**Intrinsic Structural Covariation Links 28 Cerebellum Sub-Regions to the Cerebral Cortex**

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**Introduction:** The cerebellum, long associated solely with motor control and skill acquisition, is now understood to play a role in non-motor and higher cognitive functions¹. Tract-tracing studies in monkeys have shown distinct cortico-cerebellar circuits for areas like the prefrontal and somatomotor cortex², but similar invasive studies are infeasible in humans and impossible to scale to the whole brain³. Evolutionarily, the associative cortical and cerebellar regions enlarge in humans, compared to other species⁴. Human development aligns with evolutionary evidence such that regions supporting higher cognition in the cortex and the cerebellum mature later in life⁵. However, this “big” and “small” cortex of the human brain were routinely studied in isolation. Efforts to parcel the cerebellum mainly take a winner-takes-all approach⁶, allowing only one possibility about the functional organization of the cerebellum, which may lead to an incomplete view. We hypothesize that there are multiple structural variation patterns that occur simultaneously and are spread throughout the cortex-cerebellum complex. We also hypothesize that each cerebellar subregion can be linked to several brain phenomena at the same time, and vice versa.

**Methods:** We leveraged structural whole-brain scans and 977 in-depth phenotype measurements for 38527 individuals from UKBB cohort. We parcellated the entire cerebellar cortex into 28 regions with a new functional atlas⁷, and segmented the cerebral cortex into 100 subregions⁸. Using partial least squares regression (PLSR), we estimated their structural covariation patterns (modes) at the population level. Each derived mode characterized a latent cortical score and cerebellar score that represented linear combinations of the original cortical and cerebellar measurements with maximal covariance. Robustness of the modes was determined by permutation test. We further profiled the key phenotypes associated with each mode’s latent variables to understand their real-world implications by means of phenome-wide association assays.

**Results:** Our analysis uncovered three significant population-level cortex-cerebellum covariation modes. The first and most explanatory mode revealed the interplay between broad higher-associative regions, excluding dorsal attention network (DAN), and visual, sensorimotor regions in both the cortex and cerebellum (Fig.1A). The cortical latent variable in the first mode was linked to complex reasoning, cardiovascular diseases, while the cerebellar latent variable was associated with psychomotor speed, physical activity and angiogenesis (Fig.2A). The second mode contrasted visual regions and key nodes in DAN with frontal, anterior temporal associative regions implicated in default, limbic, executive control and salience network (Fig.1B). Both its latent variables were strongly associated with watching TV and complex reasoning (Fig.2B). The third mode showed an ipsilateral pattern such that each side of cerebellum varied in the same direction as the ipsilateral side of the cortex, with few exceptions (Fig.1C).
Conclusions: Our first two modes are consistent with the higher-lower divergence of neural systems, as well as the classical double motor representation and the recently proposed triple nonmotor representation in the cerebellum. Our results support the anticorrelation between visual-attention and other higher order cognitive systems in the cerebellum, like in the cortex. Our third mode indicates a greater proportion of ipsilateral mechanisms between the cerebellum and cortex that may be overshadowed by the contralateral pathways. The distinct phenotype profiles for each mode and their latent variables revealed unique brain phenomena - behavior links that weighed differently in the cerebellum and the cortex. These findings greatly contribute to our understanding of the intricate interplay among the cortex, cerebellum and behaviors.
**References**


**Poster No 1958**

**Comparison of signal sources for real-time fMRI neurofeedback**

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**Introduction:** Extant studies have provided evidence for the feasibility of voluntarily modulating neural features using real-time functional magnetic resonance imaging (rtfMRI)-based neurofeedback (NF) approaches to affect symptoms or control of cognitive processes1,2,4-6. Recent applications of rtfMRI-NF approaches have adopted a machine learning (ML)-based accuracy to estimate NF signals rather than using neural activation (NA) within regions-of-interest (ROIs) or ROIs-based functional connectivity (FC), but no study has directly compared NF performance based on measurements. In this study, we evaluated NF training performance for voluntarily regulating smoking craving across repeated rtfMRI-NF runs depending on these measurements.

**Methods:** Thirty-one smokers performed three rtfMRI-NF runs while viewing a series of smoking-related images and receiving instructions, based on task condition, to either ‘crave’ or ‘don’t crave’. The prior run trained the ML model to be tested in the following run (Figure 1). To classify task conditions, NF signal was reflecting the distance to the hyperplane of support vector machine (3d-svm with a linear kernel implemented in AFNI1). A slider-bar integrated the feedback signal within a block and the step size for each volume was set based on the block length. To evaluate the performance of ML-based accuracy, ROI-based NA, and ROIs-based FC NF measurements, individual classification accuracy with k-fold (k = 10) nested cross-validation scheme was estimated using the percentage of BOLD signals to compare task conditions within each run. NA was measured within each ROI related to smoking craving, such as the left and right anterior cingulate cortex, posterior cingulate cortex, and insula, through the comparison of beta values in task conditions. FC was estimated between pairs of ROIs using the BOLD signals by concatenating time-series for each task condition. Pearson’s correlation coefficients were converted by Fisher’s r-to-z transformation and z-scored FC was subtracted between two conditions. Post-hoc paired t-tests and a linear regression model were performed to compare the measurements between pairs of the three runs, and across the three runs, respectively.
Results: Figure 2 presents ROI-based NA (A), ROIs-based FC (B), and individual classification accuracy (C), and the corresponding spatial patterns (D), where the weight features of classification were subjected to a one-sample t-test for group inference. From the ROI-based NA, only the anterior cingulate cortex showed marginal significance of changing activation across repeated runs and significant difference between a pair of runs was found in the left anterior cingulate cortex and bilateral posterior cingulate cortex. From the ROI-based FC, only connection between the left and right posterior cingulate cortex represented marginal significance of changes across repeated runs. From the individual classification, high accuracy (> 80%) and consistently increased performance across the repeated runs was observed for training and test sets with a statistical significance (p < 0.001) of linear regression. The left anterior insula and bilateral caudate predicted the conditions from the following runs compared to the first run and frontal regions showed decreased tendency across repeated runs. Overall spatial patterns of the insula and frontal areas showed shrinkage patterns from the third run compared to the second run.
Conclusions: Our findings demonstrate the feasibility of our machine learning based rtfMRI-NF method through the enhanced discrimination of smoking craving across repeated NF training. Future work is needed to examine the efficacy of our method against other measures of neural signal, such as network analysis. In addition, meta-analyses would be warranted to evaluate the homogeneity and heterogeneity of NF performance depending on the measurements in consideration of populations and cognitive processes.

References

Poster No 1959

Change point detection of high-dimensional graphs for early MCI classification in fMRI

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Introduction: Mild Cognitive Impairment (MCI), is a collection of precursory stages to Alzheimer’s Disease which are challenging to detect in a clinical setting [Hampel and Lista, 2016]. Functional connectivity (FC) is a method of quantifying the dependence [Biswal et al., 1995] between regions of interest (ROIs) and can be delineated into static (SFC) or dynamic (DFC), where distributions are assumed to be either constant or changing, respectively. By far the most common way of estimating DFC is through sliding windows [Shakil et al., 2016, Hindriks et al., 2016], but this technique has many shortcomings. Change point detection (CPD) is an alternative, and provides a data driven way of modelling changing FC patterns. In this work, we apply FaBiSearch [Ondrus et al., 2021] which is a novel CPD method of extracting high-dimensional, stable, DFC features for eMCI classification using non-negative matrix factorization [Ogawa et al., 1990] to model brain signals and clustering.

Methods: Data was obtained from the open source Alzheimer’s Disease Neuroimaging Initiative studies ADNI2 and ADNIGO [ADNI, 2023]. In these resting state functional magnetic resonance imaging (rs-fMRI) experiments, subjects were instructed to remain still and relaxed in the scanner. Subjects include 33 eMCI patients (mean age 72.3, 15M/18F) and 35 healthy controls (mean age 74.6, 14M/21F). Data were then pre-processed using a combination of SPM8 [SPM, 2023] and RESTplus [Jia et al., 2019] software packages. For the static condition, the entire scanning session was used to estimated FC. For both wDFC and cpDFC, we describe the hyperparameters for each condition and the values we used in Figure 1. For each subject, we ordered change points based on the p-value obtained from the statistical test during the permutation procedure. Then, the first (cpDFC1) or first two (cpDFC2) change points were used and we estimated FC between each change point. A full summary of the methods is shown in Figure 1. For each FC measure above, we generated graph theoretic features (clustering coefficient, degree, assortativity, shortest path, local efficiency, and betweenness centrality). Sure independence screening (SIS) was used for feature selection [Saldana and Feng, 2018], and we used a linear support vector machine (SVM) as the classifier model. Training and testing was done using leave-one-out cross validation.

Results: Change point detection with two change points (cpDFC2) has the best performance across almost all our four main measures of performance (accuracy; 76.47%, F1 score; 78.38%, sensitivity; 87.88%, and specificity; 65.71%). Compared to the best wDFC model (accuracy; 72.06%, F1 score; 74.67%, sensitivity; 84.85%, specificity; 60.00%), cpDFC2 only marginally outperformed it (p = 0.2496). However, compared to all wDFC models (accuracy; \( \mu = 0.5852, \sigma = 0.0483 \)), cpDFC2 had superior performance across all four main performance measures (accuracy; \( p = 3.82 \times 10^{-6} \), F1 score; \( p = 1.98 \times 10^{-5} \), sensitivity; \( p = 3.50 \times 10^{-6} \), specificity; \( p = 1.13 \times 10^{-6} \)). SFC performed poorly, achieving similar to chance performance (51.47%). A comparison of these results is shown in Figure 2.

Conclusions: In this work, we compare the predictive ability and stability of SFC, wDFC, and cpDFC for an eMCI classification task using rs-fMRI. Firstly, we show that DFC outperforms SFC for classification of eMCI, which is a difficult task. We also show that multiple cpDFC is superior to wDFC based methods for disease classification. Further, we delineate several key advantages of cpDFC in comparison to wDFC that make it attractive as a way of capturing DFC beyond just the downstream classification task. Our results demonstrate the power of CPD models with FaBiSearch for a challenging eMCI/CN classification
task, and suggest CPD is an important tool in the statistical tool box for analyzing fMRI data, and is valuable in uncovering hidden disease dynamics in rs-fMRI experiments.

Figure 1: The top panel shows a schematic of CN/EMCI classification starting from raw rs-fMRI data to predictions. Top panel is the overall pipeline, and the bottom three panels are divided across the different functional connectivity methodologies (SFC, wDFC, cpDFC). For the wDFC conditions, window size is the size of each sample over the time domain, while step size is the size between subsequent windows as they are passed over the time series. Change point detection is performed through FastSearch [Oudrus et al. 2021], and we used the following hyperparameters, $\delta = 30$, $nrun = 100$, $nreps = 100$. $\delta$ is defined as the minimum distance between change points, or the minimum sample size used in finding candidate change points. $nrun$ is defined as the number of runs to use during the fitting of the NMF model, $nreps$ is defined as the number of permuted samples to generate during the statistical analysis step of the algorithm. For more nuanced definitions, we refer readers to the original paper on this topic [Oudrus et al. 2021].

Figure 2: Results from classification study across different FC types. SFC, cpDFC, and wDFC correspond to static, change point, and window dynamic functional connectivity, respectively. cpDFC1 and cpDFC2 correspond to one or two change points, respectively. wDFC are named according to the window size (number preceding “win”), and step size (number preceding “step”).
ABSTRACTS

References

Poster No 1960

A novel non-orthogonal base decoding method for fMRI neural activation

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Evaluation and readiness signals are inevitably confounded with each other during the emotion and the reward/punishment processing. Also, the response strength differ from person to person which will cause the unbalanced base(non-orthogonal bases in this paper). In the present study, we propose a novel approach to decompose the confounded and non-orthogonal based brain activations.

Methods: In this study, we propose a novel method to decompose each participant’s brain activations under different circumstances (denoted as y) with a set of non-orthogonal basis (in the simulation, the base is set to be the form like x=(x1,x2,x3)), where each vector will represent a predefined signal model, e.g. evaluation or readiness. Specifically, non-orthogonality in this study means that any pairwise covariance of vectors not all equal zero, i.e. cov(xi,xj)=0. If cov(xi,xj)=0 (balanced base like (-1,0,1), (1,0,1)), the regression coefficients β (i.e. the strength of signals for each individual) estimated from a multiple linear model with all vectors were the same as those estimated univariately (of simple linear models).

However, in many tasks related to emotion or face response, the situation like the responses' strength are different among two directions (unbalanced base like (-1,0,1), (1,0,2)) will cause cov(xi,xj)>0. With the non-orthogonal basis, spurious correlations of signal components (i.e. β) will be introduced by related vectors (i.e. xi are correlated), thus cause the meaningless decomposition. To overcome this difficulty, we model the signals with non-orthogonal basis with multivariate linear model (Fig1), and build a statistic (Fig1) to separate the correlated signals and infer the independence. In Fig1(A), we use this method to separate simulated signals with different correlations, we can see that the statistic among varied correlations can separate the signals well. In Fig1(B), we use this method to identify independent signals at a fine-grained level, in the simulations we can find the independent signals at 0.1 correlation level with sample size=1000.

Results: In real psychology experiments, we can not know the real response strength in the unbalanced basis (e.g. (-1,0,1),(1,0,2) or(-1,0,1),(1,0,3), with our method, we can use the model and statistic in Fig1 to find the best base which can decompose the signals most properly. In Fig2, we set the real base is ((-1,0,1),(1,0,4)), only the right base ((-1,0,1),(1,0,4)) has the smallest absolute t_value (two sample t test).

Conclusions: We use a generalized linear model to model the activations and build a statistic which can infer the heterogeneity of brain signals. By implementing this method, we can identify the independent signals and separate the signal-pairs with different correlation values. In the unbalanced base(non-orthogonal base) settings, we can find the best base choice.
which can decompose the signals most properly by using this method, it will help to design the base in the experiments with emotional tasks. In the future work, we can extending our method to higher dimensions and whole brain (Berridge, K. C. (2019); Kauschke, C., Bahn, D., Vesker, M., & Schwarzer, G. (2019)).

Fig 1. Model overview and signal separation, independent signal identification. (A) Our method can separate signals with different correlations. (B) Our method can identify independent signal at 0.1 level.

Fig 2. Searching the best base. (A1-A5) Correlation values distribution with different base decoping. (B) Absolute t_value with different base decoping, correct base’s absolute t_value is the smallest.

References
Abstracts


Poster No 1961

Shared and unique fMRI responses during naturalistic movie viewing between humans and monkeys

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Introduction: Primates, including humans, share similar sensory representations due to their common ancestry. However, differences exist between species that contribute to distinct cognitive abilities. Investigating variations and similarities sheds light on fundamental questions in systems neuroscience regarding brain function, organization, and evolution. Furthermore, understanding the commonality and differences enables us to transfer knowledge obtained from studying one species to another. To establish correspondence between human and monkey brains, we conducted an fMRI study while monkeys and humans watched the same movie, “Monkey Kingdom” and applied novel comparative analyses.

Methods: We scanned 24 humans and 2 rhesus monkeys using fMRI while they freely watched 5 clips of the movie “Monkey Kingdom” (900s per clip). For the monkey scans (3T) we used contrast-agent enhanced fMRI with an isotropic voxel resolution of 1.25mm and a TR of 1s. The humans were scanned at 3T with a spatial resolution of 2.5mm and a TR of 1s. We convolved human responses with monkey HRF, and monkey responses with human HRF, to account for hemodynamic differences between species and imaging methods. To derive the fMRI response components shared between humans and monkeys, and those specific to each species, we developed a new method called multivariate variance partitioning. Each time, we trained the model using data from 23 humans and 1 monkey, withholding 1 human and 1 monkey data set for testing. We performed a group-PCA on the training data for each species separately, to derive the PC time series for each species. In this analysis, human data were concatenated across subjects along the vertex dimension. We then used multivariate ridge regression to predict human and monkey PCs based on the respective other species’ components. The brain responses explained by the other species were labeled as shared, and the residual brain responses as species-specific. This analysis yielded two sets of shared responses, one from each regression (human-to-monkey, monkey-to-human), which were concatenated. Subsequently, we performed another PCA on the 3 types of responses separately to derive the final shared, human- and monkey-specific PCs, and retained the first 30 PCs each for further analysis.

Results: In the first analysis, we examined whether brain responses of the test subjects can be explained by each of the 3 groups of components (shared, human- and monkey-specific), and specifically, in which brain regions responses can be explained by shared or species-specific components. The prediction model was trained using the test subject’s responses to the first 3 clips of the movie, and evaluated using the responses to the last 2 clips. The performance was evaluated based on Pearson correlation between measured and predicted time series of each cortical vertex, and the correlation maps were averaged across all subjects of the same species (Figure 1). In the second analysis, we examined temporal dynamics of the 3 component types. For each component type, we computed the response pattern similarity between every pair of time points, yielding a time-point-by-time-point similarity matrix. Human-specific components demonstrated a longer temporal receptive window compared to monkey-specific components (Figure 2).
Conclusions: We used a novel computational method to derive the brain response components shared between humans and monkeys, and components specific to each species. The shared components account for a substantial amount of responses in test subjects from both species. The 2 sets of species-specific components are associated with different brain parts, and exhibit different temporal dynamics. These findings provide an innovative perspective on similarities and differences between humans and monkeys in perceiving complex visual environments, offering insights into the evolutionary trajectory of brain function and neural mechanisms underlying unique human abilities.
**Poster No 1962**

**Associations between Drinking, Smoking with Psychotic, Depressive and Developmental Disorders**

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**Introduction:** Substance use is an important confounder of brain imaging findings in various diseases. Drinking (DRN) and smoking (SMK) are the two representative and prevailing addictive related disorders worldwide⁴-⁹. Individuals affected by psychotic, depressive and developmental disorders are at a higher risk for DRN and SMK. However, little work has been done to evaluate the effects of these substances on brain structure and function, which further contribute to symptoms and cognition in individuals with these disorders. Further understanding of these relationships may assist clinicians in the development of future approaches to improve symptoms and cognition among psychotic, depressive and developmental disorders.

**Methods:** Multimodal brain imaging data of DRN (n=707), SMK (n=281), psychotic disorders (including schizophrenia: SZ, n=178, schizoaffective disorder: SAD, n=134 and bipolar: BP, n=143), depressive disorder (including major depressive disorder: MDD, n=260) and developmental disorders (including autism spectrum disorder: ASD, n=421 and attention-deficit/hyperactivity disorders: ADHD, n=346) were collected across multiple consortiums⁴-⁹. Alcohol use disorder identification test (AUDIT) and fagerström test for nicotine dependence (FTND) scores were used as references to guide functional MRI (fractional amplitude of low frequency fluctuations, fALFF) and structural MRI (gray matter volume, GMV) fusion to identify the multimodal brain patterns related to DRN and SMK, respectively (Fig. 1a). Then the DRN/SMK-associated brain patterns were used as regions of interest (ROIs) to extract fALFF and GMV features from psychotic, depressive and developmental disorders, respectively (Fig. 1b). Finally, correlation analyses between the extracted brain features with symptoms and cognition were performed to evaluate the relationship of these brain regions with symptoms and cognition across 6 brain disorders (Fig. 1c).

**Results:** (1) The default mode network (DMN) and salience network (SN) were the identified multimodal brain patterns associated with DRN, whereas the DMN and fronto-limbic network (FLN) were the identified multimodal brain patterns associated with SMK (Fig. 2-I); (2) the DMN related to DRN and SMK was associated with symptom (Schizo-Bipolar Scale, SBS), whereas the fronto-basal ganglia (FBG) was correlated with cognition (Wide Range Achievement Test-IV: WRAT and Brief Assessment of Cognition in Schizophrenia: BACS) in psychosis (Fig. 2-II); (3) the middle temporal cortex (MTC) related to DRN and SMK was associated with cognition (digit symbol and Ruminative Response Scale: RRS rumination) in depression (Fig. 2-III); (4) the DMN related to DRN and SMK was associated with symptom (Social Responsiveness Scale: SRS mannerisms), whereas the SN and limbic system (LB) were associated with cognition (verbal IQ) in developmental disorders (Fig. 2-IV).

**Conclusions:** This is the first attempt to identify DRN and SMK-related brain patterns and further investigate the associations between the identified brain patterns and different clinical subdomains (symptoms and cognition) in psychotic, depressive and developmental disorders. Results suggest that DRN and SMK were related with structural abnormalities and dysfunction in DMN, SN and FLN and had significant impacts on cognition and symptoms in psychotic, depressive and developmental disorders likely via different brain networks. There are two broad implications from our results. Methodologically, co-morbid substance use has to be accounted for in neuroimaging studies of psychotic, depressive developmental populations. In clinical terms, alcohol and tobacco use disorders are extremely common and especially difficult to treat amongst mentally-ill populations. Understanding the brain pathophysiology in these co-morbid conditions may assist clinical scientists in the development of better substance cessation approaches.
(a) AUDIT/FTND-guided fusion were performed for DRN and SMK groups individually to identify DRN and SMK related multimodal brain networks.

(b) DRN/SMK associated brain regions were used as ROIs to extract features from 6 disorders:
- Drinking
- Smoking
- SZ: n=178
- SAD: n=134
- BP: n=143
- MDD: n=260
- ASD: n=421
- ADHD: n=346

(c) Correlation analyses were performed between DRN/SMK and 6 different disorders:
- SZ
- SAD
- BP
- MDD
- ASD
- ADHD

Correlation analyses were performed between DRN/SMK related features with symptoms and cognition for 6 brain disorders.
Genetic variation shapes modes of population covariation linking brain and behavior

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Introduction: Adolescence is a pivotal phase in human development marked by significant transformations in brain and behavior. As individuals transition from childhood to adulthood, the brain undergoes dynamic changes in its structure and function, influencing cognitive, emotional, and social behaviors. The development of the adolescent brain and behavior is intricately shaped by a complex interplay of genetic factors and environmental influences¹,². Yet, how genetic variation influences the multifaceted relationship between the brain and behavior remains understudied. Copy number variations (CNVs) represent a notable source of genetic variation. This class of genetic mutations is defined as either a deletion or duplication of sequences of nucleotides more than 1000 base pairs long³,⁴. It is increasingly recognized that many CNVs exert far-reaching consequences throughout the body, making them a sharp imaging-genetics tool for interrogating the effects of genetic modifications on brain physicality and behavioral differentiation⁵,⁶. We thus hypothesize that CNVs shape the complex brain-behavior relationship.

Methods: We leveraged data from 8,549 children aged 9 to 11 years from the ABCD study (Fig. 1A). Based on our CNV calling pipeline⁷, 616 children carried a deletion, 1,628 carried a duplication, and 6,305 did not carry any CNV >=50Kb. In the next step, using canonical partial least squares deployed in the children without any CNV, we estimated modes of population covariation linking brain architecture represented by 148 regional volumes according to the Destrieux atlas with 962 behavioral variables spanning 20 categories (Fig. 1B). The robustness of derived modes was assessed by cross-validation and permutation testing²,⁸. Finally, using a cross-validation scheme, we quantified the effects of deletions and duplications on the identified brain-behavior modes (Fig. 1C).
Results: Our analysis uncovered three significant modes of brain-behavior covariation. The first mode connected a vast network of brain regions with measures of cognition and demographics (Fig. 2). The second mode linked dorsal attention, somatomotor, and frontoparietal networks with measures of mental health. Finally, the third mode highlighted associations between the default mode network and environmental assessments. Importantly, carrying a CNV influences the latent brain and behavior variables (scores) across these three identified modes. We observed opposite effects of duplications on the brain second mode scores compared to deletions, which points to the previously reported mirroring effects of deletions and duplications on brain architecture$^9$ (Fig. 2A). Conversely, both deletions and duplications led to similarly-oriented effects on behavioral scores. Specifically, both CNV classes were associated with decreased cognitive functioning (Fig. 2C), mental health, and socioeconomic measures. The effects of deletions were more pronounced compared to duplications, confirming the stronger effects of deletions compared to duplications on cognitive measures observed in pediatric clinics. Our results also highlight the similar ramifications for cognition and behavior associated with deletions and duplication despite their distinct effects on brain anatomy.

Conclusions: Our study provides valuable insights into the complex interplay between genetic factors, brain architecture, and a diverse array of cognitive, behavioral, psychosocial, and socioeconomic measures during adolescence. The identified modes of population-level covariation shed light on the intricate relationships between specific brain networks and real-life functioning, underscoring the multidimensional nature of human development. Notably, our findings highlight the impact of CNVs extending beyond their known influence on cognitive abilities and language, potentially affecting various dimensions of individuals’ lives.

References
SAN: mitigating spatial covariance heterogeneity in cortical thickness data in multi-scanner studies

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Introduction: In neuroimaging studies, combining data collected from multiple study sites or scanners is becoming common to increase the reproducibility of scientific discoveries. At the same time, unwanted variations arise by using different scanners (inter-scanner biases), which need to be corrected before downstream analyses. While statistical harmonization methods such as ComBat (Johnson et al., 2007) have become popular in mitigating inter-scanner biases in neuroimaging, recent methodological advances have shown that harmonizing heterogeneous covariances result in higher data quality. Our work proposes a new statistical harmonization method called SAN (Spatial Autocorrelation Normalization via Gaussian Process) that preserves homogeneous covariance vertex-level cortical thickness data across different scanners. We use an explicit Gaussian process to characterize scanner-invariant and scanner-specific variations to reconstruct spatially homogeneous data across scanners. We demonstrate the utility of the proposed method using cortical thickness data from the Social Processes Initiative in the Neurobiology of the Schizophrenia(s) (SPINS) study registered to the fsaverage5 space with approximately 10000 vertices.

Methods: SAN uses probabilistic modeling to characterize covariance heterogeneity in multi-scanner studies. SAN decomposes data into heterogeneous (i) spatial variations and (ii) spatial variations through the Gaussian process, both revealing batch effects. Supported by extensive exploratory data analyses, SAN assumes that the underlying spatial autocorrelations are scanner-invariant while the corresponding variance terms are specific to each scanner. Although working with V=10000 vertices could be computationally intensive, we use a computationally feasible method-of-moment approach to harmonize N>300 images within 1 hour on a laptop.

Results: To characterize covariance heterogeneity, we developed a new measure called “CovarF statistic,” extending the F test statistic to covariance values. Figure 1 shows that covariance heterogeneity is prominent in localized areas of the brain including, but not limited to, pericalcarine, caudal anterior cingulate, paracentral, precentral, postcentral, superior temporal, midtemporal, and insula and entorhinal cortices. Also, covariance heterogeneity is amplified when cortical thickness data are surface-smoothed with 5mm and 10mm. Therefore, we worked on the unsmoothed cortical thickness data for harmonization. We compared the harmonization performance of SAN to other statistical harmonization methods, including ComBat (Fortin et al., 2018), CovBat (Chen et al., 2022) and RELIEF (Zhang et al., 2023). SAN was most effective in reducing the CovarF statistic throughout the brain while existing methods did not fully address covariance heterogeneity in a few regions.

Fig. 1. CovarF statistic characterizes the covariance heterogeneity in a neighbor surrounding each vertex. Higher CovarF statistic implies higher heterogeneity in covariances.
Fig. 2. After applying SAN, the heterogeneity of covariance decreases significantly when compared to other harmonization methods (ComBat, CovBat, and RELIEF).

**Conclusions:** In vertex-level cortical thickness, spatial covariance appears to be the most crucial factor that induces batch effects. SAN, which uses pairwise distance information explicitly for modeling inter-scanner effects, effectively harmonized data for downstream analysis. SAN is publicly available as an R package at https://github.com/junjypark/SAN, which supports user-friendly implementation of the method. SAN expands the spectrum of harmonization methods both to higher dimensions (vertex-level) and to methodological formations, which is expected to facilitate spatial localization of imaging biomarkers by integrating it with recent developments in spatial-extent inferences (e.g., Park et al. (2022), Weinstein et al., (2022), Pan et al., (2023)).

**Poster No 1965**

**RELIEF: A structured multivariate approach for removal of latent inter-scanner effects**

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**Introduction:** Combining data collected from multiple study sites is becoming common and is advantageous in increasing the generalizability and replicability of scientific discoveries, but unwanted inter-scanner biases are commonly observed across neuroimaging data collected from multiple study sites or scanners. While several methods for handling such unwanted variations have been proposed, most of them use univariate approaches that could be too simple to capture all sources of scanner-specific variations. To address these challenges, we propose a novel multivariate harmonization method called RELIEF for estimating and removing both explicit and latent scanner effects. Our method is the first approach to introduce the simultaneous dimension reduction and factorization of interlinked matrices to a data harmonization context, which provides a new direction in methodological research for correcting inter-scanner biases.

**Methods:**

1. **Approach:** We assume that the data matrix consists of (i) covariate effects (ii) low-dimensional patterns independent to scanners, (iii) low-dimensional patterns specific to scanners, and (iv) noise with heterogeneous variances by scanners. We use a RELIEF to achieve such decomposition and harmonize data by dropping scanner-specific patterns and rescaling the noise.

2. **Data:** We analyzed fractional anistropy (FA) data collected by the Social Processes Initiative in Neurobiology of the Schizophrenia (SPINS) study, a large multi-site, multi-scanner study on examining social cognition in schizophrenia spectrum disorder. We extracted 73 FA values using the white matter atlas from the O’Donnell Research Group. For analysis, we grouped 172 subjects from the General Electric scanners (750w Discovery 3T or 750 Signa 3T) and 179 subjects from the Siemens Prisma scanner.

3. **Evaluations:** We compared the performance of RELIEF to ComBat and CovBat, two existing batch-correction method in neuroimaging. Specifically, to evaluate covariance heterogeneity, we computed scanner-specific feature covariance matrices and compared their differences using the Quadratic Discriminant Analysis (QDA) to predict scanners from the harmonized data. We obtained the averaged prediction accuracy using the leave-one-out cross validation (LOOCV).
**Results:** RELIEF identified non-ignorable latent batch effects from the Simens Prisma 3T scanner, and our subsequent analysis showed that it can be explained by additional site effects in Siemens Prisma. To visualize the efficiency of harmonization methods, we applied each method and computed the difference of sample covariance matrices between GE and Siemens. The Figure shows its superior performance to the others. We also used machine learning methods to evaluate how well RELIEF impaired the detection of scanners. RELIEF showed prediction accuracy (49.6% for FA, 61% for MD) to the random prediction, while results of ComBat (66.1% for FA, 83.2% for MD), CovBat (59.3% for FA, 82.6% for MD) implied remaining batch effects not being harmonized.

**Conclusions:** We developed a novel batch-correction method called RELIEF, that successfully captured latent patterns of batch effects specific to scanners. It is a multivariate approach based on dimension reduction that uses all features to capture heterogeneous covariance patterns specific to scanners. We showed superior performance of the RELIEF in removing scanner effects from the SPINS study and simulation studies. The proposed methodology is made publicly available as an R package (https://github.com/junjypark/RELIEF).

**Poster No 1966**

**ISRSA Uncovers the Impact of State Anxiety on Brain Activity in the Human Extrastriate Cortex**

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**Introduction:** Emotions constitute an inherent aspect of human nature, profoundly shaping how we view the world. Among the various emotions we experience on a daily basis, anxiety holds particular significance for our survival (Bishop 2007; Fox and...
Shackman 2019; Grupe and Nitschke 2013; Hartley and Phelps 2010). The current study used functional magnetic resonance imaging (fMRI) to examine whether state anxiety modulated brain activity in response to emotionally-charged visual images.

**Methods:** Our study recruited 53 participants, and participants were instructed to complete an emotional reactivity task in the MRI scanner. Within this task, participants underwent a block design paradigm consisting of three emotional conditions (i.e., positive, negative, or neutral). After scanning, participants completed the State-Trait Anxiety Inventory (STAI; Spielberger and Gonzalez-Reigosa 1971). We then used the intersubject representational similarity analysis (ISRSA) to analyze which brain regions might reveal significant associations between individual variations in state anxiety and neural representations of the three valence conditions.

**Results:** Our results showed that the extrastriate cortex, in particular the fusiform gyrus and area MT, was the sole regions whose activity patterns across all three emotional conditions covaried with state anxiety (Figure 1). Importantly, we show that this brain-behavior association is revealed when treating state anxiety data as a multidimensional response pattern, rather than as a single composite score. Our findings suggest that ISRSA using multivariate distances may be more sensitive in identifying the shared geometries between self-report questionnaires and brain imaging data.

**Conclusions:** Overall, these findings suggest a possible influence of state anxiety on extrastriate cortical activity, which in turn may shape how we perceive and interpret the world around us. Our data provide a useful starting point for future studies that might aim to experimentally induce anxious states and document the link between extrastriate cortical activity and the perception of emotional scenes.

**References**
**Advancing replicability of structural connectivity-based multivariate brain-wide association studies**

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**Introduction:** Multivariate structural connectome-based predictive models – sCPM – are pivotal in brain-wide association studies (associating brain data with individual behavioral traits), yet the replicability of their predictive strength lacks conclusive evidence. This study aims at investigating the replicability of sCPM across diverse behavioral phenotypes using the HCP1200 dataset. Furthermore, we propose a novel data-driven feature thresholding approach and evaluate the effect of such approaches on replicability.

**Methods:** MRI and behavioral phenotype data from HCP1200 young adult cohort was utilized. To generate participant (sample size = 1000) level structural matrices of white matter connectivity, mrtrix3-based fiber tractography was performed by generating 10M streamlines. Raw connectomes (TZ, no thresholding) – serving as baseline – were used to predict 58 different phenotypes. The replicability stream consisted of a) predicting phenotypes using a Ridge regression inside of a nested cross-validation, b) repeating the sCPM on increasing sample sizes (from N = 25 to 500, steps of 25) with 100 shuffles per instance, c) calculating the replication probability (Preplicability) for each sample size as the ratio of number of significant predictions in replication set given significant predictions in the discovery set, and number of significant predictions in the discovery set. We further hypothesize that the replication curve will improve given a thresholded connectome (instead of TZ), due to factors such as noise attenuation and focus on robust connections. To achieve this, the replicability stream was applied, not on TZ, but on thresholded connectomes (Tproportionality), where the threshold (hyper-parameter) was determined as connections present in a proportion of the discovery dataset (ranging from 1% to 100% of participants). Finally, the predictive performance in terms of mean absolute error was compared for un-thresholded and thresholded methods, for the replicable phenotypes, by training-testing a regression model on the entire dataset in a nested cross-validation scheme.

**Results:** First, using the baseline model, we found that 9 (15.5%) phenotypes showed a median Preplicability > 0.7 across increasing sample sizes. Furthermore in comparison, while implementing connectomes with Tproportionality in predictive modelling, Preplicability=0.8 required comparatively less samples depending on the phenotype of interest (figure 1). Second, in terms of prediction, the mean absolute error (MAE) for sCPM with Tproportionality were lower in comparison to using TZ (figure 1 – confidence intervals).

**Conclusions:** Overall, the replicability of phenotypes is dependent on the nature of the target variable. In general, a thresholded connectome guided predictive model (e.g., proportionality thresholding) might result in a better replicability with fewer samples, in comparison with raw connectome-based (un-thresholded) sCPM. These findings suggest that leveraging Tproportionality in sCPM offers practical advantages, potentially enhancing the efficiency of predictive models and refining the accuracy of predictions in the study of various phenotypes.

**References**

**Optimizing intersubject alignment of imaging data using anatomical and functional landmarks**

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**Introduction:** Traditional neuroimaging alignment methods map from an individual’s brain to a template based on anatomical landmarks. If the anatomical locus supporting a particular function differs across individuals, functional imaging data will be misaligned by these methods. Functional alignment accounts for these differences by aligning imaging data based on functional landmarks, potentially increasing power in group MRI studies. However, alignment based on fMRI can discard useful anatomical constraints on alignment. This may be problematic in brain regions with poor fMRI signal-to-noise ratio. We tested whether an optimised combination of anatomical and functional alignment could balance the advantages of each approach and improve classification accuracy in a decoding framework.

**Methods:** We analysed 3T fMRI from 100 Human Connectome Project participants consisting of 18 contrasts from 7 different tasks. The effectiveness of alignment methods was measured by classification accuracy within a decoding framework. A linear support vector classifier was trained to decode task labels from task fMRI maps, and tested with cross-validation. Standard anatomical alignment mapped from vertex loci in source subjects to loci in the target subject (or template brain) based on anatomical similarity\(^1\). For functional alignment, a linear transformation mapped anatomical vertices in source subjects to vertices in the target subject on the basis of similar fMRI response to 1 hour of movie-viewing. This mapping captured individually specific functional localisations (Figure 1). We considered several functional alignment methods including the Procrustes method and ridge regression. In this work, we extended the functional alignment method by mapping from a source subject to a regularized target consisting of a combination of the source subject’s (weighted by \(\gamma\), where \(\gamma \in [0,1]\)) and the original target’s functional data (1-\(\gamma\)). When \(\gamma=0\), the method corresponds to pure functional alignment. When \(\gamma=1\), the method is an identity mapping, which is equivalent to anatomical alignment alone. Values of 0 < \(\gamma\) < 1 optimise both anatomical landmarks and functional co-activation.

![Figure 1](image-url)

Figure 1. Schematic of the decoding paradigm for evaluating functional alignment. Transformations were calculated from each subject to the template, based on movie-viewing fMRI responses. Subject-specific transformations were applied to each task fMRI contrast map in each subject, to align them into a common functional space. Subjects were divided into training and test sets. A linear support vector classifier was trained to decode task labels. The classifier was used to decode the task label of each contrast map in each subject in the test set. We tested whether classification accuracy was improved when task fMRI maps were not functionally aligned (i.e. anatomical alignment alone), functionally aligned, or a mixture of both.
Results: Alignment between brain maps was optimized for intermediate parameter values 0.2-0.5, demonstrating the advantage of combining anatomical and functional features (Figure 2a). The improvement in task classification accuracy when interpolating between anatomical and functional methods was robust across a range of common functional alignment methods. The optimal parameter value, calculated from one cohort, generalized to other cohorts (Figure 2b). Results were similar when resting state functional connectivity rather than movie-viewing fMRI was used for functional alignment.

Conclusions: By combining anatomical and functional information, we accounted for individual heterogeneity in functional topographies while incorporating anatomical constraints. The method improved the overlap between inter-individual brain maps beyond either anatomical or functional alignment alone, hence improving the predictive capacity of functional brain maps in a decoding framework. Modelling individual differences in this way may increase power in group MRI studies and reduce the sample sizes needed for clinically useful findings. Our findings demonstrate that macro-anatomy provides a partial lens into the inherent variability of individual neural landscapes.

References

Poster No 1969
White Matter Integrity explains 97% of age-related cognitive decline via mediation analysis

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Introduction: Research into brain aging has garnered increasing interest due to the rapid growth of the elderly population worldwide. Cognitive decline stands out as the hallmark of brain aging. Neuroimaging plays a central role in capturing both functional and structural changes in the brain associated with aging and cognitive functions. From a neurobiological perspective, the aging process triggers downward alterations in brain functions and structures, resulting in a decline in neurocognitive performance. While the three-way relationship among age, the brain, and cognitive function is important in understanding cognitive aging, the majority of current research focuses on marginal associations. The limited availability of methods addressing the neurobiological aspect of cognitive aging motivates our research. Our research aims to understand whether and to what extent the age-effect on cognitive decline can be explained by neuroimaging measures. To do this, we propose a new multivariate mediation model. The method is applied to U.K. Biobank (UKBB) data to understand the progressive loss of cognitive function with aging.
Methods: Our proposed multivariate mediation model is built on the linear structural equation model (LSEM) framework. We introduce a novel objective function. The proposed objective function is designed to maximally uncover the effect of mediation pathways by maximizing the mediation proportion. To do this, we devise an aggregate mediation factor as a sparse linear combination of multiple neuroimaging mediators and show that maximizing the mediation proportion is equivalent to optimizing the weight vector of the linear combination. We apply a sparsity-inducing penalty to identify the active brain regions involved in cognitive aging. We also developed a numerical algorithm to implement our method. We apply the method to a subset of the UKBB dataset, comprising 37,441 healthy participants aged between 40 and 70. Age is treated as the exposure variable, and two types of neuroimaging data are considered as mediators: (1) fractional anisotropy (FA) of white matter, derived from diffusion tensor imaging (DTI) data, and (2) cortical thicknesses (CT) calculated using MRI T1 data. Specifically, by following the ENIGMA-DTI analysis pipeline\textsuperscript{4}, we calculated the FA of 40 white matter tracts, and we used FreeSurfer to extract CT from 34 cortical gray matter regions in each hemisphere defined according to the Desikan-Killiany atlas\textsuperscript{2}. In our analysis, the g-factor (cognitive score) serves as the outcome variable. To assess the robustness of the result from the complete dataset, we conducted an extensive validation analysis.

Results: We identified 30 FAs involved in the mediation pathway of age-induced cognitive decline, and CT variables were not identified. To assess the consistency, we calculated the selection probabilities from the resampled data (validation analysis). The selection probabilities of FAs are generally high, with 18 FAs having a probability of 1, and another 19 FAs having probabilities between 50% and 100%. In contrast, all CTs have selection probabilities near zero, with the highest probability at 2%. The identified white matter tracts have been frequently discussed in the literature on cognitive neuroscience. For example, we identify the cingulum\textsuperscript{3} in both the cingulate gyrus regions and the hippocampal regions. The estimated mediation proportion obtained from the entire dataset is 97%. Based on the resampling, the median of the mediation proportion for the independent testing dataset was 92% (the first and third quantiles were 89%, and 95%, respectively).

Conclusions: These results confirm that first given the high mediation proportion value, we conclude that age-related cognitive decline can be almost completely mediated by neuroimaging mediators. Second, white matter integrity plays a more crucial role than cortical thickness in explaining age-induced cognitive decline. This is well aligned with previous neurobiological finding\textsuperscript{4}.

References

Poster No 1970
Deep independent vector analysis learns linked and identifiable sources from multimodal data
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Introduction: To capture interpretable and multifaceted information about the brain, it is important to develop latent variable models that effectively analyze multimodal neuroimaging data. Recently, a multiset independent subspace analysis (MISA) (Silva et al., 2020) framework has been developed encompassing multiple linear latent variable models to jointly analyze multimodal neuroimaging data. Meanwhile, identifiable variational autoencoder (iVAE) (Khemakhem et al., 2020) has been proposed to recover nonlinearly mixed sources by utilizing auxiliary variables. Built upon MISA and iVAE, we develop a nonlinear multivariate latent variable model, Deep Independent Vector Analysis (DeepIVA), to learn linked and identifiable sources that are nonlinearly mixed across multiple data modalities.

Methods: DeepIVA Overview. We iteratively optimize the iVAE loss to recover identifiable sources per modality and the MISA loss to identify cross-modal source linkage until convergence (Fig 1). Synthetic Data. We simulate multiple datasets with 2 modalities, (5, 10, 15) non-stationary multivariate Gaussian sources, (4, 8, 14) segments, and (2800, 5600) total observations. Neuroimaging Data. We utilize the UK Biobank dataset (Miller et al., 2016) including two imaging modalities, T1-weighted structural MRI and resting-state functional MRI, from 2907 unaffected subjects. We uniformly partition subjects into 14 groups according to sex and age, and extract 15 sources. Evaluation Metrics. We use two metrics to evaluate model performance: the
trimmed mean correlation coefficient between the 25th percentile and the 75th percentile (MCC) and the minimum distance (MD) based on randomized dependence coefficient (RDC) matrix.

**Results:** Synthetic Data. According to the aggregated RDC matrices (Fig 2A), iVAE can identify unimodal sources (Row I, Columns I & II) but cannot capture cross-modal linkage (Row I, Columns III & IV). In contrast, MISA can learn cross-modal linkage (Row II, Columns III & IV) but cannot identify unimodal sources (Row II, Columns I & II). DeepIVA, which unifies iVAE and MISA, can not only recover sources per modality (Row III, Columns I & II), but also identify their linkage across modalities (Row III, Columns III & IV). Furthermore, DeepIVA shows the best aggregated performance (lowest MD, highest MCC) in all simulations (Fig 2B). Neuroimaging Data. DeepIVA shows the strongest cross-modal dependence along the main diagonal (Fig 2C), suggesting that it can better capture linkage across two imaging modalities. We then color code the DeepIVA sources by sex and age groups (Fig 2D), and observe noticeable sex clusters (e.g. SCVs 12 and 15) and age clusters (e.g. SCVs 8 and 11), indicating that DeepIVA captures linked sources related to phenotype measures, with SCV 12 presenting nonlinear age effects. We next fit a separate linear line for observations from each segment. We note that slopes of fitted lines per segment are very consistent for most sources (e.g. SCVs 1-9), demonstrating that DeepIVA is capable of identifying consistent linked sources across segments. Reconstruction of DeepIVA sources also reveals linked brain biomarkers corresponding to sex and age groups (Fig 2E).
Multivariate Brain Structure-Cognition Signatures of Early Psychosis

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Introduction: Cognitive impairment is frequently observed in recent-onset psychosis, does not improve with medications, and predicts functional outcomes (Green et al., 2019). Schizophrenia presents widespread grey matter (GM) reductions and more widespread and subtle white matter (WM) abnormalities (van Erp et al., 2018; Kelly et al., 2018), but their relationship to cognitive impairment is unclear. This is the first study investigating multivariate correlations between GM-WM couplings and cognition in recent-onset psychosis individuals using a novel dimensionality technique, multiblock partial least squares correlation analysis (MB-PLS-C). Our previous MB-PLS-C studies on treatment-resistant schizophrenia individuals showed differential patterns between GM and cognitive abilities (Syeda et al., 2022). Thus, we hypothesised that MB-PLS-C would show a differential GM-WM pattern between recent-onset psychosis individuals and controls, and the differential pattern would be correlated with the cognitive abilities impaired in the patients.

Methods: We used the Human Connectome Project for Early psychosis and the Human Connectome Project Development datasets, including cognitive assessments of the NIH Toolbox, T1 and diffusion-weighted MRI data from 71 nonaffective recent-onset psychosis individuals (age 22.1±3.1) and 71 matched healthy controls (age 22.1±3.2). We performed MB-PLS-C analyses using GM thickness (GMTH) and surface area (GMSA) (Desikan-Killiany atlas) and WM fractional anisotropy (WMFA) (JHU atlas) to identify multivariate GM-WM patterns. We analysed correlations between the GM-WM patterns and cognitive abilities, including cognitive flexibility, attention, working memory, episodic memory, processing speed, reading and vocabulary.

Results: MB-PLS-C between GMTH and WMFA identified two significant GM-WM patterns explaining 29.3% of the sum-of-squares variance; one pattern (16.92%) predominantly reflected a pattern in controls: the other pattern (12.38%) comprised a differential GM-WM pattern positively and strongly mapped onto the recent-onset psychosis group (Figure 1). The differential pattern was associated with frontal and temporal regions and WM tracts, including the bilateral anterior limb of the internal capsule, left posterior thalamic radiation and retrolenticular limb of the internal capsule, and right corticospinal tract. MB-PLS-C between GMSA and WMFA demonstrated two significant GM-WM patterns explaining 72.18% of the sum-of-squares variance; one pattern (53.21%) described a widespread GM-WM pattern shared between groups: the other pattern (18.92%) showed a differential GM-WM pattern involving with frontal, temporal, and parietal regions and WM tracts including in the bilateral inferior cerebellar peduncle and posterior corona radiata and left superior corona radiata and superior longitudinal fasciculus (Figure 2). The differential GMTH-WMFA pattern was correlated with working memory (p = 0.024), episodic memory (p = 0.022), and processing speed (p = 0.006), and the differential GMSA-WMFA was correlated with word reading ability (p = 0.047) in recent-onset psychosis individuals. However, they were not significant after False Discovery Rate correction at 5%.
Figure 1. Latent Pattern of LV3 between GM Thickness and WM FA

A. Gray Matter Saliences

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Difference between groups

- Difference between groups:
  - Left: HC < ROP
  - Right: HC > ROP

B. White Matter Saliences

A) GM salience by group in controls and recent-onset psychosis individuals. Figures illustrate the GM salience difference between groups. GM saliences of HC (green) and ROP (red) with 95% confidence interval (black lines) and color-coded lobe information.

B) WM saliences shared between groups. WM tracts represented in tractography are color-coded based on the salience intensity (i) overall view, (ii) from the left, (iii) from the front, and (iv) from the bottom.

ACR = anterior corona radiata; ALIC = anterior limb of the internal capsule; BCC = body of corpus callosum; CCG = cingulum (cingulate gyrus); CGH = cingulum (hippocampal portion); CP = cerebral peduncle; CR = corona radiata; CST = corticospinal tract; EC = external capsule; FX ST = fornix (cres) / stria terminalis; GCC = genu of corpus callosum; ICP = inferior cerebellar peduncle; ML = medial lemniscus; MCP = middle cerebellar peduncle; PCT = pontine crossing tract; PCR = posterior corona radiata; PLIC = posterior limb of the internal capsule; PTR = posterior thalamic radiation; RLLC = retrolenticular part of the internal capsule; SCC = splenium of corpus callosum; SOR = superior corona radiata; SFO = superior fronto-occipital fasciculus; SLF = superior longitudinal fasciculus; SS = sagittal stratum; TAP = tapetum; UNC = uncinate fasciculus.
Conclusions: MB-PLS-C demonstrated the differential GM-WM patterns between recent-onset psychosis individuals and controls, indicating a potential signature of brain alterations in early schizophrenia. The differential pattern with GMTH was correlated with fluid intelligence, whereas the pattern with GMSA was correlated with crystallised intelligence, suggesting the relationship between the two GM metrics and two types of cognitive impairments. Identifying GM-WM differential patterns across various clinical phases could provide important information about the changes in GM-WM interaction in schizophrenia and new strategies for treating cognitive impairments.

References
Whole-Brain Patterns Related to Emotionally Valenced Images Predict PTSD Symptoms

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Introduction: Prior research on biomarkers of posttraumatic stress disorder (PTSD) has leveraged functional magnetic resonance imaging (fMRI) and emotion processing paradigms to examine brain activity. This work has found overall affective processing to be a deficit in PTSD1. Additionally, neural habituation to negatively valenced images compared to neutral images has a strong link to hyperarousal and re-experiencing symptom severity, with opponent effects found in which decreased habituation was associated with hyperarousal symptoms and increased habituation was associated with re-experiencing symptoms2. Given this prior work, we implemented machine learning methods with both habituation-related neural data and average neural signal of emotion processing to identify multivariate activation patterns that predict hyperarousal and re-experiencing symptoms.

Methods: Participants: This study included 132 military veterans (23 female; mean age: 36.1 years (s.d. 10.8) who were deployed during post-9/11 conflicts (Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn) and were recruited for this study from rural and urban regions of southwest Virginia and Houston, Texas. Clinical Assessment: Diagnosis and symptoms of PTSD were assessed using the Clinician Administered PTSD Scale (CAPS) prior to scanning. Given our prior work2, the present analyses focused on hyperarousal and re-experiencing symptoms. Experimental Paradigm: Participants were shown eight blocks each of positive, negative, and neutral-valenced images (8-10 unique images per block) in pseudo-randomized order from the International Affective Picture System3 while undergoing fMRI. fMRI Analysis: All participants underwent fMRI in a 3T Siemens Tim Trio with standard preprocessing methods4. At the individual level, valence-specific average responses were modeled as boxcar functions corresponding to each block’s duration, and valence-specific patterns of habituation and/or sensitization of hemodynamic responses were modeled as a linear parametric modulation corresponding to block order over time5. General linear models (GLMs) were used to derive individual-level beta maps. Machine Learning: For every participant, average and habituation beta maps for each valence (positive, negative, neutral) and each valence contrast were each used for a series of 12 support vector regressions (SVR). Beta maps from 100 veterans were used for each SVR, with the remaining 32 held for future out-of-sample testing. Nested cross-validation and grid search hyperparameter tuning was applied, and correlations of predicted hyperarousal score, predicted re-experiencing score, and predicted difference between hyperarousal and re-experiencing to actual scores were recorded to capture model performance. Performance was compared between SVRs predicting hyperarousal versus re-experiencing symptoms, as well as SVRs trained on average signal versus habituation.

Results: The predicted difference between hyperarousal and re-experiencing scores from an SVR trained on average neural activation in negative image blocks correlated with true difference of hyperarousal and re-experiencing across folds (r = 0.45, s.d. = 0.40). For all beta map inputs, SVR models predicting re-experiencing symptoms were significantly more accurate (p=0.002) than those predicting hyperarousal symptoms. Furthermore, beta maps from average neural responses to valenced images were more predictive of all symptom scores than were beta images from habituation beta maps (p=0.001).

Conclusions: These findings support previous results showing that neural signals related to negatively valenced images predict hyperarousal symptoms, re-experiencing symptoms, and differentials in symptom clusters in veterans. Future work will apply whole-brain multivariate weight patterns from this analysis to develop a real-time neurofeedback protocol targeting modulation of brain patterns associated with PTSD symptoms.

References
**Neural dynamics in the middle temporal gyrus predicts behavioral performance in spatial navigation**

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**Introduction:** Spatial navigation is a fundamental cognitive process that requires the integration of complex sensory information and the orchestration of precise neural dynamics. Understanding the neural substrates is a compelling and multifaceted challenge. By utilizing Stereoelectroencephalography (SEEG) recordings in patients with epilepsy and machine learning techniques, our study aimed to dissect the neural dynamics engaged during spatial navigation.

**Methods:** Twenty patients (7 females, Age: 26.3±7.9 years) were recruited, all being diagnosed with pharmacoresistant epilepsy and having SEEG monitoring. Written informed consent was obtained. SEEG recordings were conducted during each patient performing a 3D pointing task. In the task, patients navigated in the mazes and were instructed to point to the starting spot at the end of each maze (Fig. 1A). Pointing error scores were computed as the absolute difference between the pointing directions and the actual direction. The task consisted of 24 trials. In the present work, we focused on the SEEG data right at the starting spot and at the end of the mazes (7s for each). Data with a kurtosis>5 were labeled as epileptic seizures and thus excluded from the subsequent analyses. The AAL3 template were applied for assigning electrodes to the brain regions. After excluding regions with data of less than 5 patients, 25 regions remained (Fig. 1B). For each region, the SEEG signals were decomposed into five intrinsic mode functions (IMFs), based which 108 multivariate temporal neural dynamics features were extracted (Karabiber Cura et al., 2020). Finally, we ran machine leaning analyses to predict the pointing error using features extracted from the SEEG data. A LassoCV regression approach was applied. Cross-validation was done with 75% of the samples as training data, and 25% as testing data.

**Results:** Our results showed that the prediction model for the middle temporal gyrus in the left hemisphere demonstrated the best prediction performance at both the starting period ($r = 0.29, p = 1.3\times10^{-6}$) and the end of the mazes ($r = 0.33, p = 4.7\times10^{-8}$). Moreover, we found that the model based on the changes of the neural dynamics features between the end and the starting...
period of the maze also showed significant prediction performance for the pointing errors ($r = 0.29$, $p = 1.3 \times 10^{-6}$). These results suggested that the middle temporal gyrus in the left hemisphere could play a critical role in spatial cognitive map learning. The prediction models showed relatively high contribution of Hurst exponent of the original signal and the derived IMF3 mode (whose dominant frequencies are high-theta band) (Fig. 2C). The Hurst exponent of both the original signal and the IMF mode showed significant correlation with the pointing error (Fig. 2D-E).

**Conclusions:** Our results showed that the neural dynamics features in the middle temporal gyrus predicts the behavioral performance in the 3D pointing task. Hurst exponent of the neural activity contributed the most in the prediction. These results suggest critical role of neural dynamics in the in spatial cognitive map learning. Further investigation is warranted into the underlying mechanisms.

**References**

**Poster No 1974**

**Morphometricity is Biased by Image Smoothness**

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**Introduction:** Morphometricity is the proportion of phenotypic variation that can be explained by macroscopic brain morphology. It is estimated in a manner similar to heritability, with intersubject similarity of brain images replacing genetic relatedness$^4$. It provides a simple approach to summarize the link between a phenotype and high-dimensional brain data with a single value. However, recent results have found unexpectedly large morphometricity values, e.g. brain structure explaining over 90% variation in BMI$^2$. In this work we explore the role of smoothness in morphometricity in theory, simulation and real data evaluations, showing that image smoothness induces a positive bias that can help explain these unusual results.

**Methods:** Estimation of morphometricity relies on the equivalence between two linear mixed models (LMM). We call one LMM the ‘generative’ model, and it relates the response (e.g. BMI) to the voxel-wise (or element-wise) brain data. This model is impractical to fit since there are $10^4$-5-10$^6$ predictors. We call the other the ‘fitted’ model, and it relates the response to a
correlated latent random effect, where the correlation is exactly that predicted by inter-subject similarity of the brain data (Fig 1). This equivalence, however, assumes independence of the voxel-specific contributions in the generative model. Although this standard assumption might be tenable in genetics, its application in neuroimaging implies that the contribution from one voxel is independent from that of the next. This seems like a highly questionable assumption due to organisation of brain function, finite resolution of the imaging device and inevitable processing-induced blurring. We have derived a generalised version of morphometry that incorporates smoothness in the voxel-specific contributions in the generative model, and found the corresponding fitted model. Through simulations in different generative scenarios using real MRI images, we investigated the impact of model misspecification on morphometry by having smooth random influences in the generative model while assuming independence in the fitted model. We also evaluate the feasibility of recovering the true level of smoothness by model selection on the fitted model, using AIC. We use data from the UK Biobank, with N=500 subjects and M=154,055 voxel values from gray matter VBM images. In our simulations, the phenotype is directly generated from the image data and we generated 250 realisations for each scenario. We use R’s lmekin for estimating the fitted model. We also evaluated morphometry for BMI, with covariates: sex, age, intracranial volume, Townsend deprivation index at recruitment, date, assessment centre and head motion.

**Results:** We found that model misspecification due to assuming independence significantly biases estimation, with even very modest smoothness (2mm FWHM) dramatically shifting the estimates (Fig 2 top left). With the knowledge of the true smoothness, it is possible to recover morphometry on average, though there is substantial uncertainty in the estimates (Fig 2 top right). Depending on true unknown smoothness, the real dataset is consistent with anywhere from 93 to 0% of morphometry (Fig 2 bottom left). And, attempts to choose the correct generative model with AIC do not work consistently (Fig 2 bottom right).
Conclusions: Morphometricity, as conventionally computed, is biased depending on the correlation structure of the voxel-wise contributions in the generative model. If the true correlation structure is known, an unbiased morphometricity could be recovered but it appears very unstable, and learning the true correlation on real data may not be practical. All of these considerations suggest that morphometricity should be not used until new methods are developed that account for the impact of smoothness.

References

Poster No 1975
Human Reinforcement Learning (RL) in Real-world Scenarios: Brain Representation using Deep RL Agent
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Introduction: Deep neural networks have facilitated the investigation of human brain information processing across vision, speech, and language in the brain encoding framework¹. Despite the remarkable advances and utility of deep reinforcement learning (RL) in real-world scenarios with potential neuroscientific contributions², investigation using the deep RL model has
been confined to non-real-world scenarios. This study leverages a real-world human RL paradigm and Deep Q-Network (DQN) to explore the neural representations of human RL from the perspective of a deep RL agent.

**Methods:** fMRI data were acquired while subjects engaged in the Photographer paradigm. Subjects navigated Google Street View to capture images, maximizing reward reflecting similarity between image embedding of the capture and target text embedding by CLIP. In each of the five cities, every subject captured eight images. We analyzed preprocessed fMRI data from 32 subjects (M/F=16/16, mean age=23.2). They split into two groups: 16 from the 2022 experiment as group 1 and 16 in 2023 as group 2. We obtained beta-valued brain maps for capture trials using a general linear model. A DQN-based RL agent independently performed the Photographer paradigm. To extract image embeddings during street exploration, a pretrained CLIP-Image encoder was attached to the DQN. Implemented using the Pytorch, the RL agent was trained to maximize the discounted episodic return over 3,000,000 timesteps with a discount factor of 0.999. The learning rate was 0.0001 and the target update rate was maintained at 0.005. Images captured by subjects were fed to the trained RL agent, and embeddings of each layer/module were extracted. For Representational Similarity Analysis (RSA) on each subject, we calculated a representational dissimilarity matrix (RDM) of layer embedding between trials and excluded within-run blocks. Similarly, a neural RDM was obtained using the multivoxel beta-values within a searchlight with a four-voxel size radius from a center voxel. The similarity between an RL agent's RDM and a neural RDM was determined via Spearman's $\rho$, which was z-scored and smoothed with a 6 mm FWHM Gaussian kernel. One-sample t-tests were applied to individual RSA maps, generating group inference maps for all subjects or each group for reproducibility analysis.

**Results:** Subjects could learn the strategy to enhance reward scores across runs ($p=0.026$, Fig. 2a). The RL agent achieved an average score of 98.5 across the five cities, indicating training success. The capture probability of the RL agent marginally increased across runs ($p=0.09$; Fig. 2b). The trajectory revealed the RL agent's traversal across streets to capture high-
scoring images containing objects closely aligned with the target (Fig. 2c). Examining data from all subjects, lower layers of the image encoder resembled the early visual area, whereas middle layers with higher-order visual areas and higher-order cognitive areas such as frontal lobe\(^7\) (Fig. 2de). DQN hidden layers were associated with medial prefrontal\(^8\), superior parietal\(^3\), posterior cingulate cortices\(^9\), and putamen\(^10\). The output layer exhibited high similarity with the paracentral gyrus and M1. The two groups showed similar neural representations for the image encoder despite greater statistical significance in group 2 (Fig. 2fg). However, group 1 displayed a larger similarity to the DQN in the areas related to reward and cognitive functions. RL appeared more evident in group 1 than in group 2 from reward scores\(^5\), and the number of subjects who suspected object ‘person’ for high reward score differed as 11 and 6. Beta-values in the superior occipital gyrus were greater in group 2 during exploration (two-sample t-test, \(p<0.01\)).

Conclusions: To our knowledge, our study is the first to demonstrate the reproducible hierarchical neural representations of human RL in real-world scenarios using a deep RL agent.

References
ABSTRACTS


Acknowledgements
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Poster No 1976

Translating between effect size and classification accuracy

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Introduction: Biomarkers in neuroimaging are typically evaluated on the strength of their association, or effect size, with a phenotype of interest. Alternatively, machine learning models can be trained on potential biomarkers to classify individuals and evaluated on their accuracy. Although classification accuracy is dependent on the effect size of the features of interest, no work thus far has illustrated the translation of Cohen’s d effect sizes and classification accuracy in models of real-world data. We used simulated neuroimaging data to investigate the relationship between effect size and classification accuracy. We further explored the effects of variance, sample size, and reliability in both univariate and multivariate models to develop a comprehensive understanding of this relationship. We also surveyed the range of effect sizes observed in brain-behavior associations using group differences and features covariance from the UK Biobank. This work provides a contextualization of practical classification accuracies within conventional effect sizes.

Methods: We used normal probability distributions to model effect sizes between two samples. We estimated maximum classification accuracy with the cumulative distribution function of the normal distribution. This allowed us to measure the area of overlap between the two groups and therefore the best possible classifier accuracy. By convolving cumulative distribution functions, we could then observe classifier accuracy in multivariate settings. We measured the relationship between effect size and classification accuracy while manipulating the number of features and covariance between them. To contextualize these results within neuroimaging, we used the range of effect sizes and covariances in the 3,571 features of the UK Biobank.

Results: As expected, increasing the number of features while keeping Cohen’s d effect size constant between them increased classification accuracy [Fig. 1]. However, the number of parameters required for a given accuracy increased substantially with smaller effect sizes. At a Cohen’s d 0.8, accuracy of 0.9 was achieved with 10 features. At Cohen’s d of 0.2, however, the features required increased to 170. Covariance between features diminished classification accuracy [Fig. 2]. With no covariance, nearly perfect classification accuracy could be achieved with 100 features for a Cohen’s d of 0.5. However, with features correlated by Pearson’s r = 0.5, classification accuracy plummeted to just 0.65. Using 3,571 imaging features from the UK Biobank, we computed Cohen’s d effect sizes of sex differences and Pearson’s r correlation between each feature. The 50th, 75th, 90th, and 99th percentiles of Cohen’s d’s (absolute value) were 0.15, 0.43, 0.74, and 1.05, respectively, while the same percentiles of Pearson’s r’s were 0.02, 0.07, 0.19, and 0.51.
Conclusions: We developed a method to model classification accuracy of normal distributions as a function of effect size. This framework allows us to observe this relationship across data conditions, including feature count and covariance. We observed a positive relationship between feature count and accuracy and negative relationship between covariance and accuracy. The impact of covariance between features on accuracy was particularly notable, and reflects the importance of choosing orthogonal features when developing classifiers. Finally, we used real neuroimaging data from the UK Biobank to contextualize these ranges of values within imaging features.

References

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Poster No 1977
Multimodal Dynamic Fusion Captures Flexible, Time-Sensitive Structure-Function Linkages in MRI Data
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Introduction: A major goal in the field of neuroimaging centers on capturing the relationship between brain structure and time-varying functional activity/connectivity. To this end, recent approaches have estimated a single structural basis set of the brain and then sought to represent functional activation time series as a linear combination of these structural manifolds¹², a technique which can be categorized as asymmetric data fusion. Here, we introduce dynamic fusion, an ICA-based symmetric fusion approach which captures unique structural basis sets with respect to changing functional manifolds derived from dynamic functional connectivity (dFNC) states.

Methods: We analyzed functional and structural MRI data from N = 833, 310 subjects in the HCP³ (healthy controls) and FBIRN (schizophrenia [SZ]/control)⁴ datasets, respectively. We extracted dFNC states from resting-state fMRI using a sliding window Pearson correlation approach in HCP⁵ and via filter bank connectivity (FBC) approach⁶,⁷ in FBIRN, of which the latter enables both time- and frequency-resolved dFNC states. Subject-average connectomes for each dFNC state were separately fused
with subject gray matter volume (GMV) maps in independent fusion experiments via the mCCA + jICA framework\(^n\), and cross-fusion correlation was computed for both GMV and dFNC components. In FBIRN, we assessed SZ/control group differences in component loading parameters via two-sample t-tests. We also applied dynamic fusion in a sliding window manner (\(w = 10\) TR) across task boundaries in HCP working memory (WM) task fMRI to investigate the adaptive structural basis set in real time across changing functional contexts.

**Results:** We observed low cross-fusion correspondence overall for the dFNC components, which was expected as the functional input differed across each independent fusion; however, even though the GMV inputs were identical across all fusion experiments, only a few GMV components exhibited high cross-fusion correspondence, followed by a steep drop-off of cross-fusion correspondence (Fig 1A-B). This suggests most structural components are highly influenced by the joint relationship with the functional data, i.e., “dynamic”, and only a few GMV components appear consistently regardless of the dFNC inputs, i.e., “static” structural components. Of the static components, one was identified across all experiments in both HCP and FBIRN datasets, suggesting a “global static” structural component marked by higher GMV in visual/cerebellar regions, with some evident state-specific variations (Fig 1C). We observed significant group differences in GMV component loadings for static and dynamic components alike, with the strongest group differences found for dynamic components (Fig 1D). In the HCP WM sliding window experiment, we observed the emergence of structural stability in different components in clear relation to known task boundaries (Fig 2).
Conclusions: Here we propose a new approach for investigating the link between brain structure and time-varying brain function, termed dynamic fusion. Our approach is fully data driven and allows both modalities to contribute to the fusion equally (i.e. symmetric fusion), thus enforcing fewer assumptions and enabling a broader spectrum of flexibility than recent works in structural dynamics. We show that dynamic fusion identifies distinct structural basis sets that are specific to each dFNC state and are not observed when FNC from the full time series is considered at once, which challenges the notion that a single structural manifold is sufficient or appropriate for representing every time point in a rs-fMRI time series. Our results also suggest that dynamic components, which are driven by the changing linkage to the varying functional manifolds, capture stronger SZ/control group differences than static components, indicating they may encode unique aspects of clinically-relevant pathophysiology that are missed with traditional fusion approaches.

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Poster No 1978
Physiological Signatures Across the Brain
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Introduction: While fluctuations in low-frequency systemic physiology (e.g., respiration and cardiac activity) are often treated as a nuisance component in fMRI research, an increasing number of studies indicate that they contain meaningful untapped information about brain physiology and autonomic function1,2,3. Yet, the behavioral relevance of systemic, low-frequency BOLD effects, and their large-scale patterns across the brain, are largely underexplored. This study aims to fill this gap by systematically examining the patterns of peripheral physiological influences in fMRI signals and their association to individual differences in behavior.

Methods: Dataset: A subset of 375 subjects from the HCP S1200 release was utilized based on the quality of their physiological recordings5,6. Dataset included: resting-state data (4 scans/subject, 2 days with 2 runs on each day) and 51 cognitive measures based on the exclusion criteria from7 and their availability in the HCP “unrestricted” behavioral assessments. Data Prep: The % of temporal variance accounted for by respiratory volume (RV) and heart rate (HR) regressors convolved with respiratory and cardiac response function basis sets4 was calculated at each fMRI voxel. The percent variance explained (PVE) maps were deconfounded for sex, height, weight, intracranial volume, brain size, and average movement in scanner. Heritability Analysis: First, we assess the spatial similarity of BOLD physiological patterns among family members and other subjects. Next, we use SOLAR-Eclipse imaging genetic analysis package8 to quantify this similarity. Phenotype values for each individual within the cohort were adjusted for covariates including sex, age, age2, age × sex interaction, height, weight, intracranial volume, brain size, and average movement in scanner. Canonical Correlation Analysis: To investigate a linear association between BOLD physiological patterns and behavioral/cognitive variables, we employed CCA. Prior to CCA dimensionality reduction of both brain and behavior data was carried out using PCA with 30 brain and 2 behavioral PCs (a sensitivity analysis was performed on the number of PCs, not shown).

Results: BOLD physiological patterns displayed high within-subject reliability compared to a null distribution, both within and between days. Heritability (h2) is computed using SOLAR-eclipse. h2 is the proportion of the total phenotypic variance that can be explained by the genetic effects. In Fig.1, (left) voxel level maps indicates the h2, thresholded at a p<0.05 uncorrected threshold, (right) network-level averages of h2 are shown for left and right hemispheres. CCA yielded a significant first canonical mode between the physiological patterns and the phenotypic profiles of the population (p<0.018). Fig.2 displays (left) the first canonical mode and its maps of the brain CCA weights, and (right) the top 10 positive and negative CCA behavioral weights.
Conclusions: In this study, we explored the potential of BOLD physiological signatures to serve as predictors of cognitive and behavioral variables. The variability observed in physiological signals captured by BOLD signals may reflect unique characteristics of individual subjects. By considering and analyzing these measures, we gain valuable insights into the complex interplay between brain function, individual differences, and behavioral outcomes. Heritability analysis provides valuable information on the potential influence of genetic and environmental factors on the observed spatial physiological patterns. Physiological signals are closely linked to brain function and have connections to behavior. Removal of these signals should therefore depend on the study.

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Poster No 1979
Evaluation of QSM Reconstruction Pipelines for Multi-echo Gradient-echo Acquisitions
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Introduction: The NIH/NIA supports a network of 33 Alzheimer’s Disease Research Centers (ADRC) to promote translation of research to improved patient care. The neuroimaging core of the Cleveland ADRC features advanced imaging approaches to evaluate their use in guiding patient care. Of these approaches, quantitative susceptibility mapping (QSM) was included because of its potential to predict cognitive decline. However, susceptibility values can be highly dependent on choices
in the processing pipeline, and evaluation of pipeline is often confined to use in idealized datasets. In this contribution, we compare susceptibility values based on four different strategies for combining information from different echoes from MGE acquisitions on data acquired from the CADRC.

**Methods:** 70 subjects (Table 1) from the CADRC were scanned on a 3T MRI (Prisma, Siemens Healthineers, Erlangen, Germany). Imaging included 3D multi-echo gradient-echo (MGE) (FOV = 192mm x 256mm x 176mm, 1 mm isotropic voxels, TE = 16/22 ms, TR = 27 ms, FA=20o, BW = 260 Hz/px) and 3D T1-weighted image using MPRAGE sequence (FOV = 208 mm x 240 mm x 256 mm, 1 mm isotropic voxels, TE/TR = 29.8/2300 ms). QSM maps were generated using STI SUITE 3.03. 4 reconstruction pipelines (P1-P4) were developed, each reflecting a different strategy for combining data from multiple echoes (Figure 1). MPRAGE images were parcellated using freesurfer and aligned to QSM space using align_epi_anat.py. For each region, summary statistics (mean, standard deviation (SD), median) of susceptibility were calculated. One-way ANOVA among pipelines for each parcel and each statistic was performed with a Bonferroni correction for multiple comparisons, followed by post hoc comparisons with the Tukey-Kramer test. A p value < 0.05 was considered statistically significant.

**Results:** Examples of susceptibility maps from each pipeline are shown in Figure 2. Three test statistics were compared in each of all 181 regions generated by freeSurfer, leading to a Bonferroni correction factor of 3x181=543. Table 2 summarizes the results of the ANOVA analysis. As suggested by figure 1, P1 was different from the other pipelines in at least one-third of the regions, regardless of the summary statistic examined. In contrast, P2 and P4 were virtually identical. P3 was similar to P2 and P4 when using mean or median as the summary statistic, but many regions showed differences in SD, suggesting large differences of the uniformity of susceptibility across each region.

**Conclusions:** The impact of the pipeline on QSM was recently examined by Biondetti et al. in great detail in 10 healthy volunteers and found that combining phase maps prior to calculating susceptibility led to superior results than calculating a separate susceptibility map for each phase and then averaging. In contrast, our study showed that the two approaches, corresponding to P2 and P4, yielded nearly identical results. In addition to differences in the study population, differences in approach likely explain the differences among results. Here, phases were averaged, which is a simple way of implementing the weighted average implemented by Biondetti et al., and acquisitions differed, with a notable difference being in the number of echoes used. The procedure for combining echoes can affect QSM maps, but not always. Further work will be required to determine if effects from different analysis pipelines are explained by algorithmic choices or by differences among study populations.
Mostly normal, but also different: Individualised predictions from normative modelling in depression

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Introduction: Major Depressive Disorder (MDD) is a complex, multi-factorial mental illness, impacting more than 320 mio. people worldwide. The search for neuroimaging biomarkers in MDD has been impacted by unreliability, induced by small sample sizes, site effects in pooled neuroimaging data, complex interactions due to brain development, and by the heterogeneity of the disorder, paired with a group average comparison approach. We use a normative modelling algorithm that allows to deal with site effects to calculate z-scores of deviations of cortical thickness from the norm and to make individualized predictions in MDD. Our analysis is driven by two main aims: 1.) To uncover the heterogeneity in cortical thickness measures in MDD along a spectrum of deviations from the norm, stepping beyond group average comparisons. 2.) to investigate what makes individuals with extreme deviations different from individuals falling within the norm.

Methods: We trained a normative model on 35 bilateral cortical thickness (CT) measures derived from Freesurfer parcellation (Desikan-Killiany atlas) of 3181 healthy individuals and tested the model on 3645 individuals with MDD from the ENIGMA MDD consortium. This allowed us to get an estimate of region wise cortical thickness deviations of individuals with MDD under a healthy control model. To test out-of-sample generalizability, we also made predictions from a test set of 2119 healthy individuals. Beyond calculating group z-score distributions per region, we investigated into individuals with extreme deviations from the norm: Individuals with a z < -1.96 were marked to have an infra-normal score, those with z > 1.96 were marked to have

References

Figure 2. Qualitative comparison of susceptibility maps generated from each of the four pipelines (P1-P4).

Table 2. Number of regions that demonstrate significant differences among pipelines for each summary statistic (mean, SD, median) based on a one-way ANOVA. ANOVA was performed for each region and each summary statistic (p < 0.05 significant, with Bonferroni correction for multiple comparisons). Post-hoc Tukey-Kramer tests were performed to determine which pipeline drove differences. For example, differences between P1 and P2 drove differences in the mean among 63 regions.
a supra-normal score. We summarized those extreme deviations by two summary scores that target extreme deviations: a load score was calculated to summarize the number of regions with an infra- or supra-normal scores across all regions per individual, a extremity score summarized the most extreme deviation across all regions per individual.

**Results:** At group level, we found an overall trend towards decreased CT in z-score distributions of individuals with MDD for most brain regions. Those differences were in location and magnitude of previously reported effect sizes (Cohen's d: 0.01 - 0.1, overlap of distribution of z-scores: 95% 14-15, Fig 1). Similarly, we found that ~70% of individuals showed z-scores within the norm for all brain regions. For those 30% of individuals with depression that showed an extreme deviation in at least one brain region, we found widespread spatial heterogeneity of that extreme deviation (see Fig. 2). The maximum percentage of individuals that showed an infra-normal z-score in the same region was 11.8% (fusiform gyrus). For supra-normal z-scores, this number amounted to 12.2 % (both pericalcarine gyrus and cuneus). Quantifying the degree of extreme deviations in MDD by calculating load and severity scores, we found that extreme negative deviations from the norm of CT were a risk factor for remission status, number of depressed episodes, anti-depressant use patterns and age off onset of depression. Extreme positive deviations, in turn, were a protective factor and moreover, negatively associated with symptom severity and positively associated with a more favourable outcome regarding remission status and anti-depressive use patterns.

**Conclusions:** This study shows the widespread heterogeneity of extreme z-score deviations from the norm of CT in MDD that lies below previously reported thinner cortices in MDD at group level. While 70% of individuals diagnosed with MDD no extreme z-scores deviation across all brain region, the number and overall degree of extreme deviations could be used to make clinically useful predictions. This study also shows the potential of individualized z-scores from normative modelling to inform clinical predictions beyond group averages and how normative modelling may lead to additional insights in heterogeneous disorders such as MDD.
Introduction: The scarcity of medical data, particularly in the field of brain imaging, has posed a significant challenge for the development and advancement of artificial intelligence (AI) in neuroscience. The use of synthetic data has the potential to address the challenge of medical data scarcity and improve the training and validation of AI models for various medical applications. Diffusion models (Ho et al., 2020), specifically latent diffusion models (LDMs) (Rombach et al., 2022), have emerged as powerful tools for generating high-quality synthetic data that closely resembles real-world data. However, the quality of synthetic MRI data generated by LDMs is still poorly understood. Here, we aim to generate 3D synthetic MRI data using LDMs and comprehensively compare it to real-world MRI data in terms of visual appearance, morphological accuracy, and its suitability for predicting brain age.

Methods: We used T1-weighted MRI scans from 652 healthy participants aged 18 to 88 from the Cambridge Centre for Ageing and Neuroscience (Taylor et al., 2017). After strict preprocessing quality control of imaging data, our main analysis comprised 630 participants. LDMs were trained using the preprocessed data, with age and sex as conditions to generate high-quality synthetic MRI data. To ensure comparability, we acquired 630 synthetic MRI data from the trained LDMs, and matched the age and sex distributions between the original and synthetic MRI datasets. We then compared the synthetic MRI data to the original data in terms of visual quality, morphological features, and brain age prediction accuracy. For visual similarity, we computed the Fréchet inception distance (FID) (Heusel et al., 2017) and structural similarity index measure (SSIM) scores (Wang et al., 2004). For morphological feature comparison, we extracted morphological features, namely regional measures of cortical thickness (n = 68), surface area (n = 68), and subcortical volume (n = 16), from both original and synthetic MRI data using FreeSurfer (Fischl et al., 2012), and then compared their correlations with age. We further calculated Fisher’s z-values to compare the correlation coefficients between age and morphological features for original and synthetic data. We also computed the relative error between ROI feature values in original and synthetic data. For brain age prediction, we trained a support vector machine (SVM) model using original and synthetic data separately, and evaluated their performance on the same real test set. The models were evaluated using a nested 10-fold cross-validation. We quantified the performance of the models using mean absolute error (MAE) and the coefficient of determination ($R^2$) between predicted brain age and chronological age.

Poster No 1981

Quantitative analysis of synthetic 3D MRI generated by latent diffusion models

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References

Results: Figure 1 shows that the synthetic MRI data generated by LDMs closely resembles real MRI data. We obtained the FIDs of 13.18, 23.62, and 23.76 in the axial, coronal, and sagittal planes for the original data and those of 17.19, 41.34, and 34.04 for the synthetic data. The SSIM values were 0.81 for the original data and 0.82 for the synthetic data. Figure 2 shows the distribution of Fisher’s z values and the relative errors for each ROI, offering insights into the statistical differences in correlations and magnitudes of ROI features between the original and synthetic data. The brain age prediction model yielded average MAE and $R^2$ values of 6.35 and 0.81 for the original data and 9.96 and 0.55 for the synthetic data, respectively.

Conclusions: Our results collectively provide a comprehensive assessment of the synthetic MRI data generated by LDMs, covering visual, quantitative, and predictive aspects. The findings suggest a close resemblance between the original and synthetic MRI datasets, but also highlight some differences, particularly in the FID values and metrics of the brain age prediction model. We provided multifaceted assessment for understanding the strengths and limitations of LDM-generated synthetic MRI data.

References
Brain masking and registration influence QSM quantification

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Introduction: Quantitative susceptibility mapping (QSM) provides unique tissue contrast for subcortical nuclei due to its sensitivity to paramagnetic (e.g., iron) sources in the brain. However, the susceptibility map is influenced by various processing steps. Studies have compared different QSM reconstruction algorithms, however, the effects of image registration and masking have received less attention, especially at the tissue-air interface where major sources of extrinsic susceptibility complicate QSM reconstruction. Here, we investigated the effect of brain masking on susceptibilities in the basal ganglia. In addition, we propose an improved image registration approach to optimize template-based region of interest (ROI) transformation for QSM studies.

Methods: Twenty-four subjects (13 females, 12-50 years old) underwent two MRI sessions at each of two sites within eight days. A 3D multi-echo GRE was acquired; Site 1: 0.75x0.75x1 mm, TR/TE1/TE2/TE3/TE4/TE5=33/6/11.65/16.98/22.31/27.64 ms; Site 2: 0.7x0.7x1 mm, TR/TE1/TE2/TE3/TE4=30.4/7/14/21/28 ms. T1-weighted MPRAGE was acquired. QSM reconstruction: The GRE phase images were unwrapped using ROMEO1. Starting from an atlas (MNI152) template brain mask transformed into the individual space, we applied UK biobank phase reliability (PR) masking, which is based on a local phase variability map2. To find an optimal threshold value for the PR mask, we generated PR masks with threshold values falling between 0.7 and 0.97. Using each mask, the background field removal and dipole inversion were performed with QSMbox3. Hybrid template: We created two age-specific templates: adolescent (age < 20) and adult groups. We created T1w-QSM hybrid images4 with two-step registration (rigid body followed by affine) using ANTs5. The individual subject’s hybrid image was nonlinearly normalized to a template using ANTs, and ROIs for the putamen (Pu), caudate (Cd), and globus pallidus (Gp) were manually defined on the hybrid templates. This template registration consisted of 3 steps: affine, whole brain nonlinear, and basal ganglia (BG)-specific nonlinear registrations. The BG-specific nonlinear registration, with a manually defined mask tightly surrounding the BG, was necessary to achieve improved BG edge alignment. The template ROIs were transformed into individual spaces. A template orbital sinus mask was manually created and transformed into individual space. The center of mass of this individually masked unwrapped phase image (>90th-percentile image intensity) was calculated as the center of the orbital sinus. To estimate the remaining orbital sinus effects on QSM, we extracted unwrapped phase values along the line from the center of each ROI to the center of the orbital sinus and fitted the extracted values within the PR mask to a mono-exponential function.
**Results:** The combined effect of improved registration of T1w-to-QSM in creating the individual hybrid image and individual hybrid image-to-template significantly improved the accuracy of the ROI transformation, hence minimizing partial volume effects in QSM quantification. A higher PR mask threshold (i.e., more restrictive brain masking) yielded lower QSM values, and in certain cases, there was a jump in QSM values within 0.05 PR mask threshold differences. (Fig 2A, site 2, between 0.9 and 0.95). Consistently across different ROIs, there were site differences in the effect of PR mask threshold. The phase profile along the line from the center of an ROI and the center of the orbital sinus can be well-fitted as a single exponential (Fig 2C).

**Conclusions:** Because no single “right” choice for the brain mask in QSM reconstruction exists, brain masking threshold should be carefully evaluated in QSM quantification, potentially with reproducibility metrics, taking into account its site-specific nature. The residual effect of brain masking on different ROIs might be approximated by the rate of phase change between the center of the ROI to the edge of the mask at the nearby sinus.

**References**
**ABSTRACTS**

**Methods:** Participants: 117 children and adolescents (7-18 years old, 77 females). 3T MRI acquisition: T1-weighted (T1w) image 1 mm isotropic. 3D mGRE: TR/TE = 30.4/7/14/21/28 ms, 0.7x0.7x1 mm. QSM (\(\chi\)) reconstruction: Phase unwrapping using ROMEO\(^5\), phase reliability mask\(^6\), background field removal and dipole inversion using QSMbox\(^7\). R2\(^*\) values: monoeponential fitting of mGRE image intensities. Individual T1w image and QSM map were linearly combined into a hybrid image\(^8\) to create a template using ANTs. Manual delineation of subregions in the hybrid template space (Fig.1). Globus pallidus (GP): GPe/GPi (externa/interna), and wmGP (myelin-rich anterior caudal region adjacent to the Pu). Putamen (Pu): aPu (anterior), pPu (posterior), and wmPu (myelin-rich anterior medial wedge-shaped region separating the GP and Pu). Caudate (Cd): aCd (anterior), cCd (central), pCd (posterior), and vCd (vein-rich most ventromedial tip of the Cd). Posterior limb of the internal capsule (pLIC). Assumptions: 1) Distribution of myelin is well-mixed with iron within a voxel. 2) Linear additive contribution from iron and myelin components. 3) The proportion of myelin component \(f_{\text{myelin}}\) or the proportion of iron component \(f_{\text{iron}}\) scales similarly for R2\(^*\) and \(\chi\) when referenced to a highly myelinated (pLIC) or iron-rich (GPe) structure, respectively. Solving the coupled equations below: R2\(^*\) = R2\(^*\)\(_{\text{intrinsic}}\) + f\(_{\text{iron}}\) R2\(^*\)\(_{\text{iron-Ref}}\) + f\(_{\text{myelin}}\) R2\(^*\)\(_{\text{myelin-Ref}}\) \(\chi\) = \(\chi\)\(_{\text{paramag}}\) + \(\chi\)\(_{\text{diamag}}\) = f\(_{\text{iron}}\) \(\chi\)\(_{\text{iron-Ref}}\) + f\(_{\text{myelin}}\) \(\chi\)\(_{\text{myelin-Ref}}\) where R2\(^*\)\(_{\text{intrinsic}}\) = intrinsic R2\(^*\), assumed as a constant = 6 ms\(^9\). The reference values in the pLIC and GPe were obtained from the study group-average QSM or R2\(^*\) values. Summary statistics for each ROI, after transformation to the native QSM space, were used to compare \(\chi\), \(\chi\)\(_{\text{paramag}}\), and \(\chi\)\(_{\text{diamag}}\) values (Fig.2, left).

![Figure 1](image1.png)

**Results:** RETICLES-separated paramagnetic and diamagnetic images (Fig.1) show similar anatomical contrasts to those from other source-separation methods. In wmGP and wmPu with relatively high myelin content, correspondingly high \(\chi\)\(_{\text{diamag}}\) are reflected in the group, as compared to all other subregions. The posterior putamen (pPu), which is particularly sensitive to neurodegeneration, shows nearly zero \(\chi\)\(_{\text{diamag}}\). The body of the caudate (encompassing both cCd and pCd), which receives more radial fibers from the internal capsule than the head of the caudate (aCd)\(^10\), shows correspondingly higher \(\chi\)\(_{\text{diamag}}\). Notably, after source-separation, BG subregions that typically have relatively low (median \(\sim\) 20 ppb) QSM values, such as the aCd, cCd, pCd, and aPu, have substantially (approximately 50%) expanded magnitude in their corresponding \(\chi\)\(_{\text{paramag}}\) values.
Conclusions: We propose a reference tissue-based QSM source separation method that only requires linear algebraic operations between a pair of coupled $\chi$ and $R_2^*$ equations, and without additional T2 acquisition. It demonstrates reasonable anatomical contrasts and meaningful quantitative results in BG subregions. The expanded magnitude of the $\chi_{paramag}$ values in select BG subregions, presumably more accurately reflecting the underlying iron content, provides increased dynamic range and sensitivity to evaluate the potential impact of iron deficiency in adolescents.

References
A meta-analytic approach to disentangle gray matter volume and concentration in pathological brain

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Introduction: Voxel Based Morphometry (VBM) is one of the most widely used computational tools to gain insights into the neuroanatomical underpinnings of the pathological brain1. However, ongoing debates revolve around the analysis choices that have to be made to implement this technique2,3, particularly concerning those that can lead to generate measurements related to variations in gray matter volumes (GMV) or gray matter concentrations (GMC)4,5,6. In our study, we conducted a meta-analytic investigation to systematically examine potential overlaps or distinctions between these two measurements, taking Autism Spectrum Disorder (ASD) as the case of study.

Methods: Our systematic search identified 69 VBM experiments on subjects with ASD, aiming to identify consistent patterns of GMV and/or GMC variations. The primary GMV dataset included 58 experiments, for a total of 1810 subjects with ASD compared with 2003 typically developing controls (TDCs). The GMC dataset included instead 11 experiments, for a total of 210 subjects with ASD compared with 222 TDCs. Anisotropic effect-size Signed Differential Mapping (AES-SDM)7, a coordinate-based meta-analysis (CBMA) method, was employed. Data were organized into primary datasets (GMV and GMC) by grouping VBM-modulated and VBM-non modulated experimental findings, and into sub-groupings related to the age of the samples (pediatric and adult). AES-SDM facilitated a voxel-wise analysis, allowing the comparison of GMV and GMC variations, and reliability testing was performed8. Additionally, a psychological and functional association analysis using NeuroSynth9 and large-scale functional network decomposition were conducted to provide a comprehensive understanding of the neurobiological substrate of ASD.

Results: Distinct patterns of GMV and GMC variations were observed in individuals with ASD, encompassing both increased and decreased clusters compared to TDCs. Age-stratified analyses indicated dynamic variations across the lifespan, with unique patterns in pediatric and adult groups. Notable GMV changes included a decrease in the right crus I of the cerebellum and increases in various regions in the left hemisphere (Figure 1). GMC analyses highlighted areas associated with sensorimotor and executive control functions, such as the Anterior Cingulate Cortex (ACC) and Superior Temporal Gyrus (STG) (Figure 2). Psychological association analyses revealed that GMV alterations were linked to learning, memory, and social functions, while GMC alterations were associated with perception, action, executive control, and emotion. Network decomposition analysis indicated the involvement of the Default Mode Network with GMV and frontoparietal and sensorimotor networks with GMC. Contrast analyses between GMV and GMC datasets unveiled non-overlapping patterns, challenging the assumption of their equivalence.
ABSTRACTS

A) Primary

B) Pediatric

C) Adult

GMV increase  GMV decrease

A) Primary

B) Pediatric

GM increase  GMC decrease
Conclusions: The study’s findings provide clear insights into distinct GMV and GMC patterns, cautioning against assuming their equivalence. Dynamic variations across age groups underscore the complexity of ASD pathology. Associations with cognitive functions and involvement of specific brain networks contribute valuable insights into the neuroanatomical and functional aspects of ASD. The study advocates for ongoing research to unravel the complexities of gray matter alterations, aiming to enhance diagnostic accuracy and develop targeted therapeutic interventions for ASD.

References

Poster No 1985

Evaluation of imputation methods for missing values in large-scale neuroimaging data

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Introduction: With the advancement of data acquisition and analysis techniques, large-scale neuroimaging-related datasets have been established. However, missing values are inevitable in such datasets, which will introduce negative effects on subsequent data analyses. Although many imputation methods have been proposed to address the issue of missing values, there is no consensus on which method performs the best, especially for neuroimaging data. Current studies on comparisons of imputation methods for neuroimaging data have focused on some specific situations, and the evidence from large-scale neuroimaging data is still lacking. Therefore, we compared the performances of complete case analysis (CCA) and four imputation methods in multiple neuroimaging scenarios to provide a reference for selecting imputation methods for neuroimaging studies.

Methods: The Chinese Imaging Genetics (CHIMGEN) cohort (Xu et al., 2020) was used. This study was approved by the local ethics committee and written informed consent was obtained from each participant. We compared the efficacy of five methods for handling missing values in two application scenarios: first, prediction of structural/functional brain imaging measures using non-brain (behavioral) data (Scenario 1); second, prediction of non-brain data using brain imaging data (Scenario 2). In Scenario 1, 46 California Verbal Learning Test (CVLT) scores were used to predict the total gray matter volume (TGMV) obtained from structural MRI (CVLT_TGMV dataset). This dataset included 6962 subjects, and 924 had missing CVLT values with different missing patterns. In Scenario 2, regional homogeneity (ReHo) measures of 116 brain regions obtained from resting-state functional MRI were used to predict subjects’ gender (ReHo_Gender dataset). This dataset included 6953 subjects, and 763 had missing ReHo values in eight cerebellar regions. These two datasets are referred to as the real datasets, and the above models are named “prediction model”. For each dataset, 80% of the subjects without missing values were randomly sampled for 100 times. In each time, a series of simulated datasets with different percentages of missing values was created by deleting different amounts of values according to the missing patterns of the real data. The missing values of the simulated data were then handled with the following five methods: CCA, regression imputation, mean imputation, expectation maximum (EM) imputation, and multiple imputation (MI) (van Buuren et al., 2011). The performances of the five methods were assessed from three aspects: (1) differences between the imputed and the real values, (2) differences between the coefficients of the prediction models estimated from the imputed data and those estimated from the real data, and (3) differences in the prediction accuracies between the imputed data and the real data. These differences were quantified in three ways:
normalized root mean square error (NRMSE), percent bias (PB), and mean absolute error (MAE). These methods were ranked by these error measurements.

**Results:** The performances of the five methods are shown in Figs. 1 & 2. Overall, MI performed well across different error measurements and datasets: according to NRMSE, MI performed the second best in all scenarios; according to PB, MI performed the best on the CVLT_TGMV dataset and the second best on the ReHo_Gender dataset; according to MAE, MI performed the second best on both datasets. In general, CCA performed poorly in all scenarios, and the performances of other methods varied across error measurements.

**Conclusions:** In large-scale neuroimaging studies, missing values imputation could improve model correctness compared to CCA (i.e., simply deleting subjects with missing values). In general, MI showed the highest robustness and outperformed most other imputation methods regardless of the type of data and error measurements, and thus is recommended for handling missing values in neuroimaging studies.


**Poster No 1986**

Ephaptic Coupling in White Matter Fibre Bundles: A Generative Model for EEG/MEG Spectral Densities

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**Introduction:** Axons are generally regarded as isolated units that faithfully transmit neural signals to the synapse. In the 1940s, seminal experiments (Katz and Schmitt 1940; Arvanitaki 1942) demonstrated that signals traveling along parallel axons could interact with each other by changing the electric potential of the extracellular medium. Notably, these experiments showed that axons in a bundle that began firing with an initial offset, would resynchronize, by slowing down neighboring spike propagation velocities. However, this ephaptic coupling, or axonal cross-talk, was only observed in when axons were immersed in a highly resistive medium. In cortex, extracellular resistivity is low (isotropic), and ephaptic coupling is typically thought to be negligible. Recently, novel fixation techniques have revealed that unmyelinated neurons are present in significant quantities in white matter fiber bundles. Thus, densely packed (anisotropic) white matter tracts have a higher packing density and resistivity (Logothetis, Kayser et al. 2007), when the presence of unmyelinated neurons is taken into account. Thus, it is possible that axon potentials traveling along parallel axons in white matter tracts may exert subtle effects on their neighbors (Schmidt, Hahn et al. 2021). Here, we explore a novel theoretical and generative framework, the white matter ephaptic coupling model (WMEC), and test its ability to explain the relationship between white matter morphology, spike propagation dynamics, and log-linear spectral densities observed in brain activity data.

**Methods:** We developed a computational modelling framework, based on cable theoretic principles including contributions from both myelinated (Liewald, Miller et al. 2014) and unmyelinated neurons (Wang, Shultz et al. 2008) across a range of axonal calibers, (Figure 1). To model bi-directional communication in the form of “recursive spike volleys” propagating along axonal fibre bundles, we embedded the canonical microcircuit (CMC) model within the white matter cable model. To generate time-frequency estimates, we extracted white matter geometric properties from diffusion MRI (dMRI) data from a subset of 95 subjects in the HCP 1200 data set, where both structure (dMRI) and functional data (MEG) were available. We used DSI Studio to perform tractography analysis on these data using the JHU White Matter Atlas. Derived measures (number of tracts, mean path length (mm), curl, diameter, and volume) were used as inputs into our generative model (Figure 2 a, b). The model was used to furnish estimates of spike propagation velocities across fiber caliber and myelination for all white matter tracts for each subject. These estimates were used to generate time series and spectral density predictions for each subject.

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**References**


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Figure 1: A) Circuit diagram representations for a section of an unmyelinated axon, where arrows indicate the direction of current. $r_m$, $r_e$, $r_{in}$ are the axial, membrane and extracellular resistance, $C_m$ is membrane capacitance, and $V_{in}(x)$ and $V_{ex}(x)$ are intracellular and extracellular voltage as B) Circuit model for composite cable shown for a portion of a myelinated axon, with nodal and myelinated resistance ($r_x$, $r_y$, and capacitance ($C_x$, $C_y$), respectively C) Axon diameter and frequency of observation reported in (Wang et al. 2008), D) Inner diameters for and frequency of observation from (Liewald et al. 2014). Diameters were sampled from these distributions for generative purposes.
ABSTRACTS

Results: Superposition of spectral predictions across all white matter tracts, produced time series and spectral decompositions across a range of ephaptic coupling strengths. Ephaptic coupling at strengths of 10 or higher showed log-linear characteristics (Figure 2 c-h). A kappa of 12.5 had the maximum cross-correlation with the empirical MEG distribution. At a kappa of 15, there is a diminution in the higher frequency power, though the “alpha peak” appears to be correlate with the empirical data.

Conclusions: The subtle effect of ephaptic coupling may play an influential role in entraining neuronal signaling. Here, we showed that signaling along white matter fiber bundles may show 1/f characteristics, should the effects of ephaptic coupling be significant. While this phenomena is widely studied in the peripheral nervous system, it is unclear how prominent its effects are in brain. Further work and perturbation studies are needed to better understand ephaptic coupling, lead field embedding, and the potential for white matter signaling to contribute to EEG/MEG recordings.

References

Poster No 1987

Brain Asymmetry in Structure-Function Decoupling: Perspective from Graph Signal Processing
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Introduction: The left and right hemispheres of the human brain are structurally interconnected but functionally relatively independent two modules. Although, convergent evidence has highlighted exist the white-matter architecture asymmetry underlying for the function activity asymmetry, however, there is no direct studies on regarding whether and how the
hemispheric white-matter architecture supporting coordinated fluctuations in neural activity, differs between the two hemispheres. Here, by combining the network science\(^2\) and graph signal processing\(^3\), we explored the hemispheric effect and the “sex X hemispheric” interaction effects on degree of structure-function dependency, which was quantified by the structural decoupling index (SDI)\(^4\).

**Methods:** 922 healthy adults from the HCP S1200 release were included for whom both T1, resting state fMRI and diffusion MRI were available (425 males, aged 22–37 years old). All subjects provided written informed consent, and the research protocol was approved by the Institutional Review Board of Washington University. Please refer to Van Essen et al., (2013) for more details. For rs-fMRI processing procedures were performed by using GRENTA toolkit\(^6\), including linear detrending, regression of WM and CSF averaged signals, temporal bandpass filtering (0.01-0.1 Hz). For the diffusion MRI, the whole brain tractography were performed by using the MRtrix3 [http://www.mrtrix.org/] with the following operations: multi-shell multi-tissue response function estimation, constrained spherical deconvolution, tractogram generation with 100 million output streamlines and SIFT. To construction the individual structural connectome construction, the intrinsic connectivity of homotopic areas (AICHA) atlas was used to define the network nodes. Finally, for each subject, 2 hemispheric structural networks were constructed. For each participant, we calculated the hemispheric-level structural decoupling index (SDI) for each hemispheric region, by using the graph signal processing methodological pipeline proposed by previous studies\(^5\). To test hemisphere and sex effects on the hemispherical SDI, we applied a linear mixed model\(^7\), in which “hemisphere”, “sex”, and “hemisphere × sex” were fixed effects and “individual identity” was a random effect. To correct multiple comparisons, we used the Bonferroni method at 0.05 level.

**Results:** As shown in Figure 1 A, the overall patterns of hemispheric SDI map were highly similar between two hemispheres no matter which weighted strategy were used (mean map: averaged \( r = 0.74, p < 10^{-5} \)). For FN-weighted and FNr-weighted networks, regions in visual, sensory, motor and auditory cortices had the lowest SDI values (dark blue nodes) while cortices dedicated to higher-level cognitive function mainly located in dorsal anterior cingulate cortex, retro splenial Cingular cortex (light blue, yellow and light red nodes) presented relatively higher SDI values. However, the spatial pattern of SDI from the FA-weighted networks were inversed, with visual cortices showed the highest SDI values. The AI maps also affected by the weighted strategy. The regions with “Sex X hemisphere” interactions are shown in Figure 2A. For FN-weighted network, the regions mainly focus on superial frontal gyrus, parietal, SMA, thalamus. For FNr-weighted network, the regions mainly focus on frontal, middle temporal, hippocampus, Para hippocampal, and thalamus.

**Conclusions:** Our findings indicates that the weighted of structural networks affects the asymmetry patterns of structural-functional relationship.
Hierarchical Multivariate Bayesian Reference Tissue Modelling of PET Data

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Introduction: Positron emission tomography (PET) is an in vivo imaging methodology essential for studying the molecular pathophysiology of psychiatric and neurological disease. PET analysis is conventionally performed as a two-stage process of quantification followed by analysis. Quantification typically involves fitting pharmacokinetic (PK) models to each time activity curve (TAC) from each region of each individual independently to estimate several PK parameters. For analysis, the parameter representing target binding is entered into a statistical model. We recently introduced SiMBA (Simultaneous Multifactor Bayesian Analysis)1, which is a hierarchical model which performs quantification for all regions of all individuals at once. In this way accuracy of parameter estimates is improved by borrowing strength across the sample. Moreover, SiMBA performs both quantification and analysis simultaneously, improving inferential efficiency through both effective error propagation, as well as by exploiting multivariate relationships between all of the estimated PK parameters. Until now, SiMBA has been restricted to invasive models, i.e. which require the collection of arterial blood data. We have now extended this approach to a non-invasive reference tissue implementation which applies the simplified reference tissue model (SRTM)2.

Methods: We applied the model to PET data with the radioligand [11C]AZ10419369, which binds selectively to the serotonin 1B receptor, using the cerebellar grey matter as reference3. We created simulated datasets based on the mean and variance of the estimated parameters. In simulated data, we assessed accuracy of the estimated PK parameters, as well as the power, precision and false positive rate of simulated treatment effects relative to placebo in a two-group design. Next, using data collected at three different PET centres (n=139, n=47 and n=39), we examined the consistency of estimates of regional rate of change of receptor availability with age, which has previously been reported4. We also compared inferences made using a combined model with those derived from each individual centre.

Results: In simulated data SiMBA improves quantitative accuracy, reducing error by 60% for BPND, and 74% for R1 compared to conventional approaches. There was no increase in the false-positive rate throughout. Inferential efficiency was greatly improved, with precision of estimated differences and power equivalent to inferences made using conventional means with approximately double the sample size for 20 or more participants per group. However these improvements were modest for
Examining empirical age associations between centres, we observe previously shown decreases in BPND across centres which are replicated across all three samples. Furthermore, across centres we also replicate the regional differences in the rate of these changes, with the dorsal brain stem exhibiting the most rapid age-related decreases in BPND, and the ventral striatum and thalamus showing the least rapid decreases in BPND. Finally, the estimates from the combined model are not only consistent with individual estimates from each of the centres, but also exhibit greater precision.

Conclusions: We present a novel approach for non-invasive quantification and analysis of PET time activity curve data which not only improves quantification and inferences, but also yields inferences which are highly consistent across data collected at different PET centres, and allows combining data from different centres into a single model. The primary disadvantage of this approach is its high computational burden, taking up to a week to run for typical sample sizes. Another obstacle to its adoption is the necessity for defining priors over all parameters, however this can also be seen as an advantage as it allows for the incorporation of outside knowledge into the model definition.

References
Bloodstream: a BIDS App for Processing of Blood Data for Analysis of PET Data

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Introduction: Positron emission tomography (PET) is an in vivo imaging method for measurement of the concentration of specific proteins, peptides and biochemical functions. With its much higher biochemical sensitivity and specificity, PET serves a complementary role to MRI. The gold standard for quantification of PET data involves modelling together with an arterial input function (AIF). This requires sampling the arterial blood throughout the PET examination, from which the blood plasma must be extracted, and from which the relative concentrations of the parent compound and its radiometabolites must be determined. This procedure is labour-intensive, can be uncomfortable for participants, and requires experienced staff for arterial cannulation, blood measurement, as well as analysis. Although non-invasive reference tissue methods or simplified semi-quantitative approaches can serve as reasonably good substitutes for blood sampling for some targets, there exist many targets for which blood sampling is required for valid quantification. With the recent incorporation of PET into the BIDS specification, PET and its associated blood data can now be shared in a standardised and machine-readable format. With the increase of data-sharing practices, there are an increasing number of PET datasets which include blood data being shared. Research groups who regularly work with blood data have mostly developed their own in-house approaches for storing and processing this data for later modelling. However even in many PET-focused research groups, the skills and experience are lacking to work with blood data.

Methods: To this end, we have developed bloodstream, which is a BIDS application for automatically processing blood data so that it can be used for invasive PET quantification. When applied directly to the data without any configuration file, bloodstream will combine the different measured curves into an interpolated arterial input function which can be used for modelling using simple linear interpolation. For the application of more complex approaches, in which models are fit to one or more of the constituent series of measurements, a configuration file can be created which specifies the models which should be applied and allows the customisation of various attributes prior to fitting. To ease the creation of these configuration files, we have created a web app with drop-down menus to select the models and customise their settings, and the output can be downloaded. The bloodstream BIDS app returns not only the interpolated curves, but also a full analysis notebook with diagnostic plots. bloodstream is developed in R and based on functions in the kinfitr R package. For datasets requiring more tailored modelling and analysis, the code used to perform all the modelling can be retrieved from the output notebooks to allow users to run the analysis interactively at each step with greater customisation. bloodstream can be installed as an R package, or invoked from within a docker container, which further simplifies its use.

Results: bloodstream is shared on GitHub at the following link: https://github.com/mathesong/bloodstream. It has been successfully applied to one open dataset using the [11C]PS13 radiotracer, as well as several soon-to-be-open datasets.
have also recorded a demonstration video covering the theory of PET blood processing, as well as a hands-on tutorial of the application of bloodstream to an open dataset linked on the GitHub README.

**Conclusions:** In summary, we present a new tool for performing reproducible blood processing and modelling for PET analysis, which can be used for later invasive quantification of PET data. In this way, access is improved to complex and costly datasets for groups lacking experience working with blood data. Moreover, this tool incentivises the curation of PET data to the BIDS structure both for internal use of this tool, but also hopefully leads to more externally shared datasets.

**References**

**Poster No 1990**

**Sex differences and test-retest stability of synaptic density in human brains by F-18 SynVesT-1 PET**

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**Introduction:** Synaptic vesicle protein 2A (SV2A) is an established marker of synaptic density and can be imaged by F-18 SynVesT 1 positron emission tomography (PET). Here we report a large young cohort on sex difference (n=40, f/m 14/26). Previous reports of differences in in-vitro determinations of synaptic density in human tissue are contradicting and based on low sample numbers in only a few brain regions. No differences were found recently in vivo for a group with a wide age range with a similar PET method (C-11 UCB-J). Additionally, a subgroup of the sample was tested twice on consecutive days (n=20) in order to evaluate the test retest stability of the method.

**Methods:** F-18 SynVesT-1 PET list mode (90 min) data and T1-weighted magnetic resonance (MR) data were collected in 40 healthy volunteers (mean age: 27.5± 6.5 years (range: 20-45 years)) using an integrated 3 Tesla MR/BrainPET system. PET data and corresponding MR data were realigned, co-registered, segmented and spatially normalized using PMOD Neuro Tool. SV2A was quantified by the simplified reference tissue model 2 with centrum semiovale as reference region. The intersection of individual normalized gray matter segments with the AAL brain atlas was used for readout.

**Results:** We found no sex difference in synaptic density in most of the brain regions investigated. In the bilateral amygdala region binding potential BPND was higher in female participants (3.9±0.37 SD) in contrast to 3.4±0.37 SD in male participants (p=0.0007). The volume of the individualized amygdala atlas region of interest was not sig. different (1.81 vs. 1.82mL). Regarding reproducibility scores, the relative differences between scans were in the range of -1.4 to 0.5%, absolute differences between 3.8 and 6.9% and intraclass correlation coefficients between 0.75 and 0.87.
Conclusions: Our results suggest that there is no general global sex difference in synaptic density in humans and that the non-invasive quantification of synaptic density is reproducible and reliable in a short time frame. The observation in the amygdala is intriguing and warrants confirmatory and follow up investigations.

Poster No 1991

A Novel Algorithm to Produce Population-Based Input Function for Arterial Input Function

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Introduction: The [11-C]DPA-713 is a second-generation TSPO ligand and a putative PET imaging biomarker for neuroinflammation that has shown promise in preclinical and clinical studies. Accurate quantification of tracer uptake and metabolism in the tissue through kinetic modeling is crucial but requires the invasive measurement of the tracer concentration in the arterial blood over time. Non-invasive alternatives, like IDIF and population-based input function (PBIF) have gained attention, but their accuracy still relies on additional arterial or venous samples, undermining the non-invasive advantages. We propose a completely non-invasive approach that uses the PBIF technique but does not require calibration samples of any kind, utilizing machine learning to learn the input function calibration factor from very limited and easily-available clinical-demographic data. We propose a further ML step to improve the resulting kinetic modeling outcomes, in this case the regional Logan volume of distribution.

Methods: The workflow begins with the generation of Time-Activity (TAC) Curves. These curves undergo the Peak Alignment process to derive the AIF, which is normalized by area under the curve (AUC) of true AIF. The PBIF is obtained as the mean of normalized time activity curves from all subjects. The 1st ML Model is a Gradient Boosting Regressor, which serves as an AUC Predictor, using its output to de-normalize PBIF and estimate subject-specific pAIF. Kinetic modelling is then done to derive Logan VT from both empirical and predicted AIF for each region. Following which, Logan VTs from pAIF are validated against VT of the same regions using empirical AIF through Pearson correlation. The workflow concludes with the 2nd ML Model which estimates the slope of the VT-VT relationship. The predicted slope is a scalar per subject utilized to improve the fit between VTs from empirical and predicted AIF.

Results: The Results of our two ML models are displayed in the uploaded Figures. The first figure shows the computational steps to get our PBIF curve as well as the predicted AIFs. A shows the raw TACs before processing. B shows the TAC curves after linear interpolation and peak alignments. We divided TACs in B by their corresponding AUCs, and averaged those to get the PBIF curve (C). D shows the AUC predictions from our Gradient Boosting model. Then in E, we took the PBIF and multiplied by the subject-wise predicted AUCs to form our predicted AIF curves. F displays the root mean-square error results accompanied with the average of pAIF lines. The second figure illustrated the results of our Slope Re-scaling method. Subplot A shows the scatter plot of Logan VT computed by kinetic analysis using subject-specific AIFs against those computed using input function obtained from a naive population-based averaging. B: Scatter plot of gold standard Logan VT against that obtained using our PBIF. The Pearson correlation between the two methods give R² = 0.952, which is significantly higher than the naive method in Panel A. C: The Logan VT predictions after slope re-scaling. In this plot, most of the data points align with the diagonal line, giving an even higher R² = 0.986. Panels D, E, F show the effect of subjects’ diagnosis, sex, and genotype, respectively, reporting their Pearson’s R on the side. There is no significant difference in the predictions, suggesting our results are not biased by these groupings. Panels G, H, I show the distribution of predicted Logan VT corresponding to those categories respectively.
**Conclusions:** On both tasks we report excellent accuracy, as tested on a cohort of healthy subjects and patients with Parkinson’s disease. This study may pave the way for future utility of quantitative microglial imaging using [11-C]DPA-713 in a data-sparse environment without the need for any blood sampling.

**References**
Assessing Reactive Astrocytosis in Alzheimer’s Disease Using [18F]Fluorodeprenyl-D2 PET Imaging

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Introduction: The progression of Alzheimer’s Disease (AD), the most common cause of the dementia, is often accompanied by neuroinflammation, which manifests prior to significant cognitive decline. Reactive astrocytosis is a hallmark of such inflammation, potentially serving as an early biomarker for AD pathology (I). Our study employs [18F]fluorodeprenyl-D2 ([18F]F-DED) positron emission tomoscopy (PET) imaging to in vivo quantify astrocytosis comparing AD with healthy controls and examines its correlation with cognitive deterioration in AD.

Methods: We conducted a cross-sectional analysis involving 12 patients within the early stages of the AD spectrum and 11 cognitively healthy controls. All participants underwent [18F]F-DED and MRI imaging. AD patients were identified based on CSF amyloid-β42/40 ratios below 5.5% and Mini-Mental State Examination (MMSE) score below 27. Controls scored 27 or higher on the MMSE and displayed no amyloid-β pathology. Differences in [18F]F-DED uptake between groups were evaluated through region-of-interest (ROI)-based analyses. The preprocessing of [18F]F-DED data was performed in PMOD software, and the quantification of cortical uptake was determined by computing the volume of distribution, which is the ratio of the radioligand concentration in target tissue (expressed in kBq/cm³) to that in the image derived plasma (in kBq/mL) at equilibrium. In a ROI based analysis we employed the Automated Anatomical Labeling (AAL) atlas, which was adapted to individual gray matter masks and then conformed to the individual [18F]F-DED maps. We computed the median uptake value for each ROI. Cortical amyloid deposition was measured using [18F]flutemetamol β-amyloid-PET imaging. Cerebrospinal fluid (CSF) biomarkers, including Aβ42, Aβ40, and phosphorylated tau (p-tau), were measured using the Lumipulse G1200 platform from Fujirebio. Cognitive performance was tested using the Mini-Mental State Examination (MMSE). We explored the associations between cognitive performance metrics and [18F]F-DED uptake utilizing linear regression models, controlling for age and sex, conducted in the R statistical environment.

Results: The study involved participants with an average age of 71, featuring an equal distribution of genders. Notably, we detected a pronounced increase in [18F]F-DED uptake in Alzheimer’s Disease (AD) impacted areas, specifically in the bilateral occipital (Left: T:2.28, p=0.03; Right: T:2.51, p=0.02), temporal (Left: T:2.21, p=0.03; Right: T:2.22, p=0.03), and frontal lobes (Left: T:2.46, p<0.02; Right: T:2.45, p<0.02). These uptakes were significantly correlated with cognitive assessments. Specifically, enhanced uptake in the temporal regions was strongly linked to lower cerebrospinal fluid amyloid-β ratios and reduced scores on the Mini-Mental State Examination (MMSE) (p<0.01). These relationships persisted after adjusting for age and gender factors.

Conclusions: Our findings suggest that [18F]F-DED PET imaging can detect reactive astrocytosis in regions vulnerable to AD pathology, potentially before the onset of severe cognitive symptoms. The correlation between increased tracer uptake and cognitive decline reinforces the utility of [18F]F-DED as a biomarker for AD progression. These insights into the spatial patterns of neuroinflammation offer a promising avenue for early diagnosis and monitoring of AD, paving the way for interventions that target neuroinflammatory processes in the disease’s early stages.
Neuroplasticity-based Parcellation Using Continuous Microstructural Learning-induced Changes

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Introduction: Brain's connectivity can be represented by different modalities, such as the functional connectome, which reflects similarities of brain function across regions, or the structural connectome, which reflects the number of streamlines connecting each pair of regions (Sporns et al., 2005; de Reus & Van den Heuvel, 2013). Both of these metrics are commonly used to portray the brain as a network and provide distinct and valuable insights into its underlying nature. Over the course of our lifetime, the brain undergoes constant changes. For instance, when we acquire new skills structural and functional modifications occur, referred to as learning-induced neuroplasticity. Microstructural training-induced changes can be detected after short learning periods using Magnetic Resonance Imaging (MRI) (Sagi et al., 2012; Tavor et al., 2013, 2020; Hofstetter et al., 2017; Brodt et al., 2018; Jacobacci et al., 2020). A complementary, less studied avenue to a network-level perspective on the human brain is studying similarities in structural neuroplasticity patterns across brain area during learning. Such learning-derived modifications in structural connectivity can reveal information sourced in the brain's ability to change and adapt. In this study, we aim to explore how the brain's structural changes during the learning process relate to its connectivity. We'll characterize the continuous microstructural changes by adding the time dimension to structural MRI scans and use this characterization to offer a neuroplasticity-based parcellation of the brain.

Methods: To follow on continuous microstructural changes during (rather than following) learning, we developed a unique protocol of diffusion tensor imagining (DTI) (Basser et al., 1994) employed while participants perform a learning task within the MRI scanner. Fifty-eight right-handed healthy volunteers were scanned while performing a finger tapping task (Karni et al., 1995) or as a passive control. Using a sliding window method, we calculated continuous measurements of tissue diffusivity indices such as mean diffusivity (MD) and fractional anisotropy (FA). From those ‘microstructural time series’ (i.e., the change in MD or FA over time), we parcellated the brain into “plasticity networks” based on the correlation of different areas’ continuous changes and using an hierarchical clustering algorithm.

Results: Gray matter motor-related areas displayed a significant decrease in MD, and several tract systems showed an increase in FA following learning (P < 0.05, FDR-corrected) (fig 1a). Different areas demonstrated distinct change patterns, for example, while the parahippocampal gyrus (PHG) displayed a gradual decrease in MD during the learning process, the right cerebellum and the hippocampus displayed a steep decrease in the middle of the learning process (fig 1b). We computed the correlations between the continuous diffusivity indices changes across brain areas, and then used hierarchical clustering to derive a whole-brain plasticity-based parcellation (fig 2).

Conclusions: In this work we offer a novel, network-level perspective on brain connectivity by examining similarities across regions in short-term training-induced microstructural changes. By adding the time dimension to 3D structural measurements, we were able to detect different in the patterns of change over time during learning, in task-related areas which show similar changes when comparing pre- vs post-task images only. By continuously tracking microstructural changes within brain tissue throughout task execution and clustering brain areas according to their neuroplasticity patterns, we provide a unique approach which may shed new light on brain connectivity and function while learning.
Figure 1. Training-induced structural change. A 2 (task vs. control groups) by 2 (prepost) ANOVA revealed a significant interaction effect. (A) Clusters of MD decreases were found in the right PHG, the right hippocampus, and the right cerebellum following learning. Clusters of FA increases were found in the middle cerebellar peduncle and the superior longitudinal fasciculus. (B) The MD and FA change in the specific cluster displayed in A, for both groups. (C) The continuous MD decrease of three gray matter areas. In each, a change-point, based on the change in slope of the curve, is marked in a green line. The timepoint was determined as the maximum change between the slope if the two parts of the divided curve.

Figure 2. Neuroplasticity-based parcellation. (A) Correlation Matrix for all gray matter areas based on Pearson’s r of the continuous MD change within different areas of the brain, ordered by hierarchical clustering algorithm and parcellated to six “plasticity networks”. The optimal number of clusters (marked in red on the dendogram) was determined by finding the knee point of the distance between clusters. (B) The five main networks displayed on the brain.
Unsupervised Hippocampus Segmentation: Translating Deep Learning Models from Research to Clinic

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Introduction: Hippocampus volume (HV), typically measured via MRI segmentation, is a well-established biomarker for Alzheimer’s disease (AD). Most automated segmentation methods have been developed and validated for research datasets. However, domain shifts between clinical and research datasets often significantly degrade model performance. Due to differences in imaging acquisitions (scanner shift) or disease severity (population shift), current segmentation methods are often unsuitable for clinical populations. We investigated the performance of popular segmentation methods on a clinical AD dataset. Fig 1a shows a schematic of the current data setting.

Methods: For the clinical dataset we used a sample of 29 patients from the Oxford Brain Health Clinic (BHC) with labels only used for evaluation. The HarP dataset was used as a research dataset, consisting of 133 labelled MRI volumes. We explored the impact of increasing the number of inputs by splitting images into hemispheres, and also of mirroring each hemisphere. Both datasets included cognitively unimpaired individuals, Mild Cognitive Impairment (MCI) patients and dementia patients. Fig 1b compares the true left HV between HarP and BHC populations. We tested several publicly available out-of-the-box (OOB) tools for automatic segmentation: FSL FIRST, FreeSurfer and SynthSeg on the clinical dataset. For a deep learning (DL) baseline, we used a UNet trained on the HarP data as our labelled reference. To investigate generalisation to the unlabelled clinical data, we expanded the UNet with data augmentation and unsupervised domain adaptation (UDA) approaches. Augmentation is an effective technique for improving a model generalisability by increasing robustness to likely data variations. We explored both standard (affine transformations, flips, noise, intensity changes) and MRI-specific augmentation (motion, bias field). We implemented a UDA model by including a domain classifier to enable adversarial training, which aims to do the main task while learning domain invariant features. The domain classifier does not require segmentation masks and was trained using unlabelled clinical data.

Results: Fig 1c shows the Dice scores (DSC) for the segmentation methods, tested on the HarP and BHC datasets. The increase in training data size improved most models. OOB models, which are commonly trained and/or validated against research populations, all struggled with our clinical population. As shown on the violin plot in Fig 1d, FreeSurfer and FIRST, had instances of failing (DSC = 0). The UNet models with augmentations improved performance compared to OOB methods. However, the performance on BHC data was worse than on HarP data, with some particularly low-performing outliers. UDA was comparable to the augmentation methods for most participants, however, the UDA method led to particularly low DSC for certain individuals, possibly due to correlation between disease state and scanner leading to the removal of important information during DA. The UNet with basic augmentations was the best-performing model and used for further analysis. Fig 1e shows a positive correlation (r=0.70, p=1.31x10-9) between true HV and achieved DSC, showing that larger volumes had higher DSC. This may be expected as individuals in HarP are on average younger and healthier than BHC, thus larger BHC.
hippocampi are more similar to those in the HarP training data. Performance was worse for MCI/dementia patients. Fig 2 shows the brains corresponding to (a) highest and (b) lowest DSC; brains in the latter have visibly larger ventricular atrophy.

**Conclusions:** Our findings highlighted that domain shifts between research and clinical data extend beyond acquisition differences. Despite model generalisation or UDA techniques, population shifts due to disease severity and extent of atrophy may also cause challenges for translating research tools to clinical practice and should be considered in future model development.
UniFed: A unified segmentation framework for partially labelled, distributed neuroimaging data

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Introduction: Deep learning models are powerful tools for neuroimage analysis but their current clinical impact is limited. The required pooling of data to capture clinical populations leads to two major challenges: first, the harmonisation problem created by scanner differences; second, data privacy as medical images are inherently personal. Federated learning (McMahan2016) (FL) has been used with distributed data to protect privacy, but most approaches make infeasible assumptions that data from all sites are both fully labelled and available at training time. Thus, we propose UniFed, a unified FL framework (Fig. 1) formed of three processes: a federated network for partially labelled datasets; model selection for an unseen, unlabelled site, and model adaptation to the unseen, unlabelled site.
**Methods:** We used the ABIDE dataset (Martino2013), split into 16 distributed sites, preprocessed using the FSL ANAT pipeline. We split the sites into four sets: Reference site (NYU), Labelled and Unlabelled sites in the federation, and Unseen sites. We considered segmentation of four subcortical structures (brain stem, thalamus, putamen and hippocampus), using FSL FIRST (Patenaude2011) generated labels. A UNet architecture and Dice loss were used and features from the second to last layers were considered. Dice Score was used to assess performance. The framework is unified by two key concepts: encoding each learned feature as a 1D Gaussian distribution, enabling feature distribution information to be communicated without violating data privacy, and the use of the Bhattacharyya distance (DB) to calculate the distance between sites in feature space. Partially labelled FL: For every site in the federation, local training minimises a combination of two loss functions: the main task loss, if labels are available, and the DB between the local and global feature distributions for all data. The local models are aggregated equally (Dinsdale2022) to create the global model; the global feature distribution is the average across supervised sites. Model selection: Given a model zoo of pretrained models, we hypothesise that the best choice for a new unlabelled dataset has the shortest DB between the source global features (shared already for FL) and the features for the target data for that model. We used the models trained in Partially Labelled FL for the model zoo. Model adaptation: We follow our previously published SFHarmony (Dinsdale2023), a source-free domain adaptation (SFDA) approach, which adapts the network to the unseen site by minimising the DB between the source and target feature. We considered two source models – the NYU-only model and the UniFed model trained on 6 labelled sites.

**Results:** Partially labelled FL: We considered increasing numbers of supervised sites (1-6) and percentages of labels available (1,5,10% across 5 sites with NYU fully labelled), and compared to standard FL methods (McMahan2016,Li2018), semisupervised FL methods (Bdair2021) and domain adaptation FL methods (Peng2020,Dinsdale2022). Our approach matched or outperformed existing methods across all degrees of supervision. Fig 2a shows the results for 2 fully supervised sites: improved performance on the Unseen sites is clear, despite only sharing the \(\mu\) and \(\sigma\) of the features. Model selection: Each site showed a negative correlation between Dice score and the DB. The slope was significant for each unseen site (p<0.05). Our federated models were selected for 4/5 unseen sites, showing that UniFed models generalise better. Model Adaptation: For both source models our approach outperformed existing methods (Bateson2022) for SFDA. Model selection is clearly important: although the performance of the NYU-only model increased from 52.02 to 68.65, the performance was much worse than with the UniFed model (83.14 to 85.43).
Conclusions: UniFed enables the training of high-performing models for distributed and partially labelled datasets. The approach is generalisable across segmentation tasks and imaging studies.

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**Poster No 1996**

**3D assessment of fetal brain development in the second trimester from ultrasound volumes**

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**Introduction:** Recent advances in fetal MRI have allowed the complex 3D growth of the developing cortical plate (CP) to be characterised¹⁴. This advance has improved our understanding of sex differences², asymmetrical development²⁻³, and differences between healthy and at-risk pregnancies⁴. However, these studies are often limited by small sample sizes and a focus on the third trimester of pregnancy. In contrast, large ultrasound (US) datasets throughout pregnancy are obtainable as US has a short acquisition time and is routinely used across the world in clinical practice unlike MRI⁵. However, current methods for studying the 3D growth of the CP are limited to MRI and are not directly transferable to US due to significant domain differences. In this study, we propose an automated deep-learning pipeline to characterise the CP from 3D US scans, as shown in Fig. 1.

**Methods:** To measure the CP’s properties, it must first be delineated. In US, large shadows often obstruct regions of the CP, leading to holes within the extracted surface that make further analysis extremely difficult. To overcome this, we used a deep learning-based topology-preserving segmentation network: TEDS-Net⁶. TEDS-Net (gθ) learns a deformation field (φ) that deforms a prior shape (P) to produce a segmentation (Ý), anatomically guiding the segmentation in the regions of shadows. For this task, we used a CP label from an US atlas⁷ as P, to minimise the requirement for complex deformations. To train and evaluate the network, we used n=643 transabdominal US volumes between 18 and 26 weeks’ gestation collected as part of the INTERGROWTH-21st (IG21) Project⁸. The trained network was then applied to a further n=2,188 unseen, unlabelled, IG21 volumes, and both global and local properties were measured from the predicted topologically-correct CP surfaces.

![Fig 1: An overview of the proposed cortical plate analysis pipeline. Using a deep-learning network, the cortical plate are first segmented and then parcellated, before global and local cortical properties are extracted. The cortex is segmented by deforming a prior shape (P) using a learnt field. Each field has been designed to be invertible, allowing population to be made by propagating each individual’s measurements back onto the prior template and averaging across a set of individuals, as shown in green.](image-url)
**ABSTRACTS**

**Results:** Our network achieved topologically correct segmentations with a Dice overlap of 80% compared to the manual CP labels. The segmentation performance was found to decrease significantly with increasing gestational age (Pearson correlation test: $p<0.01$); this is likely due to the greater calcification of the skull, which increases US artefacts making the CP boundaries less well defined. Volume (range = 5 - 55 cm$^3$), surface area (range = 40-150 cm$^2$) and 3D Sylvian Fissure (SF) depth (range = 5-12 mm) measures were consistent with previous MRI studies$^{3,8}$ and a 2D US study$^9$, as shown in Fig. 2A. As the chosen P was based on an atlas, it could be parcellated into five lobes (frontal, parietal, occipital, temporal and insula) by aligning P to a fetal MRI parcellation map$^1$. Using φ, the parcellation map was registered to each individual’s CP segmentation generating a personalised parcellation map (L), enabling regional measures of local features. The average cortical depth (D), thickness (T) and volume for each lobe are shown in Fig. 2B. The insula deepened and thickened at the fastest rate, which is expected due to SF opercularisation. The volumes of the frontal, parietal, and temporal lobes increased most across this gestational period, closely aligning with previous MRI growth curves$^{10}$. As the transformation fields, φ, are invertible, the CP local properties, e.g. thickness and cortical depth, can be propagated back onto P and averaged across the population, facilitating a direct comparison between individuals and gestational weeks, as shown in Fig 2C.

**Conclusions:** In summary, we have developed the first automated pipeline for extracting and analysing the 3D CP from challenging US scans, taking less than 10s per scan. Our chosen approach enables efficient volume parcellation and groupwise comparisons, and the findings were consistent with previous MRI and US studies. Furthermore, this pipeline demonstrates that in-depth neurodevelopmental studies can now be conducted using US, potentially paving the way for more research in this modality in the future.

**References**

Geometric influences on the regional organization of the mammalian brain

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Introduction: Since Brodmann’s seminal work1, studies have aimed to divide the brain into spatially contiguous areas or parcels that are functionally or anatomically homogeneous. These parcellations have historically been based on histology, but recent works have derived them by combining neuroimaging with sophisticated algorithms2,3. However, current approaches are not generalizable and offer no insight into the generative mechanisms that may have shaped the regional organization of the brain. Here, we draw on evidence that regional patterning in the brain is strongly shaped by geometrically constrained gradients of gene expression4 to develop a novel parcellation approach using the eigenmodes of brain geometry5. We show that the resulting geometry-derived parcellations are more homogeneous across hundreds of diverse anatomical, functional, cellular, and molecular properties than many existing parcellations of human, non-human primate, and mouse brains.

Methods: Figure 1A shows the steps to construct a geometric parcellation of the human cortical surface modeled by a triangular mesh derived from T1w-MRI. The mesh is used to solve the eigenvalue problem5: \( \triangle \psi = -\lambda \psi \), where \( \triangle \) is the Laplace-Beltrami operator, which captures the mesh’s geometry, and \( \psi \) are the geometric eigenmodes with eigenvalues \( \lambda \). We use the zero-crossings (i.e., white areas in Fig. 1A) of the first non-constant geometric eigenmode (i.e., anterior-posterior mode) to divide the cortex into two regions. We repeat the process hierarchically, subdividing the regions from the previous iteration, and use the eigenvalues to define cut-offs for constructing parcellations with an arbitrary number of parcels. We apply this method to parcellate human, macaque, and marmoset cortices (Fig. 1B). We also apply it to 7 human subcortical nuclei (e.g., hippocampus, thalamus) and mouse isocortex in volumetric rather than in surface space (Fig. 1C).

Results: We evaluated our geometric parcellations against 53 other parcellations, based on different approaches, in human, macaque, marmoset, and mouse. Performance was evaluated using regional homogeneity6, estimated from 342 different maps capturing brain function, microstructural, cellular, molecular, and genetic properties. We matched the number of regions of our and each comparison parcellations and controlled for parcel size in the homogeneity calculations. In human cortex, our parcellations were more homogeneous in >70% of 245 brain maps relative to 17 of 18 benchmark parcellations (Fig. 2A). In the subcortex, our parcellations had similar or greater homogeneity than other nucleus-specific parcellations (Fig. 2B).
2B). In macaque, our parcellations were more homogeneous in all 3 brain maps relative to 7 of 10 benchmark parcellations (Fig. 2C). In marmoset, our parcellations were always more homogeneous relative to 4 benchmark parcellations. In mouse, our parcellation was more homogeneous than the Allen brain atlas in >86% of 88 brain maps. We further verified that our approach can be generalized to other mammalian species (e.g., chimpanzee, squirrel, guinea pig) for which no parcellations and minimal imaging data exist. Finally, we simulated a reaction-diffusion model with chemical sources at the poles of the anterior-posterior axis, consistent with evidence that patterning genes are expressed along this axis. We found that the model generated parcellations matching our simple geometric approximations (data not shown), suggesting its plausibility as a generative mechanism of our approach.

Conclusions: We introduce a new geometric approach for brain parcellation that is highly generalizable and can be applied to both the cortex and subcortex of any species, obtaining a reasonable first approximation of regional organization. The strong performance of the approach in obtaining highly homogeneous regions across diverse anatomical and functional properties emphasizes a fundamental role of geometry in shaping the regional organization of the mammalian brain.

References
A single model to segment brain tissues in any species

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Introduction: Atlas-based methods for brain segmentation rely on specific templates in order to define spatial priors. Automatic segmentation is thus available only for the few species mostly used in neuroimaging experiments, and adaptation to unseen species requires building of specific atlases, which use might in addition introduce biases in subsequent interspecies comparison studies. Having an efficient single model to segment the brain of many species would be of great interest for evolutionary biology [Milham 2022]. An example of today’s limitation is the Brain Catalog database (https://braincatalogue.org) [Heuer 2019] where manual segmentation is still necessary in most cases. Deep learning methods offer promising alternatives for brain tissue segmentation, but current models are trained for a specific species only. In this work, we evaluate the potential of training on synthetic data generated from a few species, and study whether the model can generalize to unseen species.

Methods: We used the synthetic framework [Billot 2023] because 1) it alleviates the need for real data for training and 2) the predictions are robust to variations in MRI contrast. We used the same generative process and training model (3D Unet) as described previously [Valabregue 2023]. In this study, we considered 5 different species for training: 1 adult human, 3 newborn humans from the dHCP, 3 fetal rhesus macaque, 1 adult rhesus macaque and 1 mouse lemur [Data]. The objective was to segment 13 structures in all these species (Head / CSF / Ventricles / Gray Matter / White Matter/ Cerebellum Gray Matter / 7 deep nuclei (Caudate Putamen, Pallidum, Thalamus, amygdala, accumbens, Substantia nigra ), all structures being present n the different species. The only exception was for fetal data where the deep nuclei are merged in a single structure. When such examples were seen during training, we merged the models predictions and computed the loss regarding the deep nuclei as a whole. We validated our results on 5 different test sets : rhesus macaque (5 brains, private dataset), adult HCP (40 brains from the HCP project), dHCP Young (20 youngest subjects from the dHCP), dHCP Old (20 oldest subject from the dHCP) and new species (dog, horse, and 6 different primate species) [ref Data]. For the human test sets, we chose the Freesurfer segmentation as pseudo ground truth, for the macaque we used gray matter extracted with https://github.com/Macatools/macapype and for the new species we used a manual segmentation of the whole brain (without CSF). In this case, we added the predicted label to construct a brain mask for the evaluation.

Results: Figure 1a) shows the Dice score for the Gray Matter (GM) for the different test sets. Although the performance of the model trained on multiple species was a bit lower compared to a model trained on a specific species, its performance was constant among all species in contrast to the species-specific models. Figure 1b) shows the Dice score for the brain mask, including the same test sets as above with the addition of the new species test set. We obtained similar results as for the GM but now the model trained on multiple species was the best-performing on new unseen species. A full validation on each tissue for new species is a difficult task because of the lack of ground truth labels, we therefore show some examples of segmentations for a visual quality check (Cf Figure 2).
Conclusions: Having a unique model to segment the brain in any species is an ambitious objective but with a potential high impact for comparative anatomy and evolutionary neurobiology. We demonstrate its feasibility with synthetic training: the model shows good generalization to unseen species. Our preliminary results are promising and we hope they will motivate additional work towards universal brain segmentation methods.

References
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Segmentation of Epileptic Focus from Multi-Channel Magnetic Resonance Images via Deep Learning

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Introduction: Epilepsy is one of the most prevalent neurological disorders. About 50 million individuals worldwide suffer from epilepsy¹. Focal cortical dysplasia (FCD), characterized by changes in cortical thickness, blurring of gray-white matter junctions, abnormalities in gyrus structure, is one primary cause of drug-resistant epilepsy (DRE)²³. Resection of the epileptic focus (EF) through neurosurgery is the most effective treatment of DRE-FCD. However, it is still challenging to localize EF based on neuroimaging due to the subtle structural changes of brain cortex. Computer-Aided Diagnosis (CAD) has been applied to localize EF by analyzing magnetic resonance (MR) images of FCD patients. However, conventional methods usually employ low-level artificial features, which is time-consuming and lack of feature representation capacity. The artificial intelligence represented by deep learning has promoted the development of intelligent CAD technology⁴⁵. However, the intelligent diagnosis of epilepsy is still under-explored. This article will investigate the use of deep models to segment EF from multi-channel MR images of FCD patients.

Methods: A deep learning based model is proposed in this paper to segment FCD EF. The proposed model receives a sub-volume sampled from multi-channel MR images and generates a EF probability map. The model architecture consists of a CNN encoder, a ViT encoder⁶ and a CNN decoder. CNN encoder is a 4-level convolutional network responsible for extracting local detail features. ViT encoder is employed to extract the global semantic features. CNN decoder is composed of 4 Fusion blocks which are capable of fusing features from CNN encoder, ViT encoder and previous Fusion block. A ShapeMatch block is employed to reshape and upsample the ViT feature to match with CNN feature before fusion. Upsample block is inserted between two consecutive Fusion blocks to double the feature size. At last, a convolution operation with kernel size of 1 and a softmax operation compose a Output block to convert features into EF probability map.
Results: We utilized a public open data set of FCD type II, provided by the Department of Epileptology at the University Hospital Bonn and approved by the ethics committee of the University of Bonn. This data set includes information from 85 patients, each offering T1 and FLAIR sequences. Ground truth (GT) of EF was delineated on FLAIR by two experts of epilepsy imaging. We used FSL to perform intro-registration between T1 and FLAIR (along with GT) as well as inter-registration with MNI-152 brain atlas. The aligned T1 and FLAIR, as well as their x-axis flipped images, are concatenated into 4-channel MR image. The dataset are divided into training and testing set with a ratio of 8:2. Model was trained with a hybrid loss function composed of dice loss and binary cross-entropy loss using Python 3.8 and PyTorch 1.10. For fair performance comparison, we re-trained 3DResUNet, 3DAttentionUNet and UNETR on the same dataset. The evaluation metrics include subject-level sensitivity (Sens-sub), voxel-level sensitivity (Sens-vox) and Dice coefficient (DC). Evaluations were conducted on the testing set. The proposed model achieved the best performance with Sens-sub of 88.2%, Sens-vox of 0.564±0.313, DC of 0.416±0.257, better than 3DResUNet (64.7%, 0.380±0.316, 0.369±0.300), 3DAttentionUNet (82.4%, 0.370±0.272, 0.349±0.247), UNETR (52.9%, 0.279±0.296, 0.275±0.280).
Conclusions: This paper introduces a deep neural network to segment EF from MR images of FCD patients, which shows superior performance compared to the three other models. However, there is a performance discrepancy between the segmentation of EF and other structures. Some cases remain undetectable. These underscore the considerable challenges associated with EF segmentation. Future work will explore pre-training the encoders of our proposed model based on self-supervision models, expecting to further enhance model performance.

References
**Developing a secure, browser-based and interactive image segmentation system for medical images**

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**Introduction:** The clinical diagnostic process involving manually delineating regions of interest (ROI) is a time-consuming endeavor. Moreover, it requires a significant level of domain expertise for the precise interpretation and segmentation of pathologies. Advancements in deep learning (DL) have the potential to address these challenges by enabling the automatic extraction of meaningful insights from medical imaging data (Liyanage et al., 2019). Notably, the Segment Anything model (SAM)(Kirillov et al., 2023) has demonstrated its capability in zero-shot segmentation. Such an approach could accelerate the demanding segmentation task for clinicians. However, the translation of such models to clinical applications is hindered due to patient privacy considerations, complex software setups and limited hardware resources. Moreover, existing tools present limitations, some necessitate server components to run DL models, others require complex software installations, and some are limited in their support for image formats, which impede their widespread deployment (Aljabri et al., 2022; Gorman et al., 2023; Masoud et al., 2023). Therefore, we aim to develop a zero footprint, user-friendly, interactive and secure browser-based deployment of DL models supporting various medical imaging formats for clinical environments. This abstract showcases a proof-of-concept with its core features: visualization, lesion detection with a fine-tuned SAM and refining annotation (https://iishiishii.github.io/deepsyence/).

**Methods:** To address the challenge with diverse medical image formats, the proposed platform utilizes the NiiVue package (Niivue, n.d.) for a versatile viewing experience. This platform caters various formats including voxel-based, mesh-based, mesh overlay, tractography and DICOM across all major browsers. Upon image upload, users access various functions for visualization and processing, offering an intuitive environment to interact with medical images. The automated annotation process relies on the SAM model, which has been fine-tuned for a stroke lesion annotation task. This serves as a blueprint for generalization across various models aimed at similar annotation tasks in medical imaging. To ensure the interoperability of the platform for models trained using different frameworks, we leverage the Open Neural Network Exchange (ONNX) (ONNX: Open Neural Network Exchange, n.d.), a model representation format. The model is converted to the ONNX format and executed via ONNX Runtime Web, a lightweight JavaScript library that enables the execution of ONNX models locally within web browsers. ONNX Runtime Web is resource-efficient and supports a wide range of hardware, including CPUs, GPUs, and TPUs, which makes it adaptable to various setups. The only software dependency on the clinician’s computer is a web browser. The computing is performed in parallel in the browser using Web Worker threads to enable a responsive user interface. Crucially, image data stays local in the browser sandbox and all computing is performed client-side, setting it apart from the prevalent server-side embedding seen in most available tools. This edge-computing approach ensures data privacy and enables the processing of medical imaging datasets - even behind hospital firewalls without requiring a complex setup.

**Results:** The proof-of-concept application implements a fine-tuned SAM to segment brain lesions within medical images that runs fully client-side (see Figure 1). The automatic annotation process consists of two steps: encoding the image and selecting the ROI. Once encoded, the segmentation can be done interactively on the image. These segmented ROI are displayed as a starting point for manual refinement.

**Conclusions:** The goal of this project is an open-source platform supporting DL models without complex installation, fostering collaboration among institutions. We are working on improving the execution concurrency to accelerate the runtime and integrating more models to enable various segmentation workflows.
References

Figure 1. The platform is developed as a single-page application using the React framework. It comprises two core components: the NiVue viewer allowing users to visualize and annotate on the main canvas in the main thread; and the computing session on worker threads aiding in processing each uploaded image.
Individual parcellations defined from connectivity improve heritability of cortical thickness

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Introduction: Current studies often consider surface phenotypes defined from regions stemming from an atlas projected on individuals via spatial normalization driven by the curvature of the largest cortical folds. This strategy is suboptimal relative to interindividual variations of the spatial organization of the architectural entities making up the cortical surface (particular region topography (Glasser 2016) or rare folding architecture (Mangin 2019)). To propose an alternative, we used a structural-connectivity-based subdivision (Lefranc 2016) - Constellation atlas - of the Desikan atlas (Desikan 2006) further projected on 1004 individuals (Langlet 2023) of the Human Connectome Project dataset (Van Essen 2013) according to their structural connectivity fingerprint. Here, we assessed the relevance of these individual parcellations by comparing them with 1000 randomly generated subdivisions of the Desikan atlas on the regional cortical thickness phenotype. We then performed a heritability study on the regional cortical thickness phenotype defined from the individual parcellations.

Methods: The 1000 randomly generated parcellations were obtained using Voronoi diagrams with the same granularity as the Constellation group atlas and act as group atlases. Firstly, we separately aggregated the thickness standard deviations of Constellation-based parcels and Voronoi-based parcels and performed a Student T-test under the null hypothesis: (Given a Desikan region, Constellation subdivisions have a lesser thickness standard deviation than the ones defined from Voronoi parcellations). In significant regions, the Constellation subdivisions provide better estimation of the regional thickness phenotype than random splits with similar sizes. Secondly, in these significant regions, we studied how the regional thickness of Constellation parcels relates to the ones yielded by the Voronoi parcellations. As regions cannot be matched across template parcellations, we paired their regional thicknesses on a vertex basis. We then averaged each regional thickness across the 1004 subjects and computed the Z-scores of the regional thickness stemming from Constellation subdivisions in the distribution yielded by the 1000 Voronoi subdivisions. Finally, we performed a twin-based heritability study of the regional thickness phenotype defined from Constellation individual parcellations, using the SOLAR algorithm (Almasy 1998). As covariates, we took into account the effect of age, age², sex and age × sex. We thus obtained heritability scores for the Constellation subdivisions and Desikan base regions. We kept scores that remained significant after Bonferroni correction for the number of regions of each parcellation scheme.

Results: The selection process using thickness standard deviation yielded a total of 23 significant regions across the two hemispheres. In these 23 regions, Figure 1 shows how the regional thickness differs for the Constellation method compared with random subdivisions. We observe that the individual parcellations better segregate areas with extreme cortical thicknesses thus possibly separating different structural entities. We show results of the heritability study in Figure 2 and observe that, by using individual parcellations, we tend to focus the heritability score of the Desikan regions on one subdivision. This even performed better in some regions such as the left paracentral: the heritability score of the Desikan region is 0.60 whereas one subdivision has an heritability score of 0.65.

Figure 1: Standard score of the Constellation regional thickness averaged across 1004 subjects by comparison with averaged regional thicknesses yielded by Voronoi parcellations. Blue (resp. red) means that the Constellation regional thickness is, on average, smaller (resp. greater) than chance. Colored regions have a significantly lower thickness standard deviation for Constellation subdivisions than randomly generated ones.
Conclusions: To conclude, we argue that the use of individual parcellations better captured structural entities than would random parcellations. The heritability study confirmed this result especially in associative areas, as heritability scores were focused on one sub-region. In a recent study, highly connected regions were found more heritable (Arnatkeviciute 2021) - in line with the results proposed here - hence these individual parcellations could be of use for further genetic studies.

References

Poster No 2002
Biologically Constrained Augmentation for Optimal Segmentation of MRI with Ventricular Abnormality
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Introduction: Tissue segmentation of brains with marked ventricular abnormalities is complicated by the heterogeneity of the associated patterns of anatomical distortion, obscuring underlying structure-function relationships. Conventional segmentation models employing standard augmentation techniques exhibit brittleness to ventricular morphology, and this can only be definitively corrected by representations of the space of possible ventricular appearances. A principled approach to augmenting standard segmentation models is to simulate, in a biologically plausible manner, the effects of ventricular pathology across its full range.

Methods: In this study, we develop a novel approach to biologically plausible augmentation of MR brain images based on topologically constrained deformation of the ventricular compartment. We utilised two distinct head MRI datasets: the publicly accessible OASIS-3 (Marcus et al., 2007), without examples of cerebrospinal fluid (CSF) flow disorders and that could be reliably segmented by traditional techniques, and a local dataset from UCL Queen Square Institute of Neurology, encompassing a variety of CSF flow disorders and that could not be reliably segmented using traditional techniques. A deep learning model was trained to produce augmented brains. The input to the model is the ventricle class from OASIS-3 brains segmented using Geodesic Information Flows (Cardoso et al., 2015), and the output is a deformation field that is applied to the input to produce an augmented ventricle segmentation. The model is trained by optimising a three-part objective: to maximise, within constraints, the relative growth in ventricle size, to minimise overall deformation magnitude, and to maintain spatial smoothness across the deformation field. This model was then used to produce a set of augmented scans (Fig 1).
with corresponding precise tissue class segmentation maps. A 3D U-Net model (Ronneberger et al., 2015) was trained on a) only the unaltered scans and b) a combination of unaltered and altered scans. Some local scans were used for training both models, in cases where traditional segmentation approaches were successful. Trained models were evaluated against OASIS-3 scans, with and without augmentation, that were held out during training.

Results: The deep learning model trained on this augmented dataset exhibited superior segmentation accuracy when evaluated on the most challenging unseen brains, reflected in higher median dice scores for all 3 tissue classes (Grey Matter: 0.651, White Matter: 0.801, CSF: 0.693), compared to a model trained exclusively on unaltered scans (Grey Matter: 0.577, White Matter: 0.684, CSF: 0.666), shown in Fig 2. The improvement persisted across brains at every level of ventricle enlargement (Mean dice 0.700 for all classes when trained with augmentation and 0.6740 without). This enhancement underscores the potential of our deep learning-based augmentation pipeline in significantly improving performance for segmenting anatomically atypical brains. Moreover, a subset of the augmented brains exhibited a biologically plausible appearance, similar to that in CSF flow disorders, shown in Fig 1. This further validates the effectiveness of our approach in generating synthetic, realistic representations of rare anatomical variations.

Conclusions: The enhanced accuracy of tissue class segmentation for brains with CSF flow disorders, when using our deep learning augmentation pipeline, exemplifies the crucial role that deep learning has in benefiting patients with a broad range of anatomical abnormalities that are typically underrepresented in conventional datasets. Our approach effectively bridges the gap between the scarcity of representative data and the need for precise segmentation. This success suggests that more comprehensive generative models, capable of simulating a broader range of rare imaging variations, hold great promise for future advancements in neuroimaging and personalised medicine generally.
Segmenting the whole brain including the eye: ocular morphometrics in IIH patient

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Introduction: Ocular morphometrics now allow us to include the eye and optic nerve in a whole-brain segmentation process. A dedicated eye and retroorbital space template, as well as a new processing pipeline, were developed in our lab over the past years solely to make ocular morphometrics possible. Idiopathic intracranial hypertension (IIH) is a neurological disease mostly in overweight women in which the intracranial pressure increases without a known cause. This is reflected by a swelling of the optic nerve head and a distension of the optic nerve sheath, all of which has been show with several imaging techniques (Yiangou et al., 2023). Our lab has developed an automated pipeline to measure the ocular and ventricle changes in spacefarers. In this study, our goal is to showcase this pipeline on patients with IIH using multi-modal imaging, T1-weighted and T2-weighted high-resolution structural MRI. Ultimately, we aim to identify ocular morphometrics findings IIH patients compared with age-, gender- and BMI-matched healthy control subjects and demonstrate the applicability of the new pipeline.

Methods: We recruited fifteen patients diagnosed with IIH, aged 38.1±11.5 years, and a control group comprising twenty-seven participants (32.8±12.8 years), with identical protocol for data acquisition. Isotropic 0.75mm T1w, and T2w images were conducted on a Siemens Prisma 3T scanner. Initially, T1 and T2 modality-specific templates were generated using preprocessed MRI images. Subsequently, detailed ocular and retroorbital annotations and segmentations were manually conducted on these templates. This step was followed by extracting individualized parameters from each image by registering the template to the individual images. Our analysis aims to test the hypothesis that significant differences exist in ocular and retroorbital eye metrics between IIH patients and control subjects. In addition, we want to explore the consistency between two different modalities, T1w and T2w images (See Figure 1).

Results: The optic nerve sheath volume (cm³) was smaller in the patient T2w MRI compared with the control group (Left ONS: t(47) = 3.92, difference = 0.09, CI = [0.045, 0.140], p < 0.001; Right ONS: t(47) = 3.15, difference = 0.07, CI = [0.025, 0.114], p < 0.001), the distance of lens centre to the optic nerve tip (mm) also shortened in the patient group on both T1w and T2w MRI (Left ONS: t(49) = -3.15, difference = -0.92, CI = [-1.51, -0.33], p = 0.003; Right ONS: t(49) = -2.08, difference = -0.61, CI = [-1.196, -0.021], p = 0.043) (see Figure 2, A). We also measured the consistency of two modalities, T1w and T2w. Figure 2, B showed that the point measurement has a relatively higher consistency between the two modalities, while the volume measure has a
Conclusions: The implemented pipeline demonstrated efficient performance across T1w and T2w image modalities, aligning with the anticipated outcome. It successfully facilitates the extraction of quantification, encompassing volumetric measurements, point-based metrics, and geometric characteristics of the ocular structures. Notably, in the context of IIH patients, the pipeline captures the characteristic alterations, including the dilation of the optic nerve sheath and the reduction in the axial length of the eyeball. However, our analysis reveals a notable variance in the parameters derived from T1w and T2w images, particularly concerning volumetric measurements, which appear less consistent than point-based metrics. This discrepancy suggests a potential limitation in the reliability of volume-based metrics derived from different MRI contrasts. Thus, future research should consider this inconsistency while encompassing multimodality structural metrics.

References

Test-retest reliability of cerebellar segmentation methods

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Introduction: The cerebellum serves a crucial role in motor control and cognitive function (Buckner, 2013; Schmahmann, 2019) and has been implicated in psychiatric disorders such as schizophrenia, bipolar disorder, and autism (Phillips et al., 2015; Villanueva, 2012). Measuring cerebellar structures and analyzing potential brain changes in such disorders is dependent on accurate cerebellar segmentation. In the literature, various MRI-based segmentation methods are compared on different measures such as repeatability, reproducibility, and dice overlap to expert delineations, with varying results. (Carass et al.,
2018; Sörös et al., 2021). In this study we compared the test-retest reliability of two different cerebellar segmentation methods, and determined the correlations between the segmented volumes.

**Methods**: Test-retest reliability for cerebellar volumes was calculated on an independent sample of n = 10 healthy volunteers acquired on two separate MRI scanners. T1-weighted structural images were acquired from n = 9 of the individuals (mean age = 35.76 years; range = [26.31-59.70]; 55% male) on a 3T GE Discovery MR750 scanner, and n = 9 of the individuals (mean age = 35.8 years; range = [25.24-60.52]; 55% male) on a 3T GE SIGNA Premier scanner. On each MRI scanner, individuals were scanned twice per session with a repositioning between scans, and a two-week interval between sessions, resulting in a total of four scans each. Cerebellar volumes were estimated with two different segmentation methods; the Sequence Adaptive Multimodal SEGmentation (SAMSEG; Puonti et al., 2016) and the Automatic Cerebellum Anatomical Parcellation using U-net with Locally Constrained Optimization (ACAPULCO; Han et al., 2020). Intra-class correlations (ICC) and 95% confidence intervals (CI) were computed for each combination of segmented volume, scan platform and segmentation tool, resulting in four measures from SAMSEG (grey- and white matter for each hemisphere) and an additional 28 measures of the cerebellar lobules from ACAPULCO. Furthermore, mean overall volumes and standard deviations were calculated, with a subsequent analysis of Pearson correlations to establish agreement between the methods.

**Results**: We found ICCs > 0.9 for both methods between all sessions and scans within MRI scanner, indicating excellent reliability, apart from three lobules from ACAPULCO: Left I-III (MR750: ICC = 0.79; CI = 0.54-0.94, Premier: ICC = 0.8; CI = 0.57-0.94), Right I-III (MR750: ICC = 0.73; CI = 0.46-0.92, Premier: ICC = 0.85; CI = 0.66-0.96), and Vermis X (MR750: ICC = 0.89; CI = 0.73-0.97, Premier: ICC = 0.96; CI = 0.9-0.99). Correlations for overall volumetric output between the segmentation methods were high for whole-, hemispheric-, and grey matter-volumes (r = 0.96-0.97). However, correlations for white matter volumes were lower (r = 0.37-0.42).

**Conclusions**: Both methods showed high test-retest reliability for global cerebellum measures. The most notable difference was the estimation of white matter volumes, resulting in low correlation between approaches. The segmentation of white matter differs between SAMSEG and ACAPULCO, with the former including part of the pons and most white matter branches and the latter only isolating the white matter of the Corpus Medullare (Bogovic et al., 2013). Selecting an approach for volumetric analyses of the cerebellum should thus be made not only based on the reliability of the method, but also depending on the measure of interest.

**References**

**Poster No 2005
Optimizing WMH Segmentation for diverse clinical datasets with SynthSegCSVD**

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**Introduction**: White matter hyperintensities (WMH) are key imaging biomarkers of cerebral small vessel disease (CSVD) on FLAIR MRI scans and are associated with a range of worse clinical outcomes, including increased risk for stroke and dementia. Automated, reliable WMH segmentation is crucial but challenging due to data heterogeneity across imaging protocols and...
scanner hardware. The segmentation task is further complicated by the diverse characteristics of WMH. Existing tools often fail to generalize across varied imaging datasets. This study presents SynthSegCSVD, an advanced CNN-based tool with a UNet architecture designed for improved WMH segmentation in heterogeneous clinical datasets with varying degrees of CSVD burden.

**Methods:** SynthSegCSVD was developed using a large dataset consisting of over 1000 scans sourced from seven multi-site studies, encompassing a range of clinical populations, WMH burdens, and imaging protocols. A novel two-stage segmentation framework was developed that first leverages FreeSurfer’s SynthSeg (Billot, 2023) to generate a targeted regional mask containing two key neuroanatomical structures, and subsequently combines this mask with the FLAIR image for improved WMH segmentation. Advanced machine learning strategies, including the ensembling of three models with distinct precision-recall weightings and test-time augmentation, were utilized to ensure robust segmentation performance. The efficacy of SynthSegCSVD was evaluated by benchmarking its performance against two state-of-the-art segmentation tools, HyperMapper (Forooshani, 2022) and SAMSEG (Cerri, 2023), using several diverse test datasets.

**Results:** SynthSegCSVD exhibited superior segmentation performance across all test datasets, surpassing the benchmark tools in both accuracy and reliability (Fig. 1). Its superior performance was most evident in datasets that employed isotropic FLAIR acquisition protocols, where a significant reduction in WMH contrast was also observed (permuted p<0.001). In this more challenging segmentation scenario, SynthSegCSVD demonstrated a significant increase in the mean Dice score compared to HyperMapper and SAMSEG, with improvements of 0.19 and 0.34, respectively (permuted p<0.001). Furthermore, SynthSegCSVD exhibited robustness to variations in image orientation and header inaccuracies, maintaining remarkable stability across a range of imaging conditions and patient populations.

**Conclusions:** SynthSegCSVD represents a significant advancement in automated WMH segmentation, effectively addressing the challenges of data heterogeneity. Its robust performance across a broad spectrum of imaging conditions and patient characteristics makes it a promising tool for large-scale studies and clinical applications, particularly in populations with varying degrees of CSVD.

**References**
Enhancement of PVS analysis via T1w-based PVS segmentation: Comparison with T2-weighted Based method

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Introduction: Perivascular spaces (PVS), also known as Virchow-Robin spaces, play a crucial role in enveloping brain blood vessels¹. Typically, their assessment involves 3D T2-weighted (T2w) imaging or a combination of T1-weighted (T1w) and T2w imaging²,³. However, the acquisition of 3D T2w images for PVS evaluation can be challenging in clinical or open datasets. This study introduces a segmentation method utilizing only T1w images, overcoming the limitations associated with T2w availability. We propose a two-step algorithm to enhance visibility and create a PVS mask, comparing its outcomes with the conventional T2w-based approach and providing an alternative for PVS quantification.

Methods: [Dataset and Preprocessing] We utilized 3T 3D T1w and T2w images from the Human Connectome Project (HCP) dataset (HCP-Young Adult, 22-35 years⁴). Model training involved 927 subjects, and 45 subjects were used for model testing. Additionally, external validation was performed on an independent dataset (N=18, young adults) obtained from 3T Philips MRI. Enhanced T1w targets for training were generated through pixel-wise division of T1w by T2w (T1w/T2w) after confirming co-registration accuracy. [Network] Our T1w-based segmentation method comprises two deep learning models, as depicted in Figure 1. We employed 3D U-Net and SwinUNetR⁵ as the synthetic and segmentation models, respectively. Model updates involved multiple loss functions, combining L1 Loss, minimum intensity projection (mIP), and L1 Loss with PVS-weighted map for the enhancement step. To calculate mIP Loss, we randomly chose six consecutive slices from the complete volume and applied minimum intensity projection (mIP) to both the output and target images, subsequently utilizing L1 Loss. For the segmentation step, a combination of Dice and cross-entropy loss functions was used. [Evaluation] To assess the results, SwinUNetR was also trained using single-contrast (T2w or T1w) input. PVS segmentation volume, and the number of connected components were calculated for comparison. Pearson correlation coefficients were computed between model results to measure similarity.

Results: Figure 2 summarized our result. Figure 2-A shows the improved PVS visibility compared to the original T1w image, as highlighted in the yellow circle. Figure 2-B compiles calculated PVS volumes and numbers from the segmentation results. The proposed method exhibited improved correlation coefficients for PVS volume (0.91 to 0.95) and PVS count (0.92 to 0.93), aligning closely with T2w results in Figure 2-b-1. In the external test set, no significant differences were observed in volume, but an improvement was noted in PVS count (Figure 2-B-2).
Conclusions: This study introduces a PVS segmentation method utilizing only 3D T1w images. Results from the T1-based method demonstrated high similarity to T2w results for PVS volume and count in the brain. Our approach is expected to enhance the clinical value of PVS quantification from 3D T1w images.

References

Poster No 2007

VesselBoost: Improving Segmentation of Small Vessels in Human Brain Magnetic Resonance Angiograms

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**Introduction:** The sophisticated pial arterial vascular network plays an important role in understanding cerebral blood flow dynamics and diagnosing cerebrovascular diseases. Starting by leveraging deep-learning models to extract accurate segmentations of the trivial vessels in human brains, we aim to quantitatively characterize the architecture of the pial arterial network to provide valuable insights for cerebral blood flow estimation models and fMRI signal simulations.

**Methods:** Deep-learning methods for vessel segmentation: VesselBoost offers two main avenues for detailed vasculature segmentation: 1. Test Time Adaptation (TTA): VesselBoost adapts a pre-trained model to new data, where an imperfect segmentation is available or generated with the pre-trained model. Pre-trained models were trained on 300 μm isotropic angiograms with manual or automatic labels. 2. Self-training Model: VesselBoost trains a 3D-UNet model from scratch using a single subject’s imperfect segmentation for ‘boosting’ vessel details in the single subject data. Both TTA and the Self-training Model incorporate an innovative data augmentation technique that utilizes the self-similarity between large and small vessels to expand training dataset.

**Results:** VesselBoost generated detailed segmentation across different data set with different resolutions. Figure 2 shows that both TTA and the Self-training Model can enhance the details and improve the continuity of the vessels in imperfect segmentations. Moreover, the TTA method exhibits strong generalization capabilities across varying resolutions, despite the pre-trained models being initially trained on lower-resolution data, it has a good performance on data with 150μm isotopic resolution.
Conclusions: We developed a segmentation framework capable of extracting small vessels in magnetic resonance angiograms. This is an open-source project and currently available on https://github.com/KMarshallX/vessel_code. Future efforts are needed to firstly enhance the precision of vascular graphing, to extract quantitative measures and provide valuable input for blood flow simulations. Second future direction will be to increase VesselBoost’s generalizability on other contrasts: T1, T2*, etc. In summary, VesselBoost demonstrates effective segmentation of small vessels, enhancing vascular continuity, while the TTA method successfully translates data from low to high resolution.

References
A road map to manual segmentation of cerebral structures

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Introduction: Manual segmentation is an essential tool in the researcher’s technical arsenal. It is a frequent practice necessary for image analysis in many protocols, especially when regions of interest are required (volumetry, connectivity, etc.). Despite its evident relevance, the manual segmentation process has received little attention in the literature. Some works mention addressing strategies for specific structures (Yushkevich et al, 2015), but – to our knowledge – no publication has discussed what should be considered good practices and why. Similarly, in many papers, despite the major impact of the quality of the segmentation on the results, the details of how the segmentation was planned and carried out are often briefly or not mentioned. Although manual segmentation is an expert-dependent procedure, the upstream identification of the best methodological strategies ensures quality and reproducibility. Furthermore, recent advances in neuroimaging, such as ex vivo ultra-high field MRI, enable new acquisition modalities and the visualization of minute structures.

Methods: This work is the result of a narrative review of the literature with input from expert anatomists with manual segmentation experience. We propose the comprehensive checklist in figure 1 as a guiding tool for manual segmentation of cerebral structures, from planning to reporting.

Results: As a synthesis of reviewing the literature and our experience with manual segmentation, we emphasized different critical steps (Fig. 2) and gathered tips and tricks to make for an easier and less time-consuming task (Hashempour et al., 2019, Keuken and Forstmann, 2015, Lechanoine et al, 2021). A combination of enlightened choices before the segmentation clarifies how to deal with the limits of anatomical classes that pose the most problems with this technique. Consideration of segmentation usage, subsequent processing, and expected results is necessary to avoid certain pitfalls. Reporting these choices in articles is recommended in order to enhance reproducibility and enable comparison of the results from different studies. By describing precisely what limits were used for each anatomical class, stating if those limits were followed conservatively or liberally, and thoroughly citing the papers and atlases used, a reader will better understand which anatomical area is being referred to. The abovementioned recommendations are summarized in a checklist to be used as a tool for manual segmentation (Fig. 1).

Figure 1: Checklist to be used as a guiding tool for manual segmentation, from planning to reporting.
Conclusions: In this context of new challenges, we propose a general roadmap to optimize both the technique and the reporting of manual segmentation of cerebral structures. If implemented, it would greatly contribute to open and responsible science. Well-conducted and well-described segmentation procedures will increase the validity of research works, which is a significant issue for data reproducibility and results in neuroimaging.

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Poster No 2009
Surface-based segmentation of Focal Cortical Dysplasias using Graph Neural Networks: a MELD study
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Introduction: Focal cortical dysplasia (FCD) is a common cause of drug-resistant epilepsy, and accurate detection on MRI is critical for presurgical planning (Téllez-Zentemo et al., 2010). However, MRI identification of these subtle lesions remains a challenge. Previous FCD detection methods have been prone to high numbers of false positives due to their inability to take the entire cortex into account (David et al., 2021; Gill et al., 2021; Spitzer et al., 2022). This Multicentre Epilepsy Lesion Detection (MELD) project study aimed to develop a whole-brain graph neural network (GNN) for segmenting FCDs.

Methods: The MELD cohort includes 618 patients with FCD and 397 controls, used to train and test a novel Graph UNet model architecture (https://github.com/MELDProject/meld_graph). The cortical mesh was represented as a graph, treating vertices as nodes connected to neighbouring vertices by edges, enabling the network to learn spatial relationships through spiral convolutional filters. We trained the network on 278 patients and 180 controls to segment lesions with four parallel tasks: lesion segmentation, prediction of geodesic distance from the lesion, object detection and classification of lesional examples. These last two tasks were designed to mitigate uncertainty in manually delineated lesion masks. The network was evaluated on a withheld test dataset (260 patients, 193 controls) for its sensitivity in detecting lesions in patients (i.e. overlap between prediction and ground truth) and specificity in controls (i.e. no false positives).
Results: On the withheld test cohort, the MELD Graph model achieved a sensitivity of 67% in patients, with a specificity of 76% in controls, a significant gain in specificity in controls against patch-based approaches on the same dataset (sensitivity 67%, specificity 49%). The MELD Graph model increased the positive predictive value of a prediction being a lesion from 0.4 to 0.7. Interpretable lesion reports characterise lesion location, salient feature abnormalities, and overall prediction confidence.

Conclusions: Our study demonstrates the utility of GNNs for FCD segmentation in MRI scans. The fully-trained GNN substantially improved on previous patch-based approaches. This improvement in specificity is vital for clinical integration of lesion-detection tools into the radiological workflow, through increasing clinical confidence in the use of AI radiological adjuncts and reducing the number of areas requiring expert review.

References
ABSTRACTS

Poster No 2010

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Introduction: Ultra-low/low field MRI has drawn renewed neuroscientific interest due to lower cost and portability that may increase access (Hori et al., 2021). Several possible clinical applications require accurate head tissue segmentation (Michel & Brunet, 2019). Images acquired at lower field strengths have reduced SNR, image resolution and may also suffer from image distortions compared to higher field/cost scanners (Arnold et al., 2023). The contribution of these factors on segmentation reliability are unclear. We aimed to quantify the accuracy of automated head tissue segmentations using CHARM (Thielscher et al., 2015) on 0.064T and 0.55T images in comparison to those from a 3T image.

Methods: Data acquisition 3D T1 and T2 weighted (w) images were acquired in 2 healthy adults (ages 35 and 41) at 0.064 T (Hyperfine Swoop\textsuperscript{+}), 0.55T (Siemens Healthineers MAGNETOM, Free.Max) and 3 T ((Siemens Healthineers MAGNETOM, Vida). T1w parameters. Hyperfine, inversion recovery FSE 2x2x2 mm, TR=880 ms, TE=6.12 ms, TI=354. Freemax, 3D FLASH, TR =17 ms, TE=10.70 ms, 3T Vida, MPRAGE, 0.9 x 0.9 x0.9 mm, TR=2200 TE=2.46 ms. T2w parameters. Hyperfine 2x2x2 mm, TR=2000ms, TE=156 ms. Freemax T2 SPACE, TR=1300 ms, TE= 197 ms. Vida T2 SPACE, TR=3200ms, TE=408ms. Preprocessing Linear co-registration T1 and T2 images from all 3 scanners were oriented to the same reference location using SPM 12. Linear co-registrations were carried out using SPM 12 (Penny et al., 2007). T1 and T2 images from all field strengths were co-registered and resliced to the 3T T1w image. Segmentation creation. Head models were created using CHARM, a part of SimNIBS. CHARM requires a T1-weighted image and preferably a T2-weighted image to create a segmentation of the head into several tissue types, including white matter, grey matter, CSF, bone, scalp, eyeballs, compact bone, spongy bone, blood, and muscle. Nonlinear co-registration of segmented images To correct for distortion the following nonlinear registration was performed: (i) the skull segment was extracted from all segmentations as a binary mask; (ii) rigid & nonlinear registration was performed using mrregister (a part of MRtrix3 (Tournier et al., 2019)) to align the 0.064T & 0.55T skull segments with the 3T skull segment, using a least-squares metric with strong smoothness regularization as the geometric distortions were expected to be smooth (e.g. due to B0 and gradient non-linearity); (iii) the resulting warps were applied to the full 0.064T & 0.55T segmentations using mrtransform (also a part of MRtrix 3) using nearest-neighbor interpolation. Data analysis Low-field segmentation quality was assessed by comparison with the reference 3T segmentation, quantified using the Dice coefficient.

Results: Dice co-efficients (see figure 1) indicate that segmentation quality based on 0.55T data were high (~0.7-0.95) indicating a similar segmentation to that from 3T was achieved. In contrast, dice co-efficients for segmentations derived from the 0.064T images were significantly lower (~0.25-0.5). This appeared to be related to geometric image distortions (see figure 2). Crucially, with a nonlinear registration of the segmented images there was a marked improvement in dice coefficients for the 0.064T data (~0.65-0.82).

Conclusions: Dice coefficients based on our segmented images based on 0.55T were high, indicating a very good level of similarity with our 3T derived data. On the other hand dice coefficients derived from 0.064T data were relatively low. The segmentation similarity was substantially improved by nonlinear registration. This indicated that at 0.064T image noise and contrast might be sufficient, but improved distortion (without requiring matched high-field data) is needed.

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Figure 1. A illustrates dice coefficients pre non linear registration, B shows dice coefficients post non linear registration and C provides the exact figures in table form. Note the relatively low scores pre non linear registration in the 0.064T data and the marked improvement post non linear registration.
References


Poster No 2011

Unbiased validation of connectivity-based cohesive brain parcellation

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Introduction: We have previously introduced cohesive parcellation, a functional connectivity-based approach that was shown to be optimal for downstream, exemplar-based network analysis1. However, this results in many more parcels than traditional parcellations. Most connectivity-based metrics of parcellations are sensitive to the size and number of parcels, complicating direct comparison. Recently, the distance-controlled boundary coefficient (DCBC) was introduced, an unbiased, parcel resolution invariant measure incorporating both connectivity and distance2. We evaluate cohesive parcellation using DCBC and compare to other parcellations.

Methods: 18 healthy subjects (age 20-36, 8 female) were scanned on a 7T Siemens Magnetom (Erlangen, Germany) with a 32 channel Nova head coil (Massachusetts, USA). Whole-brain, rsfMRI were acquired (SMS multiband=3, 81.5mm slices, 128+4 volumes, TE/TR=21/2800 ms, 70° flip, FOV=192 mm², resolution=1.2x1.2x1.5 mm³). T1w images were acquired for anatomical context as well as duel-echo B0 field maps. rsfMRI data were corrected for B0 distortions, slice timing, motion3, and physiologically-based nuisances4. Subject-specific cohesive parcellation was performed based on Pearson correlations of the grey matter rsfMRI data using a 0.5 cohesion threshold1. Cohesion, homogeneity, and Silhouette were calculated at the voxelwise level, grouped by parcel, and a parcel size-weighted average determined. For DCBC, a distance-based graph was assembled from the grey matter voxels based on spatial adjacency and corrected for gyral and sulcal folds using FreeSurfer-derived white and pial surface reconstructions. For each subject, DCBC was calculated for each parcel using voxel-to-voxel correlations and geodesic distances, with a final parcel size-weighted average extracted as above2.

Figure 2: A shows raw realigned T1 and T2 images for both subjects across field strengths, B illustrates the CHARM segmentation for both subjects across field strengths, and C provides the overlays of our selected segmented tissues from our 0.964, 0.551 and 8 T1 images using an RGB color scheme (see e) white indicates a perfect overlap.
Results: Cohesive parcellation and associated parcel-based Silhouette and DCBC distributions are shown for a representative subject (figure 1, 2530 parcels; 441-3579 across all subjects). The Silhouette and DCBC for this subject was 0.329 and 0.0973, respectively. The Silhouette coefficient shows strong dependence on parcel size, while the DCBC is largely independent, except in the smallest parcels. The corresponding distributions for all measures are shown for all subjects (figure 2). Over all subjects, the size-weighted averages were 0.520±0.0038, 0.484±0.0038, 0.292±0.033, 0.0845±0.012 for cohesion, homogeneity, silhouette, and DCBC, respectively. For cohesion, homogeneity, and silhouette, these results are consistent with previous findings. The DCBC for cohesive parcellation compares favorably to previously published DCBC results across a number of traditional parcellations, including the Yeo5 (0.0213), Power6 (0.0261), and Gordon7 (0.0236) parcellations.

Conclusions: Cohesive parcellation has been shown to compare favorably to other connectivity-based parcellations across several measures at both the individual subject and group levels while providing optimal parcel exemplars for downstream brain modelling. Because cohesive parcellation is focused on generating optimal exemplars, it produces higher parcel counts, complicating evaluation with traditional metrics. The DCBC metric is invariant to parcel count, which showed that cohesive parcellation performs better than other data-driven functional parcellations. Connectivity-based brain modelling is based on exemplars derived from simple averages of underlying voxel members. Incorporating spatial context into network analysis may improve these models. Cohesive parcellation utilizes a flexible hierarchical platform for optimization. Future work will look to incorporate spatial context into this framework in a DCBC-like manner in order to further optimize parcels for downstream brain modeling.

References
Automated Pituitary and Pineal Gland Segmentation with Multi-Modal Input Channels

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**Introduction:** The pituitary and pineal glands are two subcortical structures that play pivotal roles in the human endocrine system. The pituitary gland is a bilobular organ connected to the hypothalamus via the infundibulum and secretes hormones such as human growth hormone and oxytocin (Hall 2016, chap. 76). While much less is known about the pineal gland, it is thought to control melatonin secretion and various aspects of sexual function (Hall 2016, chap. 81). Accurate segmentation of both structures is critical for imaging-based analyses related to endocrine disorders. Here, we present a supervised, deep learning-based method for automatic segmentation of the pituitary and pineal glands. This work is based on a previous segmentation frameworks for the hypothalamus (Billot et al. 2020) and subcortical limbic system (Greve et al. 2021).

**Methods:** Input data: Our dataset comprised n=32 subjects from the FreeSurfer Maintenance (FSM) Grant Data (“FsmData - Free Surfer Wiki” n.d.). Each subject was associated with four MRI modalities: T1-weighted (T1w), T2-weighted (T2w), quantitative T1 (qT1), and proton density (PD). The anterior and posterior pituitary lobes, the infundibulum, and the pineal gland were manually labeled by two labelers to provide 64 labeled data sets. (Figure 1) Data augmentation: We applied a series of randomized, spatial and intensity augmentation functions to the input data during training. These include image cropping to a 100x100x100 window, an affine transformation, left-right flipping, a gamma transform for contrast alteration, bias field simulation, Gaussian white noise addition, and min-max normalization. Augmentation (aside from cropping and rescaling) began after 50 training epochs to allow proper initialization of network hyperparameters. Network architecture: Based on the methods, we trained a U-Net to perform automatic segmentation of each label similar to the methods described in (Greve et al. 2021). Our network consisted of three layers, each with two convolution blocks composed of a 3x3x3 convolution and ELU activation. We began with 24 feature maps in the first layer; these were doubled during each decoding layer, and then halved during each encoding layer. At the end of each layer, we performed either max-pooling (encoding branch) or max-unpooling (decoding branch). Experimental validation: We trained 12 different configurations of our U-Net, each with a different combination of MRI modalities as separate input channels. Training was performed using 80% of the data (n=52) for 2000 epochs using a combination of Dice and categorical cross entropy (CCE) loss functions.

**Results:** Figure 2 displays the mean Dice scores for each label obtained using the different sets of input modalities. Overall, all models performed best in the anterior pituitary and worst in the infundibulum. We observed that when using a single input channel, the T1w image provided the best segmentations over the T2w, qT1, and PD modalities. Moreover, using a combination of MRI modalities as separate input channels. Training was performed using 80% of the data (n=52) for 2000 epochs using a combination of Dice and categorical cross entropy (CCE) loss functions.
of T1w and PD, or T1w and at least two additional input channels, offered a slight improvement over T1w alone. In these cases, all network configurations achieved a mean Dice score in each label of greater than 83% in the anterior pituitary, and greater than 75% in the posterior pituitary, infundibulum, and pineal gland.

**Conclusions:** We have presented an automated, U-Net-based framework for segmentation of the pituitary and pineal glands. We showed that utilizing multiple MRI modalities as separate input channels to our network improved segmentation results compared to use of a single input image.

**References**

**Poster No 2013**

**Cytocarchitectonic mapping and probabilistic atlas of the human claustrum**

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**Introduction:** The claustrum is often described as the brain’s most mysterious nucleus (Mathur, 2014). The mystery is a consequence of the claustrum’s complex anatomy, which poses significant challenges to investigation via in vivo neuroimaging. The dorsal claustrum, which lies between the putamen and insular cortex above the level of the central insular sulcus, is remarkably thin, often submillimeter in its dorsomedial dimension. The ventral claustrum, approaching the lower circular insular sulcus and extending into the temporal lobe, consists of diffuse grey matter islands, fragmented by intersecting fascicles. At resolutions typical of in vivo MRI, the claustrum is difficult to discern from adjacent structures, and aspects of the ventral claustrum may evade detection altogether. Therefore, neuroimaging studies would greatly benefit from the development of a high-resolution, three-dimensional, probabilistic reference atlas, to better understand variations in individual anatomy, and support the investigation of claustral structure, connectivity and function in living humans. At present, no such reference exists.

**Methods:** Here, we create a cytoarchitectonic reference of the human claustrum. We mapped the claustrum as a singular structure in 10 postmortem brains (5 female, ages 37-85), on every 60th Merker-stained coronal section at 1 micron in-plane resolution (distance between sections = 1.2mm, total sections > 400). One of the examined brains is the BigBrain, allowing mapping across a continuous series of sections (Amunts et al., 2013). Using in-house software, we delineated the claustrum’s borders according to apparent anatomy, informed by cytoarchitectonic criteria described by earlier studies (Brockhaus, 1940; Rae, 1954). Next, we reconstructed the claustrum in three-dimensions, and computed continuous probabilistic maps in the MNI-Colin27 and ICBM2009casym reference spaces, at 1mm isotropic resolution (Amunts et al., 2020).
Results: The high-resolution delineation, in both hemispheres, and across multiple brains, allowed a thorough characterization of the claustrum’s structure, whilst underscoring the inherent difficulty of claustral investigation in vivo. First, in keeping with earlier studies, we observed extraordinary heterogeneity in cytoarchitecture across the claustrum’s extent [FIGURE 1A]. Second, we observed that the claustrum appears to directly abut the olfactory tubercles, amygdaloidal complex (Kedo et al., 2018), and the piriform cortex (Kedo et al., in preparation) [FIGURE 1B]. Third, we observed that, along the anterior-posterior axis, the anterior aspect of ventral claustrum extends medially above and then below the amygdaloid complex towards the piriform cortex [FIGURE 1C], surpassing what is denoted by other high-resolution atlases (Mai, Majtanik and Paxinos, 2015; Ding et al., 2017). More generally, our cytoarchitectonic mapping, as well as three-dimensional reconstruction and probabilistic maps, revealed a high degree of intersubject variability in the shape and extent of the ventral claustrum, especially its extension into the temporal lobe. Analyzes in-progress investigate sex and hemispheric differences, and whether purported claustral subdivisions, located differently across existing atlases, have a clear basis in cytoarchitecture.

Conclusions: To the best of our knowledge, ours is the first high-resolution 3D cytoarchitectonic reference of the human claustrum, based on the analysis of multiple brains. Alongside advances in ultra-high field MRI, the maps hold significant potential to illuminate enduring questions of claustral structure-function relationships, by reducing misattribution of function to adjacent structures (and vice versa), and serving as seed regions for diffusion and functional connectivity studies. The probabilistic maps will be integrated into the growing number of subcortical cytoarchitectonic mappings in the Julich Brain Atlas (Amunts et al., 2020), accessible online, e.g. via the EBRAINS platform.

References
Comparison of Infant FreeSurfer segmentation and manual tracing in alcohol-exposed neonate brains

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Introduction: Segmentation of infant MRI brain images is challenging due to low signal-to-noise ratio, motion corruption, and maturation-related regional variation in tissue contrast and geometry¹. However, neonatal morphometric brain changes are associated with teratogenic exposures²-⁳ and later neurodevelopment⁴-⁵. Infant-specific tools are thus needed as manual segmentation is not feasible for large datasets. Infant FreeSurfer (IFS) is an automated segmentation pipeline for image processing in 0-2 year-olds⁶. Here we assess the reliability of IFS segmentation in comparison to manual segmentation of subcortical brain regions in neonates with prenatal alcohol exposure (PAE), and their relative sensitivity to detect PAE-related regional volume changes.

Methods: 64 neonates (mean gestational age at scan: 41.4±2.3 wk) born to heavy-drinking or control women were scanned unsedated on a 3T Siemens Allegra MRI scanner with a custom-built neonatal head coil⁷. A motion-navigated multiecho gradient echo sequence was acquired twice with protocol parameters: FOV 144mm, 128 slices, TR 20ms, TE 1.46/ 3.14/ 4.82/ 6.5/ 8.18/ 9.86/ 11.54/ 13.22ms, 1mm³ isotropic resolution, flip angles 5° and 20° respectively. In FreeSurfer⁸, individual echoes from each acquisition were split, tissue parameters estimated and image volumes synthesised with a 24° flip angle. Volumes of bilateral caudate, putamen, pallidum, accumbens, thalamus, hippocampus, amygdala and cerebellar hemispheres, and midbrain, pons, medulla and vermis, were obtained from manual tracing in Freeview in FreeSurfer⁹ and automated segmentation in IFS6. Reliability across methods was assessed using intraclass correlation (ICC) estimates for consistency and absolute agreement with a single-rating two-way mixed effects model and Cronbach's alpha. Sensitivity to detect alcohol-related differences was assessed using a repeated measures general linear model (GLM) for each region with main effects of diagnostic group (27 unexposed, 23 heavily-exposed non-syndromal [HE], 14 pFAS/FAS; diagnosed in early childhood) and segmentation method, and group by method interactions. To examine sensitivity in detecting PAE effects, we performed ANOVA, with ANCOVA to control for potential confounding, on data obtained from each segmentation method separately to identify regions showing volumetric group differences.

Results: Consistency between segmentation methods was moderate to excellent (> 0.5) in 60% of regions, but agreement poor (< 0.5) in 70% (Table 1). Cerebellar and brainstem regions generally showed acceptable reliability, while pallidum, accumbens and amygdala showed poor reliability bilaterally across all ICC measures. GLM analyses showed a significant main effect of segmentation method in all regions other than left hippocampus and medulla (Table 1), with manual segmentations smaller than IFS in all regions except cerebellum and brainstem. A main effect of diagnosis (p < 0.1) was observed in midbrain, medulla, and bilateral putamen and pallidum. Method*diagnosis interaction effects were seen in four regions. Fig. 1 shows regions where either manual or IFS volumes differed by group (p < 0.1). Post hoc pairwise comparisons showed smaller volumes in HE and/or pFAS/FAS groups for 7 manually traced and 9 IFS regions. After controlling for potential confounders, group differences remained in manually traced medulla and bilateral pallidum and in IFS-segmented bilateral caudate, left hippocampus, right amygdala, right accumbens, midbrain and medulla, with pFAS/FAS volumes smaller than unexposed in all but 1 region.
Conclusions: Our results show moderate region-dependent reliability between manual tracing and IFS segmentation. Both methods detected PAE-related volume reductions across basal ganglia, limbic and brainstem regions, but effects were more robust in IFS segmentations.

References

Poster No 2015
Multiscale subdivision of an anatomical cortical parcellation based on geodesic distance
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Introduction: The brain can be analyzed as a complex network of interacting regions, often referred to as the human connectome [Sporns et al., 2004]. To obtain and study the human connectome, a crucial step is to define the gray matter parcellation, over which the connectivity profiles are calculated. Some studies have focused on obtaining different levels or scales of parcellation, ranging from fine- to coarse-grained parcellations, based on a base parcellation [Moreno-Dominguez et al., 2014], [Molina et al., 2023], [Diez et al., 2015]. However, these prior works face challenges such as considerably variations in size and spatial discontinuity of regions. Additionally, parcellations in these studies are not defined with a multiscale structure. Therefore, we propose a framework for the generation of multiscale cortical parcellations on a surface representation of the cortex based on a group of 79 healthy subjects from the ARCHI database [Schmitt et al., 2012]. The method is based on geodesic distance and hierarchical clustering, and uses a tree partitioning method, depending on the maximum distance between regions in a cluster, to obtain different parcellation scales. Moreover, it efficiently calculates the subject’s connectome for each level.

Methods: Fig. 1 illustrates the proposed method. First, based on [López-López et al., 2020], centroid of each region is calculated for each hemisphere of each subject using the geodesic distance between vertices of the region in the base parcellation. Next, a distance matrix is calculated based on the geodesic distance between the centroids of each pair of regions (Fig. 1A). Then, a mean distance matrix is computed to ensure the results reproducibility and its values are entered into an affinity graph (Fig. 1B) [Molina et al., 2023]. Subsequently, an average-link agglomerative hierarchical clustering is applied on the affinity graph to obtain a dendrogram. A tree partitioning method, depending on the maximum distance (Dm) between regions in a cluster, was used to obtain different parcellation scales [Román et al., 2022] (Fig. 1C). The method establishes and saves the correspondence between all levels of parcellation. Finally, based on the Möller-Trumbore ray-triangle intersection [Möller et al., 2005], for each subject, it efficiently calculates the connectome for each level, using the whole brain tractography dataset and the subject’s labeled mesh (Fig. 1D).
**Results:** We applied the method to Desikan-Killiany atlas [Desikan et al.; 2006] as the base parcellation and obtained four parcellation scales for both symmetrical and non-symmetrical parcellations. Fig. 2A displays the multiscale symmetrical parcellation obtained using a single average matrix for both hemispheres and Dm of 10, 42, 84, and 180 mm from level L4 to L1, respectively. Structural connectivity matrices reveal the expected shape, with symmetrical connections between hemispheres and with more connections within each hemisphere. (Fig. 2B). As the parcels are merged, area of the regions and standard deviation are increasing. The highest STD corresponds, as expected, to level L1, which has few large regions (Fig. 2C).

**Conclusions:** We propose an efficient framework to create a multiscale cortical parcellation with configurable parameters and based on any base parcellation. We developed a generic algorithm which does not assume a symmetrical base parcellation, however, since our base parcellation is symmetrical, we obtained a symmetrical multiscale parcellation by using a single mean.
distance matrix for both hemispheres. The generated parcels exhibit spatial contiguity and homogeneous sizes. With the adaptive partitioning of the hierarchical tree, we can generate as many levels of parcellation as desired, depending on the number of parcels in the base parcellation and the selection of different values of maximum distance between the regions of a cluster for each level. This framework will be made available and can be applied to different fine-grained parcellations.

References

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Poster No 2017
Comparison of Functional Connectivity Changes in Humans and Primates in Psychedelic States
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Introduction: Psychedelic substances such as psilocybin and LSD have received enormous attention for their positive effects on disorders like depression and alcoholism. Functional imaging studies on these drugs often report reduced within-network functional connectivity (FC) and an increased between-network FC. Though animal models are used to characterize and evaluate psychedelics, understanding the translational validity of such assessments between animals and humans is essential for psychedelic research. This work seeks to (a) identify if psychedelic modulation of FC in anesthetized nonhuman primates (NHPs) with psilocybin may have similar findings as a human cohort with LSD previously reported, thereby (b) providing support for the use of a NHP model in psychedelic neuroimaging.

Methods: Anesthetized NHPs were maintained at 1.0-1.2% isoflurane and scanned on a 3T Siemens TIM-Trio MRI. An anatomical T1-weighted MPRAge with 1mm isotropic resolution was acquired. For fMRI, NHPs were injected with Ferumoxytol (10mg/kg) to improve SNR. An EPI sequence (TE/TR = 22/3000ms, 1.3mm isotropic resolution) was acquired during drug administration. NHP received an i.v. solution of psilocybin (N=7: 30µg/kg [N=2]; 60µg/kg [N=3]; 90µg/kg [N=2]) mid-scan. Preprocessed included slice-timing correction, motion-correction, brain extraction, template registration, bias-field correction, 4mm spatial smoothing, segmenting 15-min of resting state pre, post-drug data, grand-mean scaling, band-pass filtering, linear/quadratic trend removal, nuisance regression of motion, CSF and white matter. For human analysis, 15 human fMRI datasets with full pre-processing from OpenNeuro® from a study by Carhart-Harris et al. These data were under conditions (i.v.) of placebo and 75µg LSD. Independent Component Analysis (ICA) derived seeds were used instead of a-priori selected seeds to reduce user biases in the analysis. FSL's MELODIE was used for ICA. Seed selection and analysis was performed via: (1) Assuming 25 ICs for initial ICA model fitting; (2) Extracting non-noisy ICs from the initial 25 ICs; (3) Of those selected, identifying ICs with similar spatial distribution across species (Figure 1) as seeds. Voxel-wise Pearson's correlation coefficients were calculated and converted to Z-scores. Statistical analysis was a paired t-test of psychedelic vs non-psychedelic states and thresholded at Z>2.3 with cluster-corrected at p<0.05.

Results: Five IC networks across humans and NHP (Figure 1) with similar spatial distributions were identified for seed-based analysis. Figure 2 shows FC differences between non-psychedelic and psychedelic states in both species. Potential overlapping similarities in both NHP and human FC-MRI results are: 1) reduced FC within portions of the auditory network; 2) increased striatal FC to thalamic/hypothalamic areas; 3) reduced FC from sensorimotor areas to occipital, temporal cortices.
Human data, in general, had more widespread FC changes globally across the brain, in contrast to NHP, which were isolated to the areas indicated in Figure 2.

Conclusions: This work evaluated FC changes by psychedelics in awake humans (LSD) and anesthetized NHPs (psilocybin). Trends may support the use of anesthetized NHPs as a model for evaluating psychedelic drug states. Common characteristics across species were underscored by auditory, sensory, striatal/thalamic, and occipital cortical domains. Psychedelic mediation of cortical-striatal-thalamic circuits was also reported in a work on humans with LSD, which our findings provide support in a NHP model. Additional significance in humans may be due to larger sample size and/or use of anesthesia in NHPs. Consistency of human results with the original work by Carhart-Harris et al. is evident. Future analyses will incorporate comparisons to human data with psilocybin. We also plan to conduct FC-MRI studies on LSD in NHPs, in addition to larger NHP sample sizes.

Poster No 2018

Childhood Adversity Predicts Striatal Functional Connectivity Gradient Changes After Acute Stress

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Introduction: Childhood adversity leads to several maladaptive behavioral and brain changes. One psychopathological consequence of childhood adversity is its impact on individuals' reactivity to acute stress later in life. People with a history of childhood adversity have diminished cardiac and cortisol responses to stress, and this maladaptive change was shown in depression and other psychiatric disorders. Recent models suggest that the motivational dysregulation may contribute to this blunted stress response (Carroll et al., 2017), which identified the role of striatal network in stress coping behaviors of people with childhood adversity. However, we need more direct evidence on how the striatal connectivity varies under...
the joint impact of acute stress and childhood adversity, and methods focusing on whole brain connectivity can be highly insightful in providing the overview of this interaction. The ‘connectopic mapping’, as an emerging connectivity analysis method, could serve as an ideal tool. This data-driven method was designed to detect several topographic modes (gradients) within the region-of-interest in relation to other regions of the brain (Haak, Marquand, & Beckmann, 2018). Previous studies showed striatal gradients could be an in-vivo readout of the functionality of motivation processing (Marquand, Haak & Beckmann, 2017). Here, we utilized connectopic gradients in the dataset of the ‘Measuring Integrated Novel Dimensions in Neurodevelopmental and Stress-related Mental Disorders’ study (MIND-Set; van Eijndhoven et al., 2022), to examine if the striatal connectivity gradients change depending on childhood adversity experience, and how acute stress interacts with this pattern.

**Methods:** In the sample combining 150 psychiatric patients and 26 controls of MIND-Set, we utilized ‘connectopic gradients’ to capture the functional topographic organizations of striatal connectivity during resting-state scans before and after watching an aversive movie clip (acute stress induction). We focused on the first-order gradient which was previously proven to be associated with goal-directed and motivation behaviors. The trend surface coefficients of connectivity gradients were then linked to the index of childhood adversity (overall index and three subscale scores) by Spearman correlation (p < .05, FDR corrected). Linear mixed models and moderation models were built to clarify the role of symptom strengths in these correlations.

**Results:** Participants with different childhood adversity history didn’t show significant diverse gradients at the pre-stress resting states, as the connectopic maps could not be predicted by any types of CA (ps > 0.10). After the stress-induction, this gradient map was related to one type of adversity: the emotional neglect (r = -0.190, p = 0.042). Emotional neglect frequency also negatively predicted the stress reactive change in this connectivity mode (left: r = -0.210, p = 0.033; right: r = -0.230, p = 0.014). By visualizing the gradient maps, we found the first-order gradients of frequently neglected people tend to show a clearer gradual transition from pre-stress rs to post-induction rs. Linear mixed models and moderation models showed the observed correlations between emotional neglect and striatal gradients only existed in individuals with elevated comorbidity.
Conclusions: People who experienced frequent emotional neglect displayed distinct stress-induced alterations in the motivation-related connectivity modes. The anterior-posterior organization of striatal gradients could be a new biomarker for the symptomatology of people with frequent neglected history, by tracking stress-related brain changes in the general motivation and high-order cognition systems.

References

Poster No 2019
Core time – The rich club’s role in shaping the intrinsic cortical timescales
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Introduction: Different brain areas express different intrinsic timescales that are crucial to process stimuli on various levels of temporal persistency. The reason for the association of brain regions and specific intrinsic timescales is still unknown. Previous studies suggested that the timescales follow a gradient from unimodal to multimodal fields or from sparsely to strongly connected network nodes. However, another prominent organization has not been investigated yet: At the network level, the rich club (RC) architecture has been identified to synchronize the connectome through its slow intrinsic timescale, thus influencing the temporal layout of the cortex. This study investigates the RC’s role in shaping the timescales in direct comparison to other organizational schemes and gradients.

Methods: We collected resting state functional magnetic resonance imaging (rs-fMRI) and diffusion weighted imaging (DWI) data of 46 healthy right-handed participants (32 female, age = 21.76 ± 2.75 years). Rs-fMRI was recorded with a 3T Siemens MAGNETOM Prisma MR scanner (TR/TE = 1000/34 ms, FA = 57°, FOV = 210 x 210 mm², 66 slices, slice thickness = 2.2 mm, acceleration factor = 6). DWI data (TR/TE = 7300/90 ms, initial rotation = -90°, FOV = 320 x 320 mm², 56 slices, slice thickness = 2.5 mm, acceleration factor = 2) was collected in the same session. Functional preprocessing included the removal of the first five volumes, slice-timing and motion correction. After registering the individual functional and structural datasets we performed a nuisance regression. Intrinsic cortical timescales were calculated using a model-free approach. Next, we defined the different organizational schemes of interest: (1) The RC identification followed our previous methods. (2) We also tested the diverse club (DC) as an alternative to the RC. (3) For investigating of the anterior-posterior gradient we used the stereotactic coordinates of each area. (4) We extracted the following structural graph measures: nodal degree, betweenness centrality, closeness centrality, participation coefficient, and within-module degree z-score as well as (5) the surface area and gray matter thickness for each area of each participant.

Results: Using likelihood ratio tests, the comparisons to a null model revealed that the RC classification, χ²(2, N = 9495) = 59.07, p < .001, V = 0.06, DC classification, χ²(2, N = 9495) = 37.05, p < .001, V = 0.04, coordinates, χ²(3, N = 9495) = 193.89, p < .001, V = 0.08, structural graph measures, χ²(5, N = 9495) = 63.72, p < .001, V = 0.04, and surface area and gray matter thickness, χ²(2, N = 9495) = 192.63, p < .001, V = 0.10, significantly explained variance of the intrinsic cortical timescales. Furthermore, adding the RC classification to the other individual models significantly explained additional variance beyond the DC classification, χ²(2, N = 9495) = 32.06, p < .001, V = 0.04, coordinates, χ²(2, N = 9495) = 6.65, p = .036, V = 0.02, graph measures, χ²(2, N = 9495) = 45.69, p < .001, V = 0.05, and surface area and gray matter thickness, χ²(2, N = 9495) = 41.98, p < .001, V = 0.05. Multicollinearity checks revealed no significant dependence between the organizational schemes, all VIF < 10.
Conclusions: The results demonstrate that the differences in intrinsic cortical timescales can be explained by the membership of areas to the RC and DC, the position of the area in the cortex, the variation in different graph-theoretical measures and the surface area and gray matter thickness of the respective area. Focusing on the RC, we found that this classification explains additional variance beyond the other organizational schemes, which reiterates the importance of the RC organization for the temporal layout of the cortex.

References

Poster No 2020
Altered structural connectivity and functional brain dynamics in individuals with heavy alcohol use
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Introduction: Alcohol use disorder (AUD) is a long-term and recurring neurological condition that can continue unabated despite significant adverse effects on the person, their family, and community. In 2021, over 11% of adults in the United States had AUD. Despite this impact and prevalence, the root neurobiological causes of AUD remain unidentified, and there
ABSTRACTS

are limited effective treatment methods available. Significantly, it’s been observed that only a fraction of individuals who regularly consume alcohol eventually develop AUD. This emphasizes the urgent need to uncover biological elements that predispose a person to develop AUD, and to improve treatment paradigms. Neuroimaging studies provide evidence pointing toward neurobiological mechanisms of AUD, which likely involve differences in receptor concentration/function, brain activity patterns, and anatomy (gray and white matter) (Kuceyeski 2013). However, a unifying computational model integrating multimodal observations into a single framework has not been proposed, hampering our ability to understand the neurobiological mechanisms of AUD.

**Methods:** We used publicly available high resolution, preprocessed MRI data from the Human Connectome Project – Young Adult S1200 (van Essen 2013) in this study. Regional time-series and structural connectomes (via deterministic tractography) for HCP subjects (N = 130 AUD; N = 308 control; see Figure 1 caption for details) were extracted using the 268-region Shen atlas. Brain-states were defined via k-means clustering and network control theory (NCT)-based transition energy (TE) between every pair of brain states was calculated as described previously (Singleton 2022; Cornblath 2020). TE is the minimum energy input into a network here, the structural connectome-required to move from one brain activity state to another (Gu 2015). We calculated average TE as the average amount of energy required to transition between all four brain-states. We also counted the number of state transitions in each scan from the k-means partition of fMRI volumes. Meta-state complexity (MSC; the Lempel-Ziv compressibility of the brain-state time-series) was used to measure the information content of fMRI scans (Singleton 2022). Average TE, state-transitions, and MSC were compared across groups via ANOVA with covariates for age, sex, mean framewise displacement, and age:sex interaction. A dopamine depletion simulation was performed on a PET-derived D2 receptor (D2R) map wherein average TE for control subjects was compared using the true D2R map versus a ‘depleted’ D2R map using two-sided, paired t-tests. P-values were corrected for multiple comparisons via False Discovery Rate.

**Results:** Individuals with AUD have higher average TE and lower MSC as well as a lower number of state transitions compared to those without. On an individual level, TE is inversely correlated with both MSC and state transitions. Finally, we present an in silico evaluation linking decreases in D2 receptor levels with increases in transition energy in the brain.

**Conclusions:** The brain activity of individuals with AUD reflects a less dynamic system with less complexity and higher energetic barriers compared to individuals without and SUD. More broadly, this work demonstrates that whole-brain, multimodal imaging information can be combined under a network control framework to identify and evaluate neurobiological correlates and mechanisms of AUD.
References
Predicting connectome-wise reorganization during movie watching

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Introduction: Our recent innovation, connectome-to-connectome (C2C) state transformation modeling, can predict how an individual's functional connectome reconfigures to meet different cognitive contexts, such as behavioral tasks involving memory, emotion, and attention, solely using resting-state fMRI data1,2. In this study, we expand the untapped potential of this versatile modeling framework to predict how the connectome subtly reorganizes in response to different visual scenes within the same movie, despite their similar and neutral cognitive content.

Methods: We used the rest and movie-watching fMRI dataset (n=92) originally collected in Yoo et al.1. We excluded 15 individuals with only single session data (out of two visits) or less than 30 TR volumes for any of the six movie segments after censoring, resulting in a final set of n=77 for analysis. Image acquisition, (pre)processing, and experimental design are described in Yoo et al.1. In this study, we adapted the C2C transformation framework1,2 to construct models predicting an individual's connectome-wise reorganization from resting state to movie-watching states induced by separable visual scenes while viewing the abstract video, “Inscape.” The C2C transformation involves a three-step process: 1) extraction of subsystems from the resting-state whole-brain connectome, 2) transformation of these extracted subsystems to the movie-watching states, and 3) construction of whole-brain connectomes for the movie-watching states based on the transformed subsystems. “Inscape” can be divided into six segments with distinct visual scenes3, and we constructed and validated six C2C transformation models using an 11-fold cross-validation (CV) approach (70 training and 7 testing samples) iterated 100 times. Details of the C2C modeling framework can be found in the previous publications1,2. We evaluated the models' connectome prediction in two ways. First, we assessed the specificity for movie segments. For each testing sample, we performed a paired t-test to compare spatial similarities between predicted and observed connectomes and used fingerprinting analysis4 to estimate the identification rate of an individual's predicted connectome across the six movie segments. Second, we assessed whether connectome prediction preserves individual uniqueness. For each movie segment, we calculated the identification rate of an individual's predicted connectome across the seven testing samples.

Results: The observed connectomes were most similar to the predicted connectomes of the corresponding segment (paired t-test p<0.001) for all but one segment. The identification rate averaged across participants, CV folds, and iterations was 36.5% which significantly exceeds the chance level of 16.7% (p<0.001). In individual fingerprinting, the identification rate averaged across movie segments, CV folds, and iterations was 59.4% which significantly surpasses the chance level of 14.3% (p<0.001).

Conclusions: Our study represents the successful application of the C2C transformation framework to predict whole-brain connectome-wise subtle reorganization in response to distinct visual themes within the same (or at least similar) cognitive context. The success of our model predictions suggests that even simple linear models can capture distinct connectome-wise reorganizations in response to visually similar stimuli, paving the way for deeper investigations into the dynamics of cognitive states.

References

Contribution of slow, brain-wide patterns of activity to on-going experience in resting-state fMRI

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**ABSTRACTS**

**Introduction:** Prior work has shown that subjective experience during scanning can influence such metrics as functional connectivity (FC) and regional homogeneity\(^1\)-\(^3\) of resting-state fMRI (rs-fMRI). Also, recent work shows that approx. 30% of the variance in rs-fMRI is accounted for by three low frequency spatiotemporal activity patterns found using complex principal component analysis (cPCA)\(^4\). It remains unknown how these patterns relate to rs-fMRI on-going experience. To address this question, we use rs-fMRI scans\(^5\) annotated with subject’s reports of the content and form of their thoughts, and wakefulness levels. We use connectome predictive modeling (CPM)\(^7\) to assess how much these aspects of experience are reflected in the rs-fMRI data before and after regression of cPCA patterns.

**Methods:** Dataset: 471 rs-fMRI scans (15 mins, TR=1.4s, voxel=2.3x2.3x2.3mm\(^3\)) from the MPI-Leipzig Mind-Brain-Body dataset\(^6\). Experience Data: At the end of each scan, subjects completed the Short New York Cognition Questionnaire (sNYCQ; Fig. 1.A). sNYCQ responses shown in Fig. 1.B. The content and form responses were input into a Sparse Box-constrained Non-negative Matrix Factorization algorithm to extract linear positive combinations of questionnaire items that jointly explain variance, resulting in two summary factors that we refer to as “Thought Patterns” (TPs) (Fig. 1.C). Basic fMRI Pipeline: Discard 5 TRs, motion correction, distortion correction, registration to MNI, scaling (divide by the mean), nuisance regression (motion + 1st derivative, linear & quadratic trends, COMPCOR\(^8\) regressors), and filtering (0.01 - 0.1Hz). (Fig. 1.D-green). cPCA Pipeline: We extracted the first three cPCA patterns using 50 randomly selected scans and procedures described in Bolt et al.\(^4\) Next, we generated voxel-wise, scan-specific regressors for these patterns as in Abbas et al.\(^5\) Finally, regressors were used as additional nuisance factors (Fig. 1.D-red). FC Matrices: Constructed using the 400 ROI/7 Networks Schaefer Atlas\(^9\) extended with 8 subcortical regions from the AAL atlas\(^10\). FC matrices computed for both pipelines. CPM: We used TPs 1 & 2 and Wakefulness as prediction targets. We first attempted prediction using FC matrices from the basic pipeline. Prediction accuracy was evaluated as the correlation between observed and predicted values. As CPM is non-deterministic, we attempt prediction 100 times per target. We assess statistical significance by comparing to a null distribution generated using 10,000 randomizations. Next, we attempted prediction using FC matrices from the cPCA regression pipeline. Significant differences across pipelines evaluated via paired T-tests.

**Results:** Fig. 2.A-C show our cPCA patterns, which account for 12.3% of variance: cPC1 shows an alternating activation/deactivation of sensory regions (Fig. 2.A), cPC2 alternating activation/deactivation of the DMN (Fig. 2.B), and cPC3 alternating activation/deactivation of attention and control networks (Fig. 2.C). Fig. 2.D shows average FC across scans for basic pipeline and Fig. 2.E for the cPCA regression pipeline. Fig 2.F shows differences across pipelines [66796 edges (93%) significantly different at pFDR<0.05]. We can predict TPs 1, 2 and Wakefulness significantly above chance using the basic pipeline (Fig. 2.G). After cPCA regression, predictability of TP 1 and Wakefulness significantly improved (p<0.05), while predictability for TP 2 remained unchanged (Fig. 2.H).

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**Figure 1.** (A) Questions from the sNYCQ which was completed by the participants at the end of each scan. Participants responded on a 1-100 scale, about how well the statement described their thoughts and experience during the scan. (B) The responses to (A), with wakefulness separated on the left. The right side (all but wakefulness) were passed into the matrix factorization algorithm that generated the two TPs. (C) The relationship between questionnaire items and TPs. (D) Outline of the methods used in this project. The two different pipelines are highlighted in green (Basic Pipeline) and red (cPCA Regression Pipeline).
Conclusions: We found cPCA patterns similar to those in Bolt et al.⁴ although they differ in ordering and variance explained; likely due to disparities in applied smoothing (none here vs. 5mm in Bolt et al.⁴). Regressing cPCA patterns significantly altered FC across the brain, in agreement with similar analyses for quasi-periodic patterns⁵. Yet, cPCA regression had marginal or no effect on predictability of rs-fMRI on-going experience; suggesting that these activity patterns are not directly linked to rs-fMRI cognition.

References

Poster No 2023
Feasibility of Localizing Epileptogenic Tissue with Naturalistic Stimulation in fMRI
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Introduction: One in 300 people suffers from medication-resistant epilepsy, a condition with profound cognitive and socio-economic consequences¹. Surgery can be an effective treatment, hinges on accurate identification of lesions responsible for seizure generation. This can involve invasive electrode implantation, which is expensive and carries risk. When people undergo fMRI while watching an engaging movie, synchronized blood oxygen level-dependent (BOLD) signal is observed
broadly across the cortex, quantifiable via inter-subject correlation (ISC). This common neural synchronization may afford sensitivity to abnormality in people with epilepsy, offering safe and cost-effective localization. Specifically, epileptogenic tissue may show asynchronous BOLD patterns compared to controls. We provide proof-of-concept by demonstrating that people with epilepsy exhibit abnormalities of regional synchronization relative to controls.

Methods: Structural and functional MRI data were acquired using a 3 Tesla SIEMENS Prisma with a 32-channel head coil. T1-weighted MPR sequences had a slice thickness of 0.8 mm and 192 slices. fMRI acquisition used multi-band, accelerated EPI, acquisition (TR=1250 ms, slice thickness=2.5 mm, and 60 slices). In 47 participants, 384 volumes were acquired during an 8-minute film (‘Bang! You’re Dead’, 1961). After excluding 10 datasets due to hearing loss, stimulus issues or missing data, 19 focal epilepsy patients under evaluation for surgery (20-60 years, 9 females) and 18 controls (19-58 years) remained in the study. Preprocessing was conducted using fMRIPrep (v. 20.2.6) and FreeSurfer (v. 7.2), followed by confound removal, mapping to the fsLR 32k surface, and parcellation utilizing the multimodal Glasser atlas. The subset of regions of interest (ROIs) that exhibit significant ISC within healthy subjects, and thus sensitivity to abnormality, were identified using a non-parametric test. ISCs were calculated for each ROI using a leave-one-out method, averaged across subjects (Fig.1A). To define a null distribution for absence of synchrony, subjects’ time series were randomly circularly shifted 1000 times before leave-one-out averaging (Fig.1A). Original ISCs were compared against null, with false discovery rate (FDR) correction at q<0.01 for all ROIs. We identified regions with weaker BOLD synchrony in patients compared to within controls by subtracting patient-to-control ISC from within-control ISC. The within-control ISCs were calculated as explained, while patient-to-control ISCs were determined as the average over correlations of patients with the control group's average (Fig.1B). Statistical validation used a randomization test, comprising 10000 iterations with randomized subject labels for half of the controls and patients in null groups, thereby generating a null distribution for difference of within-control and patient-to-control ISCs (Fig.1B). FDR correction was applied at q<0.05 over ROIs with significant within-control ISC.

Results: Significant synchrony was noted in early auditory and visual ROIs among control subjects during the movie-watching paradigm, extending to certain parietal and frontal ROIs. This indicates the method’s broad coverage. Elevated within-control ISC in early sensory ROIs, compared to other regions with significant ISC, validated the synchrony induced by the paradigm (Fig.2A). Importantly, ROIs L_FOP2, R_STSva, R_A1, R_MBelt, R_LBe, R_A4, R_TA2, R_PHA3 in left inferior frontal and right temporal lobe showed significantly higher ISC within controls compared to patient-to-control comparisons, despite the variability in patients’ epileptogenic regions (Fig.2B).
Conclusions: Our results suggest ISC analysis of naturalistic fMRI could identify abnormality in epileptic patients, although patient heterogeneity calls for individualized and vertex-level analysis. However, patient specific presumed seizure localization and surgical outcomes were not available, limiting us to a broader population analysis.

References

Poster No 2024

Motion regression induces global signal related bias in functional connectivity estimates
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Introduction: Regressing out motion parameters estimated from volume registration is a common step in the preprocessing of resting-state fMRI (rsfMRI) data. A prior study has shown that rsfMRI motion parameters can exhibit BOLD-weighted bias associated with the resting-state global activity of the brain, as characterized by the global signal (GS). In this work, we demonstrate that regression with biased motion estimates can negatively bias resting-state functional connectivity (rsFC) estimates and reduce rsFC differences between young and old subjects.

Methods: We used an open source multi-echo fMRI dataset², consisting of two rsfMRI scans per subject from a sample of 181 younger and 120 older adults. Motion parameters (3 translation, 3 rotation) were separately estimated for the 1st and 2nd echo
data (denoted as e1 and e2 with TE = 14 and 30 ms, respectively) using AFNI 3dvolreg. The GS was computed from the percent change e2 data as the average signal over brain voxels. rsFC estimates were computed with correlation analysis after motion censoring (framewise displacement FD > 0.2 mm) and regression with either the e1 or e2 motion parameters. We used 7 ROIs, including 4 ROIs in the default mode network (DMN) and 3 ROIs in the task positive network (TPN). The primary metric of interest was the difference \( \Delta r = \Delta r_{e2} - \Delta r_{e1} \) between the rsFC estimates obtained by regressing out either the e1 or e2 motion parameters. Because of the greater GS-related bias in the e2 motion parameters, the difference \( \Delta r \) reflects the effect of this bias on the rsFC estimates. The corresponding differences \( \Delta z \) in z-scores were also computed. Runs were sorted into one of four groups (low/high motion; low/high GS amplitude) where the respective median values were used to define the boundary between low and high groups, and \( \Delta r \) and \( \Delta z \) were examined within each group. In addition, we looked at the differences in GS amplitude and rsFC estimates between the younger and older subject groups.

Results: Figure 1 shows that there is a negative bias (\( \Delta r < 0 \) in upper triangle; \( \Delta z < 0 \) in lower triangle) in the rsFC estimates between all pairs of ROIs for each of the four groups, with the most negative values observed in the low motion and high GS amplitude (aGS) group. This finding indicates that regression using e2 motion parameters containing GS-related bias can introduce a negative bias in the rsFC estimates, with the magnitude of this bias increasing with higher rsfMRI global activity. Figure 2(a-c) shows the differences in aGS, FD, and \( \Delta z (e2-e1) \) between young and old subjects. The young subjects show significantly higher aGS and lower FD than the older subjects and exhibit more negative \( \Delta z \) values, consistent with the trends observed in Figure 1. Figure 2(d,e) shows the age-related rsFC differences (young-old) as \( \Delta z \) (upper triangle) and effect size \( d \) (lower triangle) when regression is performed with either e1 motion parameters with minimal BOLD bias (panel d) or GS-biased e2 motion parameters (panel e). With e1 motion regression, the young subjects showed significantly higher rsFC for all but one ROI pair. Regression with e2 motion parameters reduced the rsFC difference across all ROI pairs, with 5 ROI pairs no longer exhibiting significant differences.

Conclusions: Because motion parameters estimated from rsfMRI data acquired at typical echo times (e.g. 30 ms) can exhibit GS-related bias, regression with these parameters will tend to reduce rsFC values, similar to the effect seen with global signal regression. This negative rsFC bias will tend to be greater in groups with higher GS amplitudes, and can thus alter group differences in rsFC between groups that have different mean GS amplitudes. Thus caution must be used when interpreting rsFC differences obtained when using motion regression as part of the preprocessing pipeline.
Drowsiness increases slow oscillations in rs-fMRI signal before sleep onset

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Introduction: Sleep can significantly affect the functional MRI (fMRI) signal as reported in previous studies where subjects were allowed to fall asleep during the examination (Fukunaga et al., 2006, Duyn 2019). Fluctuation in the MRI signal has been associated with the increase in functional connectivity observed during light slow wave sleep (Tagliazucchi et al., 2014). Nevertheless, a major concern arises regarding the limited understanding of the evolution of fMRI signals as a function of drowsiness, when subjects are instructed to remain awake, as typically prescribed in standard resting-state exploration (rs-fMRI). This knowledge gap primarily results from the challenge of quantifying such vigilance-related events during fMRI, as they mostly occur within the complex period of wakefulness-to-sleep transition (Ogilvie, 2001). In this study, we used the percentage of eye closure (PERCLOS index (Wierwille et al., 1994)) as a proxy of drowsiness to explore its effect on the evolution of the rs-fMRI signal.

Methods: A 45 min T2* gradient echo sequence (MRI GE 3T SIGNA Premier, TR = 1 s, TE = 30 ms, flip angle = 62°, 2700 volumes) was performed in 50 healthy subjects (26 Females, 24 Males, age = 23.3 ± 4.45) with instructions not to move, not to do constructed mental tasks and to keep their eyes open without sleeping. Subjects were asked to sleep for only 5 hours the night before and all examinations were carried out at 1 p.m. Drowsiness was assessed using video from the MRI surveillance camera allowing to automatically compute an eye closure degree called Eye Aspect Ratio (EAR). Afterwards, PERCLOS index was calculated based on proportion of the time spent with eyes closed for at least 80% of their size in a 60s window. The drowsiness state was identified according to the following thresholds of the index (awake: [0.0, 0.08]; probably drowsy: [0.08, 0.15]; drowsy: [0.15, 1]; sleep: eyes closed > 5s). Lastly, all signals were resampled to MRI’s sampling rate (1s). MRI signals were...
preprocessed using fMRIPrep 20.2.6 with each brain region being extracted through python’s nilearn library 0.10.1, using AAL3 v1mm atlas. We considered the subject’s specific mask and filtered out confounds computed in the preprocessing stage (low frequency drift and motion parameters). Signals were analyzed in a time-frequency manner using a Taper spectrogram (window length: 60s, window step: 1s, time half-bandwidth: 2.5, number of tapers: 4). Each column of spectrogram was classified using our drowsiness scale then grouped by state. Afterwards, mean amplitude by frequency band was calculated and finally projected on an inflated surface of the left hemisphere of the brain.

Results: Figure 2 shows the evolution of the power spectral density of the rs-fMRI signal as a function of the drowsiness states. We can observe that the amplitude of slow oscillations, particularly in the [0.047-0.063] Hz band, increases overall at the first sign of drowsiness. This increase clearly predominates within primary cortices (motor, somesthetic, visual and auditory), as demonstrated by a drowsiness effect in the generalized linear models computed in each 165 brain regions and corrected for Bonferroni multiple comparisons test (Wald’s χ² ranging from 21.96 to 334.1). Conversely, the deep gray structures, notably the thalamus, did not undergo the same changes.

Conclusions: This study is the first attempt in exploring rs-fMRI signals while subjects struggle against sleep by considering 4 drowsiness states. The increase in slow oscillations observed, which may underlie an increase in functional connectivity and which predominate in the primary cortices, is paradoxical given the progressive isolation of the cortex induced by the thalamus during the descent into sleep and requires further investigation.

References
Classification of Vigilance Level Based on Sympathetic Biomarkers: An fMRI-Pupillometry Study

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Introduction: Our aim is to leverage pupil size, a marker of sympathetic activity, within a resting-state fMRI dataset, utilizing it as a proxy to classify subjects into two distinct subsets: those exhibiting high arousal and those with low arousal levels. Furthermore, we intend to support this classification by identifying and correlating observed sympathetic patterns within the data, thus shedding light on the relationship between autonomic nervous system, cerebrospinal fluid (CSF) flow and cognitive states.

Methods: In our study, we utilized the “Yale Resting State fMRI/Pupillometry: Arousal Study” dataset (Lee et. al., 2022), comprising 27 subjects with an average age of 26.52 years, including 16 females and 11 males, of which 25 were right-handed. T1-weighted anatomical images were acquired using a magnetization prepared rapid gradient echo (MPRAGE) pulse sequence with the following parameters: repetition time (TR) = 2,400 ms, echo time (TE) = 1.22 ms, flip angle = 8°, slice thickness = 1 mm, in-plane resolution = 1 x 1 mm, matrix size = 256 x 256, field-of view (FOV) = 256 mm, 208 contiguous slices acquired in the sagittal plane. Functional T2*-weighted BOLD images were acquired using a multiband gradient echo-planar imaging (EPI) pulse sequence (TR = 1000 ms, TE = 30 ms, flip angle = 55°, multiband acceleration factor = 5, slice thickness = 2 mm, in-plane resolution = 2 x 2 mm², matrix size= 100 x 100, FOV = 220 mm, 75 contiguous slices acquired in the axial-oblique planes parallel to AC-PC line). Correlation maps were generated by calculating the cross-correlation between each voxel within the brain and; i)z-scored pupil size, ii)CSF signal from the 4th ventricle, and iii) whole brain average signal, across lags of +/- 10 TR. We also utilized group level ICA for identifying network patterns in two arousal groups.

Results: The z-scored pupil size served as a proxy for arousal (Pais-Roldan et. al., 2020), facilitating the classification of subjects into two distinct arousal groups. A positive z-score denotes values above the average. The number of occurrences of positive and negative z-scored pupil sizes was then tallied for each subject. Subjects exhibiting an overall higher number of positive z-scores were categorized as ‘high arousal,’ and conversely, those with a prevalence of negative z-scores were designated as ‘low arousal’ subjects. The high arousal group consisted of 17 subjects, while the low arousal group included 10 subjects. In our findings, we discovered a distinguished negative correlation in the ventricular (CSF) area, in contrast to a more positive correlation pattern within the gray matter (Fig. 1). In addition, we observed a negative correlation pattern in the insula region for the high arousal group, a pattern which did not exist for the low arousal group. Within the pupil size & fMRI correlation maps, we noted a more pronounced (negative) correlation between pupil size and the visual area in subjects experiencing high arousal (Fig. 1). Conversely, when examining the whole-brain average correlation, we observed a stronger pattern in the ventricular (CSF) and gray matter regions, which aligns with previous observations during heightened sympathetic activity, such as during light sleep (Ozbay et al., 2018) or deep breaths (Picchioni, Ozbay et al., 2020). Our exploration of ICA has yielded that, within the low arousal group exists a substantial ventricle-GM contrast as evident in component 7 (Fig. 2), emphasizing the pronounced neural differences associated with diminished arousal states. Moreover, in component 12 of the high arousal group, a distinctive negative activation profile emerged within the insula region, accompanied by a positive activation in the middle temporal gyrus.
Conclusions: In summary, our study enhances our understanding of the complex relationship between brain dynamics, pupil size, cognitive states, and CSF flow, revealing mechanisms governing arousal levels.

References

Poster No 2027
Abnormal functional connectivity of the reward network in autism spectrum disorder

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Introduction: Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder with social communication impairments as a core symptom (Sarmiento 2020). The social motivation hypothesis proposes that the social deficits of ASD are related to reward system dysfunction (Clements et al. 2018). Converging evidence indicates that brain abnormalities in ASD involve atypical functional connectivity (FC) (Picci et al. 2016). However, the abnormalities of FC patterns of the reward network in ASD have not been systematically explored yet, and the effects of age, gender and subtype on reward-related FC are largely unknown.

Methods: The reward network was defined as eight regions of interest (ROIs) per hemisphere, including the nucleus accumbens (NAc) (Janouschek et al. 2021), caudate (McNaughton et al. 2023), putamen (Kohls et al. 2018), anterior cingulate cortex (ACC) (Keifer et al. 2021), ventromedial prefrontal cortex (vmPFC) (Müller et al. 2018), orbitofrontal cortex (OFC) (Martins et al. 2021), amygdala (Janouschek et al. 2021), and insula (Gu et al. 2019). We computed both the ROI-wise resting-state FC within the reward network and the seed-based whole-brain voxel-wise FC of each ROI in 298 participants with ASD and 348 typically developing (TD) controls available through the Autism Brain Imaging Data Exchange I dataset. A two-sample t-test was applied to obtain the aberrant FCs and their relationship with clinical symptoms was explored using Pearson's correlation or Spearman's correlation. In addition, Neurosynth Image Decoder was used to generate word clouds verifying the cognitive functions of the aberrant pathways. Furthermore, a three-way multivariate analysis of variance (MANOVA) was conducted to examine the effects of gender, subtype and age on the atypical FCs.

Results: For the within network analysis, the left ACC showed weaker FCs with both the right amygdala and left NAc in ASD compared with TD, which were negatively correlated with the Autism Diagnostic Observation Schedule (ADOS) total scores and Social Responsiveness Scale (SRS) total scores respectively. For the whole-brain analysis, weaker FC (i.e., FC between the left vmPFC and the left calcarine gyrus, and between the right vmPFC and the left precuneus) accompanied by stronger FC (i.e., FC between the left caudate and the right insula) were exhibited in ASD relative to TD, which were positively associated with the SRS motivation scores. Automated decoding of these aberrant FCs further verified their cognitive implications.
are related to social cognition, such as emotion, motivation, sensation, memory, and mentalizing. The three-way MANOVA analysis revealed the main effect of age on the abnormal FC between the left vmPFC and the left calcarine gyrus, main effect of subtype on the abnormal FC between the right vmPFC and the left precuneus, main effect of age and age-by-gender interaction on FC between the left caudate and the right insula.

**Conclusions:** Our findings highlight the crucial role of abnormal FC patterns of the reward network in the core social deficits of ASD, which have the potential to reveal new biomarkers for ASD. The increasing insight into gender, subtype and age-related FC changes in reward circuit may advance the development of more effective interventions.
ABSTRACTS

References

Poster No 2028
Characterizing dynamic brain states in subjects across states of wakefulness
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Introduction: It is widely accepted that brain activity, and therefore brain state, differ between conscious and unconscious (sleeping) conditions; fMRI is used to identify and quantify these changes across space and time. Dynamic analysis methods, such as complex principle component analysis (cPCA) (Bolt et al., 2022) and quasi-periodic pattern (QPP) analysis (Majeed et al., 2011), preserve temporal information, allowing spatiotemporal network detection. There are several QPPs previously detected in BOLD signal, including global signal and patterns linked to arousal. Similar spatiotemporal patterns were found from the BOLD signal using cPCA. Components of the BOLD signal are known to correlate to infraslow neural activity, and recent studies validating this principle have also discovered considerable variations in the delays related to different states, spanning both cortical and sub-cortical areas during sleep stages, from wakefulness to deep sleep (Mitra et al, 2015). The current study utilizes these dynamic methods to detect and analyze how this infraslow activity correlate propagates spatially and temporally in healthy individuals in resting-state versus in active sleep.

Methods: The data was acquired at 3T by Yameng Gu’s group and shared on OpenNeuro (Gu et al., 2023). Of the 31 participants, each had 1 scan session, which consisted of 1 anatomical scan, 2 resting-state scans, and at least 2 sleeping scans, with simultaneous EEG recordings. Functional scans were acquired using an EPI sequence: TR=2100ms, TE=25ms, FOV=240mm, slice thickness=2mm. The raw data were preprocessed using CPAC (Craddock et al., 2013), and Brainnetome parcellations (Fan et al., 2016). The parcellated and processed data was input into a pattern-finding algorithm, similar to that used in Majeed et al, to iteratively detect and converge upon a QPP template. The data was also input into cPCA, introduced by Bolt et al. Correlation values between networks were calculated on a network-level and tested for significance across conditions using a p-value<0.05, and then corrected for multiple comparisons.

Results: The results from the two different dynamic analysis techniques used are shown in figures 1 and 2. The QPP results (fig. 1) yield some expected observations, including clear differences across limbic, visual, and somato-motor networks between resting-state and sleep. Unexpectedly, there were observed differences in VAN phase relative to other networks and the drastic decrease in the subcortical network seen in the sleep group. Figure 2, results from cPCA, is more difficult to parse out differences, showing similar expected variance, probability of components, and overall proportion for both conditions. However, using the simultaneously acquired EEG recordings, the sleeping scans were divided into three subgroups – sleep1 (score<0.5, mostly awake), sleep2 (0.5<score<0.9, likely asleep). Interestingly, the second pattern (PC2) has a higher probability of occurring vs pattern three (PC3) in sleep2 and sleep3 groups, a trend not seen in resting-state nor sleep1.<score

Conclusions: This study utilizes dynamic methods to identify differences in spatiotemporal functional patterns across resting-state and sleep in healthy individuals, including key nodes such as VAN and subcortical structures. Typically, VAN is weakly correlated with DMN and in similar phase; however, during sleep, it appears more anticorrelated and in opposite phase.
Subcortical network also changes phase relative to DMN during sleep, implying these 2 networks are heavily impacted by consciousness. The cPCA results reveal distinct differences across conditions, particularly for PC2, a network linked to arousal and DMN/TPN anticorrelation. PC2 is typically more active during task, not known for high activation in sleep (Hong, et al., 2021), but is more likely to occur than PC3. Further studies are needed on the sleep stage data and its relation to QPP and component proportionality.

**Figure 1.** (a) Depicts 2D heatmaps of (global signal removed) QPP1 linked to arousal for all 7 Yeo’s networks and subcortical areas. (b) Proximal-correlated, single-cycle waveform of QPP1 for all networks for resting-state [left] and sleep [right] conditions. (c) Statistical comparisons of intra-network correlation values at the group-level for both conditions. Statistical significance is denoted with * (p≤0.05). (d) Table of correlation values between DMN and other networks.

**Figure 2.** (a) Relative proportion of each component detected from tPCs by timepoints across all subjects. The three different colors represent the three different principle components detected. (b) Explained variance for each group. (c) Probability of each component occurring. (d) Includes the probability of each component occurring for the sleep score, broken up into those groups (categorized using EEG-informed sleep scores).
ABSTRACTS

References

Poster No 2029
Connectome Gradient Dysfunctions in Non-comorbid Never-treated Patients with Social Anxiety Disorder
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Introduction: Although increasing studies have been conducted to identify discrete functional network abnormalities in social anxiety disorder (SAD), it may be short of robust sensitivity to subtle changes1, and alterations of the continuous spatial patterns of functional connectivity among regions remain unknown. To bridge this gap, a novel gradient-based approach was introduced to characterize the spatial features of inter-regional activity along a continuous spectrum in virtue of a set of low-dimensional gradients2. Nevertheless, there is no study to investigate whether/how the functional connectome gradient is disrupted in SAD. Herein, the current study aimed to adopt this promising method to characterize aberrant patterns of principal connectome gradients in a relatively large homogenous sample of SAD patients and assess their potential clinical relevance.

Methods: 1. Data acquisition Based on the power analysis (Cohen's d = 0.5, α = 0.05, 1-β = 0.8)3, 49 non-comorbid SAD patients (aged 24.6 ± 5.3 years; 19 female) and 53 demography-matched healthy controls (HC) (aged 23.4 ± 3.3 years; 22 female) were recruited to undergo resting-state functional magnetic resonance imaging (rs-fMRI) using a gradient echo-planar imaging sequence on a 3.0-Tesla MR scanner (Siemens Trio, Erlangen, Germany). 2. Connectome gradient mapping Firstly, the preprocessed rs-fMRI images (using a standard pipeline of the toolbox for Data Processing & Analysis of Brain Imaging4) were resampled to 4-mm isotropic resolution, and individual functional connectomes were constructed at the voxel level (18933 voxels)5. Then, the top 10% connections of each voxel were retained and cosine similarity among each pair of voxels was calculated to generate similarity matrix, which was further scaled into a normalized angle matrix to avoid negative values6. Lastly, by applying diffusion map embedding, the similarity matrix was further decomposed into gradient components explaining the variance in the connectivity patterns, which were further aligned across all subjects via iterative Procrustes rotation7. 3. Gradient patterns characterization Considering the greatest explained variance of principal gradient and its close relations to the neuronal microstructure8, we focused on principal gradient. At the global level, three gradient metrics (explanation ratio, range and variation) were respectively compared between SAD and HC using nonparametric permutation tests (10000 iterations) with age, sex and head motion as covariates. At the regional level, voxel-wise gradients were compared using independent-sample t-test after controlling for age, sex and head motion, in which the Gaussian random field theory was performed to control for multiple comparisons with a significance threshold of a voxel-wise P<0.001 and cluster-wise P<0.05.

Results: In general, the principal gradient explained 11.83 ± 2.18% of the total connectome variance, which was organized along a gradual axis from the primary sensorimotor/visual networks (SMN/VN) to the default mode network (DMN; Figure 1). Compared to HC, SAD patients showed global topographic abnormalities including decreased explanation ratio, narrower range and less spatial variation in the principal gradient. Regionally, SAD group demonstrated increased gradient mainly in SMN and VN, and decreased gradients in DMN (Figure 2). Furthermore, some aberrant gradient signatures correlated with symptom severity and illness duration, suggesting pathophysiological relevance.
Figure 1. The first three connectome gradients mapping in the SAD and HC groups. Abbreviations: HC, healthy controls; SAD, social anxiety disorder.

Figure 2. Between-group differences of voxel-wise principal gradient between SAD patients and HC. Abbreviations: HC, healthy controls; SAD, social anxiety disorder.

Conclusions: Our study extended earlier SAD neuroimaging studies by identifying internally clinically-relevant disrupted patterns of principal gradient across functional connectomes in SAD, which may reflect imbalance of hierarchy bottom-up response and top-down regulation in cognitive, emotional and sensory domains. These results provide functional insights into the neurobiological underpinnings of SAD, and may advance the development of objective biomarkers for early diagnosis of SAD.

References
Exploring moment-to-moment brain signal variability before and after pregnancy: preliminary results

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Introduction: Pregnancy represents an important endocrine event and life transition in women that is associated with pronounced structural and functional changes in the brain.1-2 Increased prevalence of psychiatric symptoms during the perinatal period emphasize the importance of understanding the neural underpinnings of this life transition.3 Despite the focus of functional magnetic resonance imaging (fMRI) research on the interpretation of mean blood-oxygen-level-dependent (BOLD) signals, several studies have shown that the within-individual variability of brain responses represents a key component of neural processes.4-6 Research indicates that fMRI signal variability fluctuates over the lifespan, and neural variability has also been linked to both psychiatric symptoms and cognitive performance.6-8 In this study, we aim to examine if becoming a mother is associated with alterations in moment-to-moment variability in resting-state neural response. Here, our objective was to compare the nulliparous control group and women that want to become pregnant for the first time at baseline.

Methods: Herein, 110 women took part in a prospective cohort study, involving longitudinal data of first- (n=40) and second-time mothers (n=30), who were scanned 1) before conception, 2) at an early stage and 3) at a later postpartum stage (see Figure 1). A nulliparous control group (n=40) was scanned twice at a similar time interval as the first-time mothers (i.e., ~12 months). Resting-state fMRI was performed at all sessions. fMRI preprocessing included a manually denoising procedure.9 Briefly, independent component analysis (ICA), was used to separated brain signals into components, and manual decisions were made whether each component were neural activity or not (e.g., movement, noise). The noise components were subsequently regressed out of the signal. The standard deviation of the BOLD signal (SDBOLD) was calculated over the entire time series of a single scan per voxel (see Figure 2), allowing us to investigate whole-brain voxel-wise signal variability. To delve into possible dynamic aspects within the resting-state, the five-minute resting-state scan was also segmented into five one-minute intervals for inter-group comparisons. Case-control comparisons on resting-state SDBOLD data were performed using independent t-tests in Statistical Parametric Mapping (SPM12; implemented in Matlab R2022a). Alpha was set at p < 0.001 (whole-brain uncorrected).

Results: By use of SDBOLD resting-state data at the PRE time point, we compared the nulliparous control group (CTRL) and the group of women wanting to become pregnant (PREG) using two contrasts: 1) CTRL > PREG, 2) PREG < CTRL. No significant clusters are reported. Comparisons of the shorter one-minute segments of the resting-state data also showed no significance. Further analyses of the later time points (i.e., postpartum), to investigate longitudinal changes, in both resting-state and task-based fMRI data are still pending.

Figure 1. Visualization of the data collection time points.

Figure 2. Example of mean-centered fMRI time series within the PRE session for one random voxel of three participants. The calculated standard deviation (SD) is shown for every participant.
Conclusions: The absence of significant differences in both directions indicates that the control group and the pregnancy group do not differ in neural variability during resting-state fMRI. This was expected, given that the two groups at the PRE time point differ only in the current desire to have a child in the pregnancy group. It is known that becoming a mother renders strong changes in neural grey matter structure and neural activity. Therefore, future analyses of this longitudinal dataset may further elucidate whether pregnancy is associated with changes in neural variability. Additionally, previous research suggests that task-based variability may outperform resting-state variability. Including task-based data may therefore also provide insights into whether differences between task-based and resting-state variability are also evident in the context of pregnancy.

References

Poster No 2031
Naturalistic fMRI for Presurgical Language Mapping
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Introduction: Task-based functional MRI (task fMRI) is conventionally used for presurgical language mapping. However, neurological patients may have difficulty performing the language tasks satisfactorily, particularly if they have pre-existing language or other cognitive deficits, which could in turn affect the quality of task fMRI language mapping. To tackle this problem, we adopted naturalistic fMRI using movie clips as stimuli (movie fMRI), based on the hypothesis that movies depicting real-life conversation scenes can more completely engage the language networks supporting everyday communication. We previously demonstrated the feasibility and effectiveness of movie fMRI for mapping language areas in individual healthy subjects, and for presurgical language mapping in individual brain tumor patients. The present work compares different analytic approaches to movie fMRI for language mapping, in relation to task fMRI.

Methods: We reanalyzed data from our initial study in 22 right-handed healthy native English speakers (11 females, mean age=26.3 yrs, range: 19-39 yrs). All subjects underwent movie fMRI with a 7-min excerpt from the film “The Parent Trap”, which included 7 conversation segments interleaved with 6 non-speech scenes. Subjects also underwent language task fMRI consisting of 7 blocks of antonym generation and 7 blocks of letter case categorization, interleaved with fixation intervals. Two main analytical approaches were investigated for movie fMRI: (1) a hypothesis-driven general linear model (GLM) with (a) a regressor of weighted word count derived from the movie subtitles; (b) a regressor of conversation segments derived based on the weighted word count convolved with a hemodynamic response function. (2) A Data-driven group independent component analysis (ICA), with 34 components extracted using the Infomax algorithm, of which one language component was identified based on temporal correlation with the conversation regressor. In addition, an inter-subject correlation (ISC) analysis was performed.
Results: Figure 1a-d shows the movie group results. For GLM with the weighted word count as a linear regressor, one activation cluster was revealed in the left superior temporal sulcus (Fig. 1a), consistent with an area specialized for sub-lexical phonemic processing. For GLM with the conversation regressor, positive activation was seen in multiple putative language areas in the left inferior frontal and bilateral temporoparietal cortex, and there was also negative activation (i.e., greater in non-conversation segments) in visual areas (Fig. 1b). The ICA derived language map (Fig. 1c) was similar to the conversation GLM map (Fig. 1b) but showed no activation in visual areas (Fig. 1d). The ISC map revealed extensive areas of synchronized activation across subjects (Fig. 1d). Within the language network, the strongest cross-subject synchronization was seen in the left posterior middle temporal gyrus (Fig. 2a). The task fMRI map showed extensive activation in the frontal cortex and basal ganglia and limited activation in left posterior middle and inferior temporal cortex (Fig. 1e). Compared to task fMRI, movie fMRI revealed more superior and middle temporal activation and less insulae activation (Fig. 2c-d).

Conclusions: The results demonstrate the efficacy of movie fMRI language mapping. First, different regressors can be used in GLM analyses of movie fMRI to map different aspects of language processing, as exemplified here for phonemic perception (Fig. 1a). Second, data-driven analysis of the movie fMRI data provided more comprehensive mapping of temporal language regions than task fMRI. Third, the data-driven analysis of movie fMRI returned a specific language component, whereas the GLM-derived language map included residual visual activation. Finally, ISC analysis revealed varying levels of cross-subject synchrony during movie watching within the language network, which we will further investigate in future work.
ABSTRACTS

References

Poster No 2032
Comparing methods to analyze functional dynamics in at-rest musicians
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Introduction: A resting state pattern of anti-correlated brain activity between default mode (DMN) and task positive networks (TPN) has been implicated in attentional processing1. This pattern is quasi-periodic, completing a cycle about once in 20 seconds in humans2. We detected quasi-periodic patterns (QPPs) using an algorithm based approach and complex principal components analysis (CPCA), to compare dynamic functional connectivity in a dataset of classical, improvisational, and non-experienced musicians. Based on previous literature, we hypothesized that we would detect differences in dynamic functional connectivity between the DMN and visual network and that these groupwise differences would be robust across two methods. In improv musicians, both methods detected an increase in visual-DMN correlation during the QPP and an unexpected increase in QPP correlation between the amygdala and dorsal attention network (DAN).

Methods: Functional scans were obtained at the Psyche Lab at Northeastern University. 48 subjects were classified by musical training: classical, improvisational, or minimal (MMT). Each group had 16 subjects (n = 4 females, n = 12 males). Groups were matched in age and cognitive and musical ability. For more details see Belden et al., 2020 (3). T1 weighted structural scans and resting state functional scans were obtained on 3T Siemens scanners. T1-weighted sequences were 3D magnetization prepared rapid-acquisition gradient-echo (MPRAGE) with a voxel size of 0.8 x 0.8 x 0.8 mm3 (TR = 2.4 s, TE = 2.09 ms, flip angle = 8°, FOV = 256 mm). Resting state scans were 7.5 minutes with an echo-planar imaging sequence of 947 volumes (TR = 475 ms; TE = 30 ms; flip angle = 90°, 48 slices; FOV = 240 mm; acquisition voxel size = 3 x 3 x 3 mm3). Pre-processing and global signal regression was done with the CPAC pipeline (https://fcp-indi.github.io/) and Brainnetome atlas5. QPPs were detected with an in-house algorithm (8) then plotted as Yeo’s seven networks and one subcortical network to compare network correlations (7). We used CPCA, a dimensionality reduction method that captures the QPP4, to visualize QPPs in brain space with FSLeyes (see Fig. 1). Algorithm-based and CPCA-based waveforms were plotted (Fig. 2).
Results: In the algorithm-based QPP approach, the improv musicians showed positive correlation for visual-DMN ($r = 0.830$) while the classical ($r = -0.214$) and MMT ($r = -0.879$) groups had negative correlations. Using CPCA, the improv group's visual-DMN was also positively correlated ($r = 0.371$), and the classical ($r = -0.549$) and MMT ($r = -0.960$) groups' visual-DMN were negatively correlated. For both methods, the improv group had greater amygdala-DAN correlation ($r = 0.878$, CPCA; $r = 0.369$) than the classical ($r = 0.212$, CPCA $r = -0.275$) and MMT groups ($r = 0.014$, CPCA; $r = -0.502$). While the sign of the correlations was consistent across methods, they differed in their strength. This was expected given that networks were defined differently in each method. For example, for CPCA, the entire DMN was defined as the Posterior Cingulate Cortex while the algorithm-based method used a mask of DMN-associated ROIs.

Conclusions: We used an algorithm and a CPCA-based approach to detect QPPs, and found convergent results with both methods in a resting dataset of musicians. The increased visual-DMN correlation in the improv musicians' QPP aligned with the static functional connectivity analysis of Belden et al., 2020. Also, both methods detected a positive correlation between amygdala-DAN in improv musicians. This shows the sensitivity of QPP analysis to groupwise connectivity differences and supports a potential relationship between visual-DMN activity and creative cognition. Given the link between amygdala functional connectivity and anxiety processing\textsuperscript{6}, the novel finding of increased amygdala-DAN connectivity in improv musicians points to future studies that relate anxiety to creative training.

References

Poster No 2033
Altered resting state EEG microstates dynamics in adolescents with concussion
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Introduction: Concussion or mild traumatic brain injury (mTBI) is an urgent public health concern. Canadian and US data\textsuperscript{1} indicate an annual rate of 1100 reported mTBIs per 100,000 people, 75% of whom are children, youths and young adults\textsuperscript{2}. Children and youths are especially vulnerable: they are disproportionately affected by concussions\textsuperscript{2} and take longer than adults to recover\textsuperscript{4}. Currently, the most significant challenge in concussion management is the lack of objective, clinically-
accepted, brain-based approaches for determining whether an athlete has suffered a concussion. Previous research has demonstrated alterations in resting state following acute concussion\(^5\), however microstate dynamics of EEG\(^6\), has not yet been investigated. Microstate analysis of EEG, allows investigations of brain dynamics with millisecond resolution and reflects synchronized activities of large-scale networks. Our goal is to investigate brain dynamics in a cohort of concussed youth to evaluate the potential of EEG microstates as a brain-based biomarker for concussion identification.

**Methods:** We analyzed eyes closed resting state, 64-channel EEG data from 33 healthy male adolescent athletes (age: 16±1.2 years) and 20 male adolescents diagnosed with sports-related concussions within one week of injury (age: 15±2.1 years). Microstate analysis was conducted using the open-source Python package Pycrostates\(^7\). We employed a modified k-means algorithm to identify six microstates, by their topography (labeled A-F) according to existing literature\(^8\), using data across groups. We computed average duration, occurrence rate, fraction of total time duration and transition probabilities at an individual level. These features were then compared between groups. We used a non-parametric permutation test to assess differences in microstate features between the two groups, applying Bonferroni correction to account for multiple comparisons. To calculate the distribution of transition probabilities, random subgroups comprising 10 participants from each group were generated 10,000 times.

**Results:** We successfully identified six well-established microstates in the data, achieving a global explained variance (GEV) of 79.65% across the entire concatenated dataset. The results revealed significant differences in microstate dynamics between the two groups. Specifically, the average duration of microstates A, B, D, E, and F was significantly lower in the concussed group (p < 0.0001), while the average occurrence rate of microstates A, B, C, E, and F was significantly higher (p < 0.0001). Consequently, the concussed group exhibited more time in microstates A (p = 0.005) and C (p < 0.001) but less in D and E (p < 0.001). Regarding transition probabilities, the control group demonstrated higher stability with greater self-transition probabilities for all microstates (p<0.0001). Intriguingly, when excluding self-transition, the control group showed lower transition probabilities, which underscores the reduced state stability in the concussed group.

**Conclusions:** Extending our group’s previous work using fMRI\(^9\), our current findings highlight that individuals with concussions tend to remain in specific states for extended periods, frequently reverting to states associated with auditory and default mode (DMN) networks (states A and C) with decreased time in networks associated with attention and switching of attention (states D and E). These findings show for the first time, how concussion disrupts the rapid switching among brain networks in resting state. EEG microstate analysis may be an effective, low cost brain based marker for concussion identification as well as providing insights into the underlying neurophysiological mechanisms associated with concussion recovery.

**References**

The effect of cerebrovascular reactivity on functional connectivity in children

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Introduction: Functional connectivity (FC) based on resting-state functional magnetic resonance imaging (rsfMRI) is widely used to study neuronal network formation in typical development and neurodevelopmental conditions7. However, developmental heterogeneity may contribute to inconsistent FC findings in children. FC measures the temporal correlation between the blood oxygen level dependent (BOLD) signal of distinct brain regions. In fMRI, the BOLD signal indirectly measures neuronal activity by detecting changes in oxygenated blood flow, which occur through local blood vessel dilation. In addition to neuronal activity, vascular function can affect local oxygenated blood flow, and thus the regional BOLD signal. Cerebrovascular effects on FC have been identified in adults3, but have yet to be examined in children to understand neuronal and vascular sources of connectivity in development, which has periods of rapid and heterogeneous brain vessel growth4. Cerebrovascular reactivity (CVR), or the capacity for blood vessels to dilate in response to a vasoactive stimulus, is a key indicator of brain vascular function. Previous fMRI studies have utilized the BOLD signal response to a vasodilation challenge, such as increased CO2 inhalation, to measure CVR in adults6. However, this CVR assessment is inaccessible to pediatric populations due to the challenges of respiratory monitoring and administration of air with elevated CO2 to children. To circumvent these challenges, recent studies propose using relative CVR (rCVR) mapping derived solely from resting-state BOLD fMRI signals6,7. With this innovation, CVR analyses can be conducted on standard rsfMRI scans, which facilitates CVR studies in populations with difficulty scanning (e.g. children), increases the utility of rsfMRI databases, and enables parallel analyses of CVR and FC within a single scan. In this study, we leverage this resting-state CVR method and the Human Connectome Project-Development (HCP-D) to evaluate the effect of rCVR on FC in the default mode network (DMN) during middle childhood (9-12 years old). Characterizing cerebrovascular contributions to FC in pediatric populations will improve neuronal interpretations of FC during development and provide novel insight into neurovascular development.

Methods: HCP-D rsfMRI scans from children ages 9-12 years old were corrected for motion and slice-timing, and spatially smoothed (Gaussian kernel full-width-half-max=8mm). Volumes with framewise displacement (FD) greater than 0.2mm were scrubbed. After excluding scans with less than 75% of frames remaining after scrubbing, 83 participants (32 male) were evaluated. To generate CVR maps from rsfMRI, we used voxel-wise general linear models that regress each voxel’s BOLD signal on the frequency filtered (0.02-0.04Hz) global BOLD signal, which reflects natural changes in arterial CO2 during normal breathing8 (Fig1). CVR maps were normalized to global whole-brain CVR to produce rCVR maps. CVR calculation was performed in native fMRI space, then transformed into T1-anatomical and MNI standard space. Before FC analysis, a high-pass frequency filter (0.008Hz) was applied to all voxels to eliminate linear trends in the temporal BOLD signal. FC was calculated as the z-scored Pearson correlation between the BOLD signal of each pair of regions in the DMN, identified by the Harvard-Oxford atlas. FC between each pair of regions was regressed on average rCVR in the two respective regions, age, sex, and mean FD.
Results: There was a positive trend between rCVR and FC (Fig2) of the left angular gyrus (AG) and right AG (p=0.08) and of the left AG and the posterior cingulate (p=0.09). Effects of age, sex, and mean FD were not significant (p>0.1).

Conclusions: In school-aged children, CVR may contribute to within-network FC between DMN regions, especially the left angular gyrus. Future studies will explore the effect of CVR on FC in different networks and at different stages of development, particularly at younger ages.

References
Poster No 2035

Altered functional connectivity in children with depressive tendency and problematic smartphone use

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Introduction: The worldwide trend indicates a gradual decrease in the age at which smartphones are first used. Concurrently, the increasing use of smartphones among children in their developmental stages has brought various potential side effects, such as depression, to the forefront as serious issues. Depression symptoms serve as a key predictor of the risk of smartphone overuse. While many neuroimaging studies predict significant overlap between neurobiological changes caused by depressive tendency and problematic smartphone use, no study has examined them together. In our study, we investigated the common alternations in resting-state functional connectivity (rsFC) associated with problematic smartphone use and depressive tendency in normally developing children.

Methods: Resting-state functional magnetic resonance imaging were scanned from 74 typically developing children (40 boys, 34 girls, mean age: 10.8 ± 0.8, 10–12 years), all of whom completed the problematic smartphone use (i.e., Smartphone Addiction Scale [S-scale], Smartphone Over-dependence Scale [SO-scale], Smart Media Addictive Tendency Scale [SM-scale]), Children’s Depression Inventory 2nd Edition (CDI 2) self-report questionnaires. The institutional boards of the Korea Brain Research Institute granted ethical approval for this study (KBRI-202103-HR-002). Seed-based functional connectivity analyses were performed to examine the association between depressive tendency/problematic smartphone use and rsFC by using the CONN toolbox implemented in MATLAB. Regions where functional/structural alterations have been reported in previous studies related to depression and problematic smartphone use were selected as seeds, including insula, anterior cingulate cortex, lateral prefrontal cortex, posterior cingulate cortex, precuneus, fusiform gyrus, and amygdala. Brain maps are thresholded at P< 0.001 voxel-wise and corrected for multiple comparisons using a cluster-wise threshold of p-FDR corrected < 0.05. Conjunction analysis was performed to establish a common rsFC map for depressive tendency and problematic smartphone use. We also conducted mediation analysis to investigate the specific relationships among three variables: rsFC, depressive tendency, and problematic smartphone use. The mediation model jointly tested the following effects: 1) the effect of the rsFC (X) on the problematic smartphone use (M) (path a, indirect effect); 2) the effect of the M on the depressive tendency (Y) (path b, indirect effect); 3) the effect of the X on Y controlling for M (path c’, direct effect); 4) the effect of the X-Y relationship without considering the M (path c, indirect effect + direct effect). Mediation analysis was performed using Model 4 of PROCESS software in SPSS 21.

Results: First, we confirmed the positive association between problematic smartphone use and depressive tendency. As problematic smartphone use and depression scores increased, enhanced rsFC were common observed between the left insula and the right occipital cortex, including the cuneus and the lateral occipital cortex. Mediation analysis showed that problematic smartphone use mediated the relationship between depressive tendency and rsFC, but the direct effect between rsFC and depressive tendency was not significant (path a = .520, p = .000; path b = .534, p = .000; path c’ = .035, p > .1; path c = .312, p = .009).
Conclusions: We observed shared increases in functional connectivity in the insula-occipital cortex with increasing problematic smartphone use and depression scores, possibly reflecting increased visual processing of salient stimuli. Our mediation analysis showed that increased insula-occipital rsFC was associated with higher scores of depressive tendencies, but crucially, problematic smartphone use mediated this relationship. Taken together, enhanced connectivity between the insula-occipital cortex is strongly associated with smartphone dependence, which in turn can lead to increased depression symptoms.

References

Poster No 2036
Polyneuro cognition scores generalize from large-scale discovery to a trauma-affected smaller sample
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Introduction: Cognitive abilities rely on distributed brain networks, but it remains unclear which network connections support cognitive development at different ages and predict individual differences in children. Recent analyses of large-scale data...
show that the reliable and generalizable estimation of brain-cognition associations requires thousands of individuals (Marek et al., 2022). These sample sizes are hard to obtain in developmental neuroimaging cohorts. Inspired by approaches in genomics, the new framework of polyneuro risk scores (PNRS) leverages large-scale population-based studies to derive brain feature scores for application in smaller samples. This approach can derive such associations out of different brain feature types, including resting-state functional connectivity (RSFC). Interestingly, a recent study using RSFC data in the Adolescent Brain Cognitive Development (ABCD) study established that a weighted sum of network edges explained roughly 21% variance in general cognitive ability and 5% variance in memory (Byington et al., 2023). We tested the generalizability and sensitivity of the PNRS method to the prediction of cognitive abilities in a pediatric sample enriched with cases of childhood maltreatment.

Methods: RSFC data of 111 children aged 6-13 from the Berlin Kids2Health study were successfully preprocessed in harmonization with ABCD. All children completed cognitive testing with a battery of tasks tapping into executive function, memory, verbal comprehension, and IQ. 38 children had experienced maltreatment as assessed through extensive psychiatric assessment. We calculated PNRS for general cognitive ability and for memory based on association strengths (beta weights) obtained from ABCD (discovery sample, N=6507, ages 9-10). Correlation analyses tested the associations of the scores with cognitive outcomes and dimensions of maltreatment.

Results: PNRS for general cognitive ability explained 17% and 16% of variance in verbal and nonverbal IQ scores, respectively, but were not predictive of motor ability or conflict monitoring. This is comparable to prediction levels of these scores in ABCD. PNRS for memory were also significantly but less strongly associated with IQ scores and predicted performance on a working memory task (r = 0.31). PNRS for memory were negatively associated with childhood trauma severity (r = -0.37, p = 0.02), but not chronicity (r = -0.15, p = 0.13) and PNRS for cognitive ability showed similar trends, but the results did not reach significance in this small sample (severity, r = -0.31, p = 0.05; chronicity, r = -0.12, p = 0.21).

Conclusions: We found that PNRS derived from discovery in a population-based study captured brain-wide feature correspondence to cognitive abilities in an independent smaller target sample that differed in age, cultural background, and cognitive testing protocol. These findings support the generalizability of the PNRS method to the robust prediction of cognitive abilities in children for the use in smaller samples. PNRS for memory further captured trauma-associated variation in the multivariate network profile supporting memory functions. These findings lay a basis for further studies aiming to understand individual differences in functional brain organization that can arise in the context of developmental risk factors.

References

Poster No 2037

Neural and vascular resting-state cortical network dynamics
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Introduction: Dynamic resting state fMRI (rsfMRI) is altered in a wide range of otherwise indistinguishable disease states, revealing potential biomarkers of neurological and psychiatric disease (Brier et al., 2012; Grieder, Wang, Dierks, Wahlund, & Jann, 2018). Yet we do not know how this activity varies across spatiotemporal scales and how it relates directly to changes in neural activity. Wide-field optical imaging as a technique allows us to image both neural and hemodynamic activity across dorsal cortex in awake mice to better understand the dynamics of these resting state networks. Here we look at dynamic changes in resting-state cortical activity as measured with a voltage fluorescent sensor that is optimized to capture the subthreshold voltage membrane activity and hemodynamics across dorsal cortex (Akemann et al., 2012). This provides insight into how the dynamics of time-varying neural activity relate to dynamic changes in hemodynamics.

Methods: Awake mice (n = 5) expressing the VSFP-Butterfly 1.2 voltage-based fluorescent sensor in excitatory neurons in all layers of cortex were imaged using our wide-field imaging set-up. From this imaging technique we get voltage and hemodynamic activity per pixel, this data is processed separately through the pipeline (Fig 1). All frames were aligned to the Allen Brain Mouse Atlas (Fig 2, C), a mask of the 2D Allen Atlas was created in MATLAB and applied which set all pixels outside of cortex to zero. Further masking was performed to remove the vasculature and artifacts from the glass coverslip by cropping out the midline and part of anterior and posterior cortex (Fig 2, A) Analysis was done on a group level using the
pipeline displayed (Fig 1). Briefly, data was concatenated and the dimensionality was reduced, using spatial non-negative matrix factorization (NMF). Only spatial maps reflecting cortical activity were selected to reconstruct the original data (Ren & Komiyama, 2021). Data was then embedded into a 2D subspace using t-stochastic neighborhood embedding (t-SNE) creating a continuous embedding space. Segmenting this embedding using the inverse watershed transform resulted in distinct cortical states that can be assigned to each time point in the imaging data.

Figure 1: Preprocessing Pipeline 1) All frames across trials for all animals were concatenated and imaging data was then transformed into a 2D matrix. 2) Temporal NMF was then used to reduce the data to 50 components. 3) Through manual inspection, only spatial maps reflecting neural activity were selected. 4) These maps of weights were then multiplied by the temporal features to reconstruct the data. 5) Reconstructed data was then embedded into a 2D embedding using t-SNE. 6) The embedding space was smoothed with a 2D gausian, sigma = 5. 7) The smoothed embedding was segmented into regions using the inverse watershed transform. 8) Frames in the segmented 2D embedding space were then averaged together generating 9) The different cortical states for that data. All steps were done for the voltage and hemodynamic data separately, creating two final embeddings and two final sets of states.

**Results: A total of 13 cortical states for the voltage activity and 9 cortical states for the hemodynamic activity were identified by segmenting the respective 2D density embeddings for all animals (Fig 2. E and F). We are showing the top 6 states for each of the two signals sorted by percent dwell time (Fig 2., B and D). The obtained cortical states represent symmetrical, activation/deactivation of explicit cortical areas. This includes somatosensory areas closer to the midline, prefrontal cortex, and more lateral auditory/visual sensory areas. We found in both cases one dominant state (state 1) which represented low levels of positive activity across most of dorsal cortex aside from the somatosensory areas close to the midline which were slightly negative. Looking at the transition probabilities for different states for both signals the probability of transitioning to state 1 from any other state was the highest. Additionally, we noticed that the probability of staying within a given state was higher for the hemodynamic signal than for the voltage.**

Figure 2: Cortical States A) Example showing the field of view from dorsal cortex, with the orange box showcasing what areas were included in the analysis. B) The top 6 voltage-derived cortical states, sorted by percent dwell time. C) Schematic of Allen Atlas highlighting cortical areas. D) Same as in B but for hemodynamic activity. E) State transition matrix for all 13 states obtained from the voltage data. F) Same as in E but for the 9 hemodynamic states obtained.
ABSTRACTS

Conclusions: A challenge involved in interpreting time-varying rsfMRI connectivity metrics is that we know little about how the dynamics of neural activity relate to hemodynamics across spatiotemporal scales. We’ve found on average that dynamic changes in resting state cortical voltage activity can be summarized by a total of 13 states while hemodynamic activity is represented by 9 states. All states exhibited bilateral symmetry, a common feature of resting state activity. Observed differences across states were defined by the activation/deactivation of distinct cortical areas. For both signals, one dominant resting state existed with the probability of remaining in the same state being higher for the hemodynamics.

References

Poster No 2038

Explainable Artificial Intelligence to explore dynamic functional connectivity related to subjective

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Introduction: Resting-state brain functional connectivity dynamics can reveal intrinsic brain activity in older adults. Dynamic features are more sensitive than static features in reflecting early changes, and both local and long-range dynamic connectivity relate to cognition. However, interpreting dynamic metrics of rs-fMRI connectivity features is challenging. Explainable artificial intelligence (XAI) (Meacham, Isaac et al. 2019) can clarify dynamic connectivity for a better understanding of underlying changes in subjective and objective cognition.

Methods: This study enrolled 85 healthy individuals over 50 years old with normal cognitive function from the Northeastern Taiwan Community Medicine Research Cohort. The AD8 questionnaire (Galvin, Roe et al. 2005) and MoCA were used to evaluate subjective and structured global cognition, respectively. To be considered normal, the MoCA score needed to be above one standard deviation below age- and education-adjusted mean (Rossetti, Lacritz et al. 2011). The DynamicBC toolbox (Liao, Wu et al. 2014) was used to generate the dynamic metrics of rs-fMRI by a sliding-window approach (Kung, Li et al. 2019). Greene’s brain atlas was used to define 300 regions of interest (ROIs) that were classified into 14 predefined resting-state networks. Local dynamic connectivity of ROIs was measured by the mean dynamic amplitude of low-frequency fluctuation (mdALFF) (Liao, Li et al. 2019). Whole brain-based statistics were applied to test the dynamic functional connectivity (dFC) between ROIs. The dynamic metrics (mean, variance, and coefficient of variation (CV)) of the 300 nodes and 45000 (i.e. 300x300/2) edges were ranked by the Boruta in R software (Kursa and Rudnicki 2010). The recommended features were used in the machine learning models to predict the score of AD8 and MoCA. Three machine learning models were used to test the model performance. They were Multilayer Perceptron (MLP) (Rosenblatt 1958), XGBoost (Chen and Guestrin 2016), and LightGBM (Ke, Meng et al. 2017). Grid search was used for fine-tuning model hyperparameters. During the model training and testing, a five-fold cross-validation technique was utilized. The SHapley Additive exPlanations (SHAP) values of the selected dynamic metrics were yielded from the best-performed model (Lundberg and Lee 2017). The k-mean cluster analysis clustered the SHAP values of selected dynamic metrics features into three groups (Iktotun, Ezugwu et al. 2023). The contribution of dynamic metrics of nodes and edges to subjective and objective cognition is explained by the results of clustering.

Results: XGBoost performed superiorly, and the Boruta recommended features of 18 nodes and 16 edges for predicting the AD8 score and 10 node and 15 edge features for predicting the MoCA score. Further interpreting the k-mean cluster results of the SHAP values, subjective cognition was dependent on left SomatomotorDorsal mdALFF CV and right visual mdALFF variance (Figure 1A), as well as FrontoParietal-DefaultMode dFC CV, FrontoParietal-DefaultMode variance, CinguloOpercular-SomatotorLateral variance, and CinguloOpercular-DefaultMode variance (Figure 1B). The objective cognitive performance relied on mdALFF mean and variance of left CinguloOpercular node, mean of left DefaultMode node, and variance of left medial temporal lobe node (Figure 2A). Objective cognition was also influenced by dFC mean of DefaultMode-CinguloOpercular and CV of DefaultMode-Salience and FrontoParietal-SomatotorDorsal edges (Figure 2B).
**Conclusions:** By utilizing explainable AI techniques in machine learning models, this study has discovered the clinical significance of dynamic metrics of functional connectivity. The networks that are involved in subjective cognitive complaints include visual, motor-sensory, and triple (default-salience-executive) networks. Apart from the medial temporal memory network, the balance of the triple networks is also important for objective cognition.

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Poster No 2039

Investigation of faulty CO2 chemosensing brain regions in epileptic patients with resting-state fMRI

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Introduction: Sudden Unexpected Death in Epilepsy (SUDEP) stands as the most prevalent cause of mortality in patients with epilepsy (PWE), with “3000 deaths/year in the United States alone. While there is currently no therapeutic intervention for SUDEP prevention, PWE with generalized convulsive seizures (GCS) are presumably at higher risk. GCS events induce significant hypoxia and hypercapnia, causing damage to cardiorespiratory control sites.¹³ Therefore, one hypothesis is that the sudden death in PWE may result from a disrupted carbon dioxide (CO2) chemosensing mechanism. Fortunately, it is feasible to identify change in CO2 chemosensitivity using hypercapnic ventilatory responses (HCVR)⁴ that quantifies an increase in ventilation with rising end-tidal CO2. Using blood oxygenation level dependent (BOLD) functional Magnetic Resonance Imaging (fMRI), cerebrovascular reactivity (CVR) can be obtained to assess the vascular response to CO2 changes in cardiorespiratory control nuclei in the epileptic brainstem.⁵ However this method may not be reliable due to physical discomfort of the CO2 inhalation for subjects. Resting-state fMRI (rs-fMRI) can be an alternative option to yield CVR with regular breathing⁶-⁸ based on spontaneous fluctuations in intravascular pressure of CO2. Here, we explore CO2 chemosensory abnormality in PWE with GCS using rs-fMRI CVR.

Methods: Structural and 10-min rs-fMRI imaging at 3T were conducted for two groups: 1) 25 health subjects (12F&13M, mean age = 32.8±0.9 years) and 2) five PWEs (4F&1M, mean age = 27±3.4 years) with GCS frequency greater than 10 times per year. The rs-fMRI data underwent correction for head motions and was co-registration to its structural volume in the standard space. The normalized rs-fMRI time series was then linearly detrended, spatially smoothed (FWHM=6mm), and temporally band-pass filtered into the low-frequency band of 0.01–0.1 Hz. A reference BOLD signal was created by spatially averaging skull-stripped brain-masked time series and used as a regressor in a general linear model to estimate CVR for each voxel.⁷ CVR maps were then masked to cerebellum, brain stem, and subcortical structures (e.g., thalamus, amygdala, caudate, putamen, and hippocampus) and compared between the two groups.

Results: Group comparison shows multiple clusters with significant CVR mean increases (p<0.05) between two groups. The largest clusters were found in the cerebellum (right: lobules VII, VIII, VI, and X, left: lobule IX), caudate nuclei, midbrain (periaqueductal gray), and left thalamus. Further analysis corrected for multiple comparisons using the family-wise-error-correction method showed significant (corrected p <0.001, alpha <0.05, and minimum cluster size: 60) CVR increases in the left caudate nuclei in PWE with GCS (>10) compared to controls, Fig.1. Whole-brain group comparison demonstrated that the CVR mean of patients was bilaterally greater in cingulate gyrus compared to controls, Fig.2 (corrected p <0.001, alpha <0.1, and minimum cluster size: 100).
Conclusions: Increase in rs-fMRI CVR mean was observed in the cingulate cortex and caudate nuclei in PWE with GCS (>10). Consistent with previous animal studies showing increased CO2-activated cells within these areas,9 our findings align with the importance of the human cingulate cortex in respiratory control according to previous electrophysiological analyses.10 This study demonstrated the identification of faulty CO2 chemosensing areas with rs-fMRI CVR, offering a less demanding alternative to CO2 inhalation experiments. Future research should explore high-resolution BOLD rs-fMRI for more detailed insights into chemosensitivity areas.

References
Altered Functional Gradient Organization in Adolescents with Symptoms of Depression and Anxiety

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**Introduction:** Functional gradient mapping represents high dimensional brain features in a lower dimensional space and has been leveraged in exploring brain-behavior relationships in clinical samples. Despite this progress, recent studies characterizing alterations in major functional connectivity gradients in mood disorder patients are primarily based on adults. Here, we addressed this gap in the literature by investigating the functional architecture of the cerebral cortex in a sample of adolescents with mood disorders, with a hypothesis that the severity of depression and anxiety symptoms would be associated with alterations in functional connectivity gradient organization.

**Methods:** Two hundred and four participants aged 14-17 years old (134 female) completed a resting state functional MRI (fMRI) scan and mood symptom questionnaires. Of the 204 participants, 141 presented with an active mood disorder diagnosis, whereas 63 were healthy controls. Symptom severity was assessed using the Revised Child Anxiety and Depression Scale (RCADS). fMRI data were preprocessed and denoised in the CONN toolbox. We used diffusion map embedding to derive cortical gradients of intrinsic functional connectivity, representing a set of dimensions along which the similarity of connectivity profiles is organized. We focused on the three most dominant gradients of intrinsic functional connectivity (Figure 1A). Relationships between individual-level vertex-wise gradient values and RCADS scores were assessed using multiple linear regression controlling for participant age, sex, and head motion (Figure 1B). We then performed a series of post-hoc seed-based connectivity-behavior analyses using the resulting significant clusters from each gradient as seeds (Figure 1C).

**Results:** Higher RCADS scores were associated with more positive Gradient 1 values in cortical areas that are part of the somatomotor network ($r = .26, p < .001$), suggesting a compression of this gradient from its somatomotor end linked to more severe symptoms. Our post-hoc analysis using seed-based connectivity (SBC) revealed that this compression was driven by stronger connectivity between the somatomotor seed and association networks related to more severe symptoms. Higher RCADS scores were also associated with more positive Gradient 2 values in the visual network ($r = .27, p < .001$), suggesting an expansion of the gradient from the visual network end. This was further supported by our SBC results showing weaker connectivity between a visual network seed and cluster in the somatomotor network related to more severe symptoms, which anchors this gradient at the opposite end. Higher RCADS scores were also associated with more negative Gradient 2 values from several regions in the salience network (e.g., insula, mid-cingulate cortex) ($r = -.32, p < .001$), suggesting reorganization of its connectivity along this gradient. Our SBC analysis identified a salience network seed exhibiting stronger connectivity with the somatomotor network linked to more severe symptoms, suggesting greater affiliation with the somatomotor end of this gradient. Finally, higher RCADS scores were correlated with more negative Gradient 3 values in the default mode and somatomotor networks ($r = -.30, p < .001$), consistent with a compression of this gradient from this end. Our SBC results supported this interpretation, revealing stronger connectivity between a default mode network seed (anterior temporal lobe) and the attentional networks linked to more severe symptoms.

**Figure 1.** Functional gradient alterations in adolescents with mood symptoms and post-hoc seed-based characterization.
Conclusions: These findings identify the robust cross-sectional associations between intrinsic functional connectivity gradients and the severity of depression and anxiety symptoms in a clinical adolescent sample. These results may point to the role of functional connectivity gradients as a useful imaging biomarker for disorder prognostication and outcome monitoring in this population.

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Poster No 2041

Acute effects of acupuncture treatment with GV20 on functional connectivity in patients with PSCI

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Introduction: Post-stroke cognitive impairment (PSCI) associates with adverse effects, including physical disability, sleep disruption, depression, personality changes, and other neuropsychological alterations, collectively contributing to a diminished quality of life. Approximately 44% of individuals experience global cognitive impairment 2 to 6 months post-stroke2. Acupuncture may have a distinct capability to directly enhance cognition-related brain regions and regulate areas associated with phonological, semantic, and attention functions3. Resting-state functional magnetic resonance imaging (MRI) allows us to study the brain regions that are temporally correlated during subject not performing any task, which is crucial for validating the efficacy of acupuncture treatment4. Therefore, the aim of the study was to estimate the immediate effect of Baihui (GV20) acupoint on resting-state functional connectivity (RSFC) in patients with PSCI.

Methods: Right-handed participants were recruited from the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, including 24 patients with PSCI (mean±sd age: 59.3±6.9 yr, 5 females) and 20 health controls (mean±sd age: 60.7±6.6 yr, 5 females). Two sets of rs-fMRI data were performed on a 3T Skyra Scanner (Siemens, Erlangen, Germany) using a gradient echo EPI sequence (TR=2000 ms, TE=30 ms, flip angle=90°, FOV=220 mm, voxel size 3.4×3.4×3.0 mm3) pre- and post-acupuncture treatment with GV20. A set of high resolution T1-weighted structural images were acquired using an MPRAge sequence (TR=2000 ms, TE=1.97 ms, flip angle=8°, FOV=256 mm, voxel size 1.0×1.0×1.0 mm3). Pre-processing was conducted using afni_proc.py in AFNI® including the following standard procedures: realignment, regression, and blurring. All images were registered to a 3×3×3 mm3 Talairach-Tournoux (TT) standard space. Independent component analysis (ICA) and dual regression were performed in FSL®. Fourteen resting state networks (RSNs) were identified from 20 group components using FSL-MELODIC on the 20 healthy controls. Voxelwise analysis was performed using FSL-randomise to identify significant clusters showing RSFC differences within each RSN. Values for mean z-scores were obtained in each cluster. We only report results that survived at cluster threshold of p<0.01 and α<0.05.

Results: Regions showing significant increases (p<0.01) in RSFC in 4 regions within 3 networks in patients with PSCI after receiving acupuncture treatment on the GV20 compared to themselves before the treatment (Figure 1), including right (R) precentral gyrus in somatosensory network, left (L) and R cuneus in visual network, and R thalamus in salience network. Cluster size, peak coordinate, and location of each region of interest (ROI) is shown in Table 1.
Conclusions: Elevated resting-state functional connectivity (RSFC) in the precentral gyrus indicates the positive effects of acupuncture treatment on object recognition, texture discrimination, improved sensory-motor feedback, and enhanced social cue exchange. Working in tandem with the secondary somatosensory cortex, the precentral gyrus oversees body sensations and potentially transmits signals to the motor cortex for executing reactions and appropriate motor responses. Increased RSFC bilaterally in the cuneus provides additional evidence of acupuncture’s impact on alertness, visual processing, and visual-motor control crucial for vision-motion coordination movements. Increase in RSFC in thalamus, known for salience control involving sensory, emotion, and attention systems, suggests acupuncture treatment on GV20 could influence emotion and behaviour regulation.

References
An adaptive sliding-window based dynamic functional connectivity analysis for AD classification

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Introduction: Dynamic functional connectivity (dFC) has been proven effective in quantifying the temporal dynamics of brain networks1, for example, abnormal connectivity in the frontal and temporal cortices using resting-state fMRI (rs-fMRI) in Alzheimer’s disease2 (AD). However, the fixed window size used in the most widely implemented sliding window analysis for dFC estimation must be large enough for good low frequency resolution and small enough to capture the inherent dynamics1. We utilize an adaptive sliding window3 derived from Empirical Mode Decomposition (EMD) that captures the local frequency characteristics. We also computed different dFC metrics for both adaptive and fixed window sizes and evaluated their ability to classify AD in a multiclass classification setting.

Methods: rs-fMRI data was obtained from 53 cognitively normal (CN) (20 male; age:76.7± 6.2 years), 58 mild cognitively impaired (MCI) (31 male; age:76.1 ± 7.8 years) and 61 AD (33 male; age:77.1± 7.3 years) participants, all amyloid-beta positive (standardized uptake value ratio5, SUVR ≥ 1.1) from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). rsfMRI acquisition parameters : TR/TE/resolution = 3000ms/30ms/3.3x3.3x3.3mm3, flip angle = 80, 48 slices and 140 timepoints. Data were minimally preprocessed and group Independent Component Analysis (ICA) based on FastICA6 was implemented to obtain 100 independent components (ICs). Then 54 ICs spanning 9 major resting-state networks (auditory, cerebellum, cognitive control, default mode, frontal, subcortical, somatosensory, temporal, and visual) were shortlisted. An adaptive time dependent sliding window7 based on the instantaneous period of the IMFs (frequency range between 0.01 Hz and the 0.16 Hz (Nyquist frequency)) from the Hilbert transform7.8 was used. The Pearson’s correlation matrix (54x54) calculated using this window was concatenated across time for each subject and then across all 3 groups. Dynamic brain states were then estimated by running a k-means clustering. Subsequently, we computed subject specific dFC metrics9 and tested for group differences for EMD and fixed window sizes (10, 15, 20, 25 and 30 TR). We built a Randomforest classifier using these features (dFC metrics, dFC metrics + EMD metrics (log profiles of the instantaneous period and energy profiles)) to classify AD in a multiclass scenario with 3 classes (CN, MCI, and AD). Recursive feature elimination based on permutation feature importance was used for feature selection.

Results: Three dynamic functional brain states were obtained from clustering for each of the window sizes (fixed and EMD) as shown in Figure 1A. Figure 1(B1-B3) shows the different dFC metrics obtained for the EMD approach. Only EMD showed significant group differences in the dFC metrics, specifically in the probability of transition from state 3 to state 1 (One way ANOVA : F statistic = 4.15, p-value = 0.02). No significant differences were observed in other metrics for all window sizes. Figure 2(A1) shows that the use of an adaptive window size results in better classification of AD (mean AUC-ROC= 0.65) compared to a constant window size. The significant feature identified in Figure 1(B1) had the highest feature importance in the classifier model, see Figure 2(A2). When dFC metrics were combined with EMD metrics, frontal and default mode networks showed the highest AUC-ROC (mean = 0.94) while somatosensory had the least value (mean = 0.73). The optimal feature set of this model consisted only of EMD metrics, primarily from IMF2 and IMF3 with peak frequencies at 0.025 Hz and 0.045 Hz, respectively.
Conclusions: Our analysis shows that only a time-dependent window size based on the local frequency characteristics best captures the dynamics of the brain’s intrinsic functions. Also, the estimated dFC metrics from this approach show better classifier performance for AD compared to fixed window sizes and the best performance when combined with the EMD-derived metrics.

References
Cross-species Comparison of Spontaneous Brain Activity Propagation across Sleep-wakefulness States

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Introduction: Understanding the brain's dynamic processes, particularly traveling waves in resting-state fMRI (rsfMRI), is the key to unraveling its complex functionalities. These waves, which are tied to electrophysiological measures in animal models, have been increasingly recognized for their role across various brain activity scales. These directionally constrained waves are found to propagate along a spatial axis representing cortical hierarchical organization. Ongoing arousal fluctuations are found to be associated with global waves of spontaneous brain activity in both rodents and humans, by using physiological arousal indicators. However, it is yet to be understood how traveling waves propagate under different sleep/wakefulness states in these species. A comprehensive examination of the relationship between cortical hierarchical organization and propagation patterns of traveling waves under different sleep/wakefulness states is not only critical for illuminating the underlying mechanism of dynamic brain connectivity, but also essential for providing insights into the evolutionary aspects of functional architecture of the brain across species.

Methods: Two open-source datasets (Dataset 1: OpenNeuro ds003768; Dataset 2: Mouse sleep fMRI with simultaneous ECoG) were employed in this study. Dataset 1 included simultaneous EEG-rsfMRI data from human sleep, and Dataset 2 included simultaneous ECoG-rsfMRI data from mouse sleep. The synchronized electrophysiological data were used to classify sleep/wakefulness stages. To extract propagation patterns of spontaneous brain activity, each subject’s global mean signal was segmented into chunks based on peak global activity, and in each chunk, every voxel’s rsfMRI signal peak had either an advance or a delay relative to the global signal peak. This was used to form a specific vector containing time delay information. The vectors of the same sleep/wakefulness stage were grouped together to be merged into a matrix. Singular value decomposition was applied to each matrix, extracting the principal propagation delay profile for each sleep/wakefulness stage. To obtain cortical hierarchical organization for each sleep/wakefulness stage, functional gradients were calculated using the average resting-state functional connectivity matrix of that stage based on the diffusion embedding algorithm. Spatial correlations between propagation delay profiles and functional gradients were assessed to determine their relationships.

Results: Fig. 1a shows human propagation delay profile of each stage was spatially similar to the principal gradient of that stage, indicating the propagations of spontaneous brain activity at different stages followed cortical hierarchical organization. Fig. 1b shows similar relationships in the mouse brain, but in the awake state, the propagation delay profile was similar to the secondary functional gradient instead, indicating the difference between these two species. Fig. 2 shows the comparison of propagation delay profiles between these two species. Specifically, under the awake state, the propagation in the human brain occurred between default mode regions and primary sensory areas (Fig. 2a). In the mouse brain, it was between the anterior cingulate and primary sensory cortex plus the amygdala (Fig. 2d). Under NREM, the propagation in the human brain involved the visual cortex and limbic system at one end, and primary sensory areas at the other end (Fig. 2b and c). In the mouse brain, one end of the propagation still included the primary sensory cortex, but the amygdala was no longer involved (Fig. 2e).
Conclusions: This study reveals the relationship between cortical hierarchy and propagation patterns of spontaneous brain activity across wakefulness and NREM states in both human and mouse brains. The propagation features conserved between the human and mouse brains open avenues for further research into the evolutionary aspects of dynamic brain connectivity across species.

Figure 1. Relationships between propagation delay profiles and functional gradients in the human and mouse brains.

Figure 2. Comparison between human and mouse propagation delay profiles.

References
Interaction Effects Driven by Control Conditions: Does It Disqualify Your Results?

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Introduction: In randomized controlled trial (RCT), demonstrating a significant interaction effect on outcome measurements is the gold standard way of proving the effects of therapy. Post-hoc analyses can be conducted to discern which direction the outcome variable moved. The ideal scenario would be that there is significant effect in the intervention group while no significant changes were detected in the control group (Figure 1A). However in reality, researchers often encounter unexpected outcomes, e.g., X-shaped crossing (Figure 1B), or significant changes in waitlisted groups after insignificant wait times. These results are often regarded as false positives driven by unintentional bias introduced in the trial procedure, which leads the peer-reviewers and readers to question the credibility of the findings. In this study, I will demonstrate, through computer simulation, how the current practice of performing post-hoc tests only on a few clusters identified by interaction analysis can structurally bias the post-hoc test results to show more false positives in control condition.

Methods: In this simulation study, two different cohorts were divided into two (active treatment vs. control treatment), and the measurements were taken pre- vs. post-. No intervention was provided in control group. Tests were performed 10,000 times (representing 10,000 voxels or brain regions). The treatment effects were expected to be found in 1,000 “voxels.” All measures were z-scored (normally distributed). The simulation was repeated for varying degree of treatment effects (0.1-1.0), levels of nonspecific effects of test-retest relative to the interindividual variability (0.1-1.0), and sample size (10-100 per group). Interaction effects were assessed (treatment group vs. time) for all tests, and p-values were corrected with false discovery rate (estimating q-values). q<0.05 was considered significant. For the test results of which the interaction effects were identified to be significant, post-hoc analyses were performed using paired t-test. The ratio of false positive results in control condition among true interaction effects were calculated, and fitted against the sensitivity of results (ratio of significant interaction effects out of 1,000 simulated treatment effects).

Results: In all simulations, the false positive rates of interaction effects were maintained below 0.7%. The true positive rates (sensitivity) were noticeably different across simulated conditions (0-100%), which was significantly associated with increased effect of treatment, decreased level of test-retest variability, and larger sample size (p<0.001). Among the true interaction effects, varying degree of false positives were observed in control condition (0-100%), which was significantly associated with the sensitivity (adj. R2 = 0.828; Figure 2).
Conclusions: Our simulation results show that the sensitivity of the interaction effect analysis is inversely proportional to the ratio of false positive control effects (Figure 2). In other words, if the interaction effect tests only identified 20% of true effects, 9% of these significant test results will show false positives in control condition. If the sensitivity is lowered to 5%, 20% of these will show false positives in control condition. This relationship was not observed in false positive interaction effects (adj. R² = 0.0009). In conclusion, the present simulation study confirms that the false positivity rate of control condition can increase if sensitivity of the interaction effect is low (which is almost always the case in neuroimaging studies with 2x2 design), and thus the presence of significant effects in control condition does not disqualify the results of active condition, and it should be interpreted in the context of implicit bias of performing post-hoc tests only in the limited number of clusters identified in the voxel-based interaction effect analyses.

References

Poster No 2045
Exploring Neurophysiological Markers of Brain-Computer Interface Performance in Children
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Introduction: Brain-computer interfaces (BCIs) are a promising new access technology for children with quadriplegic cerebral palsy who are unable to move or speak (Jadavji et al., 2021). Despite great advances in the field, some users are unable to effectively control BCI systems, leading to the expenditure of valuable time and effort from the user and support personnel that would be better directed towards alternative BCI solutions (Edlinger et al., 2015). Electroencephalographic (EEG)-based metrics may predict adult BCI user’s performance but there are no such pediatric studies to date (Blankertz et al., 2010; Ahn et al., 2013; Bamdadian et al., 2014). The aim of this exploratory study was to generate a machine-learning model that best predict BCI performance in children using neurophysiological parameters, and explore features best correlated with success in BCI use.

Methods: Typically-developing children (n=29, age=10.07±2.19, 58% female) were recruited and attended the BCI4Kids laboratory. 120-180 seconds of resting-state EEG recordings were collected prior to motor-imagery based BCI training and task sessions. The primary outcome of BCI performance was the classification accuracy score of the training sessions. A 60% classification accuracy score from the BCI training was used to classify participants into two groups. Data from 17 active channels were analyzed. The resting-state EEG data were cropped to 100 seconds and notch-filtered at 60Hz. The following features were calculated from the resting-state EEG recordings for the theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz) bands: 1) The functional network, using the weighted-phase lag index 2) The normalized power spectrum, using the Welch’s method
3) The aperiodic components of the power spectrum (offset and exponent), and 4) Graph theory metrics (global efficiency and characteristic path length). These values were averaged between electrodes for the given brain regions: frontal, central, parietal, and occipital. Random forest models (RF) and support vector machine (SVM) models were tested. Five predictive models were generated for each RF and SVM model type, each testing a different subset of EEG features: All features, Power, Connectivity, Aperiodic power, and Graph theory features. Each of these models were generated 50 times, ensuring that the same training and testing sets were used between the models each time. The performance of these models were analyzed using the mean balanced accuracy (BA) and F1 scores. Feature importance was also analyzed.

**Results:** For both SVM and RF models, running a feature subset of all 36 connectivity features showed high mean balanced accuracy scores, but with a high variability in performance (SVM model: BA = 61±19%, F1 = 5.6±1.8; RF model: BA = 61±19%, F1 = 5.6±2.0) (Fig. 1). A feature subset of 15 power features using the SVM model showed the second highest scores, again with high variability (BA = 60±17%, F1 = 5.6±1.6) (Fig. 1). For the power-based RF model, features within the alpha and theta bands in the parietal regions had high feature importance (alpha parietal = 10.4±2.9%; theta parietal = 9.6±2.7%) (Fig. 2A). For the connectivity-based RF model, features within the alpha band in various regions had high feature importance (alpha parietal = 8.3±2.9%; alpha global = 6.9±2.3%) (Fig. 2B).
**Conclusions:** In this exploratory study, we generated predictive models of BCI performance in typically developing children using SVM and RF models for the first time. Models using power and connectivity features had the highest mean performance; however, they are currently variable in their performance. EEG connectivity and power within the alpha band may be important correlates of BCI performance. An increased sample size would better evaluate the models proposed above. Understanding which factors best predict pediatric BCI performance would help users to find optimized BCI strategies, and potentially allow the utilization of these factors to improve a child’s performance in BCI tasks.

**References**


**Poster No 2046**

**Intuitive avatar gait control through multimodal EEG and eye-gaze brain-machine interface**

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**Introduction:** Brain-machine interface (BMI) provides a direct intention pathway between brain and external devices, inferred by spectral power changes in scalp electroencephalograms (EEG)¹. Event-related desynchronization (ERD) of sensorimotor rhythm (SMR) has been traditionally used in BMI paradigms to decode human motor intention in simple tasks². However, the decoded contents were limited to flexion or extension of the shoulder, wrist, or fingers. Here, to improve intuitive user experience by estimating complex intention beyond the single action related to a hand, this study has proposed a novel BMI paradigm in which the gait of an avatar in a virtual environment is controlled by motor imagery (MI) of walking.

**Methods:** In this study, ten healthy, right-handed subjects participated (22.5±1.0 years), and their EEG and gaze directions were processed in real-time to control an avatar navigating a circular course in a virtual reality space. During experiment, EEG signals were recorded at a sampling rate of 1000 Hz using a 128-channel scalp EEG cap (Hydrocel Geodesic Sensor Nets, Electrical Geodesics, Inc.), and eye-gaze signals were recorded binocularly at a sampling rate of 1200 Hz using a screen-based eye tracker (Tobii Pro Spectrum, Tobii AB). In our BMI protocol (Fig. 1-A), presence of movement intention (GO/STOP) was decoded based on SMR-ERD related to motor imagery, and preferred movement direction was estimated based on conscious eye movement. As for movement direction, we implemented an eye-gaze control architecture supported by semantic segmentation performed in real-time, recognizing clusters of pixels that form distinctive categories in an external virtual environment. All participants controlled the avatar configured to move forward based on MI of walking (Foot-model) and unclenching right hand (Hand-model), following experimental procedure shown in Fig. 1-Ba. After training of MI (Fig. 1-Bb), avatar control session (Fig. 1-Bc) was conducted twice, each session followed by questionnaire. For the evaluation of BMI which realizes intuitive gait control of an avatar, we posit that sense of ownership (SoO)³, and sense of agency (SoA)⁴ are significant other than the quality of EEG or success rate of control. Originating from rubber hand illusion⁵, employment of virtual reality reframed the main question to address SoO and SoA in terms of experiencing a virtual body representation as our own. Hence, the intuitive experience of users is clarified by whether they perceive the avatar as an extension of themselves or merely as a tool.
RESULTS: In sessions, a virtual gauge ranging from 1 to 20 represented transition of SMR-ERD, and decoded presence of movement intention. The gauge follows time-frequency map in the same timeline, where avatar moved straight while the gauge exceeded 10. A frequency characteristic of both beta rhythm (18-23 Hz) and mu rhythm (8-13 Hz) were observed in Foot-model (Fig. 2-Aa), whereas only mu rhythm in Hand-model (Fig. 2-Ab). Topographic representations of SMR-ERD were observed around primary sensorimotor cortices, left and right in Foot-model (Fig. 2-Ba); only left in Hand-model (Fig. 2-Bb) respectively. Overall success rate of completing the course was comparable when participants used Foot-model (77%) or Hand-model (73%). On the other hand, ERD durability defined as the proportion exceeding the threshold, was significantly higher (p<0.05) in Hand-model (62.61%) compared to Foot-model (51.88%). Meanwhile, despite both models induced significant SoO (*p<0.001) and SoA (*p<0.001), SoO was significantly higher in Foot-Model (**p<0.01) as a result of Wilcoxon signed rank test being conducted (Fig. 2-C).

CONCLUSIONS: Together, these results show that the difficulty of avatar control does not depend solely on the quality of EEG. Furthermore, significant differences in ERD durability and SoO suggest that a synchronization between MI task and avatar movement enhances intuitiveness, improving the operability of eye-gaze control.

REFERENCES

POSTER NO 2047

Use EEG to Explore the Impact of Mindfulness Meditation on Physiological and Neurological Responses

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INTRODUCTION: Mindfulness meditation has been shown to have numerous benefits for mental and physical health, include reducing stress, and increased emotional regulation. However, there is a lack of understanding about the underlying neural mechanisms of these benefits. In this study, we would analyze the electroencephalography (EEG) signals to investigate changes in physiological and neurological responses, such as changes in brainwave activity and heart rate, so as to investigate the potential benefits of mindfulness practice. The study would contribute to the existing literature on mindfulness meditation, and provide insights into how to improve mental and physical well-being assisted by EEG.
Methods: One middle age man (50 years old) participated in this longitudinal study using wearable EEG to investigate the neurophysiological change during a one-month consecutive vipassana mindfulness practice. Both EEG and heart rate responses were recorded each time, before (5 minutes), during (20 minutes), and after (5 minutes) meditation sessions. The EEG and HR data were analyzed by Matlab and EEGLab to examine changes in brainwave activity and heart rate. A self-assessment report was conducted immediately after the practice.

Results: Alpha peak frequency (APF) is significantly higher after mindfulness meditation, as shown by comparison of APF before mindfulness (pre-5) and during mindfulness practice (med-20), and comparison between APF of pre-5 and after mindfulness practice (post-5). The same is with the beta peak frequency. While for theta peak frequency, it is significant lower during mindfulness meditation (med-20), when comparing to either pre-5 or post-5. See figure 1 a. The alpha power first decreased and then increased, the beta power increased, and the theta power decreased, before, during and after meditation. Throughout the testing stage, the theta frequency, alpha power and heart rate showed the same change trend, but there was no significant correlation between the heart rate and theta frequency and alpha power. The theta power changed most significantly before and after meditation, which is consistent with previous studies showing that the theta power is the most sensitive index for loving-kindness meditation (LKM) training. See figure 1b. Meanwhile, we find significant change in standard deviation (SD) of heart rate between meditation and non-meditation mental states, as shown in table 1. The Self-assessment report shows that the scores of body-comfort, mind-comfort and mindfulness breathing are higher than the scores of body-movement, wandering-mind and fall-asleep. We can tentatively assume that meditation contributes to the comfort of the body and mind, and positive to mindfulness breathing. Meanwhile, meditation may help reduce body movement and wandering thoughts.

Conclusions: The study provides insights into the underlying neurophysiological mechanisms of mindfulness meditation using wearable EEG devices. It demonstrates that in term of EEG measurement, spectrum frequency can be more sensitive than spectrum power, and heart rate variability as measured by SD is more sensitive than the mean. Furthermore, mindfulness meditation can regulate brain wave frequency, help us regulate our emotions and reduce stress, multiple consecutive meditations with timely feedback helps to improve brain health as evidenced by traits analysis, a significant reduction in peak
frequency of alpha waves with increasing number of meditations as well as correlations with numerous other physiological indicators. The findings support the idea that mindfulness meditation can induce a meditative state and improve cognitive and emotional regulation. Moreover, the proposed study contributes to the literature by using wearable EEG devices to collect data in a more accessible and convenient manner.

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Poster No 2048
Normalizing Go/NoGo ERP in the children with cerebral palsy using motor imagery-based BCI training
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Introduction: Cerebral palsy (CP) is a neurological disorder that affects movement, posture, and coordination, resulting from damage to the developing brain, often occurring before or during birth. This condition manifests in various forms, impacting muscle control and coordination, and is characterized by impaired motor function. In the context of the brain, cerebral palsy is associated with abnormalities in the motor cortex. The damage to this area disrupts the communication between the brain and muscles, leading to difficulties in coordinated movements and muscle control. The severity and specific manifestations of cerebral palsy vary among individuals, encompassing a spectrum of motor impairments that may affect different parts of the body. Early intervention and rehabilitative strategies play a crucial role in managing and improving the quality of life for individuals with CP. In this study, we employed a motor imagery-based brain-computer interface (BCI) EEG system, conjoined with a BCI-controlled robotic arm, to design BCI training games for children with CP. The objective was to improve the function of the primary motor cortex and alleviate muscle tones in the upper extremities of children with CP.

Methods: Sixteen children with CP, exhibiting varying degrees of severity, were screened by an occupational therapist at the Hemei Experimental School in Changhua, Taiwan, and participated in the study. The study employed an 8-week training protocol, conducted weekly with each session spanning one hour, and aimed at enhancing the modulation of the primary motor cortex in children with CP. In our study, a custom-made EEG spectrometer was used to capture the alpha suppression associated with the motor imagery processing as the feature to trigger a robotic arm in real-time to move a plastic ball along a designated track as the BCI-based training facility. After the 8-week training protocol, the effectiveness of the training was evaluated using a pre- and post-training Go/NoGo EEG experiment conducted using a 64-channel ANT EEG system (ANT Neuro, Hengelo, Netherlands) sampled at 1000 Hz. The EEG data were preprocessed and analyzed using EEGLAB (Delorme and Makeig, 2004) in the Matlab environment (MathWorks Inc., Boston, USA).

Results: Results revealed that 10 of the 16 children exhibited the emergence of a N200 ERP component in the frontocentral midline region post-training, a phenomenon absent in the pre-training assessments. However, for those with severe CP, the BCI training failed to rectify the aberrant ERP patterns induced by the No/NoGo task.

Conclusions: This nuanced exploration sheds light on the potential efficacy of motor imagery-based BCI interventions in ameliorating motor-related neurophysiological signatures in children with CP and explores the feasibility of implementing this intervention. This work was supported in part by the National Science and Technology Council, Taiwan (NSTC110-2511-H-A49-012-MY3 and NSTC110-2221-E-A49-038).

References
Neuronal avalanches as potential features for Brain-Computer Interfaces

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Introduction: Brain-Computer Interfaces (BCIs) constitute a promising tool for communication and control. However, controlling non-invasive BCI remains a learned skill difficult to develop for 15-30% of users (Allison et al., 2010). This is mainly due to our poor understanding of the dynamic processes underlying BCI performance. Identifying the dynamical features that are relevant to the execution of a task could be the key to improving the diffusion of the BCI. Current features rely on local measurements without considering the interconnected nature of brain functioning. Whole-brain functional imaging is dominated by ‘bursty’ dynamics, aperiodic perturbations called “Neuronal Avalanches” spreading across the whole brain (Tagliazucchi et al., 2012). Neuronal avalanches spread preferentially across the white-matter bundles (Sorrentino et al., 2021), are affected by neurodegenerative diseases (Sorrentino et al., 2021). Here we hypothesise that they could improve BCI classification performance. To test our hypothesis, we used source-reconstructed EEG signals in a BCI framework, where 20 subjects were compared in resting state and while performing a motor imagery task. We obtained the probabilities of each pair of regions being recruited sequentially in an avalanche (Sorrentino et al., 2021), and we used them as features to perform the classification.

Methods: Here, we applied the neuronal avalanches approach to EEG data recorded during a BCI training session performed by a group of 20 healthy subjects (aged 27.5±4.0 years old, 12 men). They were instructed to control the vertical position of a moving cursor by modulating their neural activity via a motor imagery task (Corsi et al., 2020). The signal was then zscored (over time) and thresholded, and set to 1 when above threshold, and to zero otherwise (threshold =|3|). An avalanche was defined as starting when at least one region is above threshold, and as finishing when no region is active. For each avalanche, we have estimated an avalanche transition matrix (ATM) containing the probability that regions j would be active at time t+1, when region i was active at time t. Then, for each subject, we obtained one ATM per trial. We explored the performance of the ATMs in the decoding of the task. We compared the ATMs and the Common Spatial Patterns (CSP) approaches, widely used in the BCI domain (Blankertz et al., 2008). In each case, the output was classified using a Support Vector Machine (SVM). The classification scores for all pipelines were evaluated with an accuracy measurement using a random permutation cross-validator. To enable a statistical comparison of the CSP+SVM and the ATM+SVM approaches, 50 re-shuffling and splitting iterations were performed.

Results: At the group-level (Fig 1, panel A), the classification performance was greater for ATM+SVM (0.80+/−0.10) with a reduced inter-subject variability as compared to CSP+SVM (0.75+/−0.15). For each subject, we ran t-tests to compare the 50 success rates obtained with CSP+SVM to the 50 success rates obtained using ATM+SVM. ATM+SVM yielded better classification accuracy than CSP+SVM for 12 subjects. In 4 subjects, CSPs yielded better accuracy than ATMs (Fig. 1, panel B). In 5 subjects, there was no statistically significant difference between the two approaches. We examined the variability of the estimates across the splits. Steady estimates are important to train online algorithms and high variability might be partly responsible for ineffective training. We observed marginally higher intra-subject variability in CSP+SVM (median value of 0.07) as compared to ATM+SVM (median value of 0.06). In particular, the standard deviation across the split is smaller for the ATMs for most subjects.

Classification analysis. (A) Group-level classification performance. (B) Individual-level classification performance.
Conclusions: This first proof-of-concept study might capture part of the processes that were typically overlooked in a more oscillatory perspective. Our work paves the way to use aperiodic activities to improve classification performance and tailor BCI training programs.

References

Poster No 2050
Synthesizing Brain Signals to Control Motor Brain-Computer Interface Using Generative Neural Network
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Introduction: The cortical representation of motor components, such as kinematics or kinetics, appears differently depending on their behavioral characteristics and is distributed widely over the cerebral cortex (Kim et al., 2023). The brain-computer interface (BCI) system should utilize the cortical representation to increase accuracy and reliability. However, constraints on neural data acquisition can limit such utilization. For example, acquisition methods such as intracranial EEG (iEEG) have a high spatial resolution but limited spatial coverage (Sejnowski et al., 2014). Thus, obtaining appropriate brain signals representing the behavior could be challenging. We speculated that artificially synthesizing the primary brain signals representing the behavior using the signals of the secondary brain area could address such limitations. Here, we show a novel method using the generative deep neural network model for synthesizing the cortical signals for controlling BCI.

Methods: We employ the generative adversarial neural network (GAN) model based on the HiFi GAN (Kong et al., 2020), which was introduced to translate signal data. We trained the model to learn the spectrotemporal features of the primary motor cortex’s signal waveforms during the hand-reaching movement for the target (Fig 1).

Results: When source signals of a motor-related area, such as the intraparietal sulcus (IPS), entered the model, it synthesized the signal waveforms of the motor cortex (M1) by translating the spectrotemporal characteristics of IPS into those of M1. We found that the signal features of synthesized M1 signals contain the unique characteristics of motor cortex (Fig 2). Furthermore, kinematics trajectories of hand-reaching movement could be decoded from the synthesized M1 signals.
Fig. 2. Signal synthesize result. (Upper) Averaged signal waveforms and normalized spectrograms. (Middle) Crosscorrelation between M1 and other signals. (Low) Decoded hand-movement trajectories

Conclusions: We conjecture that such findings may help to address the limitation regarding to spatial coverage or augmenting neural datasets for BCI.

References

Poster No 2051
Learning on the Manifold of Human Brain Activity through Real-Time Neurofeedback
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Introduction: Learning a new behavior is constrained by the geometry, or intrinsic manifold, of neural population activity supporting that behavior. Recent work highlights the importance of manifolds that capture low-dimensional neural dynamics for brain-computer interface learning (Sadtler et al. 2015). Through invasive BCI, non-human primates can learn to operate
neural prosthetics more efficiently with a device controlled via activity on the intrinsic neural manifold (Oby et al. 2019; Sadtl et al. 2014). Recent studies have trained humans to self-modulate brain activity through real-time neurofeedback, to enhance perception (Shibata et al. 2011), attention (deBettencourt et al. 2015), or emotion regulation (Keynan et al. 2019), with variable efficacy. Prior work has not considered the neural constraints underlying their neurofeedback training. Here, we leverage manifolds in a human neurofeedback paradigm to expedite learning and unveil dimensions which facilitate learning effects.

**Methods:** We enrolled 20 participants (9 female; 25.8 ± 5.5 y) in a 4 session real-time fMRI experiment where they learned to use their brain activity to control an avatar’s movement through a virtual world. In session one, participants practiced navigating the avatar to a goal location with a joystick while fMRI data were collected. We estimated a neural activity manifold of this task from a network of navigation-related regions using the manifold learning algorithm T-PHATE (Busch et al. 2023). In subsequent sessions, participants were trained using neurofeedback to perform the same task by controlling the avatar’s movement with their brain activity. Using a closed-loop system (Wallace et al. 2022), we acquired and transmitted fMRI volumes every 2 seconds to an HPC cluster for processing and embedding onto the T-PHATE manifold. Embedded data were mapped to the direction of the avatar’s next movement in the game via one of three manifold components (i.e., intrinsic-, within-, and off-manifold mappings). These components capture the greatest, second greatest, and least variance along the manifold, respectively. Participants received feedback based on a different mapping during each neurofeedback session. Neurofeedback training used staircasing to quantify the degree each participant’s brain exerted over the avatar’s movement. Higher control (referred to as “BrainControl”) is a behavioral metric of learning in this task, as the parameter scales with performance. We also quantified the change in neural alignment along the manifold, as we predict learning to be driven by an increase in the variance explained by the manifold component yoked to the neurofeedback.

**Results:** We find neurofeedback learning effects reflected by both behavioral and neural analyses. Behaviorally, we measured learning as the change in BrainControl across the trials of a neurofeedback session. Learning increased for the intrinsic and within-manifold conditions (Fig. 1), with a greater increase for intrinsic than within-manifold condition, but not for the off-manifold condition (Fig. 2A). We calculated neural alignment with the manifold components as the change in the variance in the neural data explained by each component at the start vs end of training. When feedback was based on the intrinsic or within-manifold components, explained variance increased over the course of training, but did not for the off-manifold component (Fig. 2B).

**Conclusions:** We introduce a framework for manifold-informed non-invasive human BCI, which affords significant learning within one session. Our variance analysis indicates that neural geometry can shift along dominant manifold components, underlying behavioral changes. With manifold-based neurofeedback, we demonstrate control and reorganization of brain activity in higher-order cognitive regions. This suggests important implications for brain-based therapeutic and behavioral interventions.
References

Poster No 2052
Analyze the Characteristics of Event Related Potential of the Hand gesture for Multimodal Bio signal
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Introduction: Many studies have reported on Brain-Machine Interface (BMI) using bio signals such as Electrocardiogram (ECG), Electroencephalogram (EEG), and Electromyogram (EMG). A lot of BMI works were developed for the purpose of rehabilitation, but also the same time, it has brought improvements in the monitoring and analysis technologies¹. In the previous study, we developed the Hand gesture classification system using multimodal Bio signal using a Field programmable gate array (FPGA) which implements a deep learning model². Our system shows high classification accuracy in the case of using an EMG and combining EMG and EEG. Only in the case of using EEG shows lower accuracy than other reports. This study aims to investigate the possibility of improving the classification accuracy when other various characteristics of EEG were applied to the hand gesture classification system in the feature extraction layers. Also, comparison results of Event-related Potential
(ERP) characteristics for each hand gesture of different types of grasp can be expected to determine a modified experimental protocol or model in future studies.

Methods: This study used the data from previous works to prepare a Hand gesture classification system consisting of bio signal sensors and a processing board that contains Convolution Neural Networks (CNN) based deep Learning Model Implemented FPGA chip. The experiment consisted of a cue time and performance time (5 sec) and a rest (3 sec). The subjects were ten healthy subjects (three females and seven males, 25 ± 5.5 years) (2021005-HR-63-01-02). The gestures (large/medium-diameter grasp, three-finger, sphere grasp, prismatic pinch grasp, power flat grasp, cut, and rest) were chosen to improve the performance on the Toronto Rehabilitation Institute Hand Function Test (TRI-HFT) and the Jebsen-Taylor Hand Function Test. The system was connected to each EMG and EEG sensor and acquired signals in an on-device format. Ultracortex Mark IV Headgear and cyton board (OpenBCI Inc.,) were used to acquire the EEG data with 8-channels (F3, F4, C3, C2, C4, P3, Pz, and P4) with 250Hz sampling frequency. The signal is preprocessed by Ultra96-V2 Board which contains an Arm cortex Multiprocessor system on a chip (MPSOC) and Xilinx Zynq series FPGA. Implemented deep learning model are based on a convolutional neural network (CNN), which extracts features from data with time series data. The proposed CNN implementation includes a downstream multilayer perceptron (MLP) layer to learn nonlinearities for gesture classification. Input sources of EEG were filtered in 5-50Hz (band-pass) with 60Hz Notch, but analyzed in ERP to see a peak and Latency components in the mu rhythm (8-12Hz) range. ERP signals were measured from the C3 area for the seven different hand gestures.

Results: ERP signals were measured from the C3 area for the seven different grasp gestures. Each signal shows an average of 10 subjects for all gestures except rest. at approximately 500 ms, Maximum peak components were observed. Statistical analyses were performed with SPSS 25 (IBM Inc.,) using repeated-measures analysis of variance (ANOVA), and one-way ANOVA using the type of grasp gesture as the variable, no significant differences in maximum peak (p = 0.139) were found. However, the latency components show significant differences (p = 0.042), and between time gap of large diameter grasp is significantly faster than medium diameter grasp (p<0.05) in Bonferroni analysis.

Conclusions: This study investigated the possibility of improved classification accuracy when other features of EEG were applied to the system. Most of the ERP patterns showed similar to general gesture results, and the statistical significance shown in latency also indicates the time points of peaks for each EEG data also need to consider not only simple features such as Root Mean Square (RMS) in the time series signal in the model. In further, these results would help to develop more effective rehabilitation orthosis.

References

Poster No 2053
Towards generative AI-based fMRI paradigms: reinforcement learning via real-time brain feedback
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Introduction: In traditional human neuroimaging experiments, researchers create experimental paradigms with a psychological/behavioral validity to infer the corresponding neural correlates. Here, we introduce a novel approach called Reinforcement Learning via Brain Feedback (RLBF), that inverts the direction of inference; it seeks for the optimal stimulation or paradigm to maximize (or minimize) response in predefined brain regions or networks (fig.1). The stimulation/paradigm is found via a reinforcement learning algorithm (Kaelbling et al., 1996) that is rewarded based on real-time fMRI (Sulzer et al., 2013) data. Specifically, the reinforcement learning agent manipulates the paradigm space (e.g. via generative AI) to drive
neural activity in a specific direction. Then, rewarded by measured brain responses, the agent gradually learns to adjust its choices to converge towards an optimal solution. Here, we present the results of a proof of concept study that aimed to confirm the viability of the proposed approach with simulated and empirical real-time fMRI data.

**Methods:** We build a streamlined setup: a soft Q-learner (Haarnoja et al., 2017) with a smooth reward function (fig 1. “Reinforcement Learning”) and simple visual stimulations to implement the paradigm space (fig 1. “Paradigm Generator”). We present the participants various versions of a flickering checkerboard, with contrast and frequency as free parameters of the paradigm space, and a contrast of zero equal to no stimulation. The reward signal is calculated from responses in the primary visual cortex (fig.2b), measured by a linear model fitted to a single block of fMRI data (5s stimulation, 11s rest). The hypothesis function is convolved with a conventional double-gamma HRF. Here, the agent’s task is to determine the best contrast-frequency configuration that maximizes a participant’s brain activity in the primary visual cortex. First, we test our method through simulations with realistic effect size estimates. The optimal ground truth is defined as a linear function of contrast and frequency, with maximum activation at maximum contrast and 7Hz frequency. The agent has 100 trials in which it selects a contrast and frequency value and updates its Q-table using the reward calculated by our ground truth equation, with Gaussian noise added. We fine-tune the hyperparameters for the models using realistic initial conditions (signal-to-noise: 0.5 - 3.0; q-table smoothness: 0.5 - 4.0; soft-Q temperature: 0.2; learning rate: 0.05 - 0.9). Then, with parameters chosen on the simulation results, we measure data for n=5 participants. In the scanner, we presented the checkerboard in 45 blocks with a TR of 1 second (10 minutes) and allowed the reinforcement learner to optimize the visual stimulation based on brain feedback.

**Results:** Simulation results show that the proposed implementation provides a robust solution in a relatively wide range of initial conditions and a small amount of trials. High smoothing power appears to function well with higher SNRs, while lower SNRs seem to require lower learning rates for optimal training (fig.2a). The models display a remarkable stability with a wide range of learning rate values. Results from the empirical measurements (fig.2b) are in line with knowledge about the contrast and frequency dependence of the checkerboard-response (Victor et al., 1997) and provide initial confirmation for the feasibility of the proposed approach.

**Conclusions:** Here we presented a proof of concept for the RLBF method, a novel experimental approach, which aims to find the optimal stimulation paradigm to modulate individual brain activity in predefined regions/networks. While this proof of concept study employed a simplified setup, future work aims to extend the approach with paradigm spaces constructed by generative AI solutions. By inverting the direction of inference (“brain -> behavior”; instead of “behavior -> brain”) the proposed approach may emerge as a novel tool for basic and translational research.
Poster No 2054

Finger-specific representations are sharpened during a fatiguing motor task

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Introduction: Motor fatigability is a frequent symptom in neurological disorders. It can be quantified through the decrease in movement speed, when low-force movements are performed repeatedly with maximal speed. In this study, we measure motor fatigability in healthy with fast finger tapping. Previous research has shown that the decrease in movement speed, or motor slowing, is associated with a rise in BOLD activity, a reduction in surround inhibition in the primary sensorimotor cortex (SM1), and an increase in co-activation of antagonistic muscle groups involved in the movement (Bächinger et al. 2019). However, it remains an open question of whether motor slowing and the associated release of inhibition causes a reduction of signal-to-noise ratio for movement-specific information. Here, we aim to answer this question by assessing finger representations using representational similarity analysis (RSA) when participants perform fatiguing tapping with the index or middle finger (Fig 1A).

We hypothesized that a reduction of movement-specific information would be associated with the index and middle finger representations in SM1 getting “blurred” over time due to a gradual break-down of surround inhibition. Thus, if the signal-to-noise ratio of movement-specific information decreases in parallel with motor slowing, we would expect finger representations to become more overlapping than is predicted by BOLD activity changes alone. Vice-versa, if the signal-to-noise ratio of movement-specific information increases despite motor slowing, we would expect sharper finger representation than purely predicted by the BOLD activity increase (Fig 1B).
**Methods:** 26 healthy young participants performed a motor slowing finger tapping task during functional MRI. The participants performed 30s of maximal speed finger tapping with the index and the middle finger, alternating between trials. For the first-level general linear model, the fingers were regressed separately and the 30s of tapping were further split into 3 x 10s regressors (time bin 1, bin 2, bin 3). We performed RSA separately on each 10s regressor for the anatomically defined regions of interest (ROI) M1 and S1 hand area (Diedrichsen, et al. 2013; Walther et al. 2016) and therefore obtained a dissimilarity measure for each time bin (Fig 2B&E, actual dissimilarity, purple). A mixed effects model with the factor time was used to test whether dissimilarity changed across time bins. Since the change in dissimilarity over time bins might purely be explained by changes in BOLD activity, we extracted an estimate for BOLD activity for each time bin and used a mixed effects model with the factor time to test whether activity increased. We then predicted expected dissimilarities for bin 2 and bin 3 based on the changes in activity (Berlot et al. 2021; Fig 2B&E, predicted dissimilarity, pink). Using another mixed effects model with the factor dissimilarity type (predicted, actual) and time (bin2, bin3), we tested whether the predicted and actual dissimilarities differed. Post-hoc comparisons were then performed on each time bin. These analyses were done separately for each ROI.

**Results:** Behaviourally, motor slowing was observed, as tapping speed significantly decreased in each finger over time ($F(1,85)<10.67, p<.001$, Fig1A). BOLD activity increased over time for S1 and M1 ($F(2,50)<20.09, p<.001$, Fig 2A&D). Comparison of the predicted versus the actual dissimilarity revealed a significant difference in both ROI ($F(1,75)<37.62, p<.001$). Post-hoc comparison showed that time bin 2 and bin 3 both have significant differences between predicted and actual dissimilarity in both ROI ($p<.005$, Fig 2B&D).
Conclusions: We conclude that the finger representations in the sensorimotor cortex become more distinct with motor slowing, even when correcting for the increase in activity. This suggests that the signal-to-noise ratio of movement-specific information is increased, potentially to compensate for supraspinal changes caused by fatigability.

References

Poster No 2055
Evaluating functional connectivity during motor imitation using diffuse optical tomography
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Introduction: Autism spectrum disorder (ASD), a neurodevelopmental disorder traditionally characterized by heterogenous phenotypes, comprises a central affected domain of impaired social communication¹. Current research suggests that deficits in motor imitation may be associated with impaired development of social-communicative skills²,³. However, due to the limitations of functional neuroimaging modalities, there is insufficient work assessing brain activity during motor imitation. Here, in a proof-of-principle study in neurotypical adults, we utilize High-density diffuse optical tomography (HD-DOT), a functional neuroimaging modality that facilitates an open scanning environment and has reduced sensitivity to motion-based artifacts, to measure cortical activity during complex gross motor imitation⁴. We apply independent component analysis with reference (ICAR)⁵ to HD-DOT data and obtain subject-specific spatiotemporal components that display differential pattern of functional connectivity (FC) during motor observation and imitation. Furthermore, FC between the components show correlation with both behavioral and imitation fidelity scores.
**Methods:** Data were acquired from 45 adults (28 females, ages 18-31, no prior diagnosis of ASD) using a HD-DOT system consisting of 128 sources and 125 detectors, with over 3,500 measurement pairs. During the observation task, participants watched stimulus videos, whereas, during the imitation task, they imitated a series of upper extremity movements (Fig 1.B). Motor imitation fidelity score was computed using the computerized assessment of motor imitation (CAMI) algorithm\(^6\) (Fig.1.C). Social Responsiveness Scale (SRS-2), a measure of social reciprocity, was also collected. Data were processed using the NeuroDOT\(^7\) pipeline in MATLAB with motion detection and censoring performed using global variance in the temporal derivative\(^8\). Gordon parcellation atlas\(^9\) was used to generate a spatial reference for the ICAR algorithm via the GIFT toolbox\(^10\). The ICAR algorithm produces a spatiotemporal representation of the subject data based on the spatial reference while minimizing the mutual information between components. Significance in FC changes (observation-imitation) was assessed using paired t-test at a p cut-off of 0.05 with multiple comparison correction using false discovery rate (FDR, q-value cut off < 0.0480). Pearson correlation (r) quantified the linear relation between behavioral scores (SRS-2, CAMI) and all possible FC pairs calculated from observation or imitation. The statistical significance of the linear relation was evaluated by computing an adjusted q-value < 0.0460.

**Results:** 18 spatial reference-based independent components were estimated. A subset of the derived components (7 out of 153 FC pairs) had significantly different temporal activation during motor observation and imitation sessions (p < 0.0084). During observation, four FC pairs showed positive correlation with the CAMI score (Fig.2.A-D). During imitation, another four FC pairs showed positive correlation with the CAMI score (Fig. 2.E-H). While there was no linear relation between FC during observation sessions and SRS-2, FC between cingulo opercular and frontoparietal regions and between dorsal attention and ventral attention regions were positively (\(r = 0.4489\)) and negatively correlated (\(r = -0.4828\)) with the SRS-2 scores, respectively.
Conclusions: ICAR estimates individualized spatiotemporal representation of brain activation during motor observation and imitation. The FC derived from the ICAR components show differential activation during observation and imitation and are correlated with both the SRS-2 score measuring social reciprocity and the motor imitation fidelity score. While this analysis focused on adults without ASD, our future work aims to further extend this analysis in adults with ASD and in school-age children (7-16 years).

References

Poster No 2056
Neural origin of impaired grip force direction control in stroke survivors
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Introduction: Many stroke survivors suffer from persistent impairment in hand function, even after completing a full course of rehabilitation services (Lawrence et al. 2001). Hand impairment diminishes stroke survivors’ abilities to perform activities of daily living and thus lowers their functional independence and quality of life (Steward and Cramer, 2013). One primary function of the hand is gripping and manipulating objects for activities of daily living. Biomechanically, secure grip of objects can be hindered by abnormally directed grip force post stroke (Seo et al., 2015). The objective of this study was to investigate the neural origin of the impaired grip force direction control post stroke.

Methods: Three studies were conducted. First, the role of the sensorimotor integration was investigated using short-latency afferent inhibition (SAI) which represents the responsiveness of the primary motor cortex to somatosensory input (Ackerley et al. 2014). SAI was quantified as the extent to which the motor evoked potential (MEP) induced by transcranial magnetic stimulation (TMS) applied to the primary motor cortex of the lesioned hemisphere is suppressed by preceding electrical sensory stimulation targeting the median nerve in the wrist of the affected hand. The association between SAI and grip force direction control in the paretic hand was investigated in 10 chronic stroke survivors. In two additional studies, the role of structural connectivity and the role of functional neural connectivity within the brain's sensorimotor network were investigated using diffusion tensor imaging (DTI) in 22 chronic stroke survivors and using electroencephalography (EEG) in 12 chronic stroke survivors, respectively. The association between structural connectivity and grip force direction control as well as the association between functional connectivity and grip force direction control were investigated, with the lesion volume (measured from brain MRI) accounted for as a covariate.

Results: The poor performance in grip force direction control in stroke survivors was associated with less SAI (r = 0.63). In addition, the poor performance in grip force direction control was associated with the lower structural connectivity in the network involving bilateral Rolandic, ipsilesional SMA, and contralesional thalamus (r = 0.34) (Schranz et al. 2023). It was also associated with lower functional neural connectivity between the premotor and primary somatosensory cortices of the non-lesioned hemisphere in the alpha frequency band (r = -0.57) (Baker et al., 2023).

Conclusions: Impaired performance in grip force direction control in the hand affected by a stroke may be manifested as a result of impaired sensorimotor integration as measured by SAI. We postulate that the performance may be facilitated by utilizing the residual neural resources including the unaffected hemisphere. This study contributes to improved
understanding of neural mechanisms behind impaired hand function post stroke. This knowledge is expected to pave the way for development of novel treatments. For example, future studies may examine if SAI or cortical functional connectivity could be reinforced via novel interventions such as repetitive brain stimulation targeting the SAI pathway or the unimpaired sensorimotor network in conjunction with targeted hand rehabilitation therapy. Such development of novel treatments may address the impaired grip force direction and thus improve stroke survivors’ hand grip function.

References

Poster No 2057
Motor phenotypes: Multivariate associations with sleep, mental health, and grey matter volume
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Introduction: Motor behaviour plays an important role in our ability to interact with the world. Higher levels of physical activity and motor performance are associated with better sleep quality and mental health1,2. Previous studies mainly assessed univariate associations between individual measures rather than exploring the interplay between the latent dimensions of sleep, mental health, and motor behaviour. Furthermore, the neurobiology underlying their interplay remains unclear. In this study, we aimed to assess multivariate links between motor behaviour and the combined factors of sleep and mental health. Additionally, we discerned the interindividual neuroanatomical basis of their interaction through a predictive machine-learning approach in a large-scale sample.

Methods: We analysed data from 5853 participants (mean age=64, SD=7.7; 2907 female) without neurological diseases from the UK Biobank3. In total, 9 sleep health (e.g., insomnia symptoms) and 15 mental health (e.g., tiredness) variables were derived from touchscreen-based assessments3,5. Motor behaviour was assessed using self-reported physical activity, accelerometer, grip strength, reaction time, and trait-making tasks. To prevent data leakage between the analyses, participants were split based on neuroimaging data availability. Regularized Canonical Correlation Analysis (rCCA) was applied to 1806 participants to identify multivariate associations between sleep/mental health (X) and motor behaviour (Y), validated through 5 repeated hold-out split and permutation tests5. The rCCA weights were then used to project the remaining 4047 participants, obtaining a motor latent variable for each participant and each rCCA mode. These variables were then used as targets for prediction with grey matter volume (GMV) data, parcellated using Schaefer 1000 ROIs, Melbourne Subcortical, and SUIT cerebellar atlases2,3. The 4047 participants were divided into 80/20 training and testing subsets. The training subset underwent nested 5-fold cross-validation using XGBoost. The final model was then retrained on the entire training set for out-of-sample predictions on the test subset.

Results: Significant associations were identified between sleep/mental health and motor behaviour (p- omnibus: mode 1: 0.001, mode 2: 0.002), revealing two distinct association modes (Fig.1). The first mode showed higher grip strength and lower physical activity, which was positively associated with snoring, napping, and intermediate chronotype, and negatively associated with neuroticism, morning chronotype, and insomnia symptoms. The second mode highlighted higher self-reported physical activity and grip strength, associated with less depressive symptoms, less difficulties in awakening, and a tendency
toward morning chronotype. The same modes were not observed after removing age and sex effects. Initially, predictive analyses of the motor latent variable of both modes showed moderate links to GMV (mode 1: R2=0.17, mode 2: R2=0.18; Fig.2). However, the predictability of mode 1 substantially dropped after linearly adjusting features for age and sex in the predictive analysis (R2=0.04, r=0.19) or when adjusting the rCCA for age and sex (R2=0.02, r=0.15). A similar pattern was observed for mode 2.

**Conclusions:** We found two distinct motor latent phenotypes intricately associated with sleep/mental health and modestly linked to GMV variability. The first phenotype, characterised by increased strength but low physical activity, correlated with lower neuroticism and increased snoring/napping. The second, indicating higher self-reported physical activity was linked to better sleep health and reduced depressive symptoms. These findings highlight potential links between sleep/mental health with motor behaviour on multiple levels. They further underscore the importance of a thorough evaluation of age and sex-related effects and show potential of exploring psychologically and biologically informed phenotypes for brain-based predictive models.
Participants showed a significantly increased HBR response when evoked in NEAR, with respect to FAR (Fig 1), as shown in previous literature1,4. PRE-STIMULUS analysis showed a significant effect of POSITION, i.e. an overall lower cortical activity in PRE-STIMULUS_FAR with respect to PRE-STIMULUS_NEAR. Also, a significant POSITION * BA interaction indicated a greater activity in BA4 and 3 in PRE-STIMULUS_NEAR. In STIMULUS condition, significant effects of BA and HEMISPHERE were found, indicating greater activation of BA4 and 3, in particular in the left hemisphere, and a significant deactivation of BA44 in the NEAR with respect to the FAR condition (Fig 2).
Conclusions: Stimulus preparation varies according to arm position, particularly in somatosensory and motor areas, predisposing the system to an increased response, or conversely deactivating the system when a response is not required, in a “energy saving” mechanism when the stimulus is implicitly perceived as not risky. These areas remain active after stimulus reception, with no significant difference between positions. After the stimulus BA44, corresponding to the inferior frontal Gyrus, appears to be deactivated. BA44 has been associated with the judgement of the position of visual and somatosensory stimuli relative to their body midline, and also with risk assessment and aversion. At present it has not been possible to confirm the involvement of the VIP-PZ circuit in HBR modulation.

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Poster No 2059

Spontaneous in-scanner motion is related to a dopamine D2 receptor enriched cortical network
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Introduction: Spontaneous movement has become a topic of increasing interest, with it being linked to widespread neural activation patterns in rodents. A potential way to study this in humans is to look at spontaneous head motion in the MRI.
scanner whilst recording brain activity. The fact that motion affects the data being recorded makes this challenging as it may be difficult to disentangle artifactual activity changes from motion-related ones. To attempt to circumvent this problem, we took large motions as spontaneous events and then related event-related maps to distributions of dopamine D2 receptors. This receptor type was chosen as it has been previously linked to spontaneous motion production.

**Methods:** Resting-state BOLD fMRI data from the Human Connectome Project (100 unrelated participants) were used along with openly available PET maps of D1 (FLB457) and D2 (SCH23390) receptor distributions. D1 receptors were included as a control. Head motion from the fMRI scans was converted to discrete events by calculating framewise displacement, Z-scoring these values, and then binarising with a threshold of Z > 3. These events were then convolved with a double-gamma HRF and entered into a GLM analysis with the fMRI data to produce maps of brain regions associated with these motion events (Figure 1A). A spatial regression was then conducted between group activation maps and a model that included both D1 and D2 receptor densities.

![Figure 1A](image1.png)

**Figure 1 (A)** Head motion parameters were converted to a Z-scored framewise displacement time series. This was then turned into a binary event matrix and convolved with a HRF.

**Results:** A network of regions including motor cortex, supplementary motor areas, and the anterior insula were associated with spontaneous motion events (Figure 1B). The distribution of regions associated with such motion was positively related to D2 receptors ($b = 0.16, t = 8.85, p < 0.001$). This relationship was differentiable from D1 receptors ($F = 37.52, p = 1e-09$). To further illustrate the association between movement-related regions and others, we used the activation map as a mask to extract D2 receptor densities and compared these between active and inactive regions, finding a higher density in the former (Mann-Whitney $U = 11754421, p = 4.82e-59$; Figure 1C).

![Figure 1B](image2.png) ![Figure 1C](image3.png)

**Figure 1 (B)** Brain network associated with spontaneous motion initiation. **Figure 1 (C)** Relative D2 receptor density between regions active during spontaneous motion and those not.
Conclusions: We provide initial evidence that spontaneous head motion in the MRI scanner may be related to a specific network of brain regions and that this network displays an enrichment of dopamine D2 receptors. Given associations between head motion patterns and some dopamine-related disorders, this may indicate a potential analysis approach for investigating such conditions. However, given the potential confounds involved in the analysis, replication with other imaging modalities is required.

References

Poster No 2060
Reward-associated modulation of motor adaptation - An fMRI study
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Introduction: Adapting to delays in visual feedback of movements is an increasingly common phenomenon with the increased use of digital devices1. Reward prediction error (RPE) at the end of movement has been shown to impact motor adaptation2. Classical theories of motor control implicate the basal ganglia (BG) to specialize in reward-based learning and timing motor commands, and the cerebellum (Cb) in sensory prediction error (SPE)-based learning, and their feedback interacting only at the cortex (Ctx) level3,4. However, there is evidence supporting the involvement of Cb in reward processing and direct subcortical connections between these two structures5,6,7. Motor adaptation studies in humans mostly address this topic from a behavioural and electrophysiological perspective. These methods cannot test the interaction between sub-cortical structures and cortex during adaptation. Using a block-event mixed paradigm with a 3T fMRI protocol, we look for the BG-Cb-Ctx activity patterns associated with the effect of reward during temporal adaptation.

Methods: 20 healthy adults (10 females; mean age 25.5 ± 2.3 yrs) performed a task where they intercepted a target moving from right to left on the screen using ballistic movements with a joystick. Outcome feedback was manipulated to study RPE such that half of the successful trials were rewarded with an auditory-visual explosion of the target and visual feedback was perturbed to study for SPE by introducing a gradually increasing lag between the joystick position and its visual feedback (cursor). Three types of trials: rewarded (R+) and non-rewarded hits (R-) and misses (M), and two types of blocks: with or without delay (Baseline) were defined (Fig.1A). The entire task consisted of two rounds of baseline blocks followed by delay blocks (Fig.1B). Kinematic variables were calculated from the cursor coordinates using custom R scripts. Temporal head error (THE) was computed as the temporal difference between the centers of the target and the joystick crossing the interception zone (positive if joystick crossed the interception zone before the target, otherwise negative). Participants practiced the task and underwent imaging using T2*-w EPI and 3D T1-w MP2RAGE at 3T (Siemens Prisma). Images were preprocessed using Presurfer and the fMRiprep pipeline6. The onsets of R+, R- and M trials; Baseline and Delay blocks; and nuisance regressors for motion, WM and CSF signals were entered in a GLM design in participants' native space. The following contrasts were computed for each participant: R- vs M for differentiating success from failure, R+ vs R- for reward prediction, and R+ vs R- in delay vs baseline for the effect of reward in sensorimotor adaptation. These contrast maps were normalized to MNI space and used for their respective one-sample t-test 2nd level analysis with Nilearn. Group-level contrasts were visually inspected for differences in activation cluster peak locations.
Results: THE, RT and movement end time didn’t differ significantly between blocks, but RT and Movement end time show a moderate correlation with THE (Fig.1C). Cb cortex, Caudate (Cau) and putamen(Put) - involved in object identity and value association activate along with insula, cingulate cortex(CC), med. sup. frontal gyrus (FG) and amygdala distinguishing feedback of success from failure (Fig.2A). R+ trials elicit activity in the dentate nucleus, Cau, and pallidum activate with Sup. FG and sup. parietal lobule, CC and SMA- areas associated with perceiving reward and motor planning (Fig.2B). For reward and adaptation coupling (Fig.2C), activations in the Cb cortex, Put, PCu, SFG and MFG, dorsal posterior CC and pre-SMA suggest reward and adaptation feedback integration via the motor planning areas9.
Conclusions: In addition to the hypothesized sub-cortical BG-Cb co-activations, consistent involvement of the salience and central executive network regions indicates an increased cognitive dependence in successful coping with temporal adaptation. 

References

Poster No 2061
Neurocognitive effects of a single bout of aerobic exercise session on medial temporal lobe
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Introduction: Engagement in aerobic exercise and increasing cardiorespiratory fitness are promising methods for promoting hippocampal health in humans, with both the structure and the function of that brain area showing either increased volume or functional connectivity after long term aerobic exercise interventions. However, although there are studies focused on
exploring the acute effects of aerobic exercise on the hippocampus\textsuperscript{3,4}, the immediate neurocognitive response to a single bout of exercise and the subsequent changes and adaptations in hippocampal structure remain less understood. Thus, the objective of this study is to investigate the neurocognitive changes observed after a single bout of aerobic moderate-intensity exercise using resting state functional magnetic resonance (rs-fMRI), and measures of mood and memory in a sample of healthy young adults.

**Methods:** Participants 47 right-handed healthy young adults (27 females; age: mean=22.4, SD=3.3, range=18-29) participated in the study. All participants had a scaled score >7 on the matrix reasoning test from the WAIS-III. Experimental procedure flow Four different sessions: 1. Moderate-intensity exercise level determination for each participant: graded exercise test to exhaustion on a treadmill to assess cardiorespiratory fitness, measuring the maximal oxygen uptake (VO2max). 2. Exercise session and cognitive measures: 20 minutes of continuous running on a treadmill with a 1% incline at a speed corresponding to the 70% of VO2max, followed by a neuropsychological assessment including the Digit Span subtest of the Weschler Adult Intelligence Scale 4th edition, a computerized version of the original Corsi Block Tapping Test\textsuperscript{5}, and the Positive and Negative Affect Schedule (PANAS)\textsuperscript{6}, performed 10 min after the acute exercise. 3. Baseline MRI session: T1-weighted BRAVO anatomical image and resting-state sequence acquisition. 4. Post-exercise MRI session: moderate-intensity exercise + T1-weighted BRAVO anatomical image and resting-state fMRI acquisition, performed 18.84±3.85 minutes after exercise. Statistical analyses Independent Component Analysis was performed with a group spatial ICA by means of the GIFT toolbox in Matlab\textsuperscript{7}. Functional connectivity strength for each individual and each resting state network (RN) at two distinct time points were calculated. Then variations between MRI sessions were computed by means of a repeated measures ANOVA test in SPSS.

**Results:** Thirteen RNs were identified by means of the ICA analyses: Primary Visual Network, Medial Visual Network, Lateral Visual Network, Auditory Network, Sensory Network, Sensory Motor Network, Medial Temporal (MT, Figure 1), Network, Default Mode Network, Precuneus Network, Salience Network, Dorsal Attentional Network, Left Frontoparietal Network and Right Frontoparietal Network. Repeated-measures ANOVA including all these networks at baseline and after exercise revealed a significant decrease of the integrity only for the MT Network \([F(41)=6.51, p=.015]\) (see Figure 2). Spearman's correlations of the decrease of MT integrity and cognitive measures revealed significant correlations with the scores in the digit span test at baseline (rho=.38, p=.020) and with backward digit span (rho=.42, p=.010), forward Corsi span (rho=.38, p=.018) and positive affect dimension of the PANAS test (rho=.46, p=.008) after exercise.

![Figure 1: Medial Temporal (MT) network](image1)

![Figure 2: Medial Temporal FC pre- and post-acute exercise MRI sessions.](image2)

**Conclusions:** Our results showed a decrease in the functional integrity of the medial temporal (MT) network from pre- to post-acute exercise MRI sessions. Furthermore, this difference was positively correlated to the scores of cognitive and mood tests, reflecting a better memory performance and an enhanced positive mood after exercise in individuals with a small decrease
Brain mechanisms of self-recognition from kinematic cues

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Introduction: Recognizing an action as one’s own from those of others is a fundamental mechanism for self-awareness. Behavioral and neuroimaging studies have been conducted to understand the mechanisms underpinning this ability. Behaviorally, individuals exhibit the capacity to identify their hand movements by observing kinematic patterns. At the neural level, the observation of self-generated actions is associated with the activation of parietal and frontal regions. However, knowledge about the neural basis of explicit action recognition based on encoding kinematic features is scant. To advance on this issue, we investigated the brain mechanisms of distinguishing between one’s own and others’ movements in the absence of aesthetic or morphological features.

Methods: Fifty healthy participants (7 females; mean age±SD: 25.7±3.9) underwent two sessions (“10 days apart”). In the first session, participants’ right-hand kinematics were recorded while performing transitive and intransitive actions in a virtual reality setting. In the second session, participants were asked to observe 5-s video clips depicting their or others’ movements and press a button to select Self/Other while undergoing fMRI (4 runs, 6 mins each, total of 96 trials). Half of the videos were participants’ movements, the other half were distractors. Functional images were acquired with a 3T Siemens scanner (1.1sec TR, 30ms TE, voxel size: 2.4 x 2.4 x 2.4mm) and preprocessed using fMRIPrep. After a subject-level GLM, a 2x2 ANOVA was performed using participants’ responses (Perceived Self vs Perceived Other) and gesture category (Transitive vs Intransitive) as within-subject factors. Group maps were corrected for multiple comparisons using cluster-based correction (voxel-wise p<0.01, corrected p<0.05).

Results: Participants identified gestures significantly above chance (accuracy: 60.5% ± 7.4%; t(14)=5.5, p<0.001). Intransitive actions (64% ± 8%) were significantly more recognizable than transitive ones (57% ± 8%; t(14)= 3.6, p<0.01). The main effect of the response factor (Fig. 1) showed significantly greater activation for the videos categorized as “Perceived Other” in the left precentral gyrus extending to the postcentral gyrus (PostCG). The main effect of the gesture category (Fig. 2) showed the recruitment of the bilateral PostCG, right superior parietal lobule, and left superior temporal gyrus during the observation of transitive actions. Instead, intransitive actions elicited increased activity in the left supramarginal gyrus, right inferior frontal gyrus, and bilateral extrastriate visual areas. No significant clusters were found for the interaction effect between response and action categories.
Conclusions: We investigated the neural bases underlying the capacity to discern one’s own gestures solely based on kinematic features. Notably, intransitive actions were more easily recognized, likely because these movements are unconstrained by the objects and yet maintain a high social value (e.g., hand waving). fMRI results confirmed dissociable neural correlates of observing intransitive versus transitive actions. Interestingly, the contrast between ‘Perceived Self’ and ‘Perceived Other’ actions showed the engagement of the hand sensorimotor cortex during the elaboration of an action recognized as being performed by others. This finding is in agreement with simulation theories of action understanding (Jeannerod & Pacherie, 2004): kinematic cues may be used to predict the sensory consequences of self-generated or other-generated observed acts, thus contributing to a sense of agency (Dewey & Knoblich, 2016). In conclusion, our results show that the idiosyncrasies in the kinematics of self-generated actions, fundamental for the recognition of one’s own gesture, elicit the activation of action-related structures that participate in the distinction self/other.

References

Feasibility testing of a new paradigm to compare Decision-making in cognitive and motor domains

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Introduction: Every movement is a choice made under uncertainty. Recent studies suggest that motor control can be viewed through the lens of neuroeconomics. Motor Decision-Making (MDM) is extensively studied in healthy subjects. We suggested extending these principles to motor rehabilitation. The goal of the present study is to develop and test the feasibility of a new experimental paradigm for motor decision-making under risk. We aim to compare risk preferences in motor and cognitive domains in healthy participants to transfer this paradigm to the clinical population.

Methods: 20 young healthy participants (10 females, age: 24 ± 2.57) were enrolled in the study. The experiment comprised two parts conducted on the same day. Cognitive part: In the cognitive part, participants performed a series of 80 binary lottery choice questions. Each question presented a choice between a sure amount and a lottery where a bigger amount can be won with a specific probability (Fig. 1). Motor part: In the motor part, we used custom-made ‘Risk&Reach’ software (https://risk-n-reach.azurewebsites.net/) on the touch-screen interface when a participant has to make reaching movements with antigravitational support (Fig. 2). This part consisted of three phases: (1) individualization of the trial duration and the most distant goal position; (2) Three types of motor baselines; (3) individualized motor lotteries. All tasks in the motor part involved performing a movement with a dominant hand. After the individualization phase, participants performed three baseline tasks (160 trials each): (a) reaching towards a single goal, (b) reaching towards the same goal in the presence of an additional goal, (c) reaching towards the same goal associated with reward in the presence of an additional goal. For the motor lotteries, participants had to perform a series of 80 motor choices with probabilities and rewards corresponding to the choices in the cognitive part. To create such lotteries in the motor domain we employed a model-based approach, mapping the probability of successfully hitting a goal using the baseline (a) data. Similar to the cognitive part, in the motor domain participants were presented with a sequence of binary choices between a sure and a risky option (Fig. 2). A sure option implied performing a reaching movement towards a proximal motor goal with a 100% probability of hit, while a risky option implied making a reaching towards a distant goal with a less than 100% probability of hit. The position of the risky (distant) goal corresponded to the hit probability. Both risky and sure options were rewarded with points converted into valuable rewards. Analysis. We compared probabilities from three datasets (baselines a, b, and c) averaged within 8 target points. Model-predicted probabilities from baseline(a) were compared to observed probabilities in baselines (b) and (c). We used two-sided t-test with Bonferroni correction to account for multiple comparisons, and GLM model to investigate the effect of task type on motor performance characteristics.

Results: The presence of a reward significantly increased the probability of the distant goal being hit compared to the trials without a reward (p = 0.002) and compared to the predicted probabilities (p = 0.032). Our analysis indicated that participants chose risky options significantly more often in motor-based compared to cognitive lotteries (p = 0.001).
Conclusions: The presence of choice did not reveal any effect on the hit probability, however, the presence of reward significantly increased the probability of reaching the distant goal. Second, we observed that participants displayed more risk-taking behavior in the motor domain compared to the cognitive domain. Concluding, we showed the feasibility of the developed MDM paradigm for reaching movements to transfer it to patients with motor impairment.

References

Poster No 2064
TMS-based neurofeedback facilitates motor imagery of different hand actions
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Introduction: Non-invasive brain-computer interfaces (BCIs) allow the user to modulate brain activity patterns in a goal-directed manner¹². To date, most non-invasive BCIs can only decode gross movements while many essential daily-life activities require much finer finger and hand control³. We have developed a novel BCI using motor imagery (MI) and transcranial magnetic stimulation (TMS)-based neurofeedback (NF) training with the aim to reinforce representations of complex hand actions in the brain. In this proof-of-concept study, we aim to investigate the utility of such a new BCI for daily-life hand function training via MI.

Methods: We designed 2 experiments to investigate the effect of the TMS-based BCI on 3 hand actions (Figure 1). In experiment 1, the desired corticomotor excitability pattern was derived from the muscle-specific mean MEPs of 6 right-handed healthy adults (data not shown). NF was provided by displaying the target lines at 3 different heights (high, medium, low) with boundary boxes indicating the desired extent of corticomotor excitability. In experiment 2, we used a more adaptive ensemble-based support vector machine (SVM) learning approach. All motor execution (ME) data were used to train the first classifier and each block of MI data was used to train a new classifier in the ensemble. NF was provided based on the group decision of classifiers in the ensemble. To assess the participants’ performance as to data separability, an SVM classifier was used to decode target hand actions by normalized MEP amplitudes of 3 finger muscles for each block. Leave-one-trial-out cross-validation was used within blocks (“Cross-validation test”). Accuracy values for each fold were averaged for the block. To understand the relationship between ME and MI, the first classifier trained on ME data in each ensemble was tested on each MI block (“Cross-condition test”). Here we report data from 8 participants (age 24±3 years, 5 females) in Exp. 1 and preliminary data from 4 participants (age 32±5 years, 2 females) in Exp. 2.
Results: We first examined the ME data to understand whether the evoked MEPs in APB, FDI, and ADM allow us to discriminate 3 hand actions. The results showed 97±1 % (mean±SD) cross-validated classification accuracy for Exp. 1 and 84±2 % for Exp. 2. This indicates that healthy adults could generate comparable corticomotor excitability patterns within a hand action and distinguishable patterns between hand actions, suggesting that ME data could be used as “ground truth” for TMS-based NF training. We then probed the MI-NF data to understand whether participants could modulate their corticomotor excitability patterns with the provided feedback. For Exp. 1, the results showed 40±2% of cross-validated classification accuracy; whereas for Exp. 2, the accuracy was significantly increased to 57±6% (t10=-7.622, p<0.001). This supports that the adaptive approach worked better than the deterministic approach for training self-modulation of corticomotor excitability patterns of 3 finger muscles. In Exp. 2, we investigated the generalizability between ME and MI (Figure 2). The cross-condition findings suggested a progressive increase in median accuracy with training. We also inspected the unnormalized MEP amplitudes of ME and MI-noNF blocks for every participant. Most participants managed to regulate the muscle-specific MEP with 3 hand actions. With training, the muscle-specific MEP patterns of MI became more similar to those of ME. This demonstrates that NF training could promote the modulation of sensorimotor activities in the brain.
Conclusions: A novel, personalized, and adaptive MI and TMS-based NF training for complex hand actions was developed and tested. Our findings suggest that healthy adults could simultaneously and selectively modulate brain activities for multiple fingers with the guidance of NF. This demonstrates that TMS-based BCI could be used for hand function training in individuals that are not able to produce overt motor output.

References

Poster No 2065
M1-PMd connectivity modulation via fMRI-neurofeedback
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Introduction: Research shows that brain connectivity during resting state highly corresponds to connectivity during a task and may predict individual difference in behavioural performance (Cheng et al., 2018). Neurofeedback (NF) could serve as a mean to explore the connection between resting state connectivity, task-related connectivity, and task performance. Evidence shows greater M1-PMd connectivity is associated with superior performance in action selection (AS) (Stewart, Tran & Cramer, 2014). However, the causal relationship has not been thoroughly examined. Therefore, this study aimed to determine if M1-PMd connectivity could be modulated through covert fMRI-NF during rest, subsequently affecting cognitive-motor function.

Methods: 20 adults took part in this counterbalanced within-subject double-blind study. Participants were trained covertly with fMRI-NF in two separate conditions to increase and decrease M1-PMd connectivity. The NF training was conducted in a
30T MRI scanner, consisting of approx 24 min (3 runs of 7min + rest). The feedback signal was fed back via a thermometer bar. The height represented M1-PMd correlation difference between the previous 20 TRs during NF and the M1-PMd correlation during the rest blocks. As a covert training, participants were just instructed that the higher the bar was, the more money they would earn. The behavioural outcome of this study was measured by the action selection (AS) task, (O’Shea et al., 2007), which participants performed inside the MRI scanner before and after the NF. The monetary incentive delay task (Knutson, Westdorp, Kaiser & Hommer, 2000) was used to measure reward sensitivity (RS), as previously shown to be associated with NF performance (Hellrung et al., 2019).

Results: During the NF training (vs rest), activity was present in various regions of the sensorimotor cortex (SMA, the precentral gyrus & PMd), see Figure 1B. M1-PMd connectivity during the NF runs was analysed between conditions, using the extracted M1 and PMd timeseries. A repeated-measures ANOVA showed no main effect of condition (p=0.75), no main effect of run (p=0.42) and no condition*run interaction effect (F(2,36) = 0.40, p=0.68), see Figure 1A. An order effect was tested for. A mixed-methods ANOVA (between order, within condition) revealed a main effect of order (p=0.04), indicating that participants who started with the increase condition, overall decreased their connectivity more. Effects of NF training on AS performance were then investigated. For the increase condition, there was no difference in reaction time (RT) between before and after NF (Wilcoxon paired signed-rank test, Z=-1.09, p=0.28). However, in the decrease condition, participants were significantly faster after the NF training compared to before (Wilcoxon paired signed-rank test, Z=-2.18, p=0.03, see Figure A.). When testing for interaction effects (condition*time), no significant difference was found in RT change between the conditions (paired t-test, p=0.47). In terms of RS, a positive correlation between RS and the overall NF performance was found (Spearman correlation r=0.39, p=0.10, Figure 2A). This relationship was due to the significant correlation between RS and NF performance in the decrease condition only, with no relationship being found with performance in the increase condition (Spearman correlation decrease: r=-0.7, p=0.002; Spearman correlation increase: r=0.02, p=0.95, see Figure 2B).

Conclusions: Overall, participants did not manage to modulate their M1-PMd connectivity at rest using fMRI-NF, resulting in no changes in cognitive-motor function. The expected areas were however being modulated (sensorimotor system), indicating some level of successful implicit learning via the covert paradigm. This suggests more training could potentially lead to the desired effect. The link between reward sensitivity and NF performance gives strong evidence for a prediction tool of training success.

References

Poster No 2066

Effects of task performance on brain activity during a bilateral leg press task: An fMRI study

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Introduction: Recent advances in neuroimaging methods have helped to characterize brain activity associated with multi-joint lower extremity motor control. (Mehta et al., 2009; Jaeger et al., 2014; Noble, Eng and Boyd, 2014; Fontes et al., 2015) However, limited work has concurrently captured joint kinematics to determine how natural movement variability is associated with brain activity. (Anand et al., 2021; Slutsky-Ganesh et al., 2023) Thus, the purpose of this study was to isolate the neural correlates of lower extremity task performance using concurrent measures of brain activity and knee joint kinematics during a resisted bilateral leg press task.

Methods: Sixty-six (15.7±1.5years, 164.1±7.1cm, 64.1±11.7kg) right-leg dominant adolescent female athletes participated in the current study. Structural and functional (fMRI) neuroimaging data was obtained using a 48-channel head coil on a 3T GE Signa Premier scanner. fMRI data was acquired during a leg press task. (Slutsky-Ganesh et al., 2023) The leg press task engaged bilateral hip, knee, and ankle movement against elastic resistance bands (~9.1kg) and was performed as a block design (Figure 1). Number of cycles, knee sagittal (flexion/extension), and frontal (adduction/abduction) range of motion (ROM) were used as measures of task performance. Leg press cycle was defined as the sine wave between two consecutive peak knee flexion angles. ROM (sagittal and frontal) was the difference between minimum and maximum knee joint angle within each cycle and was averaged across the entire cycles to calculate a mean ROM value for each plane. All fMRI data analyses underwent standardized preprocessing steps, which included brain extraction, motion correction, slice timing correction, intensity normalization, spatial smoothing, and non-linear registration to standard space (MNI-152 2mm brain). After preprocessing, an independent component analysis for automatic removal of motion artifacts (ICA-AROMA) was used to denoise and reduce motion-induced signal variations (Pruim et al., 2015), and a high pass filter at 100 s was applied to the data. Subject-level analyses were performed with individualized cerebrospinal fluid and white matter regressors to prioritize the activation in the gray matter. Three separate group-level mixed-effect analyses were completed to investigate brain activity that was positively and/or negatively associated with demeaned number of cycles, sagittal and frontal ROM. In the group-level analyses, a gray matter voxelwise covariate was used as a covariate of no interest to control for variations in gray matter across subjects. Number of cycles was added as a covariate of no interest to control cycle variation for ROM analyses. A priori cluster-corrected significance threshold of z=3.1 and an alpha level of p =.05 were applied to all analyses.
Results: Greater mean knee sagittal ROM (26.4±11.7º) was positively associated with greater brain activity in the right lateral occipital cortex (z=4, p=.0004) (Figure 2). There were no significant relationships between brain activity and mean knee frontal ROM (3.3±2º) and number of cycles (73.5±5.1).

Conclusions: The current study identified a distinct cortical representation for knee sagittal ROM in the right lateral occipital cortex, which might be due to increased afferent information resulting from increased knee ROM. (Edin and Abbs, 1991; Jami, 1992; Strong et al., 2023) Brain activity appears to be influenced by natural task performance of sagittal plane ROM and may be less sensitive to identify the relationships with frontal plane ROM and number of cycles during the resisted bilateral leg press task in adolescent female athletes. Future studies should 1) compare in-scanner and functional task joint kinematics, such as the drop vertical jump, to better understand how in-scanner movement represents out of scanner movement and 2) correlate out of scanner functional movement to brain activity during the leg press task.

References

Poster No 2067
Non-primary Motor Cortical involvement in Reaching Behavior after Stroke: a TMS + MRI study
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Introduction: Motor impairments following a stroke cause decreased quality of life. Our overall goal is to improve motor function after stroke by combining neuromodulation and motor task practice. First, we must understand the neural mechanisms underlying voluntary arm movements, particularly reaching. It remains unclear how (or whether) non-primary motor areas that support reaching change their connections to M1 after stroke. Here, we investigate premotor and parietal connectivity during reaching by measuring resting state and task-related BOLD responses, and by disrupting these areas with transcranial magnetic stimulation (TMS) in patients with small subcortical strokes and in healthy participants. The results will provide the foundations for neuromodulatory strategies to maximize therapeutic outcomes.
Methods: Resting-state fMRI (rs-fMRI) and task-related fMRI (tr-fMRI) focused on functional connectivity among bilateral dorsal premotor cortex (PMd), ventral premotor cortex (PMv), posterior parietal cortex (PP) and primary motor cortex (M1). FMRI used 3T Siemens Prisma scanners with a repetition time (TR) = 0.8 seconds on 21 subjects. The rs-fMRI data was acquired over two 9-minute runs while the subjects kept their eyes open, and the tr-fMRI data was recorded while the subjects performed 60 trials of 10-second planning and hand-movement tasks, which in total take around 10 minutes. Preprocessing and statistical analysis were completed with FSL and SPM12 to estimate the functional connectivity among our regions of interest (ROIs). For rs-fMRI data, we utilized independent component analysis (ICA) and dual regression to explore the seed-based correlation and generate spatial maps at p < 0.001 statistical significance level. For tr-fMRI data, we developed generalized linear models (GLM) to extract the stimulus-induced signals and separated those signals based on events to create activation maps at a corrected cluster significance threshold of p = 0.05. Then we created dynamic causal models (DCM) to study the effective connectivity among the ROIs. For TMS experiments, participants performed planar forward and backward reaches with their right or impaired hand inside a robotic exoskeleton. We delivered triple-pulse 10 Hz TMS 100ms before the reaction time at 80% resting motor threshold (RMT), 120% RMT, and no stimulation over 7 locations: left and right PMd, PPC and the post-central midline (control).

Results: 18 normal participants and 5 stroke-affected individuals (all internal capsule stroke) have been studied. Resting State Connectivity: Analysis of normal participants showed expected correlations among non-primary motor areas (including PP) and M1. Stroke participants, in general, showed reduced connectivity, particularly between hemispheres. Task-based DCM: We focused on each region’s connection strength with M1. The method separated connectivity in different phases of the task: rest, plan, and move. The majority of significant connections were negative and in the rest phase. The stroke participants showed differences in connectivity as compared to the normal participants, and particularly in positive connections during the plan and move phases. But overall, the significance of the connections was low. TMS: In healthy controls, PMd stimulation contralateral to the hand increased the length of the total movement, endpoint error, and initial angle and shortened the distance traveled at the time of maximum velocity. The stroke group had variable outcomes. In two patients, stimulation at RPPC, RPMv, and LPMd perturbed right hand movements and increased the initial movement burst.

Conclusions: Connectivity measures were overall consistent between RS-fMRI, DCM, and TMS, although the DCM method was problematic in terms of statistical significance. TMS data demonstrate that the PMd to M1 connection remains effective even into the execution phase of reaching and it, and other connections, are altered after even small subcortical strokes.

References
Unique temporal profiles for planned and unplanned termination of movement in Parkinson’s Disease

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Introduction: Parkinson’s Disease (PD) is a common movement disorder affecting millions worldwide. Individuals with PD have been shown to exhibit impaired inhibitory control, at times, leading to impulsivity and error, especially in tasks that demand high cognitive effort. Experimentally, inhibitory control is often assessed using a standard stop task. In this task participants respond to a go signal with a button press. However, on a minority of trials the go signal is followed by another stimuli (a “stop signal”) indicating that participants should halt their initiated response. A challenge with the use of this task is that the cognitive process underlying the sudden need to inhibit a motor response is intertwined with the motor output itself. This complicates interpretation of behaviour and physiology during this task. To address this limitation, we have used a novel stop task called the continuous movement task (CMST), which assesses planned and unplanned inhibition of movement. Participants move a computer mouse during a countdown and halt the movement in response to a stop signal which occurs either at the end of the countdown or at an earlier, unpredictable, time. Here the process of suddenly having to inhibit a movement (unplanned stopping) can be directly compared with the planned stopping of movement - allowing a more clear isolation of the cognitive component. The goal of this study is to examine differences in planned and unplanned stopping as a measure of inhibitory control in PD.

Methods: The continuous movement stop task (CMST) was assessed in a cohort of 25 healthy age-matched controls and 26 individuals with PD during acquisition of electroencephalogram (EEG). Individuals with PD arrived OFF medication (12 hours of medication abstention) and completed the CMST. Participants then took their medication and CMST was performed again (all in the same day). For healthy controls, subjects performed the CMST while EEG was measured in the same way. The CMST consists of 80 planned and unplanned stop trials. In planned trials, subjects were required to move the cursor in a circular motion upon seeing the ‘Go’ cue, follow a countdown from 6-1, and stop moving the cursor when the ‘stop’ cue appeared on the computer screen. In unplanned trials, the ‘stop’ cue appeared at an unpredictable time before the countdown reached 1. The stop completion time (SCT) was assessed for both planned and unplanned trials, measured as the time from the appearance of the ‘stop’ cue to when the cursor movement came to a full stop. The go reaction time (GRT) was also measured as the time from the appearance of the ‘go’ cue to the initial movement of the cursor.

Results: Our findings demonstrate significant differences in SCT and GRT between groups, as revealed by paired t-tests. The SCT was significantly higher in unplanned than planned stop trials across all groups (p<0.01) (Figure 1). Additionally, individuals with PD, both OFF and ON medication, exhibited higher SCT compared to healthy controls in both planned and unplanned trials (p<0.05) (Figure 2). Conversely, the GRT was higher in individuals with PD OFF medication compared to those ON medication (p<0.05) and there was no difference between patients and controls. EEG findings are forthcoming.

Fig. 1. Stop completion time (SCT) between across healthy control and individuals with Parkinson’s Disease (ON and OFF medication state) for planned and unplanned trials
Stop completion time (SCT) between planned and unplanned trials in healthy control and individuals with Parkinson's Disease (ON and OFF medication state)

**Conclusions:** These results indicate that SCT in unplanned stopping is slower than planned stopping and that this effect is present regardless of disease or medication status. Additionally, people with PD took longer to stop compared to controls - but did not take longer to go - perhaps corresponding to a deficit in inhibition. Finally, there was no difference in stop completion time in patients ON versus OFF medication in spite of significant slowing in go reaction time in patients off medication.

**References**

**Poster No 2069**

**Exploring cerebral and cerebellar activities during hand and foot movements with 3T multi-band fMRI**

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**Introduction:** Over the past few decades, functional magnetic resonance imaging (fMRI) has been widely utilized to explore the cognitive functions of the human brain. Most of these studies have primarily focused on the cerebrum rather than the cerebellum. Recently, an increasing number of studies have shown that the cerebellum plays a crucial role in various aspects of cognitive processing, contributing to the fluidity and precision of mental processes. However, limited spatial resolution in 3T MRI has posed a significant challenge in cerebellar research. To address this issue, we used a multi-band MR pulse sequence, which achieves simultaneous multiple-slice acquisition by emitting several RF frequencies at the same time, thereby maximizing the utilization of limited MRI hardware resources to accelerate the image acquisition. In this study, we aimed to investigate the functional activations in the cerebellum using a left/right alternating movement task performed by both hand and foot at the spatial resolution of 1.66 x 1.66 x 2.5mm3.

**Methods:** We recruited twenty eight healthy volunteers, aged 18 to 60, who participated in finger tapping and foot pedaling tasks. During fMRI scanning, participants were instructed to push buttons using their left and right index fingers, as well as pedal using their feet, following the indicators flashing left and right alternately at 1 and 2 Hz within a 14-second interval. The scanning was performed in a 3.0T MR scanner (Discovery 750w, GE, Milwaukee, USA) with a 48-channel phase-array head coil in the Medical Imaging Division, China Medical University Hospital, Taichung, Taiwan. We used a multiple-slice acquisition technique to improve the spatial resolution of the fMRI images (1.66x1.66x2.5 mm3 compared to the typical 3x3x3 mm3 or 4x4x4 mm3 in regular fMRI) within 2-s TR. We used SPM12 for regular preprocessing, including slice-timing, realignment, spatial normalization, and spatial smoothing. For regression analysis, we further used MarsBaR to identify specific regions
of interest (ROIs) surviving the group analysis for finger tapping and foot pedaling tasks. Each ROI was defined by a 5x5x5 mm3 cube surrounding the selected ROIs. Mean beta values within these ROIs for each participant were then computed for subsequent regression analysis against reaction times. Due to the large amount of missing trials in the foot pedaling performance, we had to incorporate different statistical analysis strategies, including both block-design and event-related protocols, to analyze the fMRI data.

Results: The results showed that Event-related data analysis approaches exhibited a higher statistical significance compared to block-related one. Our results identified specific brain regions for finger tapping, encompassing right M1, left M1, cerebellar anterior lobe, and cerebellar posterior lobe, as well as for foot pedaling, involving cerebellar vermis and M1. ROI analysis further revealed a negative correlation between participants’ hand/foot movement reaction times and effect sizes, indicating significantly stronger BOLD signals with shorter reaction times.

Conclusions: These results indicated that multi-band MR imaging technology may provide the spatial resolution necessary to elucidate the functional activations in the cerebellum with a 3T MRI. This project was supported in part by the National Science and Technology Council, Taiwan (NSTC110-2511-H-A49 -012 -MY3 and NSTC110-2221-E-A49 -038).

References

**Poster No 2070**

**Ipsilateral premotor cortex complements complex finger movement in young but not in aging brains**

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Introduction: The human sensorimotor system is full of plasticity. The brain can recruit the sensorimotor cortices (dorsal premotor cortex [PMd], primary motor cortex [M1], primary somatosensory cortex [S1], and superior parietal cortex of Area 2) to control the ipsilateral hand. Ipsilateral sensorimotor activation can be seen when stroke patients (Lotze et al. 2006) and healthy older adults perform simple unimanual movement (Loibl et al. 2011) and even when healthy younger adults perform complex unimanual movement (Hutchinson et al. 2002). Although the clinical study suggests the importance of PMd for complementation of hand motor function among the ipsilateral cortices, it is unclear whether this is also the case in healthy younger and older adults. To address this question, we measured brain activity during simple and complex finger movements using functional magnetic resonance imaging (fMRI) in younger and older adults.

Methods: 31 healthy right-handed young adults (YA group: 22.1 ± 1.8 years, 22 males) and 48 older adults (OA group: 71.1 ± 4.3 years; 31 males) participated in this study. Motor tasks were 1-Hz button pressing with the right index finger (Simple task) and 0.8-Hz stick rotation requiring coordination between the right thumb, index, and middle fingers (Complex task). Brain activity was measured during both tasks using fMRI. Functional images were collected using T2*-weighted gradient echo-planar imaging (EPI) with a 3.0-Tesla MRI scanner (Trio Tim; SIEMENS, Germany) and a 32-channel array coil for each participant. We first identified task-related brain activity. Since we are particularly interested in the sensorimotor cortices (PMd, M1, S1, and Area 2), we defined each of these regions as region-of-interest (ROI) in both hemispheres, and examined activation and deactivation in each ROI. Next, we examined if the ipsilateral sensorimotor activity emerges in relation to motor performance (= maximum number of stick rotations in 10 seconds) which was evaluated outside the MR scanner. Finally, we examined brain regions that enhanced functional coupling with each contralateral seed region (PMd, M1, S1, and Area 2) during the complex task as compared to the simple task by conducting a generalized psychophysiological interaction analysis. We investigated these points both in younger and older adults to elucidate differences between them. The study protocol was approved by the NICT Ethics Committee and the MRI Safety Committee of the CiNet (no. 2003260010). We explained the details of the present study to all participants before the experiment, and they then provided written informed consent. The study was conducted according to the principles and guidelines of the Declaration of Helsinki (1975).

Results: In the YA group, the ipsilateral PMd, S1, Area 2 activated during the complex task, while the ipsilateral M1 remained deactivated as in the simple task. Ipsilateral PMd activity increased in individuals with poorer (less dexterous) performance (Figure 1). All of the contralateral seed regions consistently enhanced interhemispheric functional coupling with the ipsilateral PMd, which was just anterior to the ROI, during the complex task as compared to the simple task (Figure 2). In contrast, in
the OA group, all the ipsilateral cortices including the M1 activated during the complex task, but none of the cortical activity showed performance-related change. Increase in functional connectivity within the contralateral cortices rather than between-hemispheric connectivity was observed during the complex task as compared to the simple task (Figure 2).

![Figure 1](image1.png)

**Figure 1** Negative correlation between dexterity and brain activity in the YA group
(a) Ipsilateral brain regions in which activity was negatively correlated with the performance evaluated outside the MR scanner in YA group. This is superimposed on the horizontal section of $z = 60, 70$ of the MNI standard brain. (b) Across-participant correlation between the performance (maximum number of stick rotations in 10 seconds: horizontal axis) and brain activity (parameter estimates: vertical axis) in the PMd (left panel) and the S1/Area 2 (right panel) clusters. Ipsilateral PMd and S1/Area 2 activity increases in individuals with poor motor performance.

![Figure 2](image2.png)

**Figure 2** Differences in functional connectivity between YA and OA group
Brain regions (red) that enhanced functional coupling with each contralateral seed region (green: PMd, blue: M1, yellow: S1, and magenta: Area 2) during the complex task as compared to the simple task in both groups (extent threshold of $p < 0.05$ FWE corrected across the entire brain for a voxel-cluster image with an uncorrected voxel-wise threshold of $p < 0.005$). These are superimposed on the horizontal section of $z = 60$ of the MNI standard brain. Top row (a) represents the results from the YA group, and bottom row (b) represents those from the OA group. In YA group, the ipsilateral PMd, which was just anterior to the ipsilateral ROI (white section), consistently enhanced interhemispheric functional coupling with each of the contralateral sensorimotor cortices. In contrast, in OA group, increase in functional connectivity within the contralateral cortices rather than interhemispheric connectivity was observed.

**Conclusions:** The results suggest the importance of ipsilateral PMd and its complementary role of motor function when healthy young adults perform complex finger movement. Even though ipsilateral sensorimotor activation can be seen in older adults, the aging brain seems not to use this interhemispheric strategy to complement hand motor function.

**References**
**Single-trial anticipatory beta activity predicts the maintenance of efficient motor plans**

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**Introduction:** Originally considered an ‘idling rhythm’ associated with a mere lack of movement, pre-movement beta oscillations may instead carry critical information related to anticipation of forthcoming actions. They may reflect error prediction based on past movement outcomes and retention of efficient motor plans (Engel & Fries, 2010; Torrecillos et al., 2015). We tested this idea by recording participants’ oscillatory activity with magnetoencephalography (MEG) while manipulating trial-to-trial movement-execution errors in a non-ballistic, target-reaching task.

**Methods:** Seventeen healthy volunteers (mean age 46±13) performed 12 blocks of 50 consecutive trials of a reaching task with their right (dominant) hand, under normal (0°) or rotated visual feedback (25° or -30° rotation). Normal visual feedback is associated with small trajectory errors and high predictability of movement outcomes. Rotated feedback induces substantial errors, gradually decreasing as consecutive trials lead to a predictable mismatch between the expected and the actual feedback (Shadmehr et al., 2010). Participants’ brain activity was recorded via a 306-sensors MEG system (Megin Triux System). We explored whether pre-movement beta activity was influenced by (1) the error context (normal or rotated visual feedback), and (2) the error history across trials within the same block. For error history, we divided MEG data into Early and Late stages, as the association between predicted and actual outcomes is gradually refined across repetitions. We assessed statistical differences across conditions using a 2-by-2 non-parametric cluster-based statistics analysis (Maris & Oostenveld, 2007). Error context: Rotation vs No Rotation; Error History: Early vs. Late stage) across all 204 gradiometers, time points before movement onset (-2.5 to 0 s), and frequencies within the beta band (14-26 Hz). We used the Dynamical Imaging of Coherent Sources (DICS) approach to pinpoint possible significant sources of beta activity (Gross et al., 2001). Importantly, we then investigated if single-trial beta activity predicted the trial-by-trial motor outcomes (Shin et al., 2017; Fig. 1a). Specifically, we used an ARMAX (AutoRegressive, MovingAverage, Exogenous) model to predict the evolution of error amplitude across 50 trials, using beta activity as an exogenous predictor. We fixed the ARMAX architecture based on the coefficients obtained from the population for all rotation conditions. We then tested the model’s predictability through ‘leave-one-out’ cross-validation and Monte Carlo simulations (1000 repetitions; Fig. 1b).

![Image](image.png)

**Figure 1.** Single-trial analysis and results. a) Illustration displaying anticipatory beta activity averaged across trials (top time-frequency plot) and a subset of 9 trials. b) Example of the prediction for one participant (one rotation) of the ARMAX model obtained from the 17 participants across all rotation conditions. Points in red represent the participant’s motor-execution performance across 50 trials (Experimental Data); cyan lines represent the model’s prediction for each of 1000 Monte-Carlo simulations; the blue line is the average of those repetitions. c) Results of beta power contribution comparisons across all rotations (dependent t-test; ** corresponds to $p < 0.001$).
Results: We found an increase of pre-movement beta activity in the Late compared to the Early stage of the task (Main effect of Error History, p<0.001; Fig. 2). This increase was lower in the Rotation than in the No Rotation condition (Interaction: Error Context x Error History; p=0.014; Fig. 2). Source estimates revealed a network including the parietal cortices bilaterally, the left prefrontal cortex, and the right cerebellum (Fig. 2). Furthermore, the ARMAX (1,0,1) model showed that pre-movement beta amplitude could predict movement outcomes based on trial-by-trial errors across all 17 participants and rotations (normalized prediction mean square error – NPMSE for 0°: 0.31±0.6; 25°: 0.17±0.22; -30°: 0.26±0.13). The cross-validation revealed stronger beta contribution in blocks with higher predictability of motor outcomes (0° vs 25° rotation, p<0.001; 25° vs 30° rotation, p<0.001; Fig. 1c).

Conclusions: Our findings support the role of anticipatory beta activity in maintaining efficient motor plans, particularly in contexts with stable and low motor-execution errors (Engel & Fries, 2010; Torrecillos et al., 2015). These results provide novel insights into (1) the dynamics of this process, with changes of beta power predicting trial-by-trial motor execution outcomes and (2) the functional neuro-anatomical network supporting this anticipatory process that involves the cerebellum.

References

Poster No 2072

Neural substrates underlying the corrections for visuomotor errors
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Introduction: Rapid learning and acquisition of new motor skills require successful correction of errors. Using block-design functional magnetic resonance imaging (fMRI), a previous study (Diedrichsen et al., 2005) revealed human brain areas activated when the rotation of motion trajectory on a screen was introduced as a visuomotor error during a reaching task. However, the brain areas involved in the trial-by-trial correction of errors from preceding trials and the timing of these
corrective activities remain unclear. Using event-related fMRI, this study aimed to identify brain areas related to adaptive error correction during motor planning before actual movement and motor execution.

Methods: Forty-two healthy adults (14 women, 18–27 years old; one left-handed) participated in this study. They performed a reaching task using a manipulandum on a 3-T MRI scanner (Siemens Prisma) while in the supine position. During multiband fMRI scans, participants held the manipulandum arm with their right hand and manipulated a white cursor on a projected screen by moving the manipulandum with their right wrist. At the beginning of each trial, participants were required to maintain the cursor at the starting position for 2–5 s, after which a blue target appeared. The target turned red 2 s after the onset (i.e., Go cue), prompting participants to swiftly move the cursor to the target. Three trial conditions were adopted: visuomotor error (VE), no error (NE), and Catch. In the VE trials, the visual feedback (cursor trajectories) during reach movements was rotated rightward or leftward around the starting position as a visuomotor error. NE trials had no visuomotor errors, and the NE trials immediately following the VE trials were used as Catch trials. Given that corrections for errors introduced in previous trials would be induced in Catch trials but not in the other trials, we expected that brain areas involved in error corrections would show activation differences between Catch and other trial conditions. To test this, we conducted a univariate analysis using FSL FEAT (Woolrich et al., 2001) and PALM (Winkler et al., 2014) after preprocessing with fMRIPrep (Esteban et al., 2019). For group-level inference, we used a faster inference method (Winkler et al., 2016) with threshold-free cluster enhancement (Smith et al., 2009) and corrections for multiple contrasts (Alberton et al., 2020). We conducted inference for activations both after the target onset and after the Go cue onset, aiming to reveal whether error-corrective activities would be observed during action planning before the actual movement and/or during motor execution.

Results: Nine participants were excluded due to poor task performance, excessive head movement, or machine errors. The remaining thirty-three participants showed almost successful error-correcting behavior with most cursor trajectories in the Catch trials biased in the opposite directions to those in the preceding VE trials. After target onset, centro-parietal areas and the cerebellum were significantly activated in the Catch trials compared with VE and NE trials, while bilateral putamen showed greater activation in VE and NE trials than in Catch trials (P < 0.05, FWE-corrected). No significant differences in activation were observed between the VE and NE trials. After Go cue onset, broad cortical areas including the motor and parietal areas, the thalamus, and the cerebellum were more strongly activated in VE trials than in NE and Catch trials.

Conclusions: Activation differences were observed between Catch and the other two trial conditions in broad cortical areas, the cerebellum, and the putamen after target onset. Our findings indicate that these areas are likely involved in planning corrections for errors introduced in preceding VE trials, contributing to rapid motor skill acquisition through effective error correction.

References

Poster No 2073

Exploring the underlying mechanism of Autonomic Nervous Systems of impulsive action

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Introduction: Impulsive action is defined as the inability of an individual to withhold from making a certain response (Winstanley et al., 2006). While extensive physiological evidence has accumulated for impulsivity, inconsistent autonomic nervous system (ANS) results persist. For example, conflicting findings on excessive or insufficient activation of sympathetic nervous system (SNS) and impulsive behaviors contribute to ongoing discussions on ANS mechanisms (Aldrich et al., 2018; Peters et al., 2018). In addition, prior studies often measured ANS responses during task period. Few explored that in pre-task baseline and in post-task recovery periods. Thus our study aimed to examine the ANS mechanisms of impulse control through the SNS and parasympathetic nervous system (PNS). Specifically, we investigated cardiac pre-ejection period (PEP) in the...
SNS, indicative of cardiac contractility, and respiratory sinus arrhythmia (RSA) in the PNS, reflecting cardiac vagal control. The specific ANS measurements helped dissecting the mechanisms of impulsivity.

Methods: A total of 52 students at National Chengchi University, Taiwan (age: M = 21.48, SD = 1.46; 17 males and 35 females) participated in this study. The entire experiment included a sitting baseline period, a behavioral task period, and a sitting recovery period. The task used in the experiment was the Differential Reinforcement of Low-Rate Responding 20 seconds (DRL-20s), comprising 6 behavioral sessions. Participants initiated the task with a spacebar press after a ‘+’ prompt, responding to a yellow square. If the response interval exceeded 20 seconds, a green circle provided feedback; otherwise the screen remained unchanged. Reinforcement rules were learned through key presses. Behaviorally, the Efficiency Ratio (ER) was calculated, representing the number of key presses with IRT > 20s divided by the total key presses. Participants with an ER of 0% were defined as impulsive (I Group); others were non-impulsive (NI Group). The two-way ANOVAs with 2 Groups (Impulsive vs. Non-impulsive) as a between-subject variable and 8 Physiological stages (a baseline, six behavioral sessions, and a recovery period) as a within-subject variable were conducted to explore differences in PEP and RSA between I group and NI group across various stages.

Results: Behaviorally, 31 individuals were reinforced (NI Group: mean ER = 38.91%), while 21 individuals were not (I Group: mean ER = 0%). In PEP, after excluding participants with their values > 3 SDs, 49 individuals (30 non-impulsive, 19 impulsive) remained. A significant interaction \[F(7, 329) = 3.443, p = .001\] revealed stable SNS regulation for the NI group across all stages. In contrast, the I group exhibited significant PEP differences, with weakened SNS contribution as the experiment progressed. By the S5 stage, PEP was marginally significantly slower than in S1 \([p = .062]\), suggesting a decreasing SNS contribution for the I group. In RSA, after excluding participants with their values > 3 SDs, 44 individuals (26 non-impulsive, 18 impulsive) remained. A significant interaction \[F(7, 294) = 2.821, p = .007\] revealed the NI group’s gradual decreasing in RSA withdrawal as the experiment progressed, reflecting better behavioral adaptation. However, the I group showed no significant differences in RSA amplitude between the baseline, task, and recovery periods. That is, no improvement in PNS regulation for the I group.

Conclusions: Our results showed that the non-impulsive group had better ER, stable SNS contribution, with PNS adaptation. In contrast, the impulsive group displayed worse ER, decreasing SNS contribution, and lack of PNS adaptation in DRL learning. Our study implied that the inability to sustain SNS effort and the lack of PNS adaptation predicted impulsive behavior.

References
Sensorimotor representations of imagined finger movements are stable over time

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Introduction: Fingers are somatotopically organised in the human primary sensorimotor cortex (SM1), whereby neighbouring fingers are spatially represented in adjacent regions. Using functional MRI (fMRI), Kolanski et al. (2016) showed high intersubject variability in the location of these finger representations during executed movements. Yet, within participants, the fine-grained somatotopy was highly reproducible over time. Over the past years, research has shown that it is possible to activate finger maps in SM1 without overt motor execution or finger-specific sensory input, such as through observed touch (Kuehn et al., 2018), directing attention towards individual fingers (Puckett et al., 2017), and motor planning (Ariani et al., 2022). Moreover, in chronic tetraplegic patients and amputees, finger maps of the paralysed or amputated hand have been shown through attempted or phantom hand movements (Guan et al., 2022; Kikkert et al., 2016, 2021). While these findings show that top-down processes can activate sensorimotor finger representations, the stability of these somatotopic maps remains unexplored. Here, we used fMRI to first replicate the results of Kolanski et al. (2016) by demonstrating intra-subject stability of SM1 finger somatotopy over time using a motor execution task. Next, we aimed to extend these findings by exploring the intra-subject stability of top-down activated individual finger representations in SM1 using a motor imagery task.

Methods: Sixteen healthy right-handed participants (26.44 +/- 2.44 years; 8 female) underwent two identical fMRI sessions that were approximately 2 weeks apart (13.81 +/- 6.24 days; min = 7 days, max = 32 days). We used 3T fMRI (2.2 mm³ resolution) while participants performed a paced button press task or kinaesthetically imagined fingers movements with their right thumb, index, or little finger. We used similar procedures as in Kikkert et al. (2016, 2021) and Kolanski et al. (2016) to calculate the reproducibility over time of finger representations in the SM1 hand area activated through motor execution or motor imagery. For that, we minimally thresholded (Z > 2) the finger selective maps and calculated the DICE overlap coefficient (Dice, 1945) for each possible finger pairing across the first and second fMRI sessions. Additionally, we used a linear support vector machine to decode the moved or imagined finger based on the elicited brain activity patterns. To do so, we trained a classifier using the fMRI data of one session and tested it on the fMRI data of the other session.

Results: Our preliminary results demonstrated high intra-subject stability of sensorimotor representations of executed finger movements, replicating the findings of Kolanski et al. (2016). Dice coefficients showed highest reproducibility across sessions for maps of homologous fingers compared to neighbouring and non-neighbouring fingers (Fig. 1a). Importantly, sensorimotor representations of imagined finger movements exhibited a comparable pattern of reproducibility over time as that of executed movements. Our classification results showed that both executed and imagined individual finger movements could reliably be decoded across sessions in the SM1 hand area (Fig. 1b). This indicates that the voxel-wise activity patterns elicited by executed and imagined finger movements contain distinctive information for individual fingers which remains consistent over time.

Figure 1. Stability of neural finger representations in the primary sensorimotor cortex across two fMRI sessions. a) DICE overlap coefficient, separately for motor execution and motor imagery. A value of 0 indicates no overlap; a value of 1 indicates a perfect overlap of two representations. We grouped the finger pair-wise overlap of each finger representation of session 1 with each finger representation of session 2: same = overlap of the same fingers; neighbour = overlap of neighbouring finger pairs; non-neighbour = overlap of non-neighbouring finger pairs. Black dots indicate individual participant’s average for the condition. p-values refer to Bonferroni-corrected contrasts computed after conducting linear mixed effects models. b) Classification accuracy for motor execution and motor imagery. We trained a linear support vector machine on all data of one fMRI session and tested it on all data of the other session. Black dots show the mean cross-session classification accuracy per participant. To determine the significance of the mean classification accuracy across participants, we combined the 16 participants’ empirical p-values against chance level (dotted line) using Fisher’s method.
Conclusions: Our findings show that the fine-grained activity patterns and somatotopy of imagined finger movements are highly consistent across fMRI sessions, demonstrating that top-down activated finger representations are stable over time. Our results thereby provide validation for the use of fMRI tasks that activate finger representations in SM1 through top-down processes.

References

postcentral, middle frontal, superior temporal, insula, inferior parietal and cuneus regions, while other regions, such as lateral occipital, middle temporal and superior frontal regions showed negative peaks (Fig.1). Group average HRF estimation obtained in three parcels where beta bursts predicted the BOLD signal best are shown in Fig.2. Representative BOLD signal predictions obtained from one subject for the left precentral cortex is also shown in the same Figure. It suggested that beta bursts could obtain reliable prediction of HRF as well as the BOLD signal.

![Fig.1 Group-level averaged maps of estimation MSE and HRF peak. (A) The MSE between the estimated BOLD signal and observed BOLD signal in each region (after Z-Score Normalization). The lateral occipital region showed the lowest MSE regarding the whole cortex. (B) The peak of estimated HRF in each region (after Z-Score Normalization). The precentral, postcentral, middle frontal, superior temporal, insula, inferior parietal and cuneus regions showed positive peaks, while other regions showed negative peaks. Due to the similarity in results between the left and right hemispheres, only the results from the left were presented here.]

![Fig.2 Group averaged normalized HRF estimation obtained in the left precentral, left postcentral and left lateral occipital cortices. The red curve corresponds to the mean HRF curve across all subjects. The blue shaded area corresponds to the standard error. A representative BOLD prediction in the left precentral cortex obtained from one subject is shown in the lower panel.]

**Conclusions:** Beta bursts reflect the hemodynamic response, especially in the motor and visual regions. This study provides a deeper understanding of the mechanisms and relationships between hemodynamics and electrophysiology during the movement execution, indicating that beta bursts can be a biological indicator of hemodynamic dynamics.

**References**

ABSTRACTS


Poster No 2076
Corpus callosum biometry and visual(perceptual) functions in children with unilateral cerebral palsy
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Introduction: Besides motor problems, up to 60% of children with cerebral palsy (CP) present with visual (perceptual) impairments (Odding et al., 2006). The visual cortex is connected to the splenium, the posterior section of the corpus callosum (CC) (Wakana et al., 2004). Several studies showed that reduced CC length is related to worse visual (perceptual) functions in children born preterm and with developmental disorders (Eken et al., 1995; Kwinta et al., 2015). While previous findings (Maillieux et al., 2020; Weinstein et al., 2014) showed that children with unilateral CP (uCP) present with damage to the CC, little is known about the relation between CC biometry and visual outcomes in children with uCP. Hence, we investigate the relation between visual (perceptual) functions and CC biometry in children with uCP.

Methods: Visual (perceptual) functions were assessed in 38 children with uCP (age=11y17m±2y10m, 20 males) with the Freiburg Vision Test (FrACT) for visual acuity, the Titmus Stereo Fly circles subtest (Titmus) for stereocuity, the Test of Visual Perceptual Skills (TVPS-4) and the Beery-Buktenica Developmental test of Visual-Motor Integration (Beery-VMI) for visual perceptual and visuomotor functions, respectively. T1-weighted images were acquired (TE/TR/T1 4.2/9.1/760.3 ms, voxel size 0.9×0.9×0.9 mm3) using a 3.0-T scanner (Hercules, Philips Medical Systems). CC biometry (CC total length, splenium thickness; Figure 1) was measured manually according to Garel et al. (2011), using the midline sagittal T1 scan. Lesion aetiology was classified according to the MRI classification system (Himmelmann et al., 2021). To investigate the relation between visual (perceptual) outcomes and CC biometry, partial Spearman's rank correlations were computed with age and gestational age (GA) as covariates and corrected for multiple testing with a false discovery rate (FDR≤0.05). Backward multiple regression models (F≥100), including GA, birth weight, age, and lesion aetiology were used to study if CC biometry significantly predicted the outcome of the visual (perceptual) function assessments. Statistics were performed using IBM SPSS Statistics (Version 28.0.1).

Figure 1. Biometric parameters measured on the midsagittal T1 MRI scan on a storage system of the clinical workstation of the University Hospitals of Leuven (Belgium), according to Garel et al. (2011). (A) Measurement of the total length of the CC as the distance between the anterior aspect of the genu and the posterior aspect of the splenium. (B) Measurement of the thickness of the CC at the level of the splenium.
**Results:** Reduction of the CC total length showed the strongest correlations to worse visual (perceptual) outcomes (Table 1). Both reduced length of the total CC (rs=.62-.55, p.<.01) and splenium thickness (rs=.38-.43, p.<.05) were correlated with worse visual acuity, stereoeacuity, and lower scores of the TVPS-4 subtest form constancy. In the linear regression models, the CC total length explained 47% of the variance in visual acuity ($\beta$=.033, p.<.030; AdjR$^2$=.465, F(6,31)=6.350, p.<.001); 39% of the variance in stereoeacuity ($\beta$=.273, p.<.024; AdjR$^2$=.289, F(6,31)=4.919, p.<.001); 38% of the variance in the TVPS-4 visual discrimination ($\beta$=.173, p.<.001; AdjR$^2$=.380, F(6,31)=4.785, p.<.001); 22% of the variance in the TVPS-4 spatial relationships ($\beta$=.098, p.<.032; AdjR$^2$=.220, F(6,31)=2.735, p.<.030) for which lesion aetiology was also a significant predictor ($\beta$=.545, p.<.037); 40% of the variance in the TVPS-4 form constancy ($\beta$=.107, p.<.005; AdjR$^2$=.397, F(6,31)=5.068, p.<.001); 50% of the variance in the Beery-VMI visual perception ($\beta$=.94, p.<.010; AdjR$^2$=.504, F(6,31)=7.269, p.<.001) for which lesion aetiology ($\beta$=.523, p.<.010) and age ($\beta$=.178, p.<.001) were also significant predictors; and 35% of the variance in the Beery-VMI motor coordination ($\beta$=.086, p.<.026; AdjR$^2$=.350, F(6,31)=4.313, p.<.003) for which age was also a significant predictor ($\beta$=.137, p.<.010).

Conclusions: In children with uCP, both reduced CC total length and splenium thickness are related to worse visual (perceptual) functions. Our results suggest that CC biometry could serve as a potential biomarker for visual outcomes, indicating that children with uCP with a shorter total CC and splenium thickness should be followed up with visual testing. This could be also applied to young infants with uCP, in whom visual assessment might be challenging.

**References**
Cortical and subcortical proprioceptive contribution to oculomotor control in humans

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Introduction: Stretch receptors within the extraocular muscles convey information to the central nervous system about the rotation of the eyes. While precise control of limb position critically relies on proprioceptive feedback, a role for proprioception in controlling eye movements remains uncertain. To investigate whether the oculomotor network in the human brain responds to proprioceptive feedback, we acquired blood oxygen level dependent (BOLD) signal using ultra-high-field functional magnetic resonance imaging (7T fMRI), with a sequence optimized to focus on subcortical activation. Previous studies conducted at lower magnetic field strength (3T) identified bilateral activity in the central sulcus (area 3A) and premotor cortex. An unexpected finding was that the brainstem’s extraocular motor nuclei that move the left eye responded to proprioceptive stimulation of the right eye’s extraocular muscles. We aimed to replicate those findings.

Methods: Healthy adult volunteers (N=6) were asked to close their eyes and place their right index finger on the outer corner of their right eyelid. Following an auditory cue, they gently and briefly pushed the eyeball towards the nose, passively stretching the right lateral rectus muscle. Control conditions were designed to isolate motor and tactile task components. There were four conditions. Active: active eye movement; Passive: brief press (< 1 second) at the right corner of the right eye with their right index finger so that to gently move the eyeball. Touch: touch on the eyelid with their index finger, without moving the eyeball and Rest. Trials of each type were grouped in 25s blocks. Neural activity in response to eye proprioception was identified using the conjunction (Active – Rest) AND (Passive – Rest) masked exclusively with (Touch – Rest). The threshold for the conjunction was p<0.05 FDR-corrected for multiple comparisons, whereas for the exclusive mask it was more liberal (p<0.05, uncorrected). This contrast ruled out the confounding effects of finger movement or tactile stimulation on the eyelid. The task and the contrast were as described previously. All imaging was acquired using a 7T Magnetom Terra MRI scanner (Siemens, Erlangen, Germany) and single transmit, 32-channel receive radiofrequency head coil (Nova Medical Inc., Wilmington, MA, USA) with local ethical approval. Dielectric pads were used to improve the B1+ homogeneity with additional foam padding used to limit head movement. Functional data were acquired using a multi-band 2D echo-planar interleaved imaging (EPI) sequence with left to right phase-encoding and the following imaging parameters: 144 dynamics, resolution = 2 mm isotropic, 62 slices, field of view (FOV) = 192 x 192 x 124 mm, repetition time (TR) = 2500 ms, echo time (TE) = 17 ms, flip angle = 72°, multiband acceleration = 2. A short 2D-EPI scan (5 volumes) was acquired with the opposite phase encoding direction to correct for nonlinear geometric distortions. After standard preprocessing (slice timing, realignment, distortion correction, normalisation to MNI space and smoothing with FWHM= 2mm), data were analysed using a classic general linear model (3dDeconvolve in AFNI).

Results: The stretch of the right lateral rectus muscle was associated with suprathreshold activity not only in the somatosensory but also in the oculomotor network. In the brainstem we found a response to proprioceptive stimulation in the left abducens and left trigeminal nucleus which connect with the extraocular muscles of the left eye. This confirms previous findings at 3T3. We replicated the cortical activation identified previously² and found additional foci in (oculo)motor structures like cerebellum and supplementary eye fields (Figure 1-2).

Conclusions: This study confirms a proprioceptive coupling between the movement of the two eyes.

Figure 1. Subcortical activity in response to proprioceptive stimulation of the right lateral rectus muscle. Blue arrows: abducens nucleus; Purple arrows: spinal trigeminal nucleus.
Figure 2. Cortical activity. Blue arrows: Supplementary Eye Field; Orange arrows: Central Sulcus (Area 3a)/Postcentral Gyrus (Area 2); Green arrows: Frontal Eye Field.

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Poster No 2078
Interceptive sports exhibit stronger connectivity strength in the frontoparietal network during rest
Zai-Fu Yao

Introduction: Certain sports, such as badminton and table tennis, are considered “interceptive” and require athletes to have rapid response times and precise motor control, which can lead to unique brain network adaptations. These adaptations can manifest as altered neural network patterns, which can be observed using neuroimaging techniques. Previous studies have indicated that athletes have enhanced neural efficiency, but the relationship between years of training and alterations in resting-state networks (RSNs) has not been extensively studied. Therefore, the aim of this study is to investigate the resting-state brain networks of professional badminton and table tennis players and compare them to healthy controls to understand the neural basis of interceptive sports expertise. We hypothesize that athletes in interceptive sports have distinct resting-state network (RSN) patterns compared to healthy controls, due to their specialized training and sensory-motor demands. Specifically, we expect to see enhanced connectivity within the frontoparietal network, which has a crucial role in attentional processes and motor planning. This enhanced connectivity may be correlated with the athletes’ years of training, indicating a dose-response relationship between training duration and neural adaptations. Additionally, we anticipate distinct patterns in dorsal and ventral stream processing, aligning with the two-stream theory of visual processing. By examining these patterns, we hope to gain a deeper understanding of the neural basis of expertise in interceptive sports.

Methods: The study included 20 athletes, 10 males and 10 females, with an equal number of players from each sport, and 10 healthy individuals that matched the athletes. Resting-state functional MRI (fMRI) data was collected from all participants to analyze the brain networks involved in motor and visual processing. The initial analysis involved a whole-brain independent component analysis (ICA) used to identify resting-state networks. The ICA identified several resting-state networks, including the default mode network, the dorsal attention network, and the salience network. Subsequently, graph theoretical network metrics were employed to quantify network properties such as connectivity strength, efficiency, and modularity. The analysis
used the identified resting-state networks to investigate the topological organization of the brain networks. Effective connectivity, especially dynamic causal modeling, was used to investigate the interaction between different brain networks. The analysis utilized rs-fMRI data, which were collected and preprocessed using standard techniques such as motion correction, spatial smoothing, and normalization. The study focused specifically on the dorsal and ventral streams of visual processing. Network masks derived from brain atlases were used to isolate these streams and compare their connectivity patterns between athletes and controls. Finally, correlational analyses were conducted to determine the relationship between years of training and changes in network metrics.

**Results:** We observed enhanced connectivity in the frontoparietal network among the athlete group, potentially indicating a neural adaptation to the demands of interceptive sports. This would suggest that interceptive sports expertise is associated with enhanced cognitive control and visuospatial processing capabilities at rest. Differences in the dorsal and ventral stream connectivity also emerged, supporting the two-stream hypothesis in the context of sports expertise.

**Conclusions:** This study aims to elucidate the neural basis of expertise in interceptive sports. By examining resting-state fMRI data, we anticipate revealing significant differences in brain connectivity patterns between athletes and non-athletes, potentially contributing to our understanding of neural plasticity in response to specialized training.

**References**

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**Poster No 2079**

**Modularity of Brain Networks for Egocentric and Allocentric Memory-guided Reaching**

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**Introduction:** The brain can encode targets for reaching in egocentric and/or allocentric reference frames (Byrne and Crawford 2010). The differences in the cortical activation of these two representations has been described (Chen et al., 2014; Neggers et al., 2006). For example, Chen et al. (2014) identified egocentric directional selectivity in dorsal brain areas (the parieto-frontal cortex) versus landmark-centered directional selectivity in ventral brain areas (inferior temporal gyrus and inferior occipital gyrus) during a delayed reach task. However, differences in the functional organization of brain networks have not been studied.

**Methods:** Here, we performed a secondary analysis of the event-related fMRI task from Chen et al. (2014), to distinguish human brain networks involved in egocentric versus allocentric spatial representation of reach targets. Based on their previous univariate analysis we expected that the functional brain networks will differ, with increased hubness in ventral brain regions in the allocentric task. The paradigm consisted of three tasks with identical stimulus display but different instructions: egocentric reach (remember absolute target location), allocentric reach (remember target location relative to a visual landmark), and a nonspatial control, color report (report color of target). We performed a graph theoretical analysis on time series data recorded during the memory delay period, contrasting egocentric and allocentric data versus baseline and control. Network hubs, clustering coefficient, and efficiency of the networks were found. The community organization of the network into modules was determined using the Newman's spectral community detection approach (Newman, 2006) and the consensus partitioning of participant data. Dynamical measures of network connectivity, the synchrony and complexity, of network modules were quantified using the energy and Shannon entropy, respectively.

**Results:** Both the egocentric (Figure-1) and allocentric (Figure-2) brain networks showed increased functional segregation & integration, relative to control. In both tasks, there were no inferotemporal modules, rather the data were largely segregated into occipito-dorsal-parietal and & temporo-frontal networks modules, with similar organization in egocentric vs. allocentric trials. Contrary to expectations, the allocentric network demonstrated significantly stronger modularity in the occipito-dorsal-parietal module relative to the egocentric network, although it did demonstrate increased connectivity between modules as compared to the egocentric brain network. In addition, the allocentric network showed an increase in intramodular hubs (brain regions that were important for within module information transfer) and intermodular hubs (brain regions that were important for sharing information between modules) in the occipito-dorsal-parietal module. Lastly, for the allocentric network, there was increase in desynchronization and complexity in the occipito-dorsal-parietal module, relative to the egocentric network, indicating an increase in difficulty of information processing.
Conclusions: Our results demonstrate that rather than increased allocentric encoding of visual reach targets in the ventral stream, there is increased specialization in the interaction between early visual brain areas and dorsal parietal brain areas. This potentially demonstrates an importance of the dorsal parietal cortex in allocentric spatial encoding of visuomotor targets, through the integration visual information about task stimuli with object spatial information in the parietal cortex. Patients with allocentric spatial neglect similarly demonstrate an importance in the spatial encoding of objects in the parietal cortex. Specialization, however, is accompanied with integration and increased interaction with the temporo-frontal network, which likely facilitates the processing of instructions of using a landmark.

References
ABSTRACTS

Poster No 2080

Cybersickness Susceptibility: Preliminary fMRI Insights Informed by Psychological Metrics

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Introduction: Beneficial applications of immersive VR like VR medicine and education are constrained by cybersickness. Assessing overlapping psychological and neural susceptibility factors could provide novel solutions. We investigated this by combining psychological and neural measures in two studies: questionnaire-based Study 1 (S1), and fMRI-based Study 2 (S2). S1 explored psychological susceptibility measure(s). From these, we hypothesized significant differences between susceptible and resistant participants in cybersickness insula resting state (RS) functional connectivity (FC). S2 was a pilot study of those hypotheses.

Methods: S1: 71 participants (Age = 20-30) without VR/first person videogame experience (>2 hours/month) underwent a 30-min dynamic cybersickness induction. Induction used a first person cognitive task-integrated tunnel travel task², a HP Reverb G2 Omniece Edition headset and a side-to-side rotating chair (< 0.2Hz³). Susceptible participants scored >11 in the 0-20 Fast Motion Sickness Scale (FMS⁴); otherwise, they were resistant. We assessed psychological factors interoception (Multidimensional Assessment of Interoceptive Awareness 2 (MAIA2)⁵), state anxiety (Current Anxiety Level Measure⁶), trait anxiety, stress, depression (Depression, Anxiety and Stress Scale⁷), and VR immersion (iGroup Presence Questionnaire⁸) with a between-subjects t-test per measure. S2: 6 fMRI-experienced participants made up groups Susceptible (N = 3) and Resistant (N = 3). All completed 1) rest fMRI (10-min anatomical, 13-min eyes open RS), 2) cybersickness induction, and 3) cybersickness fMRI (13-min eyes open RS, 5-min anatomical). Induction was simplified into passive tunnel travel via Quest 2 headset without movement. Participants rated FMS for 20 minutes (Resistant) or until FMS>7 (Susceptible). Given the correlation between interoception and insula, we computed insular FC strength with Harvard-Oxford ROIs and produced General Linear Models with subjects random effects to assess group differences.

Results: S1: There were significant results for 4 MAIA2 categories: Not Worrying (t(49.04)=2.38, p=.021), Emotional Awareness (t(39.79)=-2.36, p=.023), and Noticing (t(54.33)=-2.23, p=.030). This indicates that, among factors like presence or trait anxiety, stress, or depression, only interoception significantly affects susceptibility. Based on this, we designed fMRI-based S2. S2: There were two significant right insula FC clusters (T(4)>8.61, k>15) (Figure 1). Cluster 1 was in the inferior temporal gyrus and temporal fusiform cortex (Centre(MNI): +44, -34, -16, size(3x3x3mm)=19, size pFWE=.081, size pFDR<.05, peak pFWE=1). Cluster 2 was in the right middle frontal gyrus and right precentral gyrus (Centre: +34, +10, -14, size(3x3x3mm)=31, size pFWE=.049, peak pFWE=1). These suggest susceptible participants’ right insula FC significantly decreased during cybersickness. There were three significant left insula FC clusters (T(4)>8.61, k>14) (Figure 2). Cluster 1 was in the right pre- and postcentral gyrus (Centre(MNI): +40, -20, +18, size(3x3x3mm)=34, size pFWE<.001, size pFDR<.01, peak pFWE=1). Cluster 2 was in the right frontal pole (Centre: +40, +52, +24, size(3x3x3mm)=16, size pFWE=.107, size pFDR=.016, peak pFWE=1). Cluster 3 was in the precuneus cortex (Centre: -62, -56, 14, size(3x3x3mm)=196, size pFWE=.022, peak pFWE=1). These suggest susceptible participants’ left insula FC significantly decreased during cybersickness.

Figure 1. Significant Clusters of Resting-State Functional Connectivity with Right Insula. Coloured voxels indicate areas of significantly decreased functional connectivity with the right insula (T(4)>8.61, k>15). Clusters were formed with thresholds: clusters-forming p < .001 voxel-level, and familywise corrected p-FDR < .05 cluster-size.
Conclusions: Informed by S1 findings, we designed S2. S1 showed interoception is a susceptibility factor, thus S2 hypothesized insula FC during cybersickness would differ significantly between groups. As predicted, susceptible participants' right insula showed decreased FC with visual processing, internal stimuli attention, and motion areas. Additionally, susceptible participants' left insula showed decreased FC with cognition, mental imagery, and symptom awareness areas. Larger studies could assess replicability.

References

Poster No 2081
Longitudinal changes in network connectivity in OCD are affected by reaction-action certainty
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Introduction: Obsessive Compulsive Disorder (OCD), typically emerges in youth, and symptom expression is known to change with age (Fernandez de la Cruz et al., 2013). OCD is characterized by the experience of intrusive thoughts or feelings (obsessions) and repetitive behaviors, typically motor responses (compulsions) enacted to relieve distress. These behaviors may impact patients’ ability to deal with relationships between perception, reaction and action (Friedman et al., 2017; Meram et al., 2021). Yet, little is known about how certainty in these relationships impact longitudinal changes in task-evoked connectomics. Here, we used a perception – reaction – action task (that relies on the motor system) to understand longitudinal connectomic changes in OCD youth. Participants were required to tap their fingers (“action”) in response to a
visual probe ("perception – reaction"). The uncertainty of the cycle was manipulated by varying the stimulus onset asynchrony (SOA) between successive presented stimuli, ranging from fixed SOA ("periodic", i.e. low uncertainty) to randomly varied SOA ("pseudo random", i.e. high uncertainty).

**Methods:** Thirteen OCD youth provided informed consent for fMRI (Siemens Verio 3T). Two conditions (unknown to participants) were used to manipulate uncertainty. During the low uncertainty, the probe was presented at periodic intervals (1s SOA). During high uncertainty, the probe was presented at pseudorandom intervals (SOA sampled from a distribution with a mean of 1s +- sd 0.5s, minimum SOA, 200 ms). Data were collected in each participant approximately 12 weeks apart (Time1, Time2). The fMRI data from both time points were preprocessed using conventional methods (SPM12). Connectomic analyses were conducted on time series extracted from 246 cerebral parcels (Fan et al., 2016)(30,135 unique pairs of regions). Undirected functional connectivity (uFC) based on zero-lag correlations was estimated under each experimental condition (low uncertainty and high uncertainty) from both time points before computing difference uFC matrices (Time2 – Time1). From the mean difference matrix across participants, the most significant (p<.01) difference scores from the distribution of the 30,135 values were identified.

**Results:** Figure 1 depicts longitudinal effects under each condition. Each chord signifies a significant longitudinal change in uFC (Blue: Decrease in uFC; Red: Increase in uFC). As seen, levels of certainty evoke a clear dissociation in longitudinal changes in uFC: Under low uncertainty there is a cross cerebral decrease in uFC with heavy representation of regions in the frontal, temporal and visual cortices, the medial temporal lobe and the thalamus. Conversely, under high uncertainty, there is a cross-cerebral increase in uFC, with heavy representation of motor regions (pre- and post-central gyrus) and the thalamus.

**Conclusions:** Certainty in the perception – action cycle is proposed to be related to predictive processing (Friston, 2019) that in turn evokes the flexible recruitment of brain network hierarchies (Muzik and Diwadkar, 2023). Low uncertainty in the perception – action evokes low predictive complexity, whereas high uncertainty evokes high predictive complexity. We suspect that the divergent longitudinal impact of these conditions on cross-cerebral coupling reflect distinct functional demands of each condition. Thus, over time, the OCD brain becomes less sensitive to predictive certainty (leading to a loss of cross-cerebral coupling). However, simultaneously the OCD brain becomes more sensitized by task complexity, leading to demand-mediated increases in cross-cerebral coupling. While these interpretations are highly speculative, they nevertheless are an attempt at recapitulating the compelling and dissociating impacts of perception – action certainty on longitudinal brain network profiles in OCD.
References

Poster No 2082
MIDMSL: A Densely-Sampled, Multimodal MRI Dataset of Motor Skill Learning
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Introduction: Neural plasticity induced by motor skill learning is characterized by a functional reorganization of the motor system1. This reorganization has been studied via functional MRI (fMRI), which is used to image task activation changes from learning, as well as resting-state fMRI, which is used to assess functional network changes not confounded by behavioral changes1. However, due to experimental design limitations, previous studies leave open questions of precisely where in the brain individuals exhibit plasticity and what the exact time course of this plasticity is. Specifically, these studies typically use group-averaged brain maps, obscuring individual variability in the functional architecture of the brain, which results in less reliable network estimates and lower sensitivity to detecting more precise brain features2. Additionally, these studies tend to sparsely sample post-training plasticity and exclusively study task activation or resting-state network changes. This limits their ability to capture the full trajectory of motor skill acquisition and the relationship between task activation changes and functional network changes, especially at different stages of learning when the mechanism of learning can differ1. To overcome these limitations, we present the Multimodal Imaging Dataset of Motor Skill Learning (MIDMSL) – a densely-sampled dataset aimed at developing more complete and precise brain maps of motor skill learning by leveraging advances in precision fMRI through collecting extensive amounts of data in single participants.

Methods: MIDMSL collects both task and resting-state fMRI data in single participants learning a novel, video game-like, visuomotor task (Figure 1) across repeated sessions over the course of 5 weeks. For twice a week each week, we collect 12 minutes of resting-state fMRI data and 30 minutes of task fMRI data per session. Complementing this data, we also collect T1-weighted and T2-weighted anatomical scans, fMRI data of a localizer task for each finger, and diffusion MRI data at different timepoints throughout the 5 weeks. This dataset will finalize acquisition with 10 scan sessions for 8 participants, and it will be released on OpenNeuro3. To demonstrate its use, we pilot analyses with one participant’s data for one session to develop a map of their brain activity throughout the task. Here, we preprocessed the data using fMRIPrep4 and ran univariate GLM analysis contrasting activity during task execution compared with rest using fitlins5. We also used the fMRI data from the localizer task to draw somatotopic maps of their index finger by contrasting activity for this finger compared with rest.
Results: Prior to scan sessions, we piloted our visuomotor task through behavioral studies acquired online (N = 10), which revealed improved motor performance across time within our experimental design (i.e., greater accuracy in more difficult levels over time). Next, using data from an example subject collected in the scanner, we show greater activation in regions in the dorsal visual stream, motor cortex, frontal regions, and cerebellum in response to the visuomotor task, compared with rest (Figure 2A). We also show a similar but more diffuse pattern of activity involving these regions for the localizer task specific to the index finger, compared with rest (Figure 2B).

Conclusions: In summary, we describe a dataset aimed at developing a more precise and complete map of neural plasticity induced by motor skill learning. In pilot analyses, we showed the recruitment of visuomotor regions involved in this task, as well as in a localizer task specific to the index finger. Such findings may be encouraging for future work to explore the integration of vision and motor systems throughout learning, as well as provide a basis for hypothesizing network changes occurring across sessions.

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Body ownership alterations emerge from proprioceptive impairment and frontoparietal network damage

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Introduction: The sense of body ownership refers to the feeling that our body belong to us and it plays a crucial role in our perception of our body’s position and movement. Alterations in the sense of ownership for the contralesional upper limb are relatively common in the acute phase after cerebral stroke, with patients experiencing difficulties in self-attributing the affected limb, visually perceived, or persistently denying ownership of it (i.e., somatoparaphrenia). Our understanding of the pathophysiological mechanisms underlying these alterations is still poor, limiting the development of effective neurorehabilitative approaches. Body ownership shares its neural substrate with multisensory integration processes and motor control. According to most accepted accounts, sensorimotor and multisensory integration deficits are key factors determining body ownership alterations in stroke patients; however experimental evidence supporting this view is scarce.

Methods: We used a virtual reality reaching task implementing a varying visuo-motor rotation, thus introducing a mismatch in visuo-proprioceptive cues about hand’s position during movement execution. We studied the weight attributed to the virtual hand in guiding reaching movements and used it as an implicit proxy of body ownership, which was also assessed by subjective ratings. We modelled body ownership as the product of an online Bayesian inference process, wherein the brain infers ownership over the virtual hand based on the degree of congruency between visual and proprioceptive inputs, influencing the extent of visual adjustments applied to reaching movements. We then performed network based lesion analysis in order to investigate the neural source of body ownership alterations in stroke patients.

Results: We found that stroke patients exhibit an increased tendency to perceive ownership for an incongruent virtual hand and to incorporate it into their motor planning when performing movements with the affected limb, compared to both the intact limb and to a group of age-matched healthy controls. Importantly, this tendency also correlated with diminished ownership for a congruent virtual hand, simulating patient’s actual limb. This constitutes novel, quantitative evidence that pathological alterations in subjective body experience affect visuo-proprioceptive sensorimotor loops underlying motor control. The Bayesian inference model effectively explained these alterations as stemming from proprioceptive deficits, reducing the ability to detect visuo-proprioceptive disparities. Finally, through the analysis of brain lesions, we further linked body ownership deficit to alterations in connectivity within the frontoparietal network, affecting connections between the intraparietal sulcus and the supramarginal gyrus with the premotor and dorsolateral prefrontal cortex. This indicates that, besides somatosensory deficits, alterations in body ownership and underlying sensorimotor loops may be attributed to a specific impairment in multisensory integration processes.

Conclusions: This paper provides, for the first time, a quantitative model explaining how somatosensory loss and multisensory integration deficits contribute to body ownership alterations in stroke patients. Moreover, it sheds light on the link between patients’ subjective bodily experience and closed-loop motor control. These findings have great relevance for neurorehabilitation: some of the current neurorehabilitation strategies (e.g., prism adaptation, mirror therapy) are based on the manipulation of multisensory feedback, but we have limited knowledge about how the interaction between sensory modalities during functional tasks might affect the efficacy of the intervention. Our framework may be used to predict the capability of a lesioned brain to process and combine multisensory information, supporting body ownership and motor control, and may allow adapting the neurorehabilitation strategy accordingly.
Fig. Results of the visuo-proprioceptive reaching task

Fig. Unisensory and multisensory contributions to body ownership alterations in stroke patients

References
Neural Dynamics During Visuomotor Adaptation in School-Age Children and Adults

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Introduction: Children and adults develop and acquire new movements through visuomotor adaptation, which involves constant updating of internal motor models. Previous studies in adults suggest that two processes mediate internal model updates: an early, attentive processing for rapid error reduction and a later, implicit stabilization1. Our recent behavioral study revealed distinct visuomotor adaptation patterns in younger children (6-8 years), older children (9-11 years), and adults2. Children consistently showed delayed movement compared to adults, and younger children showed slower initial learning with shallower curves compared to older children and adults. This suggests that the early processing stage relying on explicit movement strategies may not be fully mature before 9 years. Neural correlates of visuomotor adaptation development have not been fully understood. To fill this knowledge gap, we employed MEG to measure brain activity in children (6-11 years) and adults (22-40 years) during a child-friendly visuomotor adaptation task.

Methods: The task involved using a computer mouse to move a cartoon fish from a central starting point on a projection screen to a target that appeared randomly on the left or right side with equal frequency across a run. During baseline and de-adaptation, the fish moved in the same direction as the mouse. During adaptation and re-adaptation, visual feedback of the fish location was rotated 45° relative to the mouse direction, requiring corrective movements. There were 10 baseline, 60 adaptation, 30 de-adaptation, and 30 re-adaptation trials. MEG was recorded (306-channel MEG TRiUX) at a sampling rate of 1000 Hz. EOG, ECG, and five head position indicator coils were attached for monitoring eye movement, heartbeat, and continuous head movement. MEG data were preprocessed using spatiotemporal and extended signal-space separations, band-pass filtering (0.5–45 Hz), head movement compensation, and ICA-based artifact removal. Trial data were time-locked to target onset, and epochs were taken from 300 ms before to 1000 ms after onset. Digitized head position points were coregistered to the reconstructed scalp surface from each participant’s T1W structural MRI. MEG was source-localized to the reconstructed cortical surface using dSPM. Individual source activations mapped to the inflated cortical surface were extracted from parcellated cortical labels3 for visual, parietal, and frontal regions and compared between children and adults for latency and magnitude of the peak activity.

Results: In adults and children, peak MEG activity emerged faster during re-adaptation than initial adaptation, indicating an overall learning effect. Peak activity in motor and superior/inferior frontal areas, contralateral to the moving hand, was greater and emerged faster in adults than children, consistent with the behavioral pattern of faster movement onset in adults. Children showed greater and earlier peaks in visual areas than adults. Only adults showed pre-movement activity in motor regions at about 80 ms before target onset. Adults also demonstrated high correlations between movement onset and frontal peak MEG latency, implying a strong relationship between behavioral performance and neural processing speed.

Conclusions: Source-localized MEG allowed the exploration of neural correlates of visuomotor adaptation development. Faster and greater involvement in frontal regions, including the motor cortex, before and after the target onset may reflect increased motor preparation and attentive processing for internal model updating in adults. The enhanced processing in visual regions may be related to a reliance on the implicit component in children. Our results suggest that involvement of the frontal regions in visuomotor adaptation is not fully mature in children at this age, consistent with our behavioral findings. This study provides insight into how neural development underlies behavioral differences in visuomotor adaptation between children and adults.

References
Poster No 2085

Investigating full neuraxis correlates of hand dexterity

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Introduction: The execution of fine voluntary hand movement relies on contralateral cortical inputs to the ipsilateral ventral horn of the spinal cord. These motor functions can be disrupted in conditions related to cervical spinal cord injury. Brain functional MRI (fMRI) has been extensively used to reliably measure BOLD signal changes during a variety of motor tasks, resolving activations in regions including the primary and supplementary motor areas related to hand function1. However, due to the technical challenges of spinal cord fMRI, only a few studies have been able to identify BOLD signal changes in the spinal cord during motor activity2,3. Here, we aim to take advantage of the recent advancements in simultaneous brain and spinal cord fMRI4 to measure neural activity related to hand dexterity in healthy volunteers.

Methods: Ten right-handed healthy volunteers were enrolled in this study (Age = 40.3 ± 15.4, 6 females, 4 males) and completed 30 sequences of 15s right hand finger taps with an MRI-compatible 5-button response pad. Visual cues indicating when and which button to press were presented on a projector screen for three different dexterity levels: single-finger response 2nd digit only (low), single-finger response all digits sequential order (medium), single-finger response all digits random order (high)5. Functional images were collected with a combined brain-spinal cord EPI pulse sequence 4 with dynamic per slice shimming (3T GE SIGNA Premier scanner; 21-channel Head-Neck coil; TR=2.5s, TE=30ms, GRAPPA=2), including 30 brain slices (3.43x3.43x5.00mm) and 15 cervical spinal cord slices (1.25x1.25x5.00mm) centered at C5-C6 intervertebral disc. Axial and sagittal field maps were collected to calculate shimming parameters. Anatomical scans were acquired for the brain (T1-weighted 1.00x1.00x1.00mm) and spinal cord (T2-weighted 0.70x0.50x0.50mm). Brain and spinal cord functional data were preprocessed with similar pipelines using FSL6 and the Spinal Cord Toolbox7, respectively: motion correction, high pass filtering, physiological noise correction, white matter and cerebrospinal fluid regression, spatial normalization, spatial smoothing. Subject-level task activity maps were obtained using a general linear model and entered into a group level single-sample t-tests.

Results: Brain activity was identified in primary and supplementary motor cortex, primary somatosensory cortex, primary visual cortex, superior parietal lobule, thalamus, and cerebellum, and BOLD signal changes in these regions increased linearly with task dexterity levels. Interestingly, the activity became more bilateral with increasing dexterity (Z > 3.1, cluster corrected p < 0.05, mixed effects analysis, Figure 1). Spinal cord activity was identified in the ipsilateral side of the C6 spinal cord segment. Increase in dexterity levels was linearly associated with higher ipsilateral and medial spinal cord activity. Interestingly, higher dexterity levels were associated with larger clusters that expanded beyond the ventral horn (Z > 1.6, uncorrected, fixed effects analysis, Figure 2).

Figure 1. Brain activity in healthy volunteers during three levels of dexterity in a finger tapping task (N=30, Z > 3.1, cluster corrected for p < 0.05).
Conclusions: We identified that activity in cortical and subcortical brain regions related to motor functions increases linearly with higher dexterity levels. The increase in task difficulty was also associated with activity in cortical areas related to higher cognitive-attentional processes. We also show significant ipsilateral spinal cord activity during finger tapping, that increases linearly with the task dexterity. The protocol developed in the present study may be used for the characterization of the full neuraxis in patients with upper limb motor dysfunction due to spinal cord or nerve root injury.

References

Multivariate association between risk factors for non-communicable diseases and cortical thickness

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Introduction: Non-communicable diseases and brain health have a common set of risk factors, including unhealthy diet, hypertension, smoking, excessive alcohol drinking and physical inactivity. A biomarker used to study brain health is cortical thickness (CT). Studies linking risk factors to CT have mostly used univariate/bivariate approaches and yielded inconsistent results1-3. Moreover, bivariate/univariate approaches provide a partial view of such association, while multivariate approaches can link a wide set of risk factors to whole-brain CT. In addition, to gain a comprehensive understanding of the underlying neurobiology, multiple brain features should be analyzed, such as brain function and neurotransmitter systems. Finally, there is a male bias in biomedicine, and consequently findings might not generalize to women. Hence, gender/sex-specific analyses are needed.

Methods: We analyzed women (n=3685, 46-81 years) and age-matched men (n=3685; 46-81 years) from UK Biobank, without self-reported non-cancer illnesses. Risk factors included 70 variables, spanning body size and metabolism, physical activity, sleep, diet, smoking and alcohol consumption, among others. CT was parceled in 148 cortical parcels (Destrieux atlas).
We used a multivariate method (regularized canonical correlation analysis, RCCA) to find risk factors that correlated to CT (i.e., latent dimensions)\(^4\)\(^5\). The RCCA was embedded in a multiple-holdouts machine learning framework to optimize the generalizability and stability of the latent dimensions. We used two consecutive splits of the dataset\(^4\)\(^6\): 5 outer splits (model evaluation and statistical testing with 1000 permutations), each with 5 inner splits (hyperparameter optimisation with out-of-sample generalisability criteria). We used raw (absolute), proportional, and corrected (regressing out brain size) measures of CT. We ran 6 independent RCCAs (one per sex/gender and CT measure) and compared the loadings with Pearson's correlation and spin test\(^7\). Finally, we compared the brain loadings with an extensive set of brain features\(^8\) including functional and neurotransmitter patterns.

**Results:** We found one latent dimension linking inter-individual variability in risk factors to inter-individual variability in raw CT (Fig. 1-2) (women range=0.25-0.31, p=0.005-0.005; men range=0.28-0.32, p=0.005-0.005). Of note, this latent dimension was similar across sexes/genders, and across CT measures, on both risk factors loadings (r>0.96, p<0.001) and brain loadings (r>0.90, p<0.001). This dimension captured variability in sedentarism/physical activity, as well as body morphology and metabolism. The CT variability captured by the latent dimension described an axis from insula and anterior cingulate cortex to occipital lobe and superior parietal areas. Interestingly, this brain pattern was associated with binding potentials of neurotransmitter receptors 5-HT1a (r>0.55, p<0.001), D2 (r>0.53, p<0.001) and VACHT (r>0.50, p<0.001), as well as transporter DAT (r>0.48, p<0.001, except for men-raw CT).

**Conclusions:** metabolism to CT variability ranging from insula and anterior cingulate cortex to occipital and parietal areas. These results highlight the adipose-tissue-brain axis that has gained attention recently. In addition, our results indicated that the cortical structural pattern related to risk factors was associated with serotoninergic, dopaminergic, and cholinergic systems. Interestingly, these molecular systems have been linked to phenotypes associated to body morphometry and activation, such as physical activity, satiation, feeding behavior, obesity, or anorexia nervosa\(^9\)\(^10\). Hence, this work suggests that cortical structure related to these neurotransmitter systems may be associated with risk factors for non-communicable diseases, highlighting the multivariate and multi-level association between brain and body phenotypes.
References

Poster No 2087
The Microbiota-Gut-Brain Axis in Depression: Neuroimaging and Microbial Composition Analysis
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Introduction: Major Depressive Disorder (MDD) is a prevalent mental disorder marked by persistent low mood, loss of pleasure, and other symptoms1. Globally, 3%-4% of the population experiences depression, with up to 50% of suicides linked to it, imposing a significant economic burden2. Despite genetic and environmental factors contributing to MDD, about one-third of MDD patients show no improvement with antidepressant treatment, indicating the complexity of neurobiological mechanisms. Previous studies suggest the gut microbiota regulates the central nervous system, impacting psychiatric disorders through immune, endocrine, and neural pathways3-5. Dysfunction in the gut-brain axis is a pathophysiological aspect of psychiatric disorders. This study aims to explore disrupted gut microbiota in MDD, providing insights into the “microbiota-gut-brain axis” mechanism(Figure 1). Neuroimaging studies reveal reduced neuronal expression in brain regions in MDD6-8. fALFF (fractional amplitude of low-frequency fluctuations) is a technique used in resting-state functional MRI (rs-fMRI) to measure the blood oxygen level-dependent (BOLD) signal amplitude in the human brain, reflecting the spontaneous functional activity of the central nervous system. Symptom scores from the 17-item Hamilton Depression Rating Scale (HAM-D-17) and the 14-item Hamilton Anxiety Rating Scale (HAMA-14) were used in this study. This study, utilizing fALFF in resting-state functional MRI, observes changes in the gut microbiota in MDD patients, analyzing correlations between bacterial species, clinical scales, and brain regions. The study offers preliminary insights into the “microbiota-gut-brain axis” mechanism of depression, laying the foundation for future systematic exploration.

Methods: Thirty-nine healthy controls (HC) and sixty-four MDD subjects participated, collecting mid-stool samples. Samples were stored at -80\(^\circ\)C after processing. Sequencing raw data underwent quality control using fastp software, and DNA content was assessed using the Qubit platform. Imaging used a Magneton Skyra 3.0 T MRI scanner. BOLD imaging parameters...
Results: No differences in demographics between groups (P > 0.05). MDD group showed significantly higher HAMD-17 and HAMA-14 scores than HC (P < 0.05). The composition of the gut microbiota showed significant differences. Brain imaging revealed increased fALFF in the right inferior temporal gyrus (ITG_R) (t=3.792, P < 0.005) and decreased fALFF in the left nucleus accumbens (NAcc_L) (t=-3.715, P < 0.005) in MDD. Positive associations were found between Anaerostipes_rhamnosivorans abundance and HAMD-17 (r=0.38, P < 0.01). ITG_R showed a positive correlation with Clostridium_disporicum (r=0.246, P=0.013), while NAcc_L exhibited positive correlations with Holdemanella_biformis and Alistipes_sp (r=0.292, P=0.003; r=0.307, P=0.002). NAcc_L showed a negative correlation with Parabacteroides_sp (r=-0.252, P=0.011). (Figure 2)

Conclusions: These findings demonstrate that the gut microbiota structure is altered in MDD patients. Differential bacterial species correlate with clinical indicators and exhibit correlations with brain regions associated with emotion, attention, and sensory processing. Therefore, MDD is associated with disrupted gut microbiota, and there is involvement of the “microbiota-gut-brain axis” mechanism in individuals with depressive symptoms. This provides a new perspective for early prevention and treatment. (ClinicalTrials: ChiCTR2000059591).

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Figure 1: Pathways involved in bidirectional communication between gut microbiota and brain.

Figure 2: Correlation matrix.
Note: * indicates that P < 0.0167 is correlated, and the value indicates the r value.
Novel functional network-level glymphatic clearance associated with network connectivity in human

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Introduction: How brain extraordinary activity coordinates its complex clearance system is a fundamental question in systems neuroscience (Yeo BT et al., 2011; Mollon JD et al., 2022). Serving a role in waste clearance, glymphatic system is critical to brain health and cognitive performance (Hablitz LM et al., 2021). But how it relates with functional network within cortical regions remains elusive. Moreover, non-invasive regional assessment for glymphatic system is lacking (Kamagata K et al., 2021). Therefore, we aimed to unravel the characteristics of network-level glymphatic function and validate a potential regional assessment (i.e., free-water) for glymphatic clearance. We further explore whether network-level glymphatic clearance was integrated with network connectome.

Methods: This retrospective study included two prospective 3.0-T MRI cohorts. In Cohort 1, serial T1-weighted imaging was performed in participants before and at multiple timepoints after intrathecal injection of contrast. Cortical networks were defined based on 400-parcel Schaefer atlas (Schaefer400). Network-based glymphatic characteristics included 1) glymphatic clearance function, signal percentage change from baseline to 39 hours, and 2) glymphatic heterogeneity, the standard deviation of 39 hours percentage change within each network. Considering the disease effect, we compared glymphatic dynamics across three subgroups (i.e., neurodegenerative, peripheral neuropathy, and encephalitis). Gene set enrichment analysis was conducted to investigate the transcriptomic profile of 30 brain cell-types related with glymphatic clearance using Allen Human Brain Atlas. We further analyzed the relationship of glymphatic clearance characteristics with aging and sleep quality. Network free-water was estimated by a bi-tensor model based on DTI. In Cohort 2, participants with cerebral small vessel disease (CSVD) underwent multi-modal MRI were enrolled. Structural and functional connectomes were constructed based on DTI and functional MRI after preprocessing, respectively. To validate the main findings with Schaefer400, we also used another functionally-defined atlas, Craddock atlas with 450 clusters (CC450). False Discovery Rate (FDR) was used to correct for multiple comparisons.

Results: In Cohort 1, 84 participants were enrolled (50% female; mean age, 58 years ± 14 [SD]). Glymphatic clearance function was both region- and network-specific. Spatially, a stable glymphatic dynamics pattern was recognized even under different disease. In regions exhibiting better glymphatic clearance competence, genes related to astrocytes, endothelial cells, pericytes and two types of excitative cells were significantly enriched. Impaired network-level glymphatic function among all networks was associated with ageing and sleep disturbance, while increased network-level heterogeneity only associated with ageing. Network-level free-water positively associated with glymphatic clearance function across all networks. In Cohort 2, 557 participants were enrolled (49% female; mean age, 62 years ± 9 [SD]). Network-level free-water was negatively correlated with intra-network structural and functional connectivity. The above main results were also replicated on CC450 atlas in sensitivity analysis.
Figure 1. Regional glymphatic dynamics and its underlying gene set enrichment analysis of cell types. (A) Glymphatic signal percentage change at 4.5 h, 15 h, and 39 h across cortex based on 400-parcel Schaeffer atlas. (B) Seven networks defined by Schaeffer atlas. (C) Line graph of 4.5 h, 15 h, and 39 h signal percentage change for each network. Dot represents mean, and bar represents standard deviation. (D) Glymphatic signal percentage change at 39 h across cortex in subgroup of peripheral neuropathy disease (PN, n = 38), neurodegenerative disease (NGD, n = 19), and encephalitis (ENC, n = 16) from top to bottom. (E) Gene set enrichment analysis of different cell types associated with glymphatic clearance pattern. The solid green line denotes the running enrichment score along the ordered gene list, which increases when a gene is included in the gene set of interest and decreases when a gene is not included. The vertical lines in the middle display the locations at which the members of the gene set appear in the ordered gene list. The shaded curve at the bottom denotes the value of the ranking metric (i.e., Spearman correlation coefficient of each gene) for the genes in the ordered gene list. The enrichment score captures the degree to which the gene set is over-represented at the top or bottom of the ordered gene list, which is defined as the maximum deviation from zero of the running enrichment score. The normalized enrichment score (NES) is derived from comparing with those estimated from permutation tests (n = 10,000) with significance estimation (Pval). FDR indicates false discovery ratio corrected p value. ***, p < .001. L, left; R, right.
Conclusions: Our understanding about how glymphatic system contributes to brain homeostasis is evolving. Here, by using Glymphatic MRI, we provide network-based glymphatic features with its genetic underpinnings in human. Network-level free-water, consistent with its glymphatic clearance function, provides a promising tool for future investigations, and was proved to be relevant with network connectivity properties in a large cohort of CSVD participants. Our findings open a novel perspective to investigate network-based clearance function and further highlight a necessity for studies on interplay among glymphatic system, neuronal demand, and network integrity.

References
Quantitative Perfusion and Permeability in Brain Tumors Before and After Laser Treatment

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**Introduction:** Drug delivery to brain tumors is difficult due to the low permeability of the blood brain barrier (BBB) and highly variable permeability of leaky blood vessels in the tumor\(^1\). However, laser interstitial thermal therapy (LITT) has the capability to increase permeability in regions adjacent to the LITT ablated tumor and decrease permeability of the tumor itself, facilitating drug delivery while inhibiting leakage\(^2\). Quantitative values of perfusion (capillary-level blood flow in ml/min) and permeability (min-1) are necessary to determine the exact amount of low molecular weight molecules that can be delivered to the tumor site. Two promising imaging techniques to accomplish this are dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) and dynamic susceptibility magnetic resonance imaging (DSC-MRI) respectively. This study presents a clinical application of quantitative perfusion and permeability mapping in tumor sites before and after LITT.

**Methods:** Five consecutive patients with brain tumors were consented and underwent a preoperative MRI scan on a Philips Achieva 3T MRI scanner. In addition to anatomical reference scans, contrast enhanced DCE and DSC acquisitions were performed for the purposes of research. All image processing and analysis was done using software written “in-house” with MATLAB 2023b. One patient had two distinct tumors that underwent treatment, resulting in 6 cases in total. Within 24 hours of the preoperative scan, the patients were treated with LITT at the tumor site. Immediately after the LITT procedure, a postoperative scan was performed. The preoperative scans and some postoperative scans consisted of an echo planar imaging Look-Locker (EPI-LL) sequence for T1 mapping, then a Gadolinium based contrast agent (GBCA) was injected. The permeability of GBCA was imaged with gradient echo DCE-MRI (series of T1 weighted images) with variable flip angles for T1 mapping. A second injection of GBCA was performed followed by DSC-MRI (series of T2* weighted images) to measure perfusion of the GBCA. Following the DSC-MRI sequence, another EPI-LL was performed for T1 mapping post injection. A contrast enhanced anatomical T1 weighted image was also acquired. Quantitative cerebral blood flow (qCBF) was calculated from the DSC-MRI scan by first converting signal intensity to contrast agent concentration and deconvolving the signal with the arterial input function (AIF). The AIF was chosen automatically to reduce operator error and streamline post processing of the perfusion data. However, this calculation is very sensitive to errors in the AIF. Thus, a correction factor was implemented based on an AIF-independent steady state measurement of cerebral blood volume\(^3\). To obtain quantitative permeability from the DCE images, the transfer coefficient Ktrans was derived from compartmental analysis using the Patlak model\(^4\).

**Results:** A decrease in the permeability of the tumor was noted in all 6 cases after LITT with an average decrease of 0.66 min-1 (-58%). Patient 6 exhibited two tumors and at the time of this study, one was treated with LITT while the other was left untreated (Representative case Figure 1). The tumor treated with LITT showed a significant decrease in permeability of 0.80 min-1 (-44%) while the untreated tumor showed a decrease in permeability of 0.04 min-1 (-4%). Perfusion before and after LITT appeared to have no significant change.

Fig. Untreated brain tumor (top row) shows no significant change in permeability while LITT ablated tumor (bottom row) shows significant change in permeability (-44%)
Conclusions: A significant decrease in the permeability of brain tumors was observed and with quantitative values of perfusion and permeability. This new protocol will allow physicians to create accurate drug delivery maps to better treat patients and pave the way for MR data reproducibility.

References

Poster No 2090
The Dance and Music Training Enhanced the structure-function Coupling in the Attention Networks
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Introduction: Dance and music trainings are well known for their sensorimotor skills which recruit massive attention processes. Numerous neuroimaging studies have proven that dance and music training results in structural and functional adaptations within the attention networks (Schlaug 2015; Elst et al. 2023; Li et al. 2015; Li et al. 2021; Li et al. 2019). However, it is still blurred about the influence of these trainings on the relationship between brain structure and function within this network. Thus, we utilized graph signal processing (Preti and Van De Ville 2019) to measure the regional structure-function coupling induced by prolonged dance and music training.

Methods: Proficient dancers, musicians, and matched controls were recruited in this study. Then, 510s resting-state functional data (TR=2s, TE=30ms), T1-weighted anatomical images, and diffusion tensor images (DTI, diffusion direction=30, b=1000s/mm2) were collected on a 3T MRI scanner. Firstly, the number of streamlines connecting two regions (estimated by probabilistic streamline tractography on DTI data) divided by the region volumes (estimated on T1 data) was measured as the structure connectome. It was then used to construct graph Laplacian operator to characterize the brain as a graph. Secondly, regionally averaged BOLD signals were extracted. Thirdly, the eigendecomposition of Laplacian operator provided the harmonic components to build graph Fourier transform of functional signal. Low-frequency components represent signals that vary smoothly across the graph, whereas high-frequency components denote signals that vary highly across the graph. It means that when the frequency is higher, the functional signal is less coupled with structure. Finally, the cut-off frequency was defined as the frequency that split average energy spectral density (across time) into two parts with equal energy. Coupled and decoupled components of the functional signal were distracted by graph signal filtering. The logarithm of the ratio between the L2 norms of the two components across time was determined as structural-decoupling index to quantify the structure-function coupling.
Results: The statistical results indicated both dance and music groups significantly decreased the decoupling strength of the subcortical attention network, such as the right ventromedial putamen. Distinctly, only the dance group showed the increased coupling strength of the right inferior frontal gyrus opercular area in cortical attention network, which is associated with training intensity. Besides, the coupling FC between the right middle frontal gyrus ventral area and the left middle frontal gyrus area 46 increased only in the dance group. Furthermore, the dance group also indicated increased coupling FC between the left inferior parietal lobule caudal area and the left superior parietal lobule intraparietal area.
Conclusions: This study deepened the understanding of the regional plasticity effect of dance and music training. The enhanced structure-function coupling degree in cortical and subcortical attention network might be the neuron correlates of the skilled whole-body movement of dancer and the delicate movement of musicians. Prolonged dance training might have more positive impacts on the structure-function coupling in the attention networks.

References

Poster No 2091
Multiscale structural architecture of human neural dynamics
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Introduction: Neural dynamics are complex and heterogeneous across the cortex. Local spectral signatures are constrained by structural properties², but the relationship between neural dynamics and cortical structure remains incompletely understood. The present work explores this question by investigating the balance of extrinsic and intrinsic structural constraints on regional neural dynamics. We provide an integrated account of this interplay by combining the high temporal and spatial precision of intracranial electroencephalography (iEEG) with multiscale measures of cortical wiring, specifically inter-regional distance, structural connectivity estimated from diffusion-weighted MRI tractography, and microstructural profile similarity.

Methods: The MNI open iEEG atlas³ provides iEEG recordings acquired during conditions of resting wakefulness in 106 patients with intractable epilepsy (atlas dataset; Fig1A). By excluding channels involved in ictal and interictal activity, this dataset provides a putative reference space for normal human neurophysiology. Data pre-processing included band-pass filtering (0.5-80Hz), downsampling (200Hz), and demeaning. We computed each channel’s power spectral density (PSD; Welch’s method; 2-second blocks, 1-second overlap, Hamming window weighting). Channel PSDs were log-transformed, mapped to a single hemisphere, and parcellated⁴. Parcel-wise PSDs were cross-correlated while controlling for the average PSD across all channels and underwent Fisher R-to-Z transformation. We then applied diffusion map embedding to derive principal axes of variation in neural dynamics (Fig1B)⁵. In a second dataset of 20 patients (multimodal dataset; 13F; mean±S.D. age=33.90±9.02years), iEEG was recorded during resting wakefulness, and pre-operative, high-resolution structural (T1-weighted, quantitative T1, 0.8mm isovoxels) and multi-shell diffusion-weighted MRI (DWI; 1.6mm isovoxels) were acquired, enabling dataset-specific correlations between brain wiring and macroscale neural dynamics. We used micapipe⁶ to derive subject-specific measures of geodesic distance, microstructural profile similarity, and structural connectivity across all node pairs. Electrophysiological data underwent identical processing as in the atlas dataset. Channel-level PSDs were averaged across patients within each parcel (Fig2A), and multimodal dataset embeddings were aligned to the atlas embedding space using Procrustes rotation. We assessed structure-function coupling with a multiple linear regression model using three structural features as predictors of inter-node distances in the multimodal dataset embedding space.
**Results:** The first gradient (G1) of neural dynamics differentiated primary motor and surrounding frontal cortices from occipito-temporal regions, segregating channels with dominant beta and gamma-range activity (>13Hz) from those with high-delta, theta, and alpha-range peaks (<13Hz) (Fig1C). The second gradient (G2) differentiated unimodal sensory cortices, encompassing channels with peaks in the alpha frequency range (8-13Hz), from limbic and paralimbic regions with strong low frequency activity (<4Hz). This compact representation reflected distinct spectral signatures of unimodal sensory, motor, and association areas (Fig1D), and could be replicated in the multimodal dataset (median r=0.34; Fig2B). Structural features explained up to 60% of variance in distances within the embedding space: highest R2 values were observed in frontopolar and lateral temporal areas (Fig2C). This model outperformed models implementing different functional response variables (Fig 2D). These results show diverse contributions of cortical wiring to regional neural dynamics, with variable coupling strengths across the neocortex.
Conclusions: By mapping gradients of neural dynamics, our approach resolves macroscale trends in spectral similarity of local cortical regions and opens the way for assessments of structure-function coupling from direct measurements of neural activity.

References
Poster No 2092

Associations between Obesity Trajectories, Brain health, and Cognitive Function in Aging Population

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Introduction: Obesity in aging population is a public health challenge¹. Recent studies have increasingly focused on the long-term changes in obesity, such as longitudinal obesity trajectories²-⁵. However, these studies are either limited by small sample sizes or have typically relied on a single obesity indicator like body mass index (BMI) to identify obesity trajectories. Furthermore, whether the brain effects related to obesity trajectories are involved in modulating cognitive function in the elderly remains unclear. To address these gaps, this study integrated multiple obesity measures simultaneously to identify obesity trajectories. It also investigated their associations with brain morphology, functional connectivity (FC), and cognitive function, and determined whether the effects of obesity trajectories on brain mediate cognitive function.

Methods: A total of 502,411 UK Biobank participants over 40 were initially considered at baseline, with 54,243 undergoing 1-2 follow-ups. Of these, 50,538 had full obesity measures, including BMI, waist circumference, waist-hip ratio, and trunk, arm, leg, and body fat percentages, for trajectory analysis. For each participant, age at every timepoint was used as the independent variable and obesity measures at each corresponding timepoint as the dependent variable in linear regressions to calculate slopes of age. The z-scored slopes and baseline measures were analyzed using principal component analysis with varimax rotation and Gaussian Mixture Modeling to identify types of obesity trajectories (Fig. 1a), including the low stable, moderate stable, high stable, increasing, and decreasing trajectories. Subsequently, 33,467 exemplary health participants, without a history of major physical, neurological, or psychiatric diseases, remained. Among them, those with complete data and high-quality MRI images were selected to assess their brain cortical thickness and subcortical volumes (n = 24,663), whole-brain resting-state FC (n = 24,025), and cognitive scores across five domains (n = 14,666~16,950) for group comparison. Specifically, using the low stable group as the reference, separate comparative analyses were conducted with each of the other trajectory groups to assess differences in brain morphology and cognition via one-tailed t-tests, and in FC using two-tailed t-tests, while controlling for sociodemographic factors, lifestyle, etc covariates. Structural equation modeling was applied to examine the mediation effects of brain effects on the relationship between obesity trajectories and cognitive functions.

Results: Five obesity trajectories were identified (Fig. 1a-b). Compared to the low stable group, the high stable, moderate stable, and increasing groups had significantly thinner cortices in the temporal-frontal regions, reduced volumes in several subcortical structures, and extensive alterations in both within-network and between-network FC (Fig. 2a-i). However, the decreasing group exhibited limited cortical thinning in the frontal-temporal regions, no significant subcortical volume reduction, and minimal changes in FC (Fig. 2 j-l). The high stable and increasing groups exhibited the poorest cognitive performance. Mediation analyses suggested that the increasing obesity trajectory mediated cognitive decline in three domains (fluid intelligence, executive function, and processing speed) via alterations in cortical thickness, predominantly in the temporal-frontal regions, and FC, especially within DMN and between the DMN and other functional networks (Fig. 1c).
Panel (a) illustrates the process of identifying longitudinal obesity trajectories. This involved conducting linear regression analyses of seven obesity measures against age, resulting in seven slopes for each participant. The z-scored slopes and baseline measures were then subjected to principal component analysis. Subsequently, clustering analysis identified five distinct longitudinal obesity trajectories.

Panel (b) shows patterns of longitudinal obesity trajectory in aging population for each measure. The five trajectories show the patterns of maintaining high levels of obesity (high stable), maintaining moderate obesity (moderate stable), increasing levels of obesity (increasing), decreasing levels of obesity (decreasing), and maintaining normal levels of obesity (low stable) in our aging population. The error bar is one standard deviation.

Panel (c) shows that the increasing obesity trajectory-related changes in trail making (executive function), symbol digit substitution (processing speed) and fluid intelligence are mediated by cortical thickness (top, predominantly in the temporal-frontal regions) and functional connectivity (bottom, especially within DMN and between the DMN and other functional networks). To summarize the mediation effects in network-level functional connectivity, we calculated the proportion of significant connections with significant mediation in the sum of the functional connectivities among the brain regions in the two networks. The significance of the indirect effect was determined by corrected p-value < 0.01.

Abbreviations: Part, participant; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; APT, arm fat percentage; TFP, trunk fat percentage; LFP, leg fat percentage; SBP, body fat percentage; VIS, visual network; SMN, somatomotor network; DAN, dorsal attention network; VAN, ventral attention network; LIM, limbic network; FPN, frontoparietal network; DMN, default mode network; SUB, subcortical; MTL, medial temporal lobe; AMY, amygdala; CER, cerebellum.
Conclusions: This study reveals that in aging population, higher stable and increasing obesity trajectories are associated with more severe brain function and structural impairments, as well as cognitive deficits, indirectly suggesting that the maintenance and progression of obesity have detrimental effects on brain health and cognitive function. Importantly, this work highlights the regulatory role of brain effects related to obesity trajectory in cognitive decline.

References
Introduction: Heart Rate Variability (HRV) originates from the dynamic interplay between parasympathetic/sympathetic inputs to the heart, thus serving as an indicator of Autonomic Nervous System (ANS) regulation (Malik et al., 1996). Prior research has identified both positive and negative associations between HRV and brain morphology, including grey matter volume and cortical thickness, mainly in the cingulate cortex (Matusik et al., 2023). HRV is also linked with cognitive function, such that decreased HRV, marked by reduced autonomic balance, is related to poorer cognitive performance (Forte, Favieri and Casagrande, 2019). The connection between HRV and cognitive function could be explained by the common central autonomic network (CAN), which controls both the cardiac autonomic function and cognitive regulation (Thayer et al., 2009). However, previous literature mainly investigated healthy populations with a normal range of HRV. While the population with congenital heart disease (CHD) may show variations in HRV (Nederend et al., 2016), brain structure and cognitive function linked with the heart defect (Brossard-Racine and Panigrahy, 2023), the association between these variables in CHD remains unexplored. Thus, this study examines the brain volumetric and surface correlates of HRV and cognitive function in adolescents with CHD.

Methods: 58 adolescents with CHD who went through open-heart surgery during infancy and 86 healthy controls (52.7% males, 12.7±1.4 years) underwent neurodevelopmental testing and global executive function, and IQ were calculated. A cerebral MRI was performed on a 3T GE MR750 scanner. High-resolution T1-weighted images were acquired using a three-dimensional spoiled gradient echo pulse sequence (SPGR) with the following parameters: repetition time/echo time (TR/TE)=11/5ms; inversion time=600ms; flip angle=8°; reconstructed matrix=256×256; field of view (FOV)=26cm; 176 contiguous axial slices, 1mm slice thickness. SPGR images were segmented with Freesurfer 7.1 using standard preprocessing and an extensive quality assessment protocol. Grey and white matter volume, cortical thickness, and surface area were calculated following surface deformation to identify the cortical pial and white matter surfaces. Photoplethysmograph recordings were obtained during the MRI. HRV was quantified as the number of temporal differences (>50ms) between successive heartbeats. The associations between brain measurements, HRV and cognitive function were analysed with multiple linear regression.

Results: Adolescents with CHD showed lower HRV (p=0.004), cortical grey matter volume (p<0.001), cortical thickness (p=0.003), and pial surface area (p=0.004) than controls. HRV was positively associated with cortical grey volume (β=0.194, p=0.027) and with pial surface area (β=0.201, p=0.023) in the whole sample but not with cortical thickness (p=0.387). Positive correlations were found between IQ and cortical grey volume (β=0.436, p<0.001), pial surface area (β=0.453, p<0.001) and cortical thickness (β=0.167, p=0.033), as well as global executive function and those brain measurements. Furthermore, increased HRV was correlated with better global executive function (β=0.220, p=0.029) and higher IQ (β=0.229, p=0.017) in the whole sample and with higher IQ (β=0.388, p=0.032) in the CHD group. These associations were robust to confounders, including age, sex, and socioeconomic status.

Conclusions: Our findings highlight the anatomical underpinnings for HRV and autonomic regulation in adolescents, in line with prior research. Our results also demonstrated the association between HRV and cognitive functions, with the CHD group mainly driving the correlation, indicating the brain morphological correlates of HRV and cognitive function. Importantly, adolescents with CHD exhibit vulnerability to poorer IQ and altered brain development in connection with reduced HRV and autonomic imbalance. Future studies should elucidate more detailed mechanisms of the brain-heart interaction in CHD.

References

Poster No 2094

Organisation of higher-order cognitive functions in the posterior parietal cortex

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Introduction: Posterior parietal lobe (PPC) expansion can be observed in various branches of the primate phylogenetic tree, with its most dramatic expansion evident in the inferior parietal lobe of the human (Goldring & Krubitzer, 2017). Human PPC and nearby temporoparietal junction have been shown to be involved in a variety of cognitive challenges (Coslett & Schwartz, 2018; Rizzolatti & Rozzi, 2018; Medendorp & Heed, 2019). However, the precise neural loci and mechanisms supporting such, often uniquely human, cognitive functions remains a mystery. In this study, we aim to untangle general principles of overall organisation in the human PPC based on functional and anatomical data.

Methods: Data for our preliminary analysis, consist of functional task and anatomical data of 15 adult participants, part of the S1200 subjects release of the Human Connectome Project (HCP) database (Van Essen et al. 2013). We selected contrasts from task fMRI data for each participant provided by the HCP database. We were interested in working memory, language and social comprehension, mathematical computation, and relational processing. We also included motor behavior as a low-level baseline. General linear model analysis was applied on the task fMRI data via FSL’s FEAT resulting in individual and averaged activation maps for each contrast per task. Maps of the selected contrasts were then transformed from volumetric to surface space using HCP’s neuroimaging analysis toolbox Workbench. In order to understand how these maps relate to each other, we embed functional data projected onto the cortical surface into a 2-D space (Mars et al., 2018a).

Results: Within the whole brain, we find that motor tasks cluster closer together in space but tasks such as relational reasoning, language, mathematical computation and working memory are more spread out overall and across individuals (Figure 1A, Figure 1B). In particular, on the right hemisphere mathematical computation, working memory and relational reasoning are situated closer together in space, whereas language and social comprehension are situated further away (Figure 1B). These patterns can be reflected on the cortical surface with mathematical computation, relational reasoning and working memory activating lateral and dorsal prefrontal cortex, anterior cingulate and inferior parietal lobe (Figure 1C). On the other hand, language and social comprehension are situated further away from the other tasks across both hemispheres (Figure 2A, Figure 2B). In sum, it seems that higher cognitive functions, although not entirely separate, largely rely on different neural underpinnings in PPC.
Figure 1. All tasks whole brain embedding into 2D space. A. Left hemisphere. B: Right hemisphere. C. Surface map representation of cognitive tasks.

Figure 2. Congitive tasks PPC embedding into 2D space. A. Left hemisphere. B. Right hemisphere. C. PPC region of interest.

**Conclusions:** We plan to further push this concept by examining functional connectivity embedding within the superior and inferior division of the parietal lobe. The superior and inferior division of the parietal lobe differ according to their functional and cytoaritectonic profiles (Caspers & Zilles, 2018), thus we think we might uncover unique patterns of organization. In addition, we aim to relate this 2D functional embedding to the underlying anatomy of the PPC by examining the white matter tracts that form the connectional pattern of this region following Warrington et al. (2020). We are interested in exploring how well structure and function map to each other in the posterior parietal cortex. Lastly, our preliminary results presented here are based only on 15 subjects but we plan expand our sample size for our full analysis.
Breathing techniques modulate the magnitude and direction of cerebrospinal fluid flow

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Introduction: With mounting data indicating the relevance of CSF flow in aiding waste clearance from the brain, as well as potential pathophysiological linkages to neurodegenerative diseases (Braun & Iliff, 2020; Li et al., 2022; Simon & Iliff, 2016), developing effective strategies to enhance CSF flow in the brain is critical. Here, we attempt this using simple, widely-used breathing exercises: paced breathing and breath holding. The existing functional Magnetic Resonance Imaging (fMRI) based approach used in previous studies exclusively records CSF motion in the 4th ventricle in a singular direction, either cranial or caudal, contingent on the positioning of the scan volume (Fultz et al., 2019; Picchioni et al., 2022; Vijayakrishnan Nair et al., 2022, 2023; Yang et al., 2022). This prohibits the evaluation of net CSF flow. Therefore, an additional goal of the current study is to overcome this limitation and reconstruct net CSF movement signals through the use of breathing techniques during the fMRI scans. These challenges act as a unique physiological control condition bridging the unidirectional cranial and caudal CSF signals into net biphasic CSF movements. Furthermore, we also employ a novel methodology (Diorio et al., 2023) to estimate the velocities of these net biphasic CSF movements.

Methods: All participants’ MRI data were acquired using a 3T SIEMENS MRI scanner with a 64-channel head coil. The scans included structural T1-weighted MPRAGE, and resting state/breathing challenge fMRI. A chest belt was also worn by all participants to record respiration signals. The fMRI scans were carefully designed to capture the cranial/caudal CSF movements respectively from the brain/neck volumes, utilizing the inflow effect. The inflow effect refers to the increase in fMRI signal intensity that occurs when ‘fresh’ fluid (not exposed to radiofrequency pulses) enters a region of the imaging volume, as demonstrated in figure 1A for various inflow scenarios. The CSF inflow signals were extracted from a suitable voxel at the center of the 4th ventricle by overlaying the fMRI over the structural T1-weighted image registered to the fMRI space (figure 1B and 1C). Further, these unidirectional CSF inflow signals were converted into velocities based on fact that the maximum possible inflow signal increase occurs when the full volume of a given voxel has been “refreshed” with incoming fluid in each repetition time (figure 1A) as well as theoretical considerations from Gao et al. 1988 (Gao et al., 1988). Finally, net biphasic velocities were computed by summing the independently captured cranial and caudal unidirectional velocities (figure 1D).

Results: The group averaged time series plots of unidirectional cranial and caudal CSF velocities in the resting state and the net biphasic CSF velocities during the breathing challenges are shown in figure 2. It can be seen that the amplitude of CSF velocity oscillations is much larger during the paced breathing and breath holding challenges in comparison to resting state. In detail, the standard deviation (representing the amplitude variation) of biphasic CSF velocities during breath holding is significantly larger (p-value = 0.02) than the resting state, whereas that of paced breathing is only relatively larger (p-value = 0.85) in comparison to resting state. We also estimate that breath holding challenge generates a net volume displacement of -1.04±1.33 mL in the caudal direction, whereas paced breathing elicits a net volume displacement of 0.28±1.45 mL in the cranial direction, in comparison to a mere 0.16±0.68 mL across the entire duration of the corresponding scans.
**Conclusions:** Our results demonstrate that these respiratory challenges enhance the magnitude as well as control the direction of CSF movement in the fourth ventricle. We also successfully report our novel approach where we use these breathing challenges as a unique control condition to reconstruct net CSF velocities from independently captured unidirectional inflow signals.

**References**

Effects of deep respiration on cerebrospinal fluid flow in 4th ventricle

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Introduction: Accumulation of neurotoxic brain metabolites contributes to the development of Alzheimer’s Disease (Darst et al., 2021). Clearance of these substances is enhanced during sleep particularly deep sleep through increased transfer from brain through interstitial spaces and then into the CSF. Enhancing CSF flow might thus be beneficial (Burman & Alperin, 2023). Recent work has shown that slower and deep breathing can increase CSF oscillations and flow. CSF flow in the ventricles can be quantified with high temporal resolution (Chen et al., 2015; Dreha-Kulaczewski et al., 2015; Yildiz et al., 2017), including a steady-state free precession (SSFP) sequence (Wang et al., 2022) by measuring the shift and distortion in frequency tags. We examined the replicability of this method with a guided breathing paradigm in young adults before examining if the breathing-induced increases in CSF flow are attenuated in older adults.

Methods: Five healthy participants (mean age 24.8 years; 1 male) were studied using an IRB approved protocol. Each participant underwent five 7min 58s task runs during which breathing was guided by an expanding (inhalation) or contracting (exhalation) circle. Interspersed between 86 normal breaths (2.5s inhale, 2.5s exhale) were 6 deep breaths (4s inhale, 4s exhale; larger circle). Deep breaths were separated by either 10 or 20 normal breaths (Fig. 1). MRI scans were conducted on a 3T Prisma Scanner (Siemens Healthineers, Erlangen, Germany) using a 32-channel head and neck receiver array. Participants undertook two runs of a T2* weighted multiband (sms = 4) EPI sequence, and three using an SSFP sequence (TR 6ms; TE 3ms; flip angle 45°; slice thickness 3mm; FOV 240mm; matrix size 192 x 108; resolution 1.3mm x 1.3mm; frame rate 216ms). A hi-res (1mm isovoxel) structural MPRAGE scan was also acquired. For the SSFP sequence, a shim offset was introduced following B0 shimming to create the tags, and the frequency shift was tuned to position a tag in the 4th ventricle (Wang et al., 2022). Tag profiles (Fig 1b) were extracted across time. Offset values for each breathing epoch were baseline-corrected to the 1 second period preceding the breath. Area under the curve for the breathing-related tag distortions were calculated and normalized to the event duration to obtain the offset distance per second, which provided a surrogate measure of CSF movement. The offset distance per second for deep vs normal breaths were compared by repeated measures t-tests.

Results: Deep breaths showed significantly higher offset distance per second than normal breaths (paired t-test: t = -2.85, p<.05). This indicates that the change in CSF flow rate is not just a linear function of breath duration, but also depth of breathing, as can be seen in Fig 2.

Figure 1. A) Time sequence of guided breathing, with deep breaths (dark gray; 8s) separated by 10 or 20 normal breaths (light gray; 5s). B) A representative SSFP scan showing locations of the tags.
Figure 2. Offset distance of the 4th ventricle tag for normal vs deep breaths, averaged across all 5 participants. Error bars show SEM at each sampling point.

Conclusions: In this preliminary work, we demonstrated how CSF flow can be increased during guided breathing by increasing breath duration and depth, where deeper breathing elicited substantially higher volume of ventricular CSF flow. This could potentially benefit brain metabolite waste clearance (Burman & Alperin, 2023). Additionally, the change in CSF flow may be accompanied by a change in BOLD signal, which we plan to verify in the acquired multiband EPI scans.

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Poster No 2097

A multimodal gradient architecture for the human pulvinar

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Introduction: Integrative processes are fundamental for our brain to transform input signals from multiple sensory channels into a detailed, hierarchically organized, and meaningful representation of the environment. Pulvinar, the largest thalamic nucleus, is likely to play a leading role in such associative processes by means of a rich set of topographical connections to various cortical areas¹. Anatomical evidence in non-human primates suggests that such connectivity patterns are not limited to spatially discrete units, such as histological sub-nuclei; rather, they are organized in a continuum that mirrors cortico-cortical connectivity, reflecting cortical hierarchies of information transfer, and corresponding to some extent to cytochemical markers². Here, we directly address the question of continuous transitions in pulvinar-cortical connectivity profiles and their relationship to cortico-cortical connectivity as well as to neurotransmitter expression, by leveraging state-of-art gradient mapping techniques on multimodal imaging data.

Methods: We employed 3T structural, diffusion, and resting-state functional MRI datasets of 210 healthy subjects (males=92, females=118, age range 22-36 years) from the HCP repository³. Receptor expression data were obtained from a recently published, multicentric, multi-tracer positron emission tomography atlas⁴. For each left and right pulvinar voxel, the following measures were assessed: 1) functional connectivity (BOLD signal Pearson’s correlation) to 400 cortical regions from preprocessed, denoised rs-fMRI data; 2) structural connectivity to 400 cortical regions from preprocessed diffusion data (CSD signal modeling; probabilistic whole brain tractography; connectivity measure: streamline count); 3) averaged, normalized density values for 30 receptors including serotonergic, dopaminergic, cholinergic, and glutamatergic markers. For each of these voxel-wise features independently, diffusion embedding was employed to infer gradient maps of spatial variability within the pulvinar (distance metric: cosine similarity; alpha=0.5)⁵. Gradient-weighted structural and functional connectivity maps
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were retrieved to explore the cortical connectivity patterns associated with each gradient map. Receptor expression gradients were identified by their top 5 most correlated receptor markers. Cortico-cortical functional and structural connectivity gradients were also obtained from the same data for further comparison.

**Results:** We identified three functional connectivity gradients explaining ~90% of the variance of our data. Their cortical connectivity profiles were highly correlated to the first three cortico-cortical connectivity gradients. The main gradient, spanning from unimodal to transmodal cortical areas, was organized on the dorso-ventral axis of the pulvinar and showed high correlation to the main receptor expression gradient (left: \( r=-0.69 \); right: \( r=-0.78 \)) reflecting changes in the expression of serotonergic and dopaminergic markers, and to the secondary structural connectivity gradient (left: \( r=0.71 \); right: \( r=0.78 \)). The secondary gradient was correlated to the third cortico-cortical gradient, reflecting a transition in connectivity from multiple-demand to paralimbic areas. Finally, the third gradient, associated with the secondary cortico-cortical gradient (visual to sensorimotor region), was organized on the medio-lateral axis; it was found correlated to the main structural connectivity gradient (left: \( r=-0.58 \); right: \( r=-0.60 \)), and to the secondary receptor expression gradient (left: \( r=-0.47 \); right: \( r=-0.71 \)).

**Conclusions:** The human pulvinar hosts multiple representations of cortical connectivity, reflecting cortico-cortical gradient hierarchy. Our results support the hypothesis that cortico-pulvinar connectivity mirrors cortico-cortical connectivity and provide novel insights on the relation between pulvinar connectivity patterns and major neuromodulator systems.

**References**

Exploring the brain-eye connection: MRI-visible perivascular spaces, intraocular pressure and tau

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Introduction: The cerebral waste clearance system (CWCS) is vital for maintaining healthy homeostasis and is compromised in neurodegenerative conditions,¹ including Alzheimer’s disease (AD)². Waste removal is conducted through perivascular spaces (PVS)³. Preclinical research suggests the existence of a similar system in the eyes: the ocular glymphatic system (OGS) (Fig.1)⁴,⁵ The intraocular pressure (IOP) drives waste products from the eye through the optic nerve⁶,⁷ into the CWCS.⁴,⁸,⁹ However, human studies are scarce.¹⁰ In humans, CWCS function can be quantified with MRI-visible PVS.¹¹ Ultra-high field 7T MRI enables precise quantification of PVS enlargement.¹² Combining this with a measure for the driver of the OGS (i.e., IOP), provides a unique opportunity to explore connections between the eye and brain clearance systems. Furthermore, this eye-brain connection may also offer a means to gather insights about brain pathology. Tear fluid analysis was shown to be feasible to determine tear total-tau (T-tau) concentration (a marker for AD pathology),¹³ which was suggested as a proxy for cerebral tau presence and potentially indicative of reduced CWCS. This study aimed to uncover eye-brain connections by examining PVS and T-tau in healthy elderly and explore the connection between IOP and PVS, which could support the potential presence of an OGS in humans.

Methods: MRI acquisition: Thirty elderly subjects (mean age=66.9, 14F) underwent 7T MRI (Siemens Healthineers, Germany), including T1- and T1-weighted scans (Fig.2). Ocular measures: Bi-ocular tear fluid was collected using Schirmer’s strips while recording the tear-wetting length and analysed for T-tau (S-PLEX).¹³ In 23 subjects, the average IOP per eye was calculated over three tonometer measurements.¹⁴ PVS scoring: PVS were scored on the T2-weighted images in the basal ganglia (BG) and centrum semiovale (CSO), two regions known for PVS occurrence.¹⁵ Each hemisphere was scored in the slice with most PVS using a visual rating scale: 0 (<10), 1 (10-25), 2 (25-40), or 3 (>40).¹⁶ Two blinded raters performed consensus scoring. Anatomical brain size: White matter (WM) and BG volumes were automatically segmented on the T1-weighted images using Freesurfer (v6.0.5).¹⁷ Statistics: Partial Spearman’s correlations were determined between PVS scores and both T-tau and IOP, while adjusting for age, sex, and tear-wetting length. To adjust for atrophy effects, significant associations were further adjusted for the respective hemispheric WM or BG volumes.
Results: Elevated T-tau correlated significantly with higher CSO PVS scores in both hemispheres (Fig. 2). Lower right IOP was significantly correlated with higher right hemispheric CSO PVS scores, and a similar significant association was found between the left IOP and left hemispheric CSO PVS scores (Fig. 2). No other significant associations were found.

Conclusions: Elevated T-tau was linked to more PVS in the CSO in both hemispheres, suggesting that elevated T-tau might signify cerebral waste accumulation due to impaired clearance. This relationship was specific to the CSO, where PVS enlargement is associated with pathological protein deposition,\textsuperscript{11,16} as opposed to the BG, where its more likely influenced by vascular changes.\textsuperscript{11,16} Lower IOP was associated with more PVS in the ipsilateral CSO, in line with the presence of an OGS in humans. Reduced IOP may hinder waste-containing fluid flow through the optic nerve to the CWCS (Fig. 1).\textsuperscript{6} Notably, this relation was found ipsilaterally, but not contralaterally. This may be explained by the posterior pressure that is exerted on the fluid surrounding the optic nerve into the ipsilateral hemisphere, regardless of the optic nerve's crossing at the chiasm. While alternative indirect pathophysiological explanations for the IOP-PVS connection should be considered, our exploratory results suggest that a reduction in the pressure driving the OGS relates to impaired CWCS, bridging the gap between these two systems.

References
ABSTRACTS

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Poster No 2099

Scene-selectivity in CA1/subicular complex: Multivoxel pattern analysis at 7T
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Introduction: Univariate functional magnetic resonance imaging (fMRI) studies suggest that the hippocampal anteromedial subicular complex is a hub for scene-based cognition (Hodgetts et al., 2017; Dalton & Maguire, 2017). However, univariate analyses may be less sensitive than multivariate approaches (which utilize activation patterns across voxels) to scene-related activity in additional hippocampal subfields implicated in spatial processing (e.g. CA1). Further, as hippocampal connectivity-based functional gradients do not respect anatomical subfield boundaries, scene-selective activity patterns may be distributed across subfields (Aggleton & Christiansen, 2015; Dalton et al., 2019), so anatomical region-of-interest approaches might conceal cross-boundary category selectivity. We hypothesised that, by applying searchlight multivariate pattern analysis (MVPA) to high resolution fMRI data, scene-selective information would be identified in hippocampal regions crossing subicular complex and CA1.

Methods: Using FSL FEAT (Woolrich et al., 2001) and MVPA-light (Treder, 2020), we applied searchlight linear support vector machine classification to 7T fMRI data (voxel size=1.2x1.2x1.2mm) of 25 healthy adults (16f 18-35yrs) who undertook a visual odd-one-out discrimination task for scenes and non-scenes (faces, objects, shapes; Fig.1A,B). 1) Hippocampal searchlight classification was restricted to the hippocampal formation, designed to be sensitive, and accommodated inter-individual differences in category selectivity locations. Binomial tests were performed on individual-participant searchlight accuracy maps (for each 2-way classification between categories) against chance level. Each individual analysis resulted in 6 significant searchlight accuracy maps (scene v face, scene v size, scene v object, face v size, face v object, object v size), which were overlayed at group level (overlap maps), and then combined into scene and face ‘hotspot’ maps. The scene hotspot map was the sum of scene v face/size/object overlap maps, with face v size/object overlap maps subtracted. 2) Whole searchlight classification included the whole field of view (Fig.1C) and used conservative group-level statistics (FSL Randomise; threshold-free cluster enhancement; 5000 permutations, Winkler et al., 2014). T-maps were masked using corrected p-maps (α=0.0083; 0.05/6 tests). To isolate a ‘scene-selective map’, conjunction analysis was performed (the product of all the significance masks from searchlight contrasts that included scenes with the product of all the significance masks from the non-scene searchlights removed).
Results: 1) Hippocampal searchlight classification: Contrasting scene and face hotspot maps revealed medial-lateral (distal-proximal) category selectivity gradients, with higher values for scenes medially (distally) and faces laterally (proximally), across the hippocampus, and within the subicular complex and CA1 (Fig1.A). 2) Whole searchlight classification: Scene-selective regions (Fig1.B) overlapped with anteromedial (distal) right subicular complex (max ROI probability: 55%, MNI x=19 y=-21 z=-21) and left posterolateral (proximal) CA1 (max ROI probability: 50%, x=-33 y=-34 z=-10).

Figure 1. Methods. a) Examples of object, face, scene, and size trials (from top left to bottom right: ticks indicate the odd-one-out that the participants were asked to identify). All stimuli were trial unique. b) An illustration of the oddity task procedure. Trials were shown in mini-blocks (3 of the same category shown sequentially; 3 scene and 3 face trials are shown). Each trial was presented for 5.5s and trials were separated by a jittered inter-stimulus interval (ISI) of 0.5-2.5s. There were 45 trials of each category. Each participant FOV overlapped in MNI template space. The central yellow area indicates where all participant FOVs overlapped. The central blue indicates the whole hippocampus ROI (rendered using FSLeyes; McCarthy (2018)).

Figure 2. Hippocampal searchlight classification results a) Overlap statistical hippocampal scene (reds) and face (blues) ‘hotspot’ searchlight maps. ‘Hotspot’ maps constructed by summing together searchlight results from comparisons including scenes, with those results from comparisons including faces subtracted (reds) and by summing together searchlight results from comparisons including faces, with those results from comparisons including scenes subtracted (blues). Overlaid dots represent the locations of maximum overlap for the scene ‘hotspot’ map (yellow dot) and the face ‘hotspot’ map (light blue dot). Whole searchlight classification results b) The ‘scene-selective’ map. The four coronal ‘zoomed-in’ images, show inclusion of the right anteromedial subicular complex and lateral CA1 regions. Subfield ROIs were overlaid onto this map, and their colours correspond to the drawn subfield diagram. The subfield diagram illustrates our interpretation of the results and includes subfield delineations not possible with our current methods. The circles indicate that we consider the portion of the scene-selective map that overlaps with the medial subicular complex to incorporate distal subicular areas. We also consider the portion of the scene-selective map that overlaps with lateral CA1 to incorporate part of the proximal aspect of CA1. Images created using FSLeyes, Nilearn (Abraham et al., 2014) for Python, MATLAB, and Microsoft products.
Conclusions: Our work advances mapping of hippocampal scene-processing networks by using: a) MVPA to improve sensitivity to category-selectivity patterns of hippocampal BOLD, thereby providing evidence of scene selectivity in CA1 as well as subicular complex; b) a subfield-agnostic approach, revealing category selectivity regions that cross subfield boundaries; and c) subject-level, as well as group-based, analyses, which revealed scene selectivity gradients across the hippocampus, and individual variation in category-selective locations (also see Hodgetts et al., 2015). Our results align with a scene representation pathway described in non-human primates (Aggleton & Christiansen, 2015), including anteromedial (distal) subicular complex and lateral (proximal) CA1 regions.

References

Poster No 2100
Whole-brain fMRI reveals the notes, chords, and conductors of the cortical orchestra
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Introduction: The brain produces rich and dynamic patterns of neural activity spanning multiple spatial and temporal scales over seconds to minutes and in circuits and systems to enable a broad spectrum of complex behaviours. How does the brain instantiate this wide variety of spatiotemporal dynamics? A prevailing assumption in the field, which is currently undergoing revision, is that these features arise due primarily to the organisation of and the interactions within the cerebral cortex. In this study, we demonstrate that many features of coordinated neural activity measured by standard whole-brain functional magnetic resonance imaging (fMRI) approaches are inherently linked to the organisation of the subcortex (e.g., thalamus, neuromodulatory brainstem structures, cerebellum – Fig. 1a). Leveraging a geometrically-based eigenmode decomposition of (i.e., the "notes" of the brain; Fig. 1b) and a temporal dimensionality reduction technique, identifying time-lagged independent components (i.e., the “chords”, which are different combinations of notes – Fig. 1c), we establish a connection between slow subcortical fMRI temporal dynamics with spatially coarse cortical patterns and vice versa for fine spatial patterns.

Methods: 7T fMRI dataset: We analysed a dataset of 8 participants who undertook multiple fMRI scans consisting of alternating resting-state with visually evoked scans viewing an extensive set (~10k) of naturalistic images and responding to a behavioural recognition task. Importantly, this dataset was obtained using a 7T scanner at 1.8 mm isotropic resolution (TR = 1.6s). Low-dimensional mapping between subcortical activity and cortical modes: We extracted cortical activity into natural oscillatory modes of the physical cortex based (i.e., its spatial eigenmodes), analogous to the notes of a stringed instrument, represent the optimal basis set for the systematic decomposition of cortical neural activity. We then applied time-lagged independent component analysis (tICA) to the subcortical ROIs and cortical modes. tICA combines information from a time-lagged covariance matrix of the data to separate blood oxygen level-dependent activity into a nonlinear mixture of dynamic whole-brain modes.
Results: Our methodology reveals that activation in subcortical structures significantly precede resting-state component time series in the cerebral cortex (explained variance > 0.6). These patterns further explain the well-known alternating oscillation in dorsal attention and default mode networks (Fig. 1d). In particular, we focus on the anatomical role of these systems, as we find that diffuse projecting thalamic and neuromodulatory systems preferentially explain slow and coarse spatiotemporal patterns. This extension can be seen as a whole-brain extension to previous theoretical\textsuperscript{3–5} and empirical\textsuperscript{6–8} analyses focusing on one subcortical structure at a time. In particular, we confirm that the independent spatiotemporal whole-brain modes typically involve a coordinated orchestra of subcortical structures.

Conclusions: Our study relates how multiscale geometric cortical eigenmodes (i.e., notes of the brain) are coordinated into dynamic motifs (i.e., Chords), that are explained by subcortical activity (the conductors). This approach directly contributes to systems neuroscience by functionally linking whole-brain systems and delineating how these patterns align with subcortical anatomical connections. Nevertheless, we believe that incorporating coarse-grained subcortical systems dynamics will significantly enhance the accuracy of whole-brain computational models, and modelling will be required to understand the complex dynamical interplay of these various structures.

References
It’s not a bug, it’s a feature: Estimating bone mineral density from T1-weighted MR images

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Introduction: No brain is an island and, as such, it is intricately connected to other tissues and organs1, yet, the neuroimaging community largely dismisses the information from the closest bony structure surrounding the brain. More specifically, the skull may contain markers for bone mineral density and bone metabolism which, in turn, may affect emotion and cognition2–3, and even the risk of Alzheimer’s disease4–6. However, the bone mineral density (hereafter referred to as BMD) measures are typically not available in open-source brain imaging databases. Here we present a novel approach to calculate a proxy for bone mineral density from the skull based on a single T1-weighted image of the human brain.

Methods: Sample This research has been conducted using a subsample of 1,000 healthy subjects (M = 63.81 ± 6.27 years, age range: 46–79, 50% women) from the UK Biobank (UKB application 41655). Imaging parameters are provided in7. The sample was used to extract and validate our BMD estimate against the head BMD measure, obtained by dual energy X-ray absorptiometry (DXA)8. In addition, a subsample of 63 subjects from OASIS-3 (M = 69.27 ± 7.32 years, age range: 48–85, 54% women) was used to determine the retest reliability. Imaging parameters are provided in9. Data processing All T1-weighted brain images were processed using SPM12 (https://www.fil.ion.ucl.ac.uk/spm/) and Matlab 2021a (https://www.mathworks.com), which produced the following segments: gray matter, white matter, cerebrospinal fluid, skull, soft head tissue, and background. Of note, instead of the default setting (3 mm), we set SPM’s ‘samp’ parameter to 5 mm to ensure that non-brain tissues were properly classified. Misclassified skull segments were corrected by morphological operations. We created a template atlas of the skull regions by averaging affine and intensity-normalized T1-weighted images as well as CT data of OASIS-3, and manually labeling the skull segment tissue probability map using Slicer3D10. The atlas was mapped into individual space using the linear transformation from the SPM segmentation. The individual BMD measures were derived from the corrected SPM skull segment, by quantifying the mean intensity across the entire segment labeled as skull (or within a specific skull region), normalized by the median intensity of the CSF segment.

Results: The obtained BMD estimate of the skull was validated against the BMD measure of the head (UKB data-field 23226-2.0), left femoral neck (UKB data-field 23299-2.0), as well as the total body BMD (UKB data-field 23239-2.0). Our proxy skull BMD estimate is highly correlated to the head (r = .71, p < .001), as well as total BMD (r = .60, p < .001), and is moderately
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associated with BMD of the left femoral neck (r = .41, p < .001). The results of the validation are shown in Figure 2. In addition, we calculated the retest reliability of the BMD estimate of the skull using T1-weighted images from the OASIS-3 dataset acquired at two time points within an interval of less than 3 months (r = 0.97, p < .001).

Conclusions: We developed an approximation of skull BMD by making use of tissue classes that are normally discarded when processing brain MR images. The estimation of skull BMD from T1-weighted brain images may serve as a proxy for a person's total BMD in research studies where such information would be relevant but has not been collected. Moreover, the extracted measure could provide valuable insights into the interconnectedness of bones and brain.

References
To BMI, or not to BMI? Adiposity estimation from head T1-weighted MR images

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Introduction: Obesity has adverse effects on cognitive and brain health¹–². Nevertheless, most neuroimaging studies do not collect sophisticated body composition measures and usually rely on simple approximations by calculating the body mass index (BMI) from weight and height data. This approach has several limitations, especially when used in cohorts of older individuals³–⁴. To overcome this drawback, we present a novel method to approximate body adiposity by measuring the thickness of the head using T1-weighted brain images.

Methods: Sample This research has been conducted using a subsample of 1000 healthy subjects (M = 63.81±6.27 years, 50% women) from the UK Biobank (UKB application 41655). Imaging parameters are provided in⁵. The sample was used to extract and validate our adiposity estimate against the body composition measures, obtained by abdominal MRI⁶ and processed by AMRA Profiler Research⁷. In addition, a subsample of 63 subjects from OASIS-3 (M = 69.27±7.32 years, 54% women) was used to determine the retest reliability. Imaging parameters are provided in⁸. Data processing All T1-weighted brain images were processed using SPM12 (https://www.fil.ion.ucl.ac.uk/spm/) and Matlab 2021a (https://www.mathworks.com), which produced the following segments: gray matter, white matter, cerebrospinal fluid, skull, soft head tissue, and background. Of note, instead of the default setting (3 mm), we set SPM’s ‘samp’ parameter to 5 mm to ensure that non-brain tissues were properly classified. To approximate the adipose tissue of the head, we estimated the local thickness of the segment classified as soft head tissue. This was achieved by calculating the shortest distance from each soft head tissue voxel to the skull and to the background. The sum of both distances then yielded the estimate of the voxel-wise head thickness. A separation into different head tissues (i.e., muscle, skin, and fat) was omitted because of varying amounts of (chemical shift) artifacts and inhomogeneities across the image. Of note, the lower portions of all brain scans as well as voxels located more than 30 mm from the skull were excluded from the head thickness estimation to avoid side effects due to defacing and/or varying scanning protocols and procedures.

Results: The obtained head thickness estimate was validated against BMI (UKB #21001-2.0), body fat percentage (UKB #23099-2.0), abdominal subcutaneous adipose tissue (ASAT) volume (UKB #22408-2.0), visceral adipose tissue volume (VAT; UKB #22407-2.0), and waist circumference (UKB #48-2.0). Our head thickness estimate is moderately associated with BMI in the total sample (r = 0.53, p < 0.001), but more so in separate samples for men and women, respectively (r = 0.63 and r = 0.62, p < 0.001). Moreover, it is highly associated with visceral adipose tissue volume (r = 0.74, p < 0.001). The results of the
validation are shown in Figure 2. In addition, we calculated the retest reliability of the skull BMD estimates using T1-weighted images from the OASIS-3 dataset acquired at two time points within an interval of less than 3 months (r = 0.98; p < 0.001).

Conclusions: We developed an approximation of subcutaneous fat by making use of a tissue class (i.e., soft head tissue) that is normally discarded when processing brain MR images. Head thickness may provide valuable information beyond the typically used BMI, which has several limitations, especially when used in cohorts of older subjects\(^3,4\). As open-source brain imaging databases predominantly consist of aging adults, the adiposity measure presents a viable alternative to BMI. Our novel measure may not only find application in basic research as a marker for brain health and aging but also in intervention studies and clinical settings as an indicator (or predictor) for the effectiveness of therapies and interventions.

References
Wiring the metanetwork of language: a connectome-driven neurosurgery approach

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Introduction: Recent advances in non-invasive mapping techniques have provided invaluable insights into the organizational principles of the anatomo-functional architecture of the human brain. Specifically, the ability to measure spontaneous brain fluctuations using resting-state functional MRI has highlighted how segregation into functionally specialized areas is paralleled by integration into highly connected brain networks, while diffusion weighted imaging and tractography have proved incredibly useful in charting the wiring diagram of the brain. Even though both non-invasive mapping techniques represent powerful tools to investigate the functional and structural anatomy of the major functional systems of the brain, they have been mainly used to promote a segregated view of the brain, with parallel networks acting in isolation. Instead, adaptive and context specific behavior is thought to emerge from the continuous interaction of large-scale functional systems, suggesting that a ‘meta-network’ framework is better suited to encapsulate this view of brain functioning. Leveraging a recently developed computational approach able to integrate direct electrical stimulation (DES, a causal brain mapping technique) with connectomics, here we seek to (de)compose the meta-network of language. We found that spontaneous brain fluctuations in white matter are critical in delineating both the function specific and shared portion of the structural scaffold underlying semantics, phonology and speech articulation, core aspects of language.

Methods: We integrated white matter DES points causing transient speech arrest, semantic or phonological aphasia (N=297 patients, 485 stimulations) in combination with resting-state fMRI via lesion network mapping for deriving functional networks (N=1’000 control subjects). To corroborate the use of resting state fMRI in the white matter, we tested whether DES derived networks are predictive of future stimulation points via cross validation, and we investigated – accounting for spatial autocorrelation – the degree of correspondence in the spatial organization of spontaneous brain fluctuations and glucose metabolism (FDG-PET, N=25). For each functional category (Fig. 1), we defined resting-state fMRI driven white and gray matter hubs that were subsequently used as waypoints for tractography filtering in an independent cohort of control subjects (N=753). Individually filtered tractographies were merged, clustered, and visually inspected to remove artefactual reconstructions. Before clustering, we generated joint structural-functional maps of the white matter via track-weighted functional connectivity, and used them to predict symptom severity in a cohort of aphasic stroke patients via quantile regression (N=105).

Results: White matter DES derived functional networks accurately predict future stimulation points in the white/gray matter (94/64, 95/70, and 96/81% accuracy for phonological, semantics, and speech arrest, respectively). After FDR correction, 25/40 regions showed a statistically significant correlation between spontaneous brain oscillations in the white matter as measured...
by resting state fMRI and FDG-PET derived glucose metabolism. Our functionally driven tractography filtering procedure revealed both subnetwork specific connectivity signatures and the existence of multiple integration points across the three functional categories. Notably, we found that the overlap between lesion and joint structural functional white matter maps of semantics and phonological thresholded at the 95th percentile significantly predicted symptom severity in aphasic stroke patients \(r^2=0.34, r=0.35, p_{val} < 0.001\) after permutation testing, well beyond total lesion size \(r=0.14, p_{val} < 0.001\).

**Conclusions:** Our results suggest that language is a complex function subserved by specific subnetworks strategically wired to act in cooperation, supporting the adoption of a ‘meta-network’ framework to understand complex cognitive functions.

**References**

**Poster No 2104**

**Altered Frontoparietal Structural Correspondence Relates to Slower Processing Speed in Combat Blast**

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**Introduction:** Blast exposure within a military context has garnered increasing attention due to its potential long-term cognitive implications1. Low-level blast exposure (outgoing from missings) has been associated with slower reaction time amongst breachers2. We investigated the macroscopic structural correspondence associated with combat blast exposure and explored the potential cognitive relevance of altered frontoparietal structural correspondence3-5.

**Methods:** Eighty-two service members/veterans were included in this study, comprising 43 with blast exposure (age at time of evaluation: 37.4 [7.6] years, 40 males, years since last deployment: 6.4 [3.3] years) and 39 without blast exposure (age: 38.9 [8.4] years, 29 males, years of deployment: 7.8 [3.9] years)). Structural brain scans were acquired using T1-weighted 3D MPRAGE sequence from Siemens Skyra 3T MRI scanner with the imaging parameters: TR = 2530 ms, TE = 2.6 ms, image size 176 x 256 x 256, and voxel size 1 x 1 x 1 mm3. All images were first checked for quality assurance7 then were analyzed by voxel-based morphometry to estimate gray matter volume7. Regional frontal and parietal gray matter volumetric measures were sampled according to the LPBA-40 atlas8. Cognitive measures of processing speed (Trailmaking Test A completion time in seconds [Trails A]) and working memory (number of correct responses for Paced Auditory Serial Addition Test Trial 1 and Auditory Consonant Trigram 36-second delay) were also collected. To estimate structural correspondence between frontal and parietal lobes, we performed partial correlation analysis within each blast exposure group with age and sex as covariates. Fisher z test was used to test if correlation coefficients were significantly different between groups. To explore cognitive associates of altered structural correspondence, we used the bootstrapping approach to resample brain features, cognitive measures, and covariates (i.e. age and sex) from all subjects and re-estimated partial correlations between frontal and parietal lobes 1,000 times to create an empirical spectrum of structural correlations, on which we tested the relationship between frontoparietal structural correspondence and cognitive measures using a linear regression model that adjusted for age and sex. Multiple comparisons for cognitive measures were addressed using Bonferroni correction.

**Results:** We found that there was no significant frontoparietal correlation in the non-blast group (rho = -0.155, p-value = 0.368); however, significant negative frontoparietal correlation was found in the blast group (rho = -0.579, p-value < 0.001). Correlations significantly differed between blast and non-blast groups \(Z = 2.18, p = 0.029\) (Figure 1A). Out of three cognitive measures, frontoparietal correspondence was negatively associated with TrailsA Time \(p = 0.003, Figure 1B\); slower Trails A
Completion time was associated with higher magnitude of negative structural correlations (discrepant frontal and parietal gray matter volumes).

Conclusions: Among military personnel with blast exposure, discrepant frontal and parietal gray matter volumes was associated with slower response time, but this was not the case for those not exposed to blast. This suggested that although processing speed was similar across groups, frontal-parietal correspondence may influence processing speed in those exposed to blast. This is consistent with neuroimaging findings suggesting subtle altered connectivity in blast-related mild traumatic brain injury despite lack of long-term cognitive impairment. Microstructural features related to this macrostructural finding need to be explored to elucidate this preliminary finding.

References
**Poster No 2105**

**Cognitive control and default-mode linked partitions within the salience network**

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**Introduction:** The salience network plays a crucial role in neural processes related to reward, motivated behavior, attention, and social cognition (Menon & Uddin, 2010; Seeley, 2019), and contains representations in the ventral anterior insula and anterior cingulate cortex (Seeley, 2019). However, the extent to which the entire salience network is uniformly engaged in these processes remains uncertain, prompting an exploration of potential specialized sub-divisions within the network.

**Methods:** This study investigates discrete functional divisions within the salience network using resting-state functional connectivity (RSFC) in highly sampled individuals (precision functional mapping - PFM; n=20 (Gordon et al., 2017)) and large group-averaged datasets totaling approximately 45,000 participants from the Human Connectome Project (Glasser et al., 2016), Adolescent Brain Cognitive Development (Casey et al., 2018), and UK Biobank (Miller et al., 2016). Employing data-driven methods, we identified individual and data set-specific large-scale canonical networks.

**Results:** Comparing the salience network in group-averaged versus PFM, we observed that PFM identified salience network representation in the posterior cingulate and parietal cortex, extending beyond the canonical salience network. Further analysis revealed a consistent bipartite division in 80% of participants. The first subdivision, termed the core division, aligned with the canonical salience network, with representations in the anterior cingulate and ventral anterior insular cortex. The second, smaller division, termed the posterior division, was predominantly localized to the posterior cingulate and posterior parietal cortex. Notably, the core division demonstrated stronger correlation with the default-mode network and memory-related subnetworks (Gilmore et al., 2021), while the posterior division consistently correlated with the frontoparietal network, a key player in cognitive control and flexibility (Cole et al., 2013; Marek & Dosenbach, 2018). We created binary masks based on these two PFM identified subnetworks and used them as seeds in group-averaged RSFC, finding reciprocal connectivity between the core and posterior divisions.

**Conclusions:** These findings suggest an expanded scope for the salience network, encompassing not only the ventral anterior insula and anterior cingulate cortex but also the posterior cingulate and posterior parietal cortex. The connection between the posterior division and the frontoparietal network might provide a mechanism for motivated behaviors to influence goal-directed cognitive processes.

**References**


Correlations between inter-subject variability in tissue properties of human V1, V2, and V3

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Introduction: Over the past several decades, neuroanatomy and neuroimaging research has revealed large individual differences in the size of the human visual cortex (Stensaas et al. 1974; Andrews et al. 1997; Dougherty et al. 2003). Further studies have documented covariance amongst the size of visual areas, and between the size of visual areas and properties of other visual structures (Benson et al. 2022; Miyata et al. 2022). We wondered whether there was also substantial variability in the grey matter tissue microstructure of the visual cortex across individuals, and how such measures covary throughout the multiple cortical maps. Recent advances in structural neuroimaging provide opportunities for characterising tissue properties of cortical areas using MRI. The ratio of T1- to T2-weighted signal intensity (T1w/T2w) has become a widely used semi-quantitative measure of tissue microstructure of the brain (Glasser & van Essen, 2011; Berman et al. 2022). Here, we analysed the Human Connectome Project 7T retinotopy dataset (Benson et al. 2018), to evaluate individual differences and covariance of T1w/T2w amongst early visual areas V1, V2, and V3.

Methods: Analyses were performed on the 3T structural and 7T functional MRI data acquired from 160 subjects who participated in the retinotopic mapping experiments (Benson et al. 2018) as part of the Human Connectome Project (van Essen et al. 2012). Borders of V1, V2, and V3 (regions of interest; ROIs) were manually drawn by four researchers based on polar angle reversals in the retinotopic map (Benson et al. 2022). We identified the mid-grey surface of ROIs for each subject using neuropythy (https://github.com/noahbenson/neuropythy), and averaged T1w/T2w across voxels belonging to each ROI. We first calculated inter-subject correlations between T1w/T2w of ROI. Subsequently, we computed how much of the individual variability in T1w/T2w of each ROI could be predicted by that of the entire cortex using linear regression. We then used the residuals to evaluate whether, and the extent to which, T1w/T2w covaried amongst ROIs once the cortex-wide variability was partialled out.

Results: Figure 1 depicts correlations between T1w/T2w of ROIs across subjects for each hemisphere. Strong correlations were found between V1 and V2 (left: r = 0.92; right: r = 0.92), V2 and V3 (left: r = 0.93; right: r = 0.95), and V1 and V3 (left: r = 0.89; right: r = 0.91). T1w/T2w tended to be higher in V1, compared with V2 and V3, consistent with known anatomical differences in grey matter microstructure between V1 and V2/V3. We note that T1w/T2w of corresponding ROIs were also highly correlated between hemispheres (left vs right hemispheres for V1: r = 0.90; V2: r = 0.90; V3: r = 0.84). The high correlations were not simply due to some subjects having overall high or low T1w/T2w values in all of cortex. Figure 2 shows correlations between the residuals of ROIs after T1w/T2w of the whole-brain grey matter was regressed out. Strong correlations remained between V1 and V2 (left: r = 0.87; right: r = 0.86), V2 and V3 (left: r = 0.89; right: r = 0.90), and V1 and V3 (left: r = 0.82; right: r = 0.83).

Conclusions: We examined whether tissue properties, reflected in T1w/T2w, covaried between areas V1, V2, and V3 across 160 individuals. Results showed strong correlations between the border areas V1 and V2, as well as V2 and V3, and also between V1 and V3 though to a lesser extent, in both hemispheres, which persisted even when adjusted for cortex-wide T1w/T2w. T1w/T2w of corresponding areas in the two hemispheres were also highly correlated. Our findings generally align with the finding that the surface areas of V1, V2, and V3 are highly correlated within and across hemispheres (Benson et al. 2022), and suggest that structural covariance between early visual areas is not limited to their surface area, but also found in grey matter tissue microstructure.
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Figure 1. Correlations between T1w/T2w of areas V1, V2, and V3 across subjects (N = 160) for each hemisphere (A. left hemisphere; B. right hemisphere). Dots depict the data from each individual subject. Strong correlations were found between all three pairs of areas; with those between bordering areas (V1-V3 and V2-V3) being slightly stronger than between relatively distant areas (V1-V3) in both hemispheres. T1w/T2w tended to be higher in V1, compared with V2 and V3.

Figure 2. Correlations between the residuals of areas V1, V2, and V3 after T1w/T2w of the whole-brain grey matter was regressed out. Strong correlations remained between all three pairs of areas in both hemispheres. Conventions are identical to those used in Figure 1.

References
Comparative Analysis of Brain Connectivity and Gene Expression Divergence in Chimpanzees and Humans

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Introduction: Anatomical connectivity changes during evolution may underlie functional specialization of the human brain (Thiebaut de Schotten et al. 2022). Although chimpanzees (Pan troglodytes) are crucial as a comparative reference for investigating human brain evolution (Varki et al. 2005), comprehensive connectional analyses between human and chimpanzee brains have been limited due to lack of comparable cross-species brain atlases. Moreover, the underlying genetic association of human-specific brain connectivity also remains unclear. To address these questions, we built the Chimpanzee Brainnetome Atlas (ChimpBNA), investigated cross-species connectivity divergence and examined the associated genetic factors.

Methods: Data and Preprocessing - 46 chimpanzees were available from the National Chimpanzee Brain Resource. 40 human subjects were available from HCP dataset (Van Essen et al. 2003). Preprocessing was the same as our previous study (Cheng et al. 2021). Parcellation – Following a connectivity-based parcellation framework used previously with humans (Fan et al. 2016), we performed tractography for each initial ROI and used spectral clustering, resulting in the final parcellation of the whole brain. Connectivity divergence - We reconstructed homologous white matter tracts for each chimpanzee and human and obtained the connectivity blueprints (Bryant et al. 2020, Mars et al. 2018). We then calculated the KL divergence for each pair of subregions in ChimpBNA and HumanBNA and searched for the minimal value for each subregion in the HumanBNA. Genetic analysis – We used PLSR to identify the first component of AHBA gene expression (Hawrylycz et al. 2012), and used bootstrapping to calculated Z-score of each gene. Genes with Z-score higher than 3 were input into cell-type and gene enrichment analysis. Finally, we examined gene expression difference between two species in three regions of interest using PsychENCODE database (Sousa et al. 2017).

Results: Using the connectivity profiles, we subdivided the chimpanzee brain in 198 cortical and 44 subcortical regions, thereby building ChimpBNA, the most refined atlas of the chimpanzee brain to date (Fig 1A, 1B). Leveraging connectivity blueprints, we found that regions with the most different connectivity patterns between species were located at the middle and posterior temporal lobe, especially the pSTS, posterior IPL, anterior Pcn, anterior insula (Fig 2B, C). The connectivity divergence map showed dissimilarity with that of cortical expansion (Wei et al. 2019), indicating that the connectional changes reflect a unique aspect of brain reorganization. The first component identified from the AHBA data significantly correlated with the connectivity divergence map (r=0.39, p<.013), and 1912 genes had a Z-score greater than 3. These genes were highly enriched in excitatory neurons, specifically the L6 and L2-3 IT excitatory neurons (Fig 2D), and related to neuron projection and synapses (Fig 2E). In addition, 70 of these genes significantly overlapped with HAR-BRAIN genes (Wei et al. 2019) (p<.005). 1459 of 1912 genes overlapped with the PsychENCODE data, and showed significant expression differences in three ROIs (STC: t=15.96; DFC: t=8.16; V1C: t=-2.11, all p<.05) but a more significant effect size in the STC and DFC (STC: Cohen’s d=0.46; DFC: Cohen’s d=0.27; V1C: Cohen’s d=0.03, Fig 2F), indicating a potential association between gene expression differences and connectivity divergence between species.
Conclusions: In summary, we constructed the fine-grained ChimBNA based on anatomical connectivity and performed a comparative analysis of chimpanzee and human connectivity profiles. This revealed divergent patterns across species and associated genetic factors. Our findings indicate that connectivity changes in chimpanzees and humans likely reflect functional specialization in evolution and provide key steps toward elucidating diversity of primate brains.

References
ABSTRACTS


Poster No 2108

Hemispheric Multidimensional Feature Extraction Analysis Based on Decoupled Representation Learning

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Introduction: Human brain exhibits asymmetry in both structure and function. The conventional method for studying structural MRI asymmetry entails subtracting a certain metric between homologous brain regions to obtain asymmetry index²,³. However, this approach confines comparisons between corresponding regions/voxels in left and right hemispheres. Here, we expanded our study of structural asymmetry to the systematic level of hemispheres. We assumed that human brain could be disentangled into 3 distinct factors, i.e., left-hemisphere-specific factors, right-hemisphere-specific factors, and left-right-shared factors. Capitalizing on the recent advancements of decoupled representation learning⁴,⁵, we proposed a contrastive learning model to extract left-hemisphere-specific, right-hemisphere-specific and shared features from human anatomical hemispheres.

Methods: 907 right-handed subjects with T1w from HCP were included (Male: 397, Handedness > 40, age 22y to 36y). Illustrated in Figure 1, we proposed a deep learning model to extract the hemisphere-specific features. The model was based on contrastive VAE⁵ and the input of it was 3D hemisphere imaging data in native space. To ascertain the relationships between the hemisphere-specific features and behavioral data, we employed Partial Least Squares Correlation (PLSC)⁶,⁷. Our sole focus was on two hemisphere-dominant cognition performances: language and social. Tensor-based Morphometry (TBM) was utilized to identify loci of hemisphere-specific regions⁸. Specifically, for each subject, we generated three synthetic brains: the first one constructed only from shared features, termed counterfactual brain; the second one composed of left-hemisphere-specific and shared features, termed synthetic left brain; and the third one with right-hemisphere-specific and shared features, termed synthetic right brain. Then a template was created using counterfactual brains from all subjects. 3 Jacobian determinants were calculated between each subject’s 3 synthetic brains and the template. Paired t-tests was then used on Jacobian determinants to capture structural changes separately induced by 2 specific features, followed by multiple comparison correction using 10,000 permutations.
Results: Regarding the relationship between hemisphere-specific features and language, there was a single significant latent variable (LV) explaining 49.7% of the covariance (Fig. 2A). Remarkably, a left-specific feature showed significantly contribution to the language-related LV after the robustness assessment (BSR = 3.462, p < 0.01). For social, the result also revealed a significant LV (explaining 66.8%) and one right-specific feature significantly contributing to the social-related LV (BSR = 2.582, p < 0.01). The reproducibility validation utilizing a randomly selected 2/3 of the participants confirmed the stability of our findings. Figure 2B showed the loci of structural changes associated with hemisphere-specific features. Regions with negative values indicated compression of brain structural volume, while positive values indicated expansion. For left hemisphere, the regions with significant compression in volume were mainly located in the lateral prefrontal, lateral anterior temporal and medial occipital regions, while the regions with significant expansion were in cingulate gyrus. Right-brain-specific features exhibited significantly compression in the default mode network and significantly expansion mainly in the orbitofrontal cortex.

Conclusions: By combining the decoupled representation learning and structural MRI, we extracted the hemisphere-specific structural features of the human brain from the systematic level. Our results demonstrated that the hemisphere-specific multidimensional features extracted by our model revealed correlations with lateralized behavioral performance, indicating that the specific features could be disentangled using a data-driven approach. These findings might provide new insights about the brain asymmetry.

References
**Poster No 2109**

**Delineating Functional Subregions of the Left Precentral Gyrus: A fMRI Meta-Analysis**

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**Introduction:** The human precentral gyrus (PCG), known as the primary motor cortex, is crucial for voluntary movement control. It connects to the spinal cord via pathways like the corticospinal and corticobulbar tracts, with damage leading to motor deficits. Recent studies, however, reveal its roles in speech production (Silva et al., 2022) and motor learning (Rubin et al., 2022), challenging its traditional view as solely a motor center. This study revisits the PCG from the perspective of involved cognitions. By employing a meta-analytic approach at PCG region, we aim to parcellate PCG into subregions with distinct cognitive functions. Furthermore, HCP-released diffusion MRI data were used to examine the structural connectivity pattern among the identified subregions. We hypothesize that 1) PCG can be separated into anterior and posterior bank; 2) PCG may have a distinct dorsal-ventral parcellation in the anterior segment.

**Methods:** We searched for task-based fMRI studies on the Precentral Gyrus using Brainmap, focusing on the left hemisphere and studies from January 2010 to July 2022. Criteria excluded subjects outside 18-65 years or with illnesses, yielding 162 studies. Studies were categorized by functions as ‘emotion’, ‘language’, ‘social cognition’, ‘execution’, ‘attention’, ‘working memory’, and ‘movement’, each with at least 15 experiments. To complement ROI-based analysis, we conducted a whole-brain meta-analysis (Gentili et al., 2019), selecting studies reflecting specific behaviors. Following the previous steps, we selected 7 groups of studies. Using Brainmap GingerALE, we performed an ALE meta-analysis (Turkeltaub et al., 2002), transforming foci into a probability distribution for each voxel. Settings included FWE correction 0.01 and 10,000 permutations. ALE maps were registered to cvs_avg35_inMNI152, providing ALE values for each vertex in the left hemisphere. We clustered vertices in the left PCG based on ALE values, including ‘parsopercularis’ for its language function relevance. Clustering used k-means with cityblock distance, evaluated by SSE, silhouette coefficient, and Calinski-Harabasz index. To assess structural bases, we conducted diffusion tractography on HCP 7T dataset DWI data. Steps included converting the aparc+aseg atlas, transforming it to subject-specific space, generating a connectivity matrix, and comparing connectivity patterns between clusters for all subjects.

**Results:** In our parcellation and function decoding analysis, we found that a four-cluster solution was optimal for the left PCG. This led to identifying four distinct segments: PP, VP, DP, and the other region. MACM revealed distinct coactivation patterns for these clusters. PP showed increased coactivation in sensorimotor areas, VP in language processing and action observation regions, and DP in eye field and execution-related areas. Diffusion tractography analysis highlighted significant connectivity differences among these clusters. DP showed stronger connectivity to the left caudal middle frontal region compared to PP, while VP had enhanced connectivity to the left pars opercularis and supramarginal regions. PP, in contrast, demonstrated stronger links with sensorimotor areas like the left postcentral, putamen, and pallidum.
Conclusions: Our meta-analysis offers detailed insights into the left PCG, identifying 3 unique subregions: PP, similar to M1 in function and structure, and the anterior VP and DP, each with distinct roles. PP is engaged in basic cognitive tasks, while VP focuses on language, and DP is associated with action observation, highlighting their diverse cognitive functions and networks.

References

Poster No 2110

Designing Consistent Graph Theory: Sulcal Pattern Analysis in Schizophrenia

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Introduction: Sulcal patterns, the concave regions within the cerebral cortex, show significant inter-individual variability and are associated with cognitive abilities and pathological characteristics. Despite the widespread application of graph theory in brain network analysis, its use in analyzing sulcal patterns is relatively unexplored. This study introduces a novel graph theory

Conclusions: Our meta-analysis offers detailed insights into the left PCG, identifying 3 unique subregions: PP, similar to M1 in function and structure, and the anterior VP and DP, each with distinct roles. PP is engaged in basic cognitive tasks, while VP focuses on language, and DP is associated with action observation, highlighting their diverse cognitive functions and networks.

References
framework to examine complex sulcal patterns in individuals with a first episode of psychosis and those at high genetic risk for schizophrenia, compared to normal controls.

Methods: Subjects: We recruited 101 healthy controls, 50 unaffected relatives, and 101 first-episode psychosis patients. MRI data were processed using FreeSurfer and the HCP-pipeline. Sulcal curves were extracted as trees consisting nodes and edges using TRACE. This graphical representation forms the basis for employing graph theory tools in analyzing complex sulcal pattern patterns. Consistent graph theory: The extracted sulcal patterns were analyzed using graph theory-based methods, with a focus on entropy measures and correlation dimensions. Entropy, serving as a measure of network unpredictability and complexity, was computed based on the node degree and lengths of trees. Concurrently, the correlation dimension, a critical metric reflecting the network’s complexity, was deduced by assessing the scaling attributes of the sulcal patterns. Recognizing the absence of a ground truth in real data scenarios, we employed a novel approach that leverages the consistency of measurements across the left and right hemispheres as a benchmark. This approach addresses the inherent hemispheric variations, which are typically more pronounced across subjects than within a single subject. We introduced the Hemisphere Consistency Index (HCI), a metric specifically designed to evaluate the reliability of features based on their correlation across hemispheres. Both degree-based entropy and correlation dimension metrics exhibit limited reliability and should be avoided in analysis. Length-based entropy has higher reliability and highlights its potential for yielding consistent and reliable results in the statistical analysis of sulcal patterns.
Results: We employed ANOVA to examine the significance of age, group, and sex variables on entropy and correlation dimension measures while factoring out other covariates. The findings were in line with the HCl. Specifically, the length-based entropy analysis for both the right and left hemispheres demonstrated statistically significant differences in sex (p-values < 0.00001) and age (p-values < 0.008). In contrast, other measures with lower HCl values were not consistent in detecting effects of sex or age. The group effect was less pronounced (p-values = 0.078 right, 0.110 left). This suggests that the differences attributable to psychiatric conditions might be too subtle to be captured with the current sample size.

Conclusions: HCl emerged as a pivotal tool in our analysis, enabling a more nuanced understanding of measurement consistency in sulcal pattern analysis. Through HCl, we identified that length-based entropy, as opposed to degree-based entropy and correlation dimensions, demonstrates a higher level of reliability. This was evident in its consistent detection of sex and age effects across hemispheres. The findings underscore the importance of selecting appropriate graph theory features based on their consistency and reliability. However, the marginal group effects observed suggest for localized analytical methods, such as tensor-based morphometry (TBM), to identify subtle differences in sulcal patterns. Future research should focus on developing efficient bases for parameterizing and smoothing sulcal curves consistently across subjects. TBM offer a more detailed and region-specific analysis, potentially providing insights into localized variations in brain structure associated with psychiatric conditions. This is left as a future study.

References

Poster No 2111
Assessing Brain Microstructure in Juvenile Myoclonic Epilepsy using NODDI
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Introduction: Juvenile Myoclonic Epilepsy (JME) is the most common idiopathic/genetic generalized epilepsy (IGE), comprising 10% of all epilepsies. JME is characterized by generalized epileptiform discharges, generalized tonic-clonic seizures, myoclonus, and seizure onset in adolescence. Even when structural changes are not apparent on routine MRIs it is now evident that brain network can be disrupted in JME relative to healthy controls. Such brain differences may arise from microstructural changes leading to changes at the macrostructural connectivity disruptions. In this study, we used connectome quality multi-shell diffusion weighted imaging (msDWI) and the neurite orientation dispersion and density imaging (NODDI) model to investigate cortical microstructural alterations in JME.

Methods: Data and pre-processing: MRI images were acquired on GE 3 T wide bore with 48-ch head coil, from n=49 JME participants (20.2±3.4 years) and n=25 healthy controls (HC) (17.8±3.9 years) between 12-25 years. Briefly, msDWI data were acquired using multiband EPI (Moeller et al. 2010) with slice acceleration factor 3 and with opposite phase-encoding polarity (AP and PA). The acquisition of 2 reversed phase-encoding directions makes it possible to eliminate susceptibility distortions to a great extent. Collectively, these factors result in a much-improved characterization of WM connectivity and identification of aberrant patterns (Sotiropoulos et al. 2013). The diffusion-weighted images were acquired at b = 1,000 s·mm⁻² and b = 2,000 s·mm⁻² in an alternating fashion. There were two sets of protocol: 1) with 38 directions at 1,000 s·mm⁻², 37 directions at b = 2,000 s·mm⁻², and 9 b=0 volumes; 2) 50 directions at both 1,000 s·mm⁻² and b = 2,000 s·mm⁻², and 5 b=0 volumes. The data were pre-processed using DESIGNER (Ades-Aron et al., 2018) guidelines and NODDI measures were estimated using DMIPY (Fick et al., 2019). NODDI measures such as NDI (neurite density index) and ODI (orientation dispersion index) were calculated at the gray-matter (GM) boundary using GBSS (gray-matter based spatial statistics) (see Figure 1 for conceptual overview) framework (Vogt et al. 2020). The NODDI data projected onto the gray matter skeleton were harmonized using NeuroComBat to account for the protocol differences (Garcia-Ramos et al, 2023). Permutation testing with n=10000 permutations were used to conduct the statistical analysis with threshold free cluster enhancement (Winkler et al., 2014) for family-wise error corrections.
**Results:** Neurite density was significantly higher throughout frontal and cingulate regions as well as insular areas (Figure 2, left), along with significantly higher orientation dispersion of neurites (Figure 2, right) in bilateral frontal areas, posterior cingulate and left temporal regions compared to controls. These results support the hypothesis that defective neuronal pruning might be present in JME which enables hyperexcitable synapses in the brain (Meencke and Janz, 1984). Abnormalities in brain function, cortical thickness, positron emission tomography and EEG have been found on JME at the frontal lobe and cingulate areas, which are the most prominent areas of significant differences in this study (see Wolf et al., 2015 for a review). These findings suggest that JME is associated with microstructural deviations compared to controls throughout diverse gray matter brain regions.

![Diagram](image)

**Conclusions:** Preliminary results from the JMECP demonstrate significant gray matter microstructural differences in NDI and ODI in patients with JME. The general pattern demonstrates increased NDI and to a lesser extent increased ODI within frontal regions. These suggest a less organized and hyperconnected neural architecture within the frontal gray matter-the region partially related to seizure generation in JME. Further investigation is needed to determine how these changes relate to clinical and cognitive outcomes in JME.

**References**

Poster No 2112

Sensory Integration Mapping in Early Blindness

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Introduction: Multisensory information integrates as signals propagate from lower- to higher-order brain regions (Mesulam, 1998, Calvert, 2001; Beauchamp et al., 2004; Beauchamp, 2005; Driver & Noesselt, 2008). However, it is unclear how early-onset blindness alters the organization of sensory processing. This study compared early-blind and sighted controls using a sensory integration model, which represents cortical organization by relative relationships to primary sensory areas. With this work, we aimed to enhance our understanding of cortical reorganization in the absence of visual experience.

Methods: We included 16 early-blind participants (EB, 10F, mean age = 32.8 yrs) and 22 sighted controls (SC, 11F, mean age = 31.3 yrs) from a previously published dataset (Xu et al., 2023). SC participants underwent blindfolding during the MRI scan. The resting-state functional and T1 weighted structural MRI data were processed using Micapipe (Rodriguez-Cruces et al., 2022), with additional surface-based smoothing (FWHM = 4). The sensory integration model was established as follows (Fig.1a). Sensory-related information at each vertex was derived using a non-negative linear model, employing time series from the primary visual, sensorimotor, and auditory cortex (V1, S1, and A1, delineated in Glasser et al., 2016) as predictors. The coefficients obtained from the linear model were converted into angles through hue transformations, representing the relative combination of primary signals. The variance explained by the predictors was ordered and rescaled from 0 to 1 to derive magnitude, which reflects the dependence on signals from the primary sensory cortex. Between-group similarities in magnitudes and angles were assessed using Spearman and circular correlation (Jammalamadaka and Sengupta 2001, p176), respectively. Vertex-level comparisons involved evaluating magnitudes through a two-sample t-test and angles using the Watson-Williams test. The cluster-based permutation test (n = 5000, p < 0.05) was used to correct all statistical results for multiple comparisons.

Results: The polar and surface projections of the sensory integration model are depicted in Fig.1b for early-blind (left) and sighted controls (right). The network-wise distributions of magnitude exhibit overall similarity between the two groups (Fig.1c). Along the ventral visual stream, both groups demonstrate patterns transitioning from periphery to core, but the angular distribution of EB shows more alignment to visual domain than SC (Fig.1d). The between-group correlations of the global angles and magnitudes are 0.718 and 0.926. A significant between-group difference (vertex-level p < 0.001 and cluster-level p < 0.05) is observed in angles within the extrastriate cortex (Fig. 2a) and in magnitudes within left parietal cortex (area PFm) (Fig. 2c). The pattern in the extrastriate cortex of EB is located close to the V1 anchoring angle (0°), whereas the pattern of SC is closer to the S1 anchoring angle (120°) (Fig.2b). Although both groups were scanned without visual stimulus, the signal from V1 still plays a great role in the activity of surrounding regions of EB but not for SC. The pattern in left PFm of EB is more peripheral (Fig. 2d), suggesting a greater dependence on primary signals than SC.
Conclusions: The sensory integration model delineates distinct areas along the sensory processing stream that significantly differ between early-blind and sighted controls, especially within regions related to visual processing. The nature of the cortical reorganization in early blindness has been partially captured in the extrastriate cortex through the relative combination of signals from the primary sensory cortex and in area PFm through the dependence on these signals. Although
further exploration is needed to validate and refine these findings, they provide a novel insight to investigate the stability and flexibility of cortical organization and how they change based on experience with visual input.

References

Poster No 2113
Exploring Cortical Muscle Representations in Patients With Migraine using TMS – A Preliminary Study
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Introduction: Migraine (MIG) remains one of the leading causes of worldwide disability, resulting in 45.1 million years lived with disability at a global prevalence of twelve percent1,2. Convergent multimodal evidence points towards cortical hyperexcitability as one aspect of MIG pathophysiology3,4. Additionally, recent evidence suggests a link between cervical neuromuscular affereces and MIG pathophysiology, potentially mediated at the level of the trigemino-cervical complex (TCC)4,5. In this context, the current preliminary study employed a transcranial magnetic stimulation (TMS) paradigm to investigate cortical motor representations of the trapezius muscles in MIG patients and healthy controls (HC), given its innervation profile (C1-C3) and role within the TCC.

Methods: We prospectively recruited 12 MIG patients, who were matched with HC based on the criteria of body mass index (BMI), age, and sex. Neuronavigated TMS (nTMS) and electromyography (EMG) were used to create cortical motor representation maps via motor evoked potentials (MEPs) of the medial (TrM) and lateral (TrL) trapezius muscles on both hemispheres, with all MIG patients being investigated during inter-ictal intervals. The EMG recordings from the biceps brachii (BI) were simultaneously acquired as a control muscle. After motor hotspot determination and identification of optimal e-field orientation, the resting motor threshold (rMT) was determined for either TrM or TrL. Subsequently, cortical motor representations of the TrM and TrL were mapped using an intensity of 105% rMT. The stimulation intensities and MEP amplitudes were extracted for comparisons between MIG and HC groups.

Results: Mean age for both groups was 26±3 years, with a sex distribution of 11 females and 1 male per group. The rMT did not significantly differ between both groups (p>0.05). After Bonferroni correction, TrM and BI demonstrated significantly higher MEP amplitudes spread over the primary motor cortex (M1), supplementary motor area (SMA), and premotor cortex (PrM) in MIG as compared to HC (TrM: 2.21±1.32 μV vs. 1.90±1.16 μV, p<0.0006; BI: 16.21±10.57 μV vs. 14.91±11.10 μV, p<0.0001).

Conclusions: According to the results of this preliminary study, the observed results for MEPs across different muscle groups may be interpreted in the context of inter-ictal motor hyperexcitability in MIG patients3,4. The group differences were found for the trapezius muscles, involved in the concept of the TCC, but also for the BI, thus potentially emphasizing general hyperresponsiveness over trigemino-cervical specificity. However, given the small sample size and lack of further parameters to assess excitability and neuromodulatory effects in more detail (e.g., active motor threshold, cortical silent period), the findings of this preliminary study need to be followed up by investigations in larger samples. Specifically, future analyses need
to take into account the extent and distribution of cortical motor representations, as well as longitudinal measurements across the MIG cycle to further elucidate motor system hyperexcitability.

References

Poster No 2114
Morphological Analysis of the Inferior Frontal Sulcus in the Chimpanzee (Pan troglodytes) Brain
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Introduction: There has been considerable interest in the neuroanatomical similarities of the homologue of Broca’s region in nonhuman primates to further understanding of the evolution of language. The inferior frontal sulcus (ifs) is a critical landmark below which lie language production areas in the human brain, and its homologue may be found in the chimpanzee brain (see Fig.11-3). Defining the morphology of the ifs may provide insight into the structural blueprints that permit the development of language in human brains.
Methods: MRI scans of the brains of 50 chimpanzees (Pan troglodytes; 22 male and 28 female) from the National Chimpanzee Brain Resource (NCBR) were examined. The MRI scans were acquired using a 3T scanner (Siemens Trio, T1W images, 0.6-0.90 mm isotropic) at the Yerkes National Primate Research Center. The MRI scans were registered to an NCBR volumetric chimpanzee template using a 12-parameter registration. Cortical surfaces were reconstructed from the MRI scans using CIVET-Chimp (see reference #5 for similar methods used in CIVET-Macaque), which permitted 3D investigation of the sulcal contours and fundus. The ifs and adjacent sulci were identified in each hemisphere (100 hemispheres in total, 50 left and 50 right) on the basis of recent sulcal investigations. The morphological patterns of the ifs were then categorized by type and according to the connections with surrounding sulci. Finally, the individual surfaces were registered to a common surface template obtained by averaging the surfaces of the subjects under study. The ifs was then labeled on the resampled surfaces using Freeview. The labels were averaged across subjects, such that the spatial probability map quantifies the likelihood of each surface vertex belonging to the ifs.

Results: The ifs can be categorized into five types, each having a different frequency of occurrence. Type 1: the ifs connects posteriorly with the inferior precentral sulcus in 40% of hemispheres (46% of left; 34% of right). Type 2: the ifs connects anteriorly with the rectus sulcus, in addition to connecting posteriorly with the inferior precentral sulcus in 49% of hemispheres (46% of left; 52% of right). Type 3: the ifs connects anteriorly with the rectus sulcus only in 6% of hemispheres (4% of left; 8% of right). Type 4: the ifs is an independent sulcus with no connections to neighboring sulci in 5% of hemispheres (4% of left; 6% of right). Type 5: the ifs additionally connects to other adjacent sulci (i.e., fronto-orbital sulcus and middle frontal sulcus) in 15% of hemispheres (16% of left; 14% of right). With regard to its relationship with surrounding sulci, the connection of the ifs with the inferior precentral sulcus was completely fused in 75% of hemispheres (90% of left; 60% of right), superficially fused in 14% of hemispheres (2% of left; 26% of right) and in 11% of hemispheres (8% of left; 14% of right) there was no connection. The connection of the ifs with the rectus sulcus was complete in 12% of hemispheres (12% of left; 12% of right), superficial in 43% of hemispheres (38% of left; 48% of right), and there was no connection in 45% of hemispheres (50% of left; 40% of right). Finally, there was a complete connection of the ifs with other adjacent sulci in 9% of hemispheres (10% of left; 8% of right) and a superficial connection in 6% of hemispheres (6% of left; 6% of right). See Fig. 2 for examples of the different patterns of the ifs in three hemispheres.
Conclusions: The present study demonstrates that, despite its considerable variability, the ifs can be clearly differentiated from adjacent sulci by means of 3D examination of the sulcal contours and fundus. The morphological descriptions presented here provide a means of identifying accurately the ifs in the chimpanzee (Pan troglodytes) and contributes to a better understanding of the structural organization of a region that, in the human brain, evolved to play a critical role in language production.

References

Poster No 2115
Cerebral expression and evolutionary annotation of oxytocin pathway genes
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Introduction: Oxytocin (OT) is a neuropeptide involved in a range of functions across vertebrate species, from parturition and lactation (e.g.,[1,2,3]) to energy regulation[4,5] in different vertebrates. In humans, OT has been investigated as a treatment for mental disorders and conditions due to its link to social cognition[6], albeit with inconclusive results thus far[7]. The extent of OT’s functions suggests its evolutionary conservation. Genetic and imaging studies on selected OT genes have aided in unraveling the role of the OT system, however, more than 150 genes are involved in OT signaling. An evolutionary timeline for all genes in the pathway remains incomplete, as does their cerebral expression. A characterization of the evolutionary history and cerebral expression of genes in the OT signaling pathway might help in better understanding the system’s current function and purpose.

Methods: To assign the 154 genes in the OT pathway to different phylostrata in evolution, we deployed BLASTp and phylostratigraphy across 39 species (26 invertebrates, 13 vertebrates), ranging from bacteria to modern humans. In addition, microsynteny was used in vertebrates. The genes were categorized as ‘ancient’, ‘medium-aged’ and ‘modern’ based on the resulting genes ages. We also tested for positive selection signatures in a subset of ‘modern’ OT pathway genes. Subsequently, the differential expression of the three gene age subsets across the human body, including the brain, was assessed with FUMA. Given the results, the cerebral expression specificity of the modern OT gene set was explored using the Allen Human Brain Atlas (AHBA; preprocessed with the abagen toolbox[8] and summarized using the included Desikan-Killiany atlas). We compared the expression of the modern OT gene set in each donor in a given brain region against the whole-brain across-donor population mean of the same gene set.

Results: Of the 154 genes in the OT pathway, we classified 28 as evolutionary ‘ancient’, as they have homologs dating to 3500 – 1100 million years ago (mya). Another 28 genes had homologs dating to 1000 – 550 mya, which we classified as ‘medium-aged’. The majority of the OT pathway genes (n = 98) were ‘modern’, having evolved between vertebrate (540 mya) and homini evolution. Of those modern genes, most emerged around jawless or jawed vertebrates (540 - 530 mya), including OXTR (encoding the OT receptor), OXT (encoding the OT ligand) and CD38 (regulating OT secretion). 44% of those were under positive selection during vertebrate evolution. The medium-aged genes were up-regulated in blood vessel and the bladder, while the modern genes were up-regulated in muscle tissue and the brain. In the human brain, those modern OT pathway genes displayed significantly up-regulated expression in four cortical regions (e.g., precentral gyrus), and they were significantly down-regulated in five sub-cortical regions (e.g., hippocampus; fig. 1). Of note, OXTR and CD38 were still above-average expressed in all subcortical regions.
Conclusions: In this study we found that the vast majority (64%) of homologs in the OT signaling pathway emerged with and after vertebrate evolution and can thus be considered ‘modern’. We further show that approximately 36% of homologs of genes supporting the OT signaling pathway date further back, that is 3500 to 550 million years. OXT, OXTR, and CD38 have their earliest homolog around 540 – 530 mya. Accordingly, we suggest that the evolution of the OT signaling pathway was a gradual process in which evolutionary ancient genes first started interacting with and supporting OT signaling around the evolution of vertebrates, but other genes joined the OT signaling system afterwards. Finding that only modern genes in the OT pathway were up-regulated in the brain, specifically the cortical regions, might indicate that cognition and social behavior were not an initial function but only have evolved later when new environmental demands required it.

References

Poster No 2116

Texture Analysis as a Tool for Quantifying Cellular Architecture in the Human Brain

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Introduction: Advancements in optical methods, image analysis and 3D mapping have improved our understanding of the brain’s microstructure in the past years. Different methods have been proposed to analyze the architecture of the cerebral cortex, e.g., extracting line profiles to quantify laminar changes in cell density (e.g.,), or descriptive approaches for...
characterizing subcortical nuclei (e.g., mean cell densities, cell sizes). However, there is a lack of methods to reproducibly describe the architecture of the numerous and highly heterogeneous areas in the human brain in a more comprehensive way that considers variations in cellular distributions. Here we introduce texture feature analysis in high-resolution histological images to characterize the brain's architecture. As a proof-of-principle, it has been applied to histological images of the lateral and medial geniculate bodies (CGL and CGM)[2].

**Methods:** We analyzed 550 regions of interest from 10 human postmortem brain (resolution 1μm in-plane). We leveraged the Julich Brain Atlas for anatomical reference. The texture analysis was based on the Gray Level Co-occurrence Matrix (GLCM) method that evaluates the frequency and relationship of pixel intensity pairs neighborhoods across the images. From the GLCM, 21 modified Haralick texture features were extracted, encompassing aspects like contrast, homogeneity, energy, and correlation to quantify the cellular architecture of the tissue. A Principal Component Analysis (PCA) reduced these features to four main components, capturing 96.18% of total variance. The distinctiveness between the CGL and CGM was assessed using Independent-samples Kruskal-Wallis tests. Additionally, we examined the intra-structural differences within the CGL's six laminae, demonstrating the method's applicability to more complex neurohistological structures (Fig 1 a,b).

**Results:** The texture analysis resulted in a separation of the CGL and CGM, showing unique microstructural traits in both areas. A subsequent PCA effectively simplified the texture data, and especially the first four components stood out in how clearly they differentiated from each other. Within the CGL, we observed significant textural differences between the layers, especially between magnocellular (Lamina 1-2) and parvocellular layers (Lamina 3-6). These differences were statistically significant, with the second and third PCA components showing substantial variations across the laminae (Fig 2 a,b).
Conclusions: Texture analysis of high-res histological images quantified the brain's complex micro-architecture and parcellation going beyond basic metrics like cell density. Therefore, it seems to be a promising tool to provide new insights into the brain's architecture, both in cortical and subcortical structures. This approach excels in discerning both notable distinctions, like those between CGL and CGM, and subtler variations within CGL's magno- and parvocellular layers. The interpretation of texture features in terms of traditional histological features is sometimes not straightforward, e.g., due to the different contributions of features to PCA factors, resulting in each factor representing a mix of features. However, such complexity corroborates with microscopic observations, especially in highly heterogeneous subcortical nuclei. The present study provided first evidence that texture analysis enables a reproducible and quantitative characterization of cellular architecture, deepening our grasp on brain organization.

References
Neuroanatomical Correlates of Cognitive Phenotypes in Patients with Primary Brain Tumors

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Introduction: Patients with primary brain tumors exhibit substantial variability in neurocognitive profiles, likely related to multifactorial etiologies and different neuroanatomical locations. Cognitive phenotyping offers a patient-centered approach toward characterizing patterns of impairment and has shown utility for determining risk for disease progression in neurological disorders (Hancock et al., 2023; Hermann et al., 2007). Investigating the neuroanatomical correlates of cognitive phenotypes in patients with brain tumors may lead to a better understanding of the mechanisms underlying different patterns of cognitive impairment while also elucidating specific risk factors for cognitive decline.

Methods: Patients with primary brain tumors were recruited for a prospective, observational study examining the effects of fractionated, partial brain radiotherapy on cognition between 2014 and 2021. Neurocognitive and structural MRI data were available for 79 participants prior to radiation treatment. Patients were cognitively phenotyped using latent profile analysis in a prior study, which revealed three groups: those with generalized impairments (17.7%), those with isolated verbal memory impairments (12.7%), and those with minimal impairments (69.6%). MRI scans were acquired on a 3.0T 750 GE scanner. Anatomical images were acquired using a T1-weighted inversion recovery spoiled gradient echo sequence and diffusion data were acquired with a single-shot pulsed-field gradient spin EPI sequence with b = 0, 500, 1500, and 4000 s/mm², with 1, 6, 6, and 15 unique gradient directions for each b-value respectively. Anatomical scans were processed using FreeSurfer version 5.3.0. Diffusion tensors were calculated using mono-exponential fitting from b=0, 500, and 1500 s/mm² to extract estimates of fractional anisotropy (FA) and mean diffusivity (MD). DTI metrics were calculated from the co-registered DTI maps by sampling up to 5 mm below the white matter surface normal at each vertex and then averaging within each ROI volume. Tumor, necrotic tissue, and regions of edema were manually censored for each patient and excluded from final ROIs prior to analysis. Cognitive phenotypes were compared using ANCOVAs for CT, FA, and MD in each ROI while controlling for age, with follow up pairwise comparisons. Pearson correlations with neurocognitive test performance were examined in regions exhibiting significant differences between groups.

Results: Compared to the minimal impairment group, the verbal memory impairment group showed significantly increased CT in the left temporal pole (p = 0.032) and right parahippocampal gyrus (p = 0.022), along with reduced MD bilaterally in the parahippocampal gyrus (left p = 0.008; right p = 0.078). Greater MD in the left parahippocampal gyrus was also significantly associated with poorer HVLT Learning (r = 0.784; p < 0.001) and Delayed Recall (r = 0.528; p < 0.01) scores. The generalized impairment group showed decreased CT in the left cuneus (p = 0.039) left frontal pole (p = 0.049), right pars orbitalis (p = 0.033) and right superior parietal region (p = 0.049). Neither CT nor FA was associated with cognitive performances within the phenotypes.

Conclusions: Cognitive phenotypes in patients with primary brain tumors showed unique patterns of brain pathology, suggesting different underlying mechanisms of impairment profiles. These results demonstrate the utility of examining neuroanatomical correlates of cognitive phenotypes for identifying areas of vulnerability that may inform treatment decisions for individual patients based on patterns of neurocognitive performance, with significant brain-cognition correlations supporting the biological relevance of this approach. Examining how phenotypes evolve over the course of treatment could be additionally helpful for understanding the effects of different intervention approaches on cognition, and for identifying patients at risk for treatment-related decline.

References
Effects of Emotional Changes in Brain Neural Activity in Relation to Food Intake

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Introduction: It is believed that a ‘delicious’ meal activates the brain, creates a sense of well-being and has a beneficial effect on the body. In everyday meals, there is a mixture of pleasant emotions such as “delicious and likeable” and unpleasant emotions such as “unappetizing and dislike,” and the perception of ‘deliciousness’ varies from person to person. Our previous study found that cerebral hemodynamic changes were significantly greater in the left frontal pole and dorsolateral prefrontal cortex when chewing gum that tasted and smelled ‘unpalatable’ than when chewing gum that tasted “palatable.” However, the changes in emotions according to individual preferences are still not clear. This study aimed to clarify the effects of emotional changes on cerebral neural activity in response to food intake using test foods prepared according to each person’s food preferences (approved by the Niigata University Ethics Review Committee (2019-0216)).

Methods: Participants were 21 right-handed, healthy, dentate individuals aged 20-35 years (10 males, 11 females, 28.1 ± 3.7 years). The decision on the food to be tested was made from the answers to questions about the food using Google Forms, after the presence or absence of allergies had been confirmed. Two food-related questions were asked: closed and open questions (“What foods do you like/dislike?”). The closed question asked 40 healthy adults in their 20s other than the participants to write a score for each of the 10 foods they most frequently answered “like” or “dislike” when asked in the open question (very much to not much: 5 to 1). Priority was given to the answers to the open question, and if a test food was difficult to prepare, the answer to the closed question was taken into account when deciding on the test food. The test foods were either soft-cooked Aito® (E.N. Otsuka Pharmaceutical) as a care food or a food prepared as a paste so that it could be swallowed without chewing. Cerebral blood flow was measured using a 45-channel fNIRS (FOIRE-3000, Shimadzu) covering the bilateral frontal to parietal lobes and analysed for oxy-Hb. Experiments were performed at least 3h after a meal. A total of three foods were used: control (Aito® rice), palatable and unpalatable foods, each of which was repeatedly ingested at 4 g per spoonful. The participants repeatedly swallowed and responded on a visual analogue scale (VAS: good to bad) according to the instructions displayed on a monitor placed in front of them. The fNIRS data were analysed using a generalised linear model (GLM). Then, incorporating the influence of emotion as assessed by the VAS values, a cortical activity map was created for each subject based on the β1 value of each channel, and a one-sample t-test was conducted using SPM123 to determine the brain activation area that respond in common to the emotional change of “deliciousness” in all participants.

Results: Significantly increased activity was observed in the left dorsolateral prefrontal cortex (Brodmann area: BA 9, BA 46) when emotional valence was high during food intake. In the right hemisphere, there was also significant but slightly altered activity in parts of BA 6 (premotor and supplementary motor areas, Fig. 1). The dorsolateral prefrontal cortex is an important brain region associated with appetite control, food craving and executive functions, which are closely related to memory, attention, learning and behaviour. Changes in hemodynamic response in the dorsolateral prefrontal cortex have also been reported to be associated with reward value (reward) and control of limbic reward areas such as the striatum.

Fig. 1 Cortical areas activated by diet-induced emotions.
Conclusions: Emotional changes associated with eating behaviour that were identified in the left dorsolateral prefrontal cortex indicate that activity in the reward system associated with eating may influence higher-order functions such as memory and learning. In other words, it can be inferred that the ‘taste’ of a meal may influence changes in cognitive functions.

References

Poster No 2119
Lesion-symptom mapping of language and cognitive function in stroke patients
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Introduction: Language deficit after stroke, aphasia, is one of the frequent consequences, and the consequences affect the whole life in terms of quality of life. There has been a growing understanding of how cognitive function affects language deficits after stroke. It is crucial to understand the relationship between lesions and language deficits including the factors that affect language abilities. In this study, we investigated the core neural correlates of language function and factors that can affect language by voxel-based lesion symptom mapping (VLSM) analysis using the principal components of cognitive and language assessments.

Methods: A total of fifty-five patients with stroke enrolled in this study. All patients completed the Korean version of the Western Aphasia Battery (K-WAB) and a comprehensive cognitive function test called the computerized neuropsychological test (CNT). Also, every patient underwent MRI scanning. All MR images were acquired on a 3T Siemens Prisma scanner (Siemens, Erlangen, Germany). Lesion maps were identified by automatic lesion segmentation using fractional anisotropy (FA) image derived from diffusion tensor imaging. The lesion-symptom mapping was conducted using a Statistical NonParametric Mapping (SnPM; version 13.1.08, http://nisox.org/Software/SnPM13/) toolbox implemented in the MATLAB to run the non-parametric analysis. A principal component analysis (PCA) was conducted to lower the dimension of multiple behavioral variables; behavioral scores of language and cognitive function examinations. Lesion-symptom mapping analyses of language function and factors affecting language impairment were conducted using the principal component loadings.

Results: As a result, a rotated PCA result produced six independent principal components (PC) : language, executive control, verbal memory, visual processing, semantic memory, and attention (Figure 1). Also, VLSM results showed significant neural correlates of four factors out of six (Figure 2). The results showed that a significant relationship with language impairment was found in the cluster at the center of the left insula and frontal operculum that extended to the inferior frontal gyrus (IFG). The significant cluster related to the executive control function was in the left insula, angular gyrus and posterior supramarginal gyrus. The small cluster in the left thalamus was found to be related to the verbal memory factor. The result showed visual memory and construction functions were related to regions in the right hemisphere, right Rolandic operculum and superior temporal lobe.

Figure 1. Factor loadings of six PCs & individual scatter plot between language and cognitive factors
Conclusions: A PCA result produced six independent factors related to language function after stroke. The VLSM results found core regions related to four language and cognitive factors that could affect language deficits. The results of this study could help to decide the target area for noninvasive brain stimulation (e.g., repetitive transcranial magnetic stimulation; rTMS, transcranial direct current stimulation; tDCS, etc.) for rehabilitation of aphasia.

References

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Poster No 2120
Quantifying human infra- and supra-granular layer properties using high-resolution ex vivo MRI
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Introduction: Analyzing the structure of the human cortex is challenging due to its highly folded nature and microscopic cyto- and myeloarchitectural detail. Histology allows for visualizing the structure of the cortex at a single cell resolution. However, tissue cutting and mounting makes it infeasible to align serial sections to the level of accuracy that is required for precise modeling of laminar and cytoarchitectonic boundaries of the cortical layers in 3D. Conventional in vivo MRI provides 3D whole-brain scans that can be used to construct surface models of the cortical sheet but lacks the resolution to extend this to the cortical laminae. In contrast, the spatial resolution of ex vivo MRI scans have been pushed down to 100 micrometers (μm), where the mesoscopic structure of the cortex becomes visible. Here we use an existing dataset of ex vivo MRI scans acquired at 120um resolution⁴, and construct surface models of the border between the infra- and supra-granular layers.

Methods: The MRI scans are first processed using a state-of-the-art, cascaded, multi-resolution U-Net architecture to obtain probabilistic segmentations (values between 0 and 1) of the infra- and supra-granular layers. The white matter (WM), granular, and pial surfaces are placed using a modified version of the FreeSurfer recon-all pipeline, which was tailored to handle the additional surface (granular) and the high-resolution data. The modified pipeline: (i) generates a full volumetric segmentation at 1mm isotropic resolution using a contrast-agnostic neural network⁶-⁸; (ii) upsamples the WM mask to 120um resolution;
(iii) refines the 120um WM mask with the confidence maps for increased accuracy; (iv) generates a pseudo T1-weighted image from the WM mask and confidence masks, which includes the infra- and supra-granular layers by linearly scaling the confidence values; and (v) processes this synthetic image with the recon-all surface placement pipeline\textsuperscript{9,10} to produce the final surfaces and a cortical parcellation.

**Results:** Fig 1A shows the MRI scan, surfaces, volumetric segmentation, and parcellation for a sample case. To study if we can detect architectonic borders of the primary visual area (V1), we computed intensity gradients at 20 different cortical depths between the WM and pial\textsuperscript{2}. The gradient magnitudes were averaged over the depth excluding the first and last two depths to avoid partial volume effects. Fig 1B shows the gradient magnitude on the inflated surface of three different subjects, and Fig 1C shows the border of the V1 label, mapped from the fsaverage template, overlaid on the gradient magnitude. The label border matches the areas with increased gradient magnitude, especially on the lateral part of the V1 – indicating that the borders of V1 can be directly detected using the high-resolution surface models and MRI data. Fig 2A&B show the average thickness of the infra- and supra-granular layers (top) and its variance (bottom) over four subjects. Fig 2C shows the correlation of the curvature magnitude and the infra-granular layer thickness: the gyri (light gray) have a positive correlation whereas the sulci (dark gray) have a negative correlation, indicating that the infra-granular layers expand at the gyral crowns and compress at the sulcal fundi – which is consistent with histological studies\textsuperscript{11} and computational cortical layer models\textsuperscript{12}.
Conclusions: We have presented a preliminary quantitative analysis of the infra- and supra-granular layer properties using high-resolution ex vivo MRI data. The dataset will be expanded to include surfaces and cortical parcellations for 17 subjects, which allows for assessing the individual variability of the infra- and supragranular layers and the cortical region borders. The models can be used to inform in vivo MRI analysis paving a way for more accurate modeling of the cortex in neuroscience studies. The scans, surfaces and parcellations will be made freely available for download from the DANDI data archive.

References

Poster No 2121

Grey-matter structure markers of Alzheimer’s disease, conversion, functioning and cognition

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Introduction: Grey-matter atrophy in Alzheimer’s disease (AD) maps the neuronal and synaptic loss associated with neurodegeneration. Atrophy patterns may be used to predict the disease risk or serve as secondary endpoints in clinical trials. We sought to extend our knowledge about grey-matter regions (thickness or surface) associated with AD status, as well as those associated with Mild Cognitive Impairment, Alzheimer’s conversion, parental history of dementia, and cognitive or functional scores. All of these can inform on the progression, and nature of the grey-matter atrophy across the disease stages.

Methods: We gathered T1w MRI brain images and associated data from 10 neuroimaging cohorts (N=9,140) and from the population-based UK Biobank (N=37,664). We performed Region of Interest (ROI; Desikan-Killiani atlas) as well as vertex-wise analyses, using grey-matter measurements generated using pipelines from the ENIGMA consortium (based on FreeSurfer 6.0). Analyses included estimation of whole-brain morphometricity (fraction of explained variance by all brain [ROI or vertex-wise] measurements), as well as brain wide association studies. We considered 24 traits of interest, that focus on different disease stages (e.g. conversion within 1-5 years, MCI, AD status), disease risk (parental history) and scales (e.g. MMSE, CDR, GDS, RAVLT) that capture more specific cognitive, psychiatric or functional dimensions. To boost statistical power, we meta-analysed results from 8 cohorts, and validated the findings using replication and out-of-sample prediction in 2 independent cohorts. We contrasted the grey-matter regions associated with the different traits, or those that we identified using ROI and vertex-based approach.

Results: We found significant morphometricity between our traits and the grey-matter measurements, except for parental history of AD, and the Geriatric Depression Scale. Vertex-wise morphometricity was 3 to 21 times larger than the ROI based one, indicating that vertex-wise data captures more signal of interest. We identified 94 trait-ROI significant associations, and 307 distinct clusters of trait-vertex associations, partly overlapping with the ROI findings. For AD vs. controls (N=796 cases, 2752 controls), our results confirm atrophy of the hippocampus, amygdala and of the medial temporal lobe ( fusiform and parahippocampal gyri) and our vertex-wise results provide a precise localisation of the atrophied regions. In addition, we identified replicable atrophy in several subcortical (putamen, accumbens) and cortical regions (inferior parietal, postcentral, middle temporal, transverse temporal, inferior temporal, paracentral, superior frontal), some of which have rarely been reported. The analysis of AD conversion, MCI status and cognitive/functional scores yielded fewer associated regions, that partly overlapped with the regions associated with AD. We combined the significant ROI or vertices to build interpretable predictors, which achieved statistically significant out of sample prediction (AUC in 0.53-0.70). Lastly, we found that the AD grey-matter score could predict cognition, MCI status, conversion, genetic risk, or tau concentration from CSF in non-diseased individuals (AUC in 0.54-0.70).

Conclusions: Our large sample size, systematic replication and out-of-sample prediction provides robust maps of grey-matter atrophy in AD. Our joint analyses of AD status, conversion and cognitive/functional scores help shed light on the evolution of atrophy across the disease stages, and its relationship with cognitive or functional impairment. The vertex-wise analysis complements the ROI based approach in identifying additional brain regions and offering a localised description of the atrophied regions. All our significant findings explain a fraction of the morphometricity, suggesting that more grey-matter regions remain to be identified using larger samples, to improve prediction and unveil the full map of atrophy in AD.

**Poster No 2122**

**Neuron-Level Motor Cortex Mapping with Transcranial Magnetic Stimulation**

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Introduction: Transcranial magnetic stimulation (TMS) is a non-invasive technique that modulates brain activities by generating a time-varying electric field in the brain, capable of eliciting action potentials in cortical neurons1. By using biophysical modeling of the induced electric field (E-field) the cortical structures that are effectively stimulated by TMS can be identified2,4. We recently proposed a regression-based method to perform structure-function mappings by analyzing the relationship between behavioral modulation and local cortical stimulation strength3,7. Physiological properties of neurons, especially the orientation of the neurons with respect to the E-field, determine the firing threshold in response to TMS8. However, existing TMS modeling works neglect the diversity of neuron types and geometries across the different cortical layers. To bridge this
Our study incorporates a recently published average response model of cortical neuron\(^8\) into the regression-based TMS mapping of the motor cortex.

**Methods:** Fourteen healthy, right-handed participants (seven females, aged 21-38 years) were recruited\(^5\). High-resolution realistic head models were constructed from individual T1, T2, and diffusion weighted images acquired on a 3T Magnetic resonance imaging (MRI) scanner. Subsequently, the cortical layers were added within the primary motor cortex region of interest (ROI). A total of 900–1100 single TMS pulses were applied around the left motor hotspot with 150% motor threshold (MT)\(^5\). Coil positions and angles were randomly selected for each stimulation to sample electric field distributions and corresponding motor-evoked potentials (MEP) from the first dorsal interosseous (FDI) muscle. E-field simulations were performed for each pulse using SimNIBS v4.0 [9, 10]. Neuron firing thresholds for every element in the motor cortex were determined by computing the polar angle ($\theta$) and the percentage decay of the electric field magnitude ($\Delta|E|$) on layer 2/3 and layer 5 using the average threshold model from Weise et al.\(^8\). Subsequently, we calculated the effective E-field ($E_{\text{eff}}$) the neurons are responsive to by dividing the E-field magnitude ($E_{\text{mag}}$) by the normalized firing threshold (thresh) for each ROI element. These effective E-fields were then nonlinearly regressed with the elicited MEPs to locate their cortical origin on the cortical layer level. The highest goodness-of-fit ($R^2$) identifies the cortical site housing the relevant neuronal populations. We compared current mapping results obtained from the $E_{\text{eff}}$ (neuron-enhanced model) with those derived solely from the $E_{\text{mag}}$ (magnitude model), and the cortical column cosine model, which counts the normal component of the E-field.

**Results:** Localization results (depicted as $R^2$ maps in Fig. 1) revealed a consistent pattern when comparing the magnitude model with the neuron-enhanced model, which incorporated information from layer 2/3 and layer 5. The locations of elements with maximum $R^2$ did not show distinguishable differences across models. However, layer 5 exhibited significantly higher $R^2$ values compared to the standard method ($Z = 10$, $p = 0.013^*$, Wilcoxon test), suggesting a more precise functional localization of the cortical origin of the elicited MEPs. No significant difference was observed between the magnitude model and the layer 2/3 ($Z = 40$, $p = 0.463$, Wilcoxon test), or the cortical column cosine model ($Z = 19$, $p = 0.064$, Wilcoxon test).

![R² Maps](image-url)

Figure 1. Localization results from all 14 subjects with the magnitude model, the neuron-enhanced model on layer 2/3, and on layer 5. Subjects with the pink background indicate improved $R^2$ results on layer 5, while those with the cyan background represent a slight opposite trend. The highest $R^2$ values and the corresponding coordinates are individually displayed beneath the $R^2$ maps.
Conclusions: The current study advanced TMS modeling by incorporating neuron-specific factors, adjusting the E-field magnitude with the normalized firing threshold at the individual neuron level. The observed improvements in localization results in layer 5 emphasize the potential source of observing MEPs originating from this layer in the motor cortex. This neuron-enhanced model lays the groundwork for more comprehensive and accurate interpretations of TMS-induced effects in future works.

References

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Poster No 2123

Cortical Folding Shows Fingerprinting Ability in Early Developing Rhesus Macaques

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Introduction: Previous human studies have revealed that complex cortical folding patterns have the fingerprinting ability for individual identification as early as 30 postmenstrual weeks and remain a stable individual identifier across ages (Duan et al., 2020). However, it is unknown if this fingerprinting ability can extend to nonhuman primates with simpler cortical folds, especially during early brain development marked by dramatic cortical development. For the first time, we perform individual identification tasks based on a longitudinal dataset including 156 rhesus macaque scans during early postnatal stages. Our results have shown 100% identification accuracy, revealing the fingerprinting ability of cortical folds in macaques from birth.

Methods: In total, 156 longitudinal MRI scans of 32 rhesus macaques (18 males) from the UNC-Wisconsin Rhesus Macaque Neurodevelopment Database are used in this study (Young et al., 2017). Each macaque subject has 4 to 5 scans ranging from 0 to 3 years in age as illustrated in Fig. 1. (a). To characterize the cortical folding, we first segment the macaque brain MRI into gray matter, white matter, and cerebrospinal fluid; reconstruct cortical surfaces (Li et al., 2012); and compute the mean curvature, average convexity, and sulcal depth (Li et al., 2014) to vertex-wisely chart the cortical folding pattern. Then, we align all reconstructed cortical surfaces into a common space using an unbiased longitudinal group-wise registration strategy. (Li et al., 2015). The cortical lobar parcellation (10 regions in each hemisphere) is propagated from an atlas (Styner et al., 2007) to each individual scan. Finally, we resample all aligned cortical surfaces with 40,962 vertices to establish vertex-wise correspondence across scans and subjects. The identification task uses global-based, ROI-based, and vertex-wise frameworks in two directions: identifying a subject’s later scan using an earlier one, and vice versa. A dynamic identification pool is formed by combining a subject’s two scans at different times with the scans of all other subjects. The match is chosen by ranking pair-wise Pearson correlations using a specific feature combination. In the global-based framework, each scan is represented by concatenated features from both hemispheres, followed by subject-wise Pearson correlation ranking (Duan et al., 2020). In the ROI and vertex-wise frameworks, the selection process is performed at each ROI or within a 14-ring neighborhood from uniformly distributed vertices on both hemispheres (excluding noncortical areas), resulting in 1 candidate at each region or vertex. Then, a voting strategy is employed to count the votes for the candidate selected at each region or vertex, leading to the final decision of the match (Duan et al., 2020). The identification accuracy at each cortical region or vertex is calculated as the probability of correctly identifying the match. The vertex-wise accuracy map is averaged for each vertex, which is used repeatedly in defining neighborhood regions.

Results: Fig. 1 shows the results for different cortical feature combinations: (a) scan age distribution for each subject; (b) sulcal depth maps of human infants at 41 postmenstrual weeks and macaques at 20 months; and (c) the identification accuracies for both forward (early to late) and backward (late to early) tasks. Fig. 2 displays the maps of identification accuracy based on (a)
14-ring neighborhoods of around 2,300 uniformly distributed vertices and (b) lobar ROI for mean curvature, average convexity, and sulcal depth in the forward task. Results indicate high identification accuracy in the superior and middle temporal gyri for all cortical features.

Conclusions: This study unprecedently reveals that cortical folding patterns are reliable individual markers of rhesus macaques with high fingerprinting ability during dynamic early postnatal brain development, despite that macaques have simpler and less individualized cortical shapes than humans.

References
Optimizing Atrophy Mapping in Alzheimer’s Disease

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Introduction: Several MRI methods have been used to define atrophy in neurodegenerative diseases including Alzheimer’s disease. Raw cortical thickness measures are commonly compared across groups but are confounded by regional heterogeneity due to intrinsic differences in gyral/sulcal thickness1. To account for this heterogeneity and allow comparisons across cohorts, people have started using w-maps. A w-map is comprised of z-scores at every vertex, comparing that individual’s cortical thickness against an expected cortical thickness based on a normative group. However, it is unclear whether w-maps should be thresholded and focused on peak atrophy to exclude noise or if the more subtle variations in relative cortical thickness provide pertinent information.

Methods: In this study, cortical thickness and multiple w-mapping methods were compared using the Alzheimer’s Disease Neuroimaging Initiative cohorts (ADNI1 = 183 AD, 215 controls (CN), ADNI2 = 140 AD and 188 CN). MPRAGE MRIs sequences were processed in surface space using Freesurfer v7.2. Cortical thickness is determined on a vertex wise basis comparing the distance between the pial and white matter surfaces. These raw cortical thickness files were converted to GIFTIs and used for cortical thickness analyses. The w-maps were generated using cohort specific general linear models (GLMs) created from controls to calculate z scores while covarying for age and gender. Control subjects were excluded from their own GLM. A negative z-score occurs when the observed cortical thickness is thinner than expected by the GLM divided by the standard deviation. Unthresholded w-maps were then compared to w-maps thresholded at a z-score of negative 2 to define peak atrophy as has been done in the literature2. Methods were compared at the group and single subject levels. The w-maps were overlapped to create group level AD and CN maps for ADNI1 and for ADNI2. A two-sample t-test was performed comparing AD single subject w-maps to their Alzheimer’s Disease Assessment Scale - cognitive sub-scale (ADAS-cog) 11 scores for each cohort. The ADAS-cog 11 is a normalized test of general cognition. Reproducibility was assessed using the ground truth spatial correlation comparing ADNI1 to ADNI2.

Results: Cortical thickness analyses demonstrate sulcal/gyral differences in both AD and CNs which is not seen in unthresholded w-maps. Group level overlap maps for AD subjects for both unthresholded and z= -2 thresholded w-maps mimic known atrophy patterns in AD and highly correlate with group level AD vs CN two sample t-test maps. However, the CN group level map created from the -2 thresholded maps also resembles the AD atrophy pattern, while group level unthresholded maps do not show a clear atrophy spatial bias and do not correlate with the AD v CN map. Reproducibility between ADNI1 and ADNI2 ADAS-cog 11 was limited but higher in the unthresholded (0.22, p<0.004) compared to -2 thresholded w-maps (0.16, p<0.002).

Conclusions: In addition to normalizing cohorts, w-mapping removes regional heterogeneity seen in cortical thickness. Using unthresholded vs thresholded w-maps leads to better reproducibility and eliminates any spatial bias of atrophy within controls. These findings demonstrate the utility of w-mapping when assessing atrophy and show that the subtle variations in relative cortical thickness outside of peak regions positively impacts reproducibility.

References
Beyond tumor location: Global neurostructural reshaping in patients with left brain tumors

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Introduction: Brain tumors are known to disrupt cognitive functions according to their location. Following this idea, studies examining the structural impact of brain tumors have primarily focused on lesion location and their immediate counterparts, overlooking the dynamic interplay within brain networks. These studies have found effects in the grey matter volume of the contralesional hemisphere1–3, restricted to changes in volume in the immediate contralesional region without providing any insights for the rest of the brain. In a previous study, to actually take into account the impact within a certain network, we studied patients with tumors in the left hemisphere and focused on grey matter volume of 10 language related regions and found changes for all of them in contrast to healthy participants, regardless of tumor location4.

Methods: Consequently, this research aimed at assessing whether the presence of a tumor within the left hemisphere induced structural reshaping across the entire brain. For this purpose, we included a cohort of 39 patients with a tumor within the left hemisphere (including frontal, SMA, temporal, and parietal lesions) that were recorded in the pre-surgical stage and the longitudinal assessment of 22 of those patients 3 months after surgery. As a control, we include the data of 70 healthy participants. All participants underwent cognitive evaluations, including measures of general cognitive state, intelligence and working memory. Regarding language abilities, we obtained measures for language production, language comprehension and grammatical use. Patients completed the evaluations before and after surgery. To explore the mechanisms for structural plasticity, we collected high-resolution MRI T1 and T2 - weighted images. For patients, these images were collected before and after surgery and the lesion affected-area was manually reconstructed slice by slice in the native space by trained technicians. The overlay map by tumor location can be seen in Figure 1A. As an index of macrostructural alterations, we measured grey matter volume through voxel-based morphometry analysis (VBM)5. As a spatial constraint, we parcellated the brain according to the automatic labeling atlas (AAL)6.

Results: Results stated that, in comparison to healthy participants, patients showed volumetric decreases not only in the immediate contralesional area, as suggested by other studies, but also in the vicinity of the tumor and throughout the entire contralateral hemisphere. These results are illustrated in Figure 1B with controls depicted in dashed lines. This demonstrates that the structural effects of a brain tumor are global rather than lesion location dependent. Interestingly, patients showed no longitudinal difference in grey matter volume in either of the hemispheres 3 months after the surgical intervention. A lack of changes in volume after the tumor resection suggests that neuroplasticity mechanisms were happening already at the presurgical stage, most likely due to the nature of the lesion, which growth allows for reorganization.
**Conclusions:** Thus, by revealing a global pattern in the decrease of grey matter volume, this study challenges the traditional localizationist strategy followed when conducting structural studies in patients with brain tumors. A change is needed from studying just the contralesional area towards considering a whole-brain approach to understand the actual macrostructural impact. Overall, our findings shed light on the extent of the structural changes caused by the presence of a brain tumor, emphasizing the need to extend the scope of presurgical and intraoperative brain mapping in patients with brain tumors since the impact of a brain lesion appears to be global. Intraoperative mapping should be designed to respect the anatomical substrate that is already going through neuroplastic processes, moving to holistic treatments that would lead us to promote recovery and ultimately minimize the long-term deficits.

**References**


**Poster No 2126**

**Alcoholic and sweetened beverage intake in relation to regional cortical thickness**

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**Introduction:** Common drinks such as alcohol and sweetened beverages have been linked with multiple health outcomes including dementia in older adults. There is scarce data examining whether beverage intake is associated with regional cortical thickness (Thx), and little is known about these associations in young and middle-aged adults.

**Methods:** Using data from a community-based study of healthy adults, we examined the association between beverage intake and regional Thx, as well as the role of Thx in mediating the beverage–cognition association. We also examined the associations separately for young (20–44 yrs), middle-aged (45–59 yrs), and older (60+ yrs) adults. Beverage intake (drinks/day) information was self-reported from the Willet semi-quantitative food frequency questionnaire (FFQ) on average intake of artificially-sweetened beverage (ASB) [diet soda], sugar-sweetened beverages (SSBs) [orange/grapefruit juice, soda, and lemonade/fruit punch], and alcoholic drinks [beer, wine, and liquor] over the past year. Healthy Mediterranean diet score and total caloric intake were calculated from the entire FFQ. The global cognitive score was the average of the z-scores in memory, fluid reasoning, processing speed, and vocabulary domains. All brain images were acquired on Philips Achieva 3T MRI. Thx was evaluated in 68 regions of interest (ROIs) using Freesurfer v5.12. Linear regression models were used, adjusted for age, sex, education, total caloric intake, and Mediterranean diet score.

**Results:** The study included 436 individuals, with average age of 45.5 (SD=16) years, 16 (SD=2.4) years of education, and 55.5% females. Total alcohol intake was negatively associated with Thx in 9 ROIs. This was mainly due to liquor intake (11 ROIs) rather than wine (1 ROI) or beer (0 ROI) intake. In older adults there was a negative association between wine and 3 ROIs and between liquor and 4 ROIs, in middle-aged adults a positive association of wine with 2 ROIs, and in young adults a negative association between beer and 3 ROIs. We found that in the overall study population ASB was positively associated with Thx in the right posterior cingulate region, and fruit punch intake was associated with thickness in the left rostral middle-frontal gyrus. However, residual confounding by age may lead to these overall positive associations. Indeed, ASB and SSBs were consistently associated with lower Thx within each age group. In older adults, diet soda (rh-cuneus) and soda (lh-frontal pole) were each negatively associated with cortical thickness in 1 ROI, in middle-aged adults, diet soda with 1 ROI (rh-fusiform); and in young adults, orange juice with 8 ROIs. Alcohol drinks tended to be positively associated, while all ASB and SSBs tended to be negatively associated with the global cognitive score, although the results were significant only for total alcohol and orange juice. Thx in 2 ROIs mediated the association between soda and cognition in the overall population and in older adults.
In young adults, Thx in 5 ROIs mediated the association between orange juice intake and cognition. Thx did not mediate the relationship between alcohol drink and cognition.

Conclusions: Sweetened beverage intake was associated with lower cortical thickness and cognition in young, middle-aged, and older adults. Liquor intake was negatively associated with cortical thickness. Regions such as supramarginal, inferior parietal and superior parietal may particularly be vulnerable.

References

Poster No 2128

Influence of Estradiol and Progesterone on Neural Circuits: A Diffusion-Weighted MRI Study

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Introduction: Estradiol (E2) and progesterone (P4) are pivotal in modulating neural circuits throughout a female’s lifespan1,2. However, the precise mechanistic underpinnings of sex hormonal modulation on these neural circuits remain elusive. A growing body of cross-sectional neuroimaging studies has endeavored to unravel the intricate relationship between sex hormones and neural circuitry, employing structural and functional MRI techniques3. Recent research has also begun to emphasize the importance of densely sampled longitudinal tracking4 of hormonal rhythmic nature alongside dynamic changes in brain activity4. This approach enriches our insights into the multifaceted hormone-brain interactions by detecting also subtle changes that could be unnoticed in less frequent sampling. However, notably absent from the existing literature is an investigation utilizing diffusion-weighted MRI, a modality known for its sensitivity to microstructural tissue changes5. This study addresses this knowledge gap, aiming to provide a more comprehensive and nuanced understanding of the intricate interplay between sex hormones and neural circuits.

Methods: Three females and one man underwent extensive brain imaging across five weeks. Data collection took place mostly on weekdays in the morning. All three women were measured during their natural menstrual cycle, covering the follicular and luteal phases. One of the women underwent another complete measurement cycle while using an oral contraceptive. Hormonal E2 and P4 levels were measured daily after MRI. The dwMRI protocol consisted of a measurement with 394 volumes using a fast SMS-enabled sequence variant6 (1.5 mm iso res, max bvalue: 2700 s/mm2. Data preprocessing included denoising, determination of the frequency offset map, and the subsequent correction of susceptibility-based artifacts, eddy-current-based distortions, and rigid motion. The preprocessed data was then masked and spatially rigidly aligned to the MNI template. Subsequently, so-called peaks were calculated from the diffusion data, from which we segmented into 50 different white matter tract structures for each data set separately7. Tractograms for the diffusion properties fractional anisotropy (FA) and mean diffusivity (MD) were generated based on these tracts8 (cf Fig. 1). The changes in these tractograms over time were compared with the respective corresponding individual time courses of E2 and P4 using a permutation test.
Results: We found that the hormone level of P4 in many tracts can be used as a predictor for the temporal change of the diffusion parameter MD. This is particularly true for the tracts of the anterior thalamic radiation (ATR), fronto-pontine tract (FPT), and thalamic-premotor tract (T_PREM), where we observed very similar spatial distributions of areas between subjects (cf Fig. 2). However, we could not make this observation for the male and the female on the oral contraceptive measurement series. A correlation between the time course of the E2 level and the diffusion parameter MD could only be found in individual tracts and not consistently across the three female subjects with a natural menstrual cycle. Interestingly, no correlation of the temporal change in FA could be found with the hormones E2 and P4.
**Conclusions:** In summary, extensive brain imaging and venipuncture across the natural menstrual cycle have shown that changes in hormone levels are associated with measurable changes in diffusion parameters. Notably, the absence of correlations in the male and the female on oral contraceptives, when hormones are low or suppressed emphasizes the importance of considering the impact of hormonal dynamics on potential modulatory effects in future studies. This research contributes to a more comprehensive understanding of the nuanced dynamics between sex hormones and neural circuit microstructure, paving the way for further investigations that may elucidate the underlying mechanisms of hormonal modulation on brain connectivity.

**References**


**Poster No 2129**

**Representational geometry, not topography, best characterizes BOLD signals in multimodal brain areas**

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**Introduction:** Neural representations are characterized both as coarse topographic maps (Sereno, 1995) and embedded population codes (Churchland 2012, Mante 2013). Brain mapping hinges on stereotactic characterizations of brain function, and crucially neglects idiosyncratic fine scale embeddings, but accumulating evidence shows high dimensional embeddings exists at scales relevant to topographic maps (Sengupta, 2017). Here we use BOLD fMRI to systematically evaluate if topographic maps or embedded feature spaces provide a better account of millimeter scale population level brain organization. We show representational geometry offers a richer account of multimodal but not unimodal brain function.

**Methods:** We compare two brain encoding models using 3T BOLD fMRI data from the Human Connectome Project (N=610). One model, diereomorphic multivariate alignment (DMA), preserves local topography. The second is a novel variant of parcelwise high-dimensional alignment (fixed mean hyperalignment, fmHA) that preserves representational geometry and mean regional evoked responses, but not local topography. Models are fit to functional connectomes estimated from resting-state data (15 min/participant). We first use DMA to align pairs of individuals and then apply fmHA to resulting connectomes. Both models are tested for their ability to predict responses evoked by a battery of 7 cognitive, sensory and motor tasks in independent runs of independent aligned participants (N=305), measured in terms of improvements in pairwise a priori networks (BSC). We expect alignment of task evoked responses will improve most in transmodal networks (especially default mode [DMN], frontoparietal [FP], dorsal attention [DA] and salience), and define these as a priori networks of interest. First, resting state alignment is limited by the idiosyncrasies at rest which are greatest in transmodal areas (Gratton, 2018). Second, we expect a unique advantage for fmHA in areas dominated by population code embeddings, while DMA is expected to perform best in areas dominated by coarse scale topographic maps. The latter are undisputed in unimodal areas but topographic organization of multimodal and transmodal brain areas remains largely uncharted.

**Results:** On average across task conditions and throughout the cortex DMA categorically improves BSCs relative to surface anatomical alignment (+7.4% BSC, z-fisher r = +0.023 ± 0.0004, t305=49.0, p < 0.001). fmHA incrementally improves on DMA in transmodal networks (+2% BSC for fmHA-DMA, z-fisher r = +0.005 ± 0.0007, p < 0.001) but DMA was superior to fmHA in unimodal networks (+15% BSC for fmHA-DMA, z-fisher r = -0.07 ± 0.001, p < 0.001). Among transmodal networks, DMN (+15% BSC, z-fisher r = +0.021 ± 0.001, p < 0.001), FP (+14% BSC, z-fisher r = 0.022 ± 0.001, p < 0.001) and DA (+5% BSC, z-fisher r = 0.012 ± 0.001, p < 0.001) networks show statistically significant increases in BSC for fmHA - DMA (mean±sem, Holm-Sidak
Hyperalignment improves between subject correlations in task evoked responses relative to diffeomorphic alignment in multimodal but not unimodal regions.

**Conclusions:** Prior efforts to establish shared group level representations in the brain have been limited in scope (Haxby 2011), precision (Bazeille 2021) or are confounded by model averaging (Guntupalli 2016) and transformations which disrupt both topographic maps and evoked response amplitudes simultaneously. We use granular, interpretable models to show support for different representational organizations in different brain areas. While topographic organization offers a useful account throughout the brain, the relative superiority of fmHA in transmodal brain areas shows millimeter scale stereotactic population mapping in these regions may be invalid and recommends measures of shared representational features instead. Conversely, the disruption of functional organization of sensory motor regions by fmHA suggests topographic organization in unimodal areas may be uniquely important.

**References**

**Poster No 2130**

**Functional Implications and Heritability of Gyral Hubs in Gyral Morphological Networks**

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**Introduction:** The organization of cortical folding patterns are related to brain function, cognition and behaviors [Fischl et al., 2008]. Due to the distinct complexity and high variability of cortical morphology, it has been a challenging task to quantitatively model the cortical organization patterns. To this end, we propose a graph-based representation of human...
cortical organization-gyral morphological network (GMN) - which is constructed by an adaptive fusion model by integrating multiple morphological features, e.g. curvature and sulcal depth. More importantly, we uncovered inheritable signatures among functional brain networks and laminar areas through analyzing the properties of the nodes of the GMN.

**Methods:** Inspired by the Gyral Net (GN) recently proposed by [Chen et al., 2017], we developed a Fast and Adaptive algorithm for Constructing Gyral Morphological Networks (FAC-GMN) by integrating multiple morphological metrics such as cortical thickness, curvature and sulcal depth. The FAC-GMN model consists of five steps: (1) feature fusion, (2) gyral crest segmentation, (3) distance transform, (4) tree marching, and (5) tree connection, as illustrated in Fig. 1(B-F). In this study, we are especially concerned with nodes of the GMN, i.e., vertices where three or more edges (gyral crest lines) intersect, called gyral morphological hubs (GMHs). Given that our previous work demonstrated significant structural and functional differences between these gyral hubs and other gyral regions and sulci [Liu et al., 2022], we further analyzed the relationship between the spatial distribution of these hubs and the intrinsic functional networks and laminar areas, and their heritability (Fig.1G), thereby discovering inheritable signatures among functional brain networks and laminar areas.

**Results:** Experiments on 1081 young adults from HCP dataset demonstrated that the proposed FAC-GMN and the GN method constructed roughly similar cortical architecture. But our method obtained better results in detailed architecture, especially in some cortical regions where the contours of gyral crests are not particularly clear, as shown in Fig. 2A. In addition, the FAC-GMN method was more flexible and efficient than the GN, because the algorithm is fully adaptive. Specifically, the FAC-GMN method revealed more gyral morphological hubs, longer connected gyral crests, better gyral network integrity, shorter execution time (i.e., faster), and higher inter-individual variability. By analyzing the spatial distribution of gyral hubs in the functional networks [Thomas Yeo et al., 2011] and laminar areas [Mesulam, 1998], we found that both in left and right hemisphere, more gyral hubs are detected in the heteromodal areas including limbic and default mode networks (Fig 2B). Our findings support that these morphological hubs could serve as structural and functional hubs in brain networks, and are involved in more functional networks compared to other gyral areas, especially those related to high-order cognitive functions [Zhang et al., 2020]. Heritability analysis of the GMHs distributed in functional networks and laminar areas showed that, compared to the heteromodal areas, the spatial distribution of the GMHs in unimodal areas are more heritable (h²=0.26, p=0.0003 vs. h²=0.14, p=0.02).
Conclusions: Results suggest that the proposed FAC-GMN model outperforms the classical gyral net as well as single-feature gyral networks in terms of the length and integrity of gyral networks and capturing more gyral morphological hubs. Besides, more gyral hubs were detected in the heteromodal areas including limbic and default mode networks, which were also significantly inheritable among twins. This study provides new avenues to study the gyrification patterns of cerebral cortex in neuro-development and aging and toward better understanding the neural basis of human cognition.

References

Poster No 2131
Examining Hippocampal-Cerebellar Functional Connectivity across the Lifespan
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Introduction: Evidence from nonhuman species suggests that the hippocampus and cerebellum interact closely to support spatial cognition, with cerebellar disruption influencing hippocampal place cell coding and navigational behaviour (Rochefort
et al., 2011). Neuroanatomical studies in nonhuman species suggest that these functional interactions may be mediated by direct (Heath and Harper, 1974) and indirect pathways, with the hippocampus receiving input from disparate parts of the cerebellar cortex, including lobule HVI, HVIIA (Crus I) and paraflocculus (Watson et al., 2019). However, the hippocampal-cerebellar connectivity remains poorly understood in humans. Given that hippocampal-connected areas of the cerebellum (lobule HVIIA and HVI) appear highly sensitive to ageing (Ramanoël et al., 2013), characterising this functional interaction has implications for understanding both the properties of an extended navigation system and its potential vulnerability to ageing and neurodegeneration.

**Methods:** Using CONN toolbox (Nieto-Castanon, 2022), we applied seed-based functional connectivity analyses to task-free fMRI data from 479 adults in the Cambridge Centre of Ageing and Neuroscience (CamCAN) dataset (330F, 323M, mean age= 54.3, SD= 18.6, range= 18-87) (Taylor et al., 2017). The hippocampal seed region-of-interest (ROI) was created using the Harvard-Oxford and Julich histological atlases and split into anterior and posterior subdivisions at the uncal apex. The cerebellum was interrogated using the SUIT Probabilistic Atlas (Diedrichsen et al., 2009). For seed-based analyses, fMRI time series of our hippocampal seeds (left, right, anterior, posterior) were used as regressors to examine Fisher-transformed correlation coefficients within the whole cerebellar cortex. Results were corrected for multiple comparisons in SPM12 (p<.05 FWE) and displayed on cerebellar flatmaps using SUIT.

**Results:** We found strong functional connectivity between the hippocampus and widespread areas of the cerebellum, including the border of lobule HVI and HV, lobule HIX and lobule HVIIA. Contrasting the left and right hippocampus showed that they were preferentially connected with an area within contralateral lobule HVIIA (Fig 1a and 1b). Direct contrasts between the anterior and posterior hippocampus revealed that the anterior hippocampus displayed preferential connectivity with bilateral regions of lobule HVIIA (peak in right Crus II) (Fig 1c). In contrast, the posterior hippocampus showed stronger connectivity with lobule V (Fig 1d). Finally, we found strong age-related reductions in functional connectivity between the hippocampus and lobule HV and HVI. Similar patterns were observed for the anterior hippocampus, but the posterior hippocampus showed minimal age-related alterations in connectivity (Fig. 2).
Conclusions: These findings provide novel insights into the organisation of the hippocampal-cerebellar connectivity in humans. Aligning with nonhuman animal work, we show that the hippocampus functionally connects to widespread areas of the cerebellum, particularly lobule HVI and HVIIA (Crus I). Unlike prior anatomical work, however, we observed strong connectivity with lobule HVIIA (Crus II, rather than Crus I), as well as lobule HIX and HX. Functional connectivity differences between anterior and posterior hippocampus suggest that long-axis subdivisions based on neocortical connectivity are maintained in cerebellum. Ageing most strongly affected functional connectivity between the hippocampus and lobule HV and HVI, consistent with evidence showing age-related atrophy in lobule HVI (Ramanoël et al., 2013), which could be related to age-related behavioural deficits. Future studies are required to test novel hypotheses about the functional role of this interaction in humans, such as whether cerebellar circuits store and use forward models of hippocampal function to automate hippocampal processes, as seen in frontal lobe circuits (Ramnani, 2014).

References
From theory to practice: Cross modal organization of the human temporal lobe

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Introduction: The temporal lobe underwent considerable expansion and reorganization throughout the primate lineage. Mounting evidence suggests that beyond mere expansion we witness substantial differences in organization across modalities compared to other primates. An overarching theory on the functional implications of those evolutionary processes remain elusive. Recent evidence suggests at least one human unique principle of organization in the domain of function and structural connectivity. The current project aims at solidifying those principles of organization across meta-analytic computational anatomy and literature studies.

Methods: We investigated current literature placing the temporal lobe in a primate context. We investigated several aspects of expansion and reorganization (Braunsdorf et al., 2021), as well as underlying implications spanning different modalities using Laplacian eigenmapping of meta-analytic functional activation maps. We compared those to results of temporal lobe organization in the structural connectivity domain (Braunsdorf et al., 2023).

Results: We demonstrated a significant expansion and reorganization in the temporal lobe, exceeding mere expansion that can be expected based on total brain size. Furthermore, we showed that the ‘remapping factor’ (that is total area of input vs. output areas) is significantly bigger in humans compared to other species. We hypothesized two hotspots for semantic processing, one with a focus on categorization in the posterior temporal lobe, one involved in more abstract complex representations anteriorly. This general framework seems to hold across varied areas of cognition (Braunsdorf et al., 2022). We further demonstrated that functional principles of organization across a wide domain of cognitive processes resemble those found in structural connectivity (Braunsdorf, 2023; Blasquez Freches et al, 2020).

Conclusions: Our work hypothesized an overarching theory of temporal lobe organization in a primate context. We were able to show similarities between functional and structural organization. In the future we aim to demonstrate in how far structure follows function and how individual differences in brain anatomy influence functional organization and ultimately behavioral performance in different cognitive domains.
Poster No 2133

Annectant Gyri in Parietal Cortex Capture Dorsal Visual Stream Boundaries

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Introduction: Visual processing is separated into the ventral and dorsal streams, responsible for object recognition and spatial attention. While functional boundaries of the ventral stream have been linked to cortical folding (Witthoft et al. 2014), no such model exists for the dorsal stream. Unlike the ventral stream, most of the dorsal stream’s maps exist within one continuous sulcus, the parieto-occipital sulcus (PO) into the intraparietal sulcus (IPS). However, the field lacks a definition of intrasulcal anatomical features that could enhance our understanding of this region’s structural relationship to function. Our study explores annectant, or concealed, gyri within the PO sulcus, building on Gratiolet’s 1854 findings of buried gyri within the macaque brain. We hypothesize that there are consistent annectant gyri across the dorsal stream which overlap with dorsal stream visual field map boundaries. If structure and function are coupled in the dorsal stream, we also hypothesize that variability in PO anatomy can be related to behavioral measures such as visuospatial bias (VSB).

Methods: Employing anatomical and functional MRI, we collected data from 20 adults (mean age 33 ± 15). An average of 3.0 (± 0.4) annectant gyri were identified in the left PO and 3.2 (± 0.8) in the right. These hidden gyri are consistent to the extent that three annectant gyri in the left PO and two in the right remain visible in cortical surface averages from FreeSurfer and Human Connectome Project participants (Fischl et al., 1999). Annectant gyri extend perpendicularly across PO and IPS, and were distinguished based on their spatial positioning relative to other sulcal landmarks, such as the transverse occipital sulcus and parieto-occipital fissure. Specifically, four annectant gyri were consistently identified to overlap with retinotopically defined left hemisphere dorsal stream map boundaries in over 80% of participants for V3ab/IPS0 (89%), IPS0/IPS1 (89%), IPS1/IPS2 (83%), and IPS2/IPS3 (83%). Some of these annectant gyri partially extend across the PO sulcus, while others fully interrupt the continuity of the sulcus.

Results: We also investigated how structure-function couples to behavior, using anatomical MRI data and VSB scores from a cohort of 38 children (mean age 10 ± 2). In each child we quantify the surface area and gray matter volume of the PO sulcus in each hemisphere and derive a normalized anatomical bias score (left - right)/(left+right). Subsequently, children were stratified into two groups based on their VSB scores relative to the median, distinguishing those with strong leftward and weak rightward spatial biases. Results indicated that individuals with a pronounced rightward VSB exhibited a notable leftward bias in cortical surface area (t-stat=2.1, p=0.047) and gray matter volume (t-stat=2.2, p=0.039). This relationship was specific to PO and not observed in other sulci such as the central sulcus. To further examine development, in a subset of participants with both retinotopic mapping and structural imaging (n=18 adults; n= 7 children), we find left hemisphere predominance in surface area (p = 0.029), gray matter volume (p = 0.001), and cortical thickness (p = 1x10-06) in PO and IPS, the two sulci that contain retinotopic dorsal stream visual field maps, indicating ongoing cortical folding in the dorsal stream into adulthood. These results suggest a protracted development of the left relative to the right parietal cortex, consistent with the rightward shift of VSB throughout development.

Conclusions: Our findings reveal novel and consistent anatomical features in the parietal lobe, and suggest that dorsal visual stream organization can be predicted from cortical sheet folding. Establishing criteria for intrasulcal anatomical features can enrich analyses in populations where retinotopy data cannot be collected. The developmental dynamics observed warrant further exploration to understand the interplay between structure, function, and cognitive functions of the dorsal stream.

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Mapping neurotransmitter receptor distributions in the macaque cortex

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Introduction: Quantitative maps of neurotransmitter receptor densities are important tools for characterizing the molecular organization of the brain. We have previously presented a 3D reconstruction pipeline for 2D autoradiographs to create 3D atlases at up to 50µm resolution (Funck, et al 2022). We here use the 3D reconstruction of autoradiographs from a macaque hemisphere to investigate patterns of receptor distribution and the balance of inhibitory, excitatory, and modulatory neurotransmitter receptors.

Methods: The brain of an adult male Macaca fascicularis was removed from the skull, the hemispheres separated and each cut into a rostral and a caudal block. The unfixed tissue blocks were frozen at −40 °C and serially sectioned in the coronal plane using a cryostat microtome (CM 3050, Leica, Germany), obtaining sections of 20 µm thickness which were thaw-mounted on gelatine-coated slides and freeze-dried overnight. Alternating sections were processed for the visualization of 15 different neurotransmitter receptor binding sites using quantitative in vitro receptor autoradiography and previously published protocols (Rappan, et al. 2021). Sections were sparsely sampled from the tissue blocks such that groups of 25 sections were collected throughout the slab with 20 sections discarded between groups. Receptor autoradiographs were digitized using Axiovision (video-based image analysis system; Zeiss, Germany) resulting in 8 bit images with an in-plane resolution of 20 µm per pixel, respectively (Palomero-Gallgher & Zilles, 2018). As no MRI was acquired for the macaque brain, the MEBRAINS template brain (Balan, et al. 2023) was used as the anatomic template to which the autoradiographs were reconstructed with our pipeline. The 3D volumes were reconstructed at 1mm resolution for inhibitory (GABAA, GABAB), excitatory (AMPA, NMDA, Kainate), and modulatory (5-HT1A, 5HT2, M1, M2, D1, α2) receptors. Reconstructed receptor volumes were smoothed with a gaussian filter (FWHM=3). Receptor densities were then projected onto the 10k vertex Yerkes19 (v1.2) group average mid surface (Donahue et al., 2016, 2018) and normalized by z-score. Vertex-wise receptor gradients were calculated using all the available receptors with a principal component analysis embedding and pearson correlation kernel. The ratios of excitatory to inhibitory receptors, GABAA/GABAB, and inhibitory plus excitatory to modulatory receptors were also computed.

Results: The first and second components of the gradients explained 29% and 16% of the variance respectively (Fig.1.A). The first component highlights the visual cortex (Fig.1.A). The second component illustrates a gradient separating the precuneus, the posterior inferior parietal cortex and the posterior superior temporal cortex from rostrally and caudally adjacent regions (Fig.1.A). The distribution of neurotransmitter receptor ratios indicates that the first component appears to be driven by the ratio of glutamate to GABA receptors and the second component by the proportion of modulatory vs. glutamate and GABA receptors (Fig.1.B). The ratio of fast acting ionotropic GABAA to slower GABAB metabotropic receptors appeared less informative of the observed gradients.
Conclusions: We demonstrate gradients of receptor distribution across the macaque cortex with a particularly strong axis separating the visual cortex, which presents a conspicuously low excitatory to inhibitory ratio. The secondary axis highlights the precuneus and posterior parietal cortex, both of which are part of the default mode network (Raichle 2015). The 2D autoradiograph sections were presently only reconstructed to 1mm resolution to provide gross anatomic information. The data, however, supports reconstruction up to 50µm resolution. We will therefore be able to investigate microscale patterns of receptor distributions to elucidate the molecular architecture of the macaque brain at a previously inaccessible resolution.

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Poster No 2135

Computational correlation between the International 10-20 positioning and underlying cortical areas

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Introduction: The International 10-20 positioning in clinical practice is routinely used for electroencephalograms. Each of its 19 positions is considered adjacent to a specific cortical area, making the 10-20 positioning helpful for brain research. The 10-20 positioning has been used in several brain stimulation studies, mainly by means of transcranial magnetic stimulation¹. The F3 and F4 positions are respectively stimulated and inhibited for the treatment of depression². The point between the P3 and T3 positions (hereby denominated TP3) was previously inhibited to treat auditory verbal hallucinations³. To the best of our knowledge, few studies have directly correlated the international 10-20 electrode positioning to brain images using reproducible cortical segmentation. This study aims to determine the correlation between previously reported positions of interest (F3, F4, T3, P3, and TP3) and underlying cortical areas using a highly reproducible method.

A. Cortical areas included in the study, considering all points. B. Cortical parcellation for each point studied.
**Methods:** Patients were recruited into a robust study approved by the institutional ethics committee and gave written informed consent. Brain segmentation, 10-20 positioning, and measurements were made virtually to ensure maximum reproducibility. The head three-dimensional reconstruction was made using 3D Slicer version 5.2.2, based on a morphological magnetic resonance image. Brain segmentation was performed using FreeSurfer version 7.3.1 and imported into 3D Slicer via FreeSurfer Importer extension using the Desikan-Killiany Atlas. The International 10-20 positioning was performed using the Geodesic Slicer extension. The distances between each point and all cortical areas were measured using the Fiducial to Model extension. Preliminary results showed 100% consistency in the closest 3 cortical areas for each point, as illustrated in Figure 1. Relative distances were then calculated to quantify sub-regions of each underlying cortex, and data were plotted in equilateral triangles according to Viviani’s theorem. The normality of data was determined using the Kolmogorov-Smirnov test. Student’s t-test was used to evaluate statistical relevance among differences between skin points and the closest cortical volume point. Statistical significance thresholds were set at 0.05, 0.005, and 0.001.

**Results:** 16 patients (12 female, aged 21 to 65, all right-handed) were enrolled in this study. Calculated distances between each point and respective cortical volumes were all normally distributed. Figure 2 summarizes the measurement results for each point, according to the subjacent cortical area. F3, F4, T3, and P3 highly correlated with a specific cortical area. Although the 3 closest cortical areas from PT3 were consistent, their relative locations according to the subjacent area were not statistically significant.
Conclusions: In this study, the International 10-20 positioning was obtained using morphological magnetic resonance and open-source software. Besides, the main points of previous studies using the 10-20 system as a viable cortical map in psychiatry were evaluated according to their distance to subjacent areas. Interestingly, the closest regions to F3 and F4 were the left and right Rostral Middle Frontal Cortices, respectively. This area of the Desikan-Killiany Atlas is a solid anatomical approximation of the Dorsolateral Prefrontal Cortex, classically defined as the lateral anterior two-thirds of the frontal cortex. As expected, the most common subjacent areas correlated with T3 were the Inferior, Middle, and Superior Temporal Cortices, with the Middle Temporal Cortex being the most common. As also expected, P3 was highly correlated with the Inferior and Superior Parietal Cortices. In this study, TP3 was not solidly related to a single cortical area. We hypothesize this is due to a low number of patients or interpersonal differences in the T3 and P3 positions. Further studies are warranted to analyze this specific point.

References

Poster No 2136
A Mathematical Model Representing the Cortical Folding Disorder Hemimegalencephaly

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Introduction: The complexity of brain folding patterns make it extremely challenging to study brain diseases since there is such variability in the folding patterns across healthy individuals. There is considerable debate among biologists as to how folding patterns develop, including biochemical¹, biomechanical², and differential growth hypotheses. In previous work we developed a combined biochemical-biomechanical model to elucidate the mechanisms of cortical folding development³. In this research, we alter various model parameters and demonstrate how disorders of cortical formations such as hemimegalencephaly can be explained by parameters in our model.

Methods: The intermediate progenitor (IP) model is a biochemical biological hypothesis to explain pre-patterning of cortical folding in early development¹. Several genes have been shown to regulate cortical folding via modulating IP cell development in mice. Our biochemical model² uses a dynamically growing domain Turing reaction-diffusion system⁴ where the morphogens regulate IP cell patterning. A chemical morphogen activates IP cell proliferation in specific regions, resulting in folding patterns on the cerebral cortex caused by irregular distributions of cell populations throughout the surface. The concentration of neurons from the Turing model are used to govern the magnitude of the applied axonal tension forces in our biomechanical model. We use a linear stress-strain-elasticity model with biophysical parameters to determine displacements due to external forces. The deformation of a two-dimensional semi-circular domain representing the cerebral cortex is implemented computationally using a finite element formulation. External forces corresponding to the axonal tension-forces are applied on the boundary of the model cortex. The lateral ventricle of a brain with hemimegalencephaly is enlarged, so it may contain more IP cells compared to a healthy brain, resulting in the production of excessive number of neurons. We model the asymetrically increased cell proliferation with irregular Turing patterns. The cortex of a brain with hemimegalencephaly also has a thickened cortex⁵, which is captured by one of the model parameters.

Results: The morphogens evolve and change rapidly during domain growth and converge when growth stops. We assume the morphogen concentration is correlated to the concentration of neurons and determine the magnitude of the applied axonal tension force in our biomechanical model (Fig. 1). Irregular Turing patterns can be generated by changing the initial conditions of the model. These irregular patterns lead to asymmetric forces. When applied to the semi-circular model cortex, the asymmetric forces pull together, resulting in a deformed configuration corresponding to an enlarged hemisphere. Increasing the thickness of the cortex reduces the elongation of the asymmetric development (Fig. 2).
Conclusions: MR images of brains with hemimegalencephaly show one hemisphere to be enlarged. The hemisphere grows asymmetrically and the cortex is thicker. Modifying model parameters and initial conditions allow us to explore possible mechanisms involved in disorders of cortical formations. Irregular Turing patterns are used to represent asymmetric IP cells in the lateral ventricle of a hemimegalencephalic brain. The corresponding asymmetric forces and increased cortical thickness parameter result in an enlarged cortex configuration in one hemisphere. Our model is the first model to explore how different IP cell patterns can lead to unusual cortex configurations that can be correlated to cortical patterning disorders. This modeling and simulation research represents an important step in improving our understanding of cortical folding pattern formation.

References
**Microstructural asymmetry across cortical layers in the human brain**

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**Introduction:** Left-right asymmetry is an important feature of human brain structure and function, supporting language and related to mental health (Kong et al., 2022). Previous studies have investigated asymmetry of gross morphological features such as cortical thickness, surface area, and gray matter volume. However, little is known about the asymmetry of the cortical microstructure at the meso- and micro-scale. Here, we study the asymmetry of cortical microstructure leveraging post-mortem histological maps and in vivo MRI, and explore their association with language and mental health.

**Methods:** Whole brain cell-body staining sample with ultra-high resolution (20 um). We used surface-based data in BigBrain native space and 6-layer estimates from a previous study (Wagstyl et al., 2020), then constructed 10 equivolumetric surfaces within each layer (Fig. 1A and 1B). To probe the regional asymmetry index (AI), we employed a homologue multimodal parcellation (Glasser et al., 2016). We regressed out the mean intensity for RH and LH and obtained normalized intensity values. Additionally, we used in vivo T1w/T2w imaging for in vivo replication (Glasser et al., 2022), Human Connectome Project (HCP, n = 1101, resolution = 0.8 mm). We reconstructed 12 equivolumetric surfaces between pial and white matter and z-scored the intensity values for LH and RH (Fig. 1D). We calculated the microstructural intensity AI for each surface and/or layer by subtracting right from left hemispheres. To understand how the microstructural differentiation differs between LH and RH, we computed the microstructural profile covariance (i.e., ipsilateral patterns: from LH to LH and from RH to RH; contralateral patterns: from LH to RH and from RH to LH) and used diffusion map embedding to capture the gradients for LH and RH separately. Then we aligned RH to LH and calculated the AI for each pattern (Fig. 2A and 2B). We summarized our findings into 12 functional networks including primary visual (Vis1), secondary visual (Vis2), somatomotor (SMN), cingulo-opercular (CON), dorsal attention (DAN), language (Lan.), frontoparietal (FPN), auditory network (Aud.), default mode (DMN), posterior multimodal (PMN), ventral multimodal (VMN), and orbito-affective (OAN).

**Results:** We found an overall left-right asymmetry pattern from anterior to posterior regions (Fig. 1C and 1E). Studying how asymmetry of each region varied across layers, we observed highest variation in VMN and SMN, and lowest in Vis1 and Vis2 (Fig. 1F and 1G). Next, we investigated inter-regional asymmetry in microstructural organization. In Bigbrain, we found lan. and FPN showed a stronger laminar differentiation in LH than RH, and PMN showed a stronger laminar differentiation in RH than LH for ipsilateral pattern (Fig. 2C). In HCP, FPN and OAN showed a stronger laminar differentiation in LH than RH, and PMN showed a stronger laminar differentiation in RH than LH for ipsilateral pattern. Contralateral pattern was similar to the ipsilateral pattern. To test how the BigBrain has a spatial similarity to HCP, we correlated the asymmetry spatial pattern between individual HCP and BigBrain (Fig. 2C). It suggested no correlation with mean r = 0.03 and 0.01 for ipsilateral and contralateral patterns respectively.

**Conclusions:** We illustrate cortex-wide asymmetry in microstructure along layers and at the system level for both post mortem cytoarchitecture and in vivo imaging histology, especially for language- and attention-related regions.
Fig 1. Layer-specific asymmetry in BigBrain and HCP.

Fig 2. Asymmetry of microstructural profile covariance gradients
Longitudinal analysis of cortical dysplasia microstructure through diffusion-MRI and histology

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Introduction: Focal cortical dysplasias (FCD) are malformations of cortical development characterized by cortical layer disruption and neuronal abnormalities associated with refractory focal epilepsy (Blümcke et al. 2011). Surgical resection is available when lesions are visible through magnetic resonance imaging (MRI). Unfortunately, many of these lesions are subtle and difficult to detect by conventional MRI. Several methods to analyze MRI have been proposed aiming to unmask subtle cortical lesions (Kabat et al., 2012). However, most image-processing methods are targeted to detect the macroscopic characteristics of FCD, which do not always correspond to microstructural disarrangement. Novel quantitative diffusion-MRI (dMRI) methods provide valuable microstructural characteristics of complex tissue, including gray matter (Leuze et al. 2012). Through spatial analysis of dMRI metrics using a novel multi-tensor, we demonstrate abnormalities in an animal model of cortical dysplasia that reflect cyto- and myelo-architecture disarrangement as seen by histology.

Methods: Pregnant rats were injected with either carmustine (BCNU; 20 mg/kg) (n=3) or saline solution (n=3) at E15 (Benardete et al., 2002). Resulting pups (BCNU: n=16; Control: n=16) were scanned in vivo at 30 and 150 postnatal days using a preclinical 7T scanner. We acquired T2w images (spatial resolution 0.175×0.175×1 mm3) and dMRI (spatial resolution 0.175×0.175×1 mm3) with b values of 670, 1270 and 2010 s/mm2, each with 90 diffusion-sensitizing directions. Additionally, 14 b=0 s/mm2 volumes were obtained. After dMRI data preprocessing, we fitted the diffusion tensor (DTI) (Basser et al., 1994), and the multi-resolution discrete-search method (MRDS) (Coronado-Leija et al., 2017) that can fit up to three independent diffusion tensor profiles. To have a common anatomical descriptor of the cortex, we create a 2D grid-line system of coordinates with fifty curved lines, each one with ten vertices spanning the entire depth of the cortex. Since MRDS fits one or more tensors per voxel, resulting bundle-wise tensors were labeled as parallel or perpendicular to the grid-lines. For our statistical analysis, we conducted a longitudinal vertex-wise Linear Mixed Effect Model. Finally, to validate our diffusion metrics, we performed histological assessments using the primary antibodies myelin basic protein (MBP), and neuronal nuclear (NeuN). Myelin fiber orientations were examined through a structure tensor analysis

Results: T2w images showed normal morphological features in both groups at P30, followed by enlarged ventricles and hippocampal atrophy at P150 in BCNU rats. Metrics derived from DTI failed to reveal differences between groups at any time point. In contrast, multi-tensor metrics at P30 showed significant changes between groups in FApar, FAperp, and MPDpar (p<0.05) pointing to the deep cortical layers of the motor and somatosensory cortex. Histological assessment with NeuN revealed radial-columnar disorganization and disrupted transition between layers III-IV and V-VI. Also, MBP stainings highlighted a loss of the myelination process and disarrangement of intracortical fibers at the early stages of development (P30), while P150 displayed subtle changes in the cortex in BCNU rats. This fiber disarrangement was reflected in a loss of coherence from the structure tensor maps, being more noticeable at P30.
Conclusions: Our findings indicate that during the early stages of development (P30), macrostructural alterations in FCD are exceedingly subtle and remain undetectable through conventional MRI. However, our use of dMRI proved to be a valuable tool for identifying microstructural abnormalities. While DTI proved its limitations, our MRDS successfully pinpointed cortical regions with abnormal microstructure related to disorganized radial-tangential fibers and columnar-layer architecture, as confirmed by histology. These findings put forward the potential application of advanced dMRI for the detection of human FCD.

References
Investigation and validation for cortical laminar structures of myelin and iron using $\chi$-separation

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Introduction: $\chi$-separation (chi-separation) is an advanced quantitative susceptibility mapping method that separate paramagnetic and diamagnetic susceptibility\textsuperscript{9}. Previous studies have confirmed the relationship between iron and paramagnetic susceptibility, and myelin and diamagnetic susceptibility\textsuperscript{3,4,5,9} respectively, but quantitative layer-wise comparison with ex-vivo histology is yet to be done. Primary visual cortex (V1) can be distinguished by the presence of Gennari line\textsuperscript{2,3}. The Gennari line exhibits line-shaped distribution where both iron and myelin are more prominent than the surrounding cortex layers. Therefore, these distinctive structures can serve as valuable reference to evaluate the relationship between $\chi$-separation maps and iron and myelin accumulations. Therefore, this study aims to quantitatively assess how precisely $\chi$-separation can distinguish susceptibility sources by comparing layer-wise profiles in iron-, myelin- stained images and ex-vo $\chi$-separation maps in the V1 region.

Methods: An ex-vivo human brain specimen, containing the V1, was scanned\textsuperscript{9} at 7T MRI (Siemens Terra, Erlangen, Germany). 3D multi-echo gradient-echo and 3D multi-echo spin-echo data were from $\chi$-separation paper data\textsuperscript{9}. $\chi$-separation is conducted using local field\textsuperscript{1,10}, R2*\textsuperscript{6}, and R27 maps which are processed from acquired data. After the MRI scan, specimen was utilized for LFB myelin staining and LA_ICP_MS iron staining\textsuperscript{9}. LFB myelin staining image represents optical density, which have low intensity in myelinated areas, is transformed into absorbance map using the Beer-Bouguer-Lambert law. V1 ROI is manually segmented using AutoCAD (version 2024, Autodesk Inc.) considering microstructural and macroscopic features\textsuperscript{2} in $\chi$-separation and staining maps. Cortex boundaries were defined as follows: Interface between CSF and cortex was defined as outer contour with 0% depth. Border between deepest cortex and the white matter\textsuperscript{2} was defined as inner contour with 100% depth. Depth trajectory is defined as a line perpendicular to cortical layers, heading to the white matter. Evenly spaced trajectories are manually drawn along the cortex\textsuperscript{8}. Within the ROIs, there exist 54 depth trajectories. Additionally, cortical depth-wise points were sampled over each depth trajectory with 5% depth increments. Using depth-wise samples, laminar profile was acquired by averaging intensity at each depth. Cortical laminar profiles were z-score normalized for quantitative comparison of intermodal differences. Laminar profiles between $\chi_{\text{para}}$ and iron staining; and $\chi_{\text{dia}}$ and myelin staining were visually assessed and similarity was measured using the mean Euclidean Distance\textsuperscript{2}. 

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Segmentation in paramagnetic maps and stained maps. (a) and (b) $\chi_{\text{para}}$ and $\chi_{\text{dia}}$ maps depth-wise points. The outer cortical boundary for paramagnetic was extracted from $\chi_{\text{para}}$, which has distinctly white inner cortical boundaries. The outer cortical boundary was obtained from $\chi_{\text{para}}$, which has distinctly white outer cortical boundary. V1 ROI was set as same as possible for every map. (c) For iron, 4 depth trajectories are not drawn due to an artifact in the middle, resulting in 54 depth trajectories. The inner- and outer-cortical boundaries were manually segmented with reference to image contrast. Depth trajectories are perpendicular to cortical boundary, and histograms equidistant points along the cortical depth profiles were shown on depth points, where data were sampled.}
\end{figure}
Results: Fig. 1 depicts segmented depth-wise points in $\chi$-separation and staining map. Segmented depth-wise points agree well each other. V1 ROI, cortex boundary and depth trajectory are highlighted for detailed explanation. In Fig. 2, z-score normalized laminar profiles are plotted. $\chi_{\text{para}}$ and iron staining; $\chi_{\text{dia}}$ and myelin staining display remarkable similarity between two profiles including Gennari line peak at 65% depth. Difference of $\chi_{\text{para}}$ and iron staining is demonstrated with mean Euclidean distance of 0.357±0.043, while $\chi_{\text{dia}}$ and myelin staining demonstrated higher mean Euclidean distance of 0.909±0.143.

Conclusions: In this study, we investigated the laminar profiles of visual cortex within $\chi$-separation maps and histological maps. The results show that the profiles of iron histology and $\chi_{\text{para}}$; myelin histology and $\chi_{\text{dia}}$ coincide throughout the cortex, including a peak at the Gennari line, respectively. Although we performed manual segmentation to maximize alignment of segmented cortical boundaries, the boundaries were less distinct in the iron staining map, potentially resulting in some inconsistencies.

References
Evolution and ontogeny of cortical microstructure facilitating hand movements

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Introduction: The remarkable efficiency and precision in coordination of human hand movements surpass those of other species, including our closest living relatives, the great apes. The evolution of the human hand function was paralleled by the expansion of its functional representation in humans and great apes’ motor and somatosensory cortices. Fine motor skills of the human hand, enabling complex tool manipulation tasks, require fast and precise neuronal control facilitated by myelinated intracortical and projection fibers within the motor cortex. In humans, the hand-controlling area in the motor cortex has higher levels of myelin as compared to the face-controlling area as shown by quantitative MRI (qMRI) but it is not known whether this is a human-specific phenomenon, or if it is already observed in great apes. Herein, we compared the microstructure of the functional subdivisions within primary motor cortex in humans and chimpanzees using high resolution qMRI and characterized the lifespan trajectory of different cortical motor regions.

Methods: Sixteen post mortem chimpanzee brains (8 f, age 11-52y) were collected in field sites, sanctuaries and zoos using an ethical pipeline and studied with ultra-high resolution qMRI. In vivo qMRI data of ten human participants (6 f, 28 ± 3.6 y) from a previously published study were analyzed. QMRI were acquired at 7T using multi-parametric mapping with 500μm and 300μm resolutions for humans and chimpanzees, respectively. Magnetization transfer saturation (MTsat) served as a myelin marker, the effective transverse relaxation rate (R2*) as a marker for iron content. Cortical surfaces for both species were reconstructed using the Freesurfer recon-all pipeline. Areas within the primary motor cortex controlling the hand, face, and foot movements were manually delineated based on sulcal anatomy (Fig. 1.A). Median R2* and MTsat values were extracted for the hand, face and foot regions and compared in paired t-tests. An exponential saturation model for age-related increase of iron and myelin was fitted to R2* and MTsat values to characterize the lifespan trajectories in each cortical area. A time constant indicating the age at which around 63.2% of all age-related changes were completed was determined for each area within the motor cortex (Fig. 1.B right).

Results: Differences in microstructure of the foot, hand and face regions of the motor cortex were observed in both species (Fig. 1.B) with significantly higher R2* in hand areas as compared to the foot and face areas, implying higher levels of cortical iron and myelin in the former. A non-significant tendency towards higher MTsat values in the hand area in humans was observed. In chimpanzees, significantly higher MTsat values for hand compared to face and foot areas were found. Developmental myelination and age-related iron accumulation of R2* and MTsat in chimpanzees are shown in Fig 1.B right. Age-related iron accumulation (measured with R2*) was described by a time constant of 30y±22 for all three regions. This is slower than values reported in the human motor cortex, which found iron accumulated with a time constant of 20 years. The developmental myelination in chimpanzees measured with MTsat was characterized by time constants 2.1y±0.5, 2.4y±0.5 and 2.4y±0.6 for face, hand and foot areas, respectively.
Conclusions: For the first time we showed that microstructure of the hand knob area in the chimpanzee motor cortex is different from the subdivisions controlling other movements and thus that the evolution of hand motor skills is not only manifested in alterations to sulcal anatomy but also in pronounced changes of cortical microstructure. We found elevated myelin and iron content in the hand knob area in both species and characterized developmental myelination and iron accumulation within the chimpanzee motor cortex. These findings may enhance our understanding of the anatomical basis for distinct behaviors like remarkable tool use seen in hominids.

References
Multimodal analysis in infants to adults shows faster myelination of V1 than high-level visual areas

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Introduction: Myelination is a lifelong process that can be modified by experience and exert profound effects on circuit function, learning, and memory. Yet, how myelination contributes to the development and maturation of human visual circuits is unknown.

Methods: Here, we examined the development of myelin using a combination of ex vivo histology (immunohistochemistry, IHC) (Fig. 1a) and in vivo quantitative MRI (qMRI) of tissue relaxation rate (R1) in three functionally-distinct regions of human visual cortex: primary visual cortex (V1) and high-level face- and place-selective cortex. We chose these regions as they include both early and high-level visual areas that can be identified using anatomical landmarks alone in ex-vivo samples (Holmes 1918, Weiner 2014; Weiner 2018). IHC of myelin basic protein (MBP) was done in 6 infant samples (34 gestational weeks to 5 months old), a 9 year old, and a 25 year old. Analysis of myelin coverage was conducted using semi-automated thresholding of MBP+ immunolabeling to calculate total cortical area covered by MBP+ myelin sheaths. Cross-sectional and longitudinal qMRI was done in 80 infants (newborn-12 month olds) and cross-sectional qMRI was done in 52 5-25 year olds. In adults, R1 in cortex depends on myelin (Gomez 2017; Natu 2018) and the physiochemical tissue properties (Mezer 2013; Edwards 2018).

Results: Using IHC, we find that myelin increases in infancy in all regions, but more rapidly in the calcarine sulcus (V1), than in the collateral sulcus (CoS; place-selective) and fusiform gyrus (FG; face-selective) (Fig. 1b-d). Furthermore, while myelin levels in V1 and CoS are similar in childhood and adulthood (9 vs. 25 years old), in the FG, myelin levels are lower in the 9 year old than in the adult, suggesting continued myelination of FG during adolescence (Fig. 1b). Within visual areas analyzed, cortical layers display different developmental trajectories of myelination, where deep layers of cortex (L4-L6) and L1 myelinate earlier and more rapidly than L2/3. In the case of higher-level visual cortex (CoS and FG), both L1 and L2 continue to myelinate throughout adolescence. Cortical R1 is higher in V1 than higher-level face- and place- selective cortex at birth, and all regions show faster increases in R1 in infancy than later childhood (Fig. 2a), mirroring myelin patterns in ex vivo samples. Across the lifespan, cortical R1 plateaus earliest in V1. In contrast, cortical R1 reaches adult levels in place-selective cortex in childhood (5-9 years old), and cortical R1 is still lower in 10-12 year old children than in adults in face-selective cortex, suggesting prolonged development of face-selective cortex into adulthood (Fig 2b). Across ages and areas, there is a positive linear relationship between cortical R1 and myelin level estimated from IHC (beta=0.0069, p<0.0001, no effect of region or interaction), suggesting that in cortex linear increases in myelin will produce linear increases in R1. As we find visual cortex is largely devoid of myelin at birth, we identify a baseline cortical R1 value (0.49 s⁻¹) that is not driven by myelin.

Conclusions: Overall, we observe differential development of cortical myelin, where myelination proceeds rapidly during the first year of life and continues developing more slowly during childhood, with differential development across layers and areas. Deeper layers myelinate earlier than superficial layers, and V1 myelinates earlier than high-level regions, with face-selective cortex showing the most prolonged myelination. We confirm that developmental changes in R1 are correlated to changes in myelin and identify baseline cortical R1 value that is independent of myelin. These findings identify differences in spatiotemporal patterning of myelination within the human visual system, laying the foundation to understanding differences in functional development.
References
Human Brain Functional Modules: A Novel Detection Algorithm and A Multiresolution Comparative Study

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Introduction: Combining resting-state functional MRI (R-fMRI) and graph theory, a functional brain network, where nodes represent brain regions and edges represent functional connectivity (FC), is organized into modules defined by dense FC within each module and sparse FC between them (Meunier et al., 2009). The resolution limit of community detection algorithms (Sporns, 2018) leads to a poor explanation of the complex brain functional modular structure (Wang et al., 2021; Lin et al., 2018). An avenue is to introduce a resolution-related parameter that produces multiple solutions spanning from coarser to finer resolutions. The developing computational intelligence algorithms paved the way for a resolution-parameter-free design, which decomposes the definition of modularity into two objective functions and processes a multiobjective search. Therefore, we developed a multiobjective evolutionary algorithm (MOEA) to detect functional modular structures and conducted a multiresolution comparison of algorithms and their cognitive predictions.

Methods: Data were obtained from the HCP dataset, consisting of 310 healthy adults. After the HCP preprocessing pipeline, R-fMRI data were regressed out linear trends and nuisance signals and filtered (0.01~0.1 Hz). We utilized Power’s atlas (Power et al., 2011) and calculated the sparse group-average no-negative matrix (sparsity = 25.2%) to detect modular structure. MOEA (Fig 1A) produced a Pareto front (PF) comprising non-dominated partitions that attained near-optimal yet distinct trade-offs between the conflicting Kernel K-means (KKM) and Ratio cut (RC) (Lin et al., 2018). For the multiresolution comparison of MOEA and ten classic algorithms (Fig 1B), partitions were organized into a three-level resolution hierarchy (low/medium/high) based on the maximum-information-gain criterion. The representative partition for each algorithm at each level was selected as the one having the highest average normalized mutual information with others. We adapted the connectome-based predictive modeling (Shen et al., 2017) into a module-based approach for cognitive predictions. Modular statistics (herein, intra-module strength z-score and participation coefficient) were used to predict the principal component scores of 58 behavioral measures.

Results: We plotted the estimated 225 network partitions generated by the 11 algorithms in the RC-KKM space (Fig 1C). The PF ranges from the ‘cohesiveness-preferred’ upper left to the ‘segregation-preferred’ lower right. Only a few AFG’s and RN’s partitions were superior to the reference PF. Resolution levels L1~L3 of our hierarchy consisted of partitions with 2~6, 7~10, and 11~29 modules, respectively. While single-solution algorithms’ partitions were all at L1, multi-solution algorithms except for RN could generate partitions across all levels but with different preferences (Fig 2A). Fig 2B shows the MOEA’s representative partitions at each level. Two highlighted principal components, Comp1 and Comp2, were derived from behavioral data. While only RB’s partitions could successfully predict Comp1 in a few repetitions, the prediction for Comp2 succeeded on most partitions (significant predicted-observed correlations) (Fig 2C). As the resolution increased, the prediction accuracy of Comp2 worsened in AFG, RB, and StrC, but improved again after a decline in SpeC and MOEA (Fig 2D). Interestingly, the most accurate prediction results were obtained by SpeC at L3 and MOEA at L1.

Conclusions: This study constructs a multiresolution comparison of module detection algorithms. We use a reference front comprised of partitions generated by the proposed resolution-parameter-free multiobjective optimizer. By establishing a three-level multiresolution hierarchy and extracting representative partitions at different resolutions to predict task performance, we found the resolution preferences of multi-solution algorithms and revealed their task-performance prediction advantages.
ABSTRACTS

References
**Introduction:** White matter hyperintensities (WMHs), an established MRI-detected marker of vascular brain injury, are frequently present in Alzheimer’s disease and related dementias (ADRDs), and are known to exert an independent effect on cognitive decline in these diseases (Debette and Markus 2010). Genetically, WMHs demonstrate high heritability in twin, sibship and family studies (~70%) (Turner et al. 2004; Atwood et al. 2004). While research on WMHs, as well as the ADRDs, have mostly focussed on the brain, emerging evidence points to crosstalk between brain and body (Makin et al. 2015), (Huang et al. 2022). However, the heritability of WMHs across tissue- and cell-types in the whole body (i.e., the brain-body axis) have not been characterized. Addressing this gap in knowledge, the aims of this study are to (1) characterize WMH tissue- and cell-specific partitioned heritability in the whole body, and (2) identify common partitioned heritability components between WMHs and ADRDs.

**Methods:** Assessment of tissue-specific heritability: We ran stratified-linkage disequilibrium score regression (sLDSC) on summary statistics from genome wide association studies (GWAS) (N=3 WMH studies; N=10 ADRD studies; Figure 1) for partitioning heritability of the phenotypes (i.e., WMHs or ADRDs) across published tissue-specific binary annotations (N=10) (Finucane et al. 2015). Per GWAS study, enrichment of phenotype-associated-single nucleotide polymorphism (SNPs) within each tissue-type was calculated. Assessment of cell-specific heritability: Using sLDSC, we partitioned heritability of phenotypes across published cell-specific continuous annotations (Cao et al. 2020) for all cell-types associated with tissues enriched with WMH-associated-SNPs. -log10(enrichment_p) values were used to interpret the data and represent the strength of the association. Only significantly enriched cell types (Figure 2) are presented below (>-log10(0.05)). A 5% False Discovery Rate threshold was applied to correct for multiple comparisons.

**Results:** We found that WMH-associated-SNPs were significantly enriched in four tissues. Cardiovascular and kidney enrichments were observed in WMH only, while CNS and liver enrichments were found common to both WMH- and AD-associated-SNPs (Figure 2A). Cell analysis within the four tissues enriched with WMH-associated-SNPs shows that 16/64 cell-types were also enriched, with vascular endothelial cells (vECs) being enriched in all four tissues. The tissue with the highest proportion of cell-types showing WMH-associated-SNPs enrichment was the liver (5/9 cell-types, 55%), followed by CNS (6/18 cell types, 33%). While WMHs and AD both showed enrichment in CNS and liver tissues, in the CNS, cell-specific analysis highlighted enrichment in distinct cerebellar cell-types, with inhibitory interneurons and Purkinje cells being enriched for AD and WMHs, respectively (Figure 2B). Cell-specific analyses on liver cells showed no AD-associated-SNPs enrichment.
Conclusions: Established literature highlights brain vEC dysfunction as a pathogenic mechanism of WMHs (Hassan et al. 2003). We demonstrated that SNPs associated with WMHs were enriched in vECs not only in the CNS, but also in cardiovasculature (heart, lungs), liver, and kidney tissues. In line with our findings, WMHs have also been linked to heart hypoperfusion (Berry et al. 2019), non-alcoholic fatty liver disease (Jang et al. 2019), and worse kidney function (Makin et al. 2015). Overall, our findings lend strength to the proposition that presence of MRI-detected WMHs is indicative of an underlying multi-system endothelial disorder affecting several vascular beds (Vogels et al. 2012). In addition, the enrichment of both WMH- and AD-associated SNPs in inhibitory CNS cells may suggest common mechanistic pathways. Further follow-up studies are required to enhance our understanding of the causative pathways associated with these multi-systemic genetic findings.

References
Whole-brain Changes in Longitudinal Relaxation Rate throughout Emerging and Early Middle Adulthood

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Introduction: The specific neurobiological alterations underlying age-associated macrostructural changes in the brain remain relatively unknown. With magnetic resonance imaging (MRI), in vivo examinations of the human brain are possible – for instance, longitudinal relaxation rate (R1) is a quantitative metric sensitive to myelin and transition metals (Desmond et al., 2016; Stüber et al., 2014). Both histology stained for intracortical myelin and R1 demonstrate inverted-U trajectories across the lifespan, with both rising during early ages followed by a period of stability in middle adulthood and a progressive degeneration at older ages (Erramuzpe et al., 2020; Lintl & Braak, 1983). R1 in deep brain structures has not been studied extensively, however. Here, we characterize age trajectories of R1 across the whole brain during emerging and middle adulthood.

Methods: MRI scans were collected across five imaging sites from healthy individuals aged 16-43 years without any neuropsychiatric diagnoses. (N=43F/35M). Images were acquired on 3T GE or Siemens scanners at isotropic resolution of 1.0mm using 32-channel receive-only head and transmit RF body coils. An inversion-recovery gradient-echo T1-weighted (T1w) image (Anatomical) along with T1w images optimized to maximize (T1wHC) and minimize intracortical contrast (T1wLC) were collected as well as a B1+ map. Subcortical segmentations and cortical parcellations were created from Anatomical using FreeSurfer and the Human Connectome Project’s (HCP) minimal preprocessing pipeline and atlas (Glasser et al., 2016). In total, 28 subcortical and 180 bilateral cortical surface regions of interest (ROIs) were examined. A ratio map between the two T1w images (T1wHC/T1wLC) was calculated and scaled using site- and structure-specific factors to correct for potential inter-site variability. This and the B1+ map were then used to compute R1 maps using look-up tables calculated from Bloch equation simulations. The association between age and mean R1 was evaluated using linear regression for each ROI in R software, with p values corrected using false discovery rate (FDR). Figures 1 and 2 visualize the slope of regression lines and R2 values.

Results: Significant age effects were found in 52 ROIs, including the right putamen, pallidum and bilateral frontal and parietal cortical areas. The strongest age association in the cortex was found in the premotor cortex ($R^2 = 0.222, B = 0.0022 \text{ s}^{-1/\text{year}}, p = .005$), and the smallest age effect was observed in the subgenual area ($R^2 < 0.001, B < 0.0001 \text{ s}^{-1/\text{year}}, p = .991$). In subcortical structures, the strongest and weakest age effects were found in the right putamen ($R^2 = 0.155, B = 0.0026 \text{ s}^{-1/\text{year}}, p = .022$) and the posterior corpus callosum ($R^2 < 0.001, B < 0.0001 \text{ s}^{-1/\text{year}}, p = .981$), respectively. Overall, the putamen and pallidum showed the strongest age effects, while cerebral white matter and corpus callosum showed the weakest age effects.
Conclusions: Our analysis of age-related changes in R1 across the whole brain allowed for a direct comparison of trends across the cortex and deep brain structures. We found differential age trajectories of R1 across the cortex, with the strongest increases in motor areas and the smallest in the medial frontal cortex. These trends agree with past findings (Grydeland et al., 2019). In deep brain structures, the strongest age associations were observed in the basal ganglia, while we did not observe a significant age effect in deep white matter in this age range. These results are also in line with previous research (Hallgren & Sourander, 1958; Lebel et al., 2012), exemplifying the possibility of studying whole-brain neurobiology using R1. Whole brain R1 age trajectories in healthy controls in the future could be used as baseline data to detect abnormal trajectories in disease.

References
Poster No 2145

A normative model of cortical morphology across the lifespan

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Introduction: Understanding the intricate morphology of the human brain in health and disease is a foundational pursuit in neuroscience and current challenges in this field stem from noisy imaging data and small sample sizes, especially for clinical studies. Traditional measures of cortical morphology, i.e. thickness, volume, and surface area, are known to covary and do not capture the complex folded shape of the brain. Research is beginning to leverage normative modelling as a framework for creating robust estimates of healthy variations in brain structure across the lifespan and to assess abnormalities in patient cohorts or individuals. We aimed to extend this field by developing a normative model of brain morphology that can estimate variations in traditional structural metrics as well as novel measures of cortical morphology, and make this model available to the community.

Methods: We collated T1-weighted MRI data from several large public datasets (including HCP, NKI, OASIS, and CamCAN) and in-house studies of healthy controls across the lifespan (n>3,500, age range 6-95 years). All data were pre-processed using the standard recon-all pipeline in FreeSurfer. We utilised novel independent components of cortical morphology (Wang et al., 2020, NeuroImage) to provide nuanced measures of brain structure. We used generalized additive models to build normative models of the independent components (K, I, and S) as well as traditional measures, accounting for normative age, sex, and site effects.

Results: The normative models of traditional metrics showed age trends in line with previous research, e.g. decreases in cortical thickness with age. The independent morphological metric K also decreased with age and explained more of the variance in the data than the traditional metrics, suggesting K may be a more appropriate measure to describe ageing and detect deviations from the healthy trajectory. We introduce our analysis pipeline as a freely available web app that can take new data as input and estimate abnormalities in cortical morphology for each individual based on the normative data. Crucially, we demonstrate that, given a new dataset with a clinical group and matched healthy controls, our model can estimate abnormalities in each patient, where biological and technical covariates are corrected based on the healthy data, debiasing site effects and more accurately estimating the underlying psychopathology of clinical populations.

Conclusions: Our normative models provide robust estimations of healthy variations, and abnormalities, in brain structure across the lifespan, utilising both traditional and novel metrics. Our freely available web app offers an accessible and powerful tool to estimate nuanced measures of cortical morphology and will open new avenues for research and clinical applications for detecting brain structural abnormalities.
Introduction: Congenital Heart Disease (CHD) is one of the most common birth defects in neonates, affecting millions of infants worldwide. CHD not only impacts cardiac function but also has a significant negative effect on the development of the cerebral cortex, leading to long-term neurodevelopmental disorders. Research has revealed that the brain structural abnormalities and incidence rates of various neurodevelopmental disorders (such as Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorder) display notable gender differences. A deeper understanding of these differences can aid in the development of precise and effective treatment and intervention strategies. However, current knowledge about how gender affects brain structures in CHD patients, particularly during infancy, remains quite limited. This study aims to explore this under-researched area by utilizing magnetic resonance imaging (MRI) to reveal potential gender effects on brain development in infants with complex CHD, providing deeper insights for clinical diagnosis and treatment.

Methods: In this study, we recruited 89 infants with complex CHD (43 females and 46 males) and 87 age-matched healthy controls (HCs, 40 females and 47 males) from the Children’s Hospital of Nanjing Medical University, aged between 1 and 2 years. For each subject, T1-weighted imaging data were collected and preprocessed using a pipeline specifically designed for infants. We then parcellated the brain into 17 functional systems and calculated the regional cortical surface area (SA), cortical thickness (CT), and gray matter volume (GMV). Finally, we employed a Linear Mixed Effects Model (LMER) to compare the developmental differences in functional system between male CHD and male HC infants, as well as between female CHD and female HC infants, to capture the potential gender difference. The LMER model used age as an independent variable and morphological characteristics as dependent variables, with “diagnosis” as the grouping factor. The variable “diagnosis” was used to examine the main effect difference (i.e., intercept difference), while “diagnosis*age” was employed to evaluate the interaction effect difference (i.e., slope difference). We applied false discovery rate (FDR) for multiple correction, setting the significance level at p<0.05.

Results: Fig. 1 presents the comparative results of cortical development in functional systems for SA, CT, and GMV in male and female infants with complex CHD. As shown in Fig. 1(A), we found significant developmental abnormalities in several systems for male and female CHDs compared to HCs. The regions exhibiting abnormalities demonstrate considerable overlap across genders, particularly in the aspect of GMV. Subsequent in-depth analysis, however, uncovers significant gender effect in the developmental pattern in CHD infants, as depicted in Figs. 1(B) and 1(C). Developmental alterations in female CHDs predominantly manifested as interaction effects, contributing to 75%, 66.7%, and 71.4% of the anomalies in SA, CT, and GMV, respectively. Conversely, male CHD patients predominantly displayed main effects, with proportions of 66.7%, 100%, and 100% in SA, CT, and GMV, respectively. These findings indicate cortical development delays in both male and female CHD infants. Yet, the rate of development in female CHDs is considerably accelerated compared to that in healthy infants, whereas in males, it aligns closely with that of HCs. This suggests the potential for an earlier normalization of cortical structures in female CHD infants compared to their male counterparts.
Conclusions: This study for the first time reveals the impact of gender on brain developmental abnormalities in infants with complex CHD. The results suggest the potential for an earlier normalization of cortical structures in female CHD infants compared to their male counterparts.

References
Longitudinal Characterization of Hormone-Related Hippocampal Volume across the Pubertal Transition

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Introduction: Puberty is a period of marked changes in behavior, emotion, and cognition1-3. Well-documented sex differences in the brain also emerge during this critical developmental period4,5. The hippocampus is reported to undergo substantial structural and functional changes during puberty, and basic science studies have demonstrated that puberty-related sex hormone secretion influences hippocampal morphology6,7. While some studies in humans have documented both the emergence of sex differences8 and sex-hormone related changes9,10 in hippocampal structure during puberty, these findings have been complicated by confounding variables (such as age, menstrual cycle status), cross-sectional designs, or temporally sparse sampling of longitudinal data during a period when neurodevelopmental changes may be occurring rapidly. Here, we employed data from the ongoing “NIMH Intramural Longitudinal Study of the Endocrine and Neurobiological Events Accompanying Puberty” to document developmental trajectories of hippocampal volume and estradiol (E2) and testosterone (T) serum levels in healthy boys and girls from prepuberty to age 18 to identify associated patterns of change.

Methods: Healthy children between the ages of 8 (when they were ascertained by clinicians to be pre-pubertal) and 18 years were studied every 9 months with neuroimaging and hormonal measurements. Fasting morning blood samples to measure E2 and T levels and 3T structural MRI scans (GE MR750 scanner, sagittal acquisition, 1mm isotropic voxels; TE=1.8ms; TR=10.5ms) were collected across 566 cumulative visits of 135 healthy children (56 girls). To control for menstrual cycle-related hormonal effects, structural scans from menarchal girls were collected during the follicular phase (days 4-11 of the menstrual cycle) as confirmed by serum progesterone levels <2 ng/ml. Repeated measures correlations (R’s rmcorr package) and longitudinal mixed-effects spline models (R’s gamm4 package) were used to identify associations across age between estradiol and testosterone levels and Freesurfer-derived whole hippocampal volume.

Results: Serum E2 and T levels positively correlated with left and right hippocampal volumes in both sexes separately, regardless of age (p’s<0.0006, r’s>0.22). Mixed-effects spline-modeling of developmental relationships between hormones and hippocampal volumes showed significant age-by-T interactions for left hippocampus and age-by-E2 interactions bilaterally. Hippocampal volumes increased faster as estradiol levels increased (p’s<0.001), and a similar relationship was found with testosterone for the left hippocampus, where hippocampal volume increased faster with increasing testosterone (p=0.02).

Conclusions: Our longitudinal findings empirically document E2- and T-dependent hippocampal structural changes across puberty. The specific observation that higher gonadal hormone levels are associated with faster age-related increases of bilateral hippocampal volume suggests that the rapidity of the pubertal transition could have significant developmental impact on long-term hippocampal morphology and function and reinforces the importance of temporally high-density investigation. Finally, these changes in hippocampal volume related to variations in gonadal hormone levels during puberty may have important implications for understanding the emergence of sex differences and increases in vulnerability to neuropsychiatric disorders that are well documented during this period.

References
**Poster No 2148**

**Synthesizing Multi-session Structural MRI using Age and Patch Information**

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**Introduction:** Techniques such as normative modelling have become popular to model cross-sectional brain development with respect to a continuous variable, typically age. In neurodevelopmental conditions, quantifying individual differences or deviations from neurotypical brain development has been shown to be powerful in understanding heterogeneous conditions like prematurity, genetic syndromes and psychiatric illness. In early life, normative approaches are ideal as brain development is non-linear and, during short windows, rapid. Here we propose an extension of normative modelling to whole brain longitudinal development, modelling brain anatomy at later timepoints, given its appearance at an initial timepoint, and with deviations over time analogous to positive or negative “thrive lines” slopes in paediatric growth charts. This approach allows the identification of outliers of typical longitudinal development on a whole brain basis.

**Methods:** Images from the Brown University Assessment of Myelination and Behavioral development Across Maturation (BAMBAM) study were utilised for modelling and estimation. Images were acquired on a 3T Siemens Trio scanner with repetition/echo times varied according to expected head size described in detail in 3. At 12 months, repetition/echo/inversion times were 16/6.9/950ms, collected at a resolution of 1.4x1.4x1.4mm. From the cohort, we selected 195 subjects with 2 longitudinal scans who had age ranges of 68-4542 (scan 1), 128-5476 (scan 2) and 57-2588 days (scan interval). Image pre-processing included N4 bias correction, brain extraction and registration to template space (FSL+ANTS) as in 3. Synthetic images were generated using a method based on that seen in 4. Voxel-wise Gaussian Process regression was used to predict intensity values at the 2nd timepoint across the whole brain using two models. The 1st used age at scan and sex (age model) and was trained using the 2nd scans only as output. The 2nd used age-at-scan 1, age-at-scan 2 and sex in combination with voxel intensities from a 5x5x5 patch surrounding each voxel at time 1 (patch model), providing spatial priors for later timepoint prediction. 5-fold cross-validation was used to assess accuracy of the estimated models. Median absolute error (MAE) maps were calculated by averaging the difference between each subject’s 2nd scan and equivalent synthetic image. To assess utility of the models, Z-score abnormality maps were created by dividing the difference images by subject voxel-wise GP variance outputs.

**Results:** Both models generated synthetic images with intensity values close to those seen in the observed scans. Areas of more consistent structure, such as the basal ganglia, are more accurately modelled while more heterogeneous areas, such as the cortical surface, appear smoothed. However, providing spatial priors from time 1, significantly reduced MAE for time 2. Predicted images with abnormality maps overlays Fig 1 and demonstrate the model’s ability to detect a range of structural deformations and lesions. MAE images can be seen in Fig 2 and achieved MAE score (averaging over all voxels in the MAE image) of 0.242 for the age model and 0.222 for the patch model.

**Conclusions:** Our models can predict T1w structural images at a 2nd timepoint using either subject demographic information or by combining this with patch information from an initial time point. These images infer voxel intensity values from a typical population but, in the patch model, allowing better incorporation of subject specific tissue boundaries and structural heterogeneity. This can be seen by the lower MAE score for the patch model compared to the age model. The Z-score abnormality maps can detect an enlarged ventricle present only at the 2nd scan, an abnormal cerebellum present at both scans and a lesion in the periventricular tissue that is not present or obscured by motion in the 1st scan. Combined, these demonstrate a potential use of patch-based modelling in voxel-based neuroimaging.
References

Poster No 2149
Comparison of subcortical regions in macaque and marmoset monkeys using multimodal MRI and histology
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Introduction: Subcortical nuclei play essential roles in regulating the central and peripheral nervous systems. However, the cross-species comparison of these deep brain structures has yet to be thoroughly investigated using MRI and histology. Here,
we combined multimodal MRI data and matched histology sections with multiple stains derived from the same marmoset and macaque brains to investigate if there are any MR signal intensity or neuropil staining differences in different subcortical regions between these two species ex-vivo.

**Methods:** We scanned two adult perfusion-fixed marmoset brains and one macaque brain on a 7T scanner using mean apparent propagator (MAP)-MRI\(^2\) with 150 µm and 200 µm resolution, respectively. We acquired 112 or 256 diffusion-weighted images with multiple b-values (bmax=10000s/mm\(^2\)), diffusion gradient pulse duration δ=6 or 8 ms, and diffusion time ∆=28 or 20 ms. In each voxel, we estimated the MAP and computed microstructural diffusion tensor imaging (DTI) and MAP parameters: fractional anisotropy (FA); mean, axial, and radial diffusivities (MD, AD, and RD, respectively); propagator anisotropy (PA), return-to-origin probability (RTOP), return-to-axis probability (RTAP), return-to-plane probability (RTPP), non-gaussianity (NG), and the non-diffusion attenuated (amplitude) image, which provides a T2W contrast. We also estimated the fiber orientation distribution functions (fODFs)\(^3\) in each voxel. Following MRI acquisition, we prepared both brain specimens for histological processing with multiple stains\(^4,5\). An alternating series of 50 µm thick coronal sections were processed with AchE, Prussian blue (iron stain), and Nissl or antibodies against neurofilament protein (SMI-32), parvalbumin, NeuN, and ChAT. The high-resolution images of these stained sections were manually registered to corresponding maps of MRI volumes to allow analysis in histologically defined subcortical regions.

**Results:** We found distinct MR signal intensity differences between the marmoset and macaque monkeys in some subcortical regions. For example, the subregions of the basal ganglia (pallidum and substantia nigra) and the deep cerebellar nuclei exhibited significantly more hypointense signals in the T2W images of macaque than in the marmoset (Fig. 1). The MRI studies in primates have interpreted this hypointense signal to a high level of intracellular iron deposit\(^6,7\). We confirmed this finding in the histology sections derived from the same macaque and marmoset brains stained with Perls Prussian blue. In the macaque, the neuropil of the basal ganglia subregions and the deep cerebellar nuclei stained intensely with Prussian blue confirm the presence of a high-level iron. The spatial location of these intensely stained regions matched well with the hypointense signal intensity found in these deep brain structures in macaque T2W images. In contrast, these subregions in the marmoset revealed very faint staining with Prussian blue, confirming a very weak iron deposit, and it corresponded well with the significantly less hypointense signal in T2W images (Fig. 1A-F). We also found other differences in the subcortical white matter in T2W images. For example, the anterior limb of the internal capsule, cerebral peduncle, anterior commissure, and the deep cerebellar white matter exhibited more hypointense signal in the marmoset than in the macaque (Fig 2A, B). In MAP-MRI (DEC-FOD)\(^8\), we found alternating bands of fiber bundles with different orientations in the fascia dentata (FD) of the macaque hippocampus but not in the marmoset (Fig. 2C, D). In contrast, the hippocampal CA1 of the marmoset revealed more mediolaterally oriented fibers than in the macaque (Fig. 2E).

**Conclusions:** High-resolution multimodal MRI combined and correlated with histology can elucidate structures that were previously invisible radiologically and offer a roadmap toward identifying subcortical nuclei and their subregions based on differences in microstructural and chemoarchitectonic properties.
Fig. 1. Comparison of subcortical regions in macaque and rhesus monkey brains. (A–F) Subregions of the basal ganglia (caudate/putamen-ct/ACh, external and internal segments of the globus pallidus GPi/GPe), substantia nigra (SNp), parvicellular division of the red nucleus (RIPct), and the deep cerebellar nuclei (dentate nucleus-DN, anterior interposed nucleus-AN, posterior interposed nucleus-PN, fastigial nucleus-FN) in the macaque and rhesus monkey coronal T2W images. Matched histology sections with similar subcortical regions from the same macaque and rhesus brains stained with Prussian blue for detecting intracellular ferric iron. Note that in the macaque (A–D), these basal ganglia subregions (except caudate-ct) and the deep cerebellar nuclei stained intensely with Prussian blue that matched well with the strong hypointense signal found in these subregions, as revealed in T2W images. In contrast, these deep brain regions stained weakly with Prussian blue that matched well with the significantly less hypointense signal found in these subregions in T2W images (D–F).

Abbreviations: 3rd-oculomotor nucleus; 3e-oculomotor nerve; CC-corpus callosum; ca-internal capsule; CPU-cerebral peduncle;ModeslSuperior colliculus; GPe-globus pallidus externa segments; GPi-globus pallidus interna segments; SNr-substantia nigra, anteromedial; SNp-substantia nigra, posteromedial; SNmedial nucleus; SNc-cerebellar nucleus; RNred nucleus; RNpo-red nucleus; parvicellular divisions; STN-subthalamic nucleus; VP-ventral pallidum; VPM-ventral posterior medial nucleus; Scale bars: 5 mm.
References


Association between hippocampal subfield development and socio-emotional outcomes in preterm infants

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Introduction: Each year, more than 1 in 10 neonates are born prematurely (<36 weeks gestational age [GA]) worldwide1. Premature birth carries long-term consequences, including an increased risk of socio-emotional difficulties during childhood2. The hippocampus is a crucial brain region for socio-emotional abilities as it conducts functions such as the flexible manipulation of relational memories which is essential for understanding social interactions and behaviour regulation3. Prior studies showed that children born very preterm (<32 weeks GA; [VPT]) exhibit reduced total hippocampal volumes compared to their term-born peers at school-age4 and that volume reduction is associated with impaired memory functions5. Recent studies in healthy adults have suggested that the hippocampus functional topography may be region-specific6. However, investigations of early hippocampal subfield development and how they may relate to functional outcomes are sparse in VPT infants. With the recent refinement of Hippunfold, a validated automatic magnetic resonance imaging [MRI]-based hippocampal subfield segmentation pipeline7, we may now have the tools to fill this gap in knowledge. Therefore, this ongoing study aims to 1) quantify total and subfield hippocampal volumes at term-equivalent age [TEA] in VPT infants and 2) explore the relationships between volumes at TEA and socio-emotional competencies at 12 months corrected age.

Methods: Enrolled VPT infants completed a brain MRI under natural sleep at TEA on a 3.0 Tesla MRI system (Achieva X-Series, Philips Healthcare) using a 32-channel head coil. High-resolution (1 mm isotropic) T1-weighted images were acquired and pre-processed using Hippunfold. Pre-processing steps included N4 bias field correction, resampling to a 0.3mm isotropic subvolume, linear registration to an age-appropriate template, cropping to coronal-oblique subvolumes and left-right flipping of the left hippocampi sub-volumes. Automatic segmentation of the hippocampi and 7 subfields (subiculum, cornu ammonis [CA]1-4, dentate gyrus [DG] and Stratum Radiatum, Lacunosum, and Molecular [SRLM]) was also performed in Hippunfold. Lastly, manual correction was performed when necessary. At 12 months corrected age, parents completed the Brief Infant-Toddler Social and Emotional Assessment (BITSEA)8, which yielded results divided into two subscales: Problem (e.g., anxiety, aggression and defiance) and Competence (e.g., prosocial behaviors, empathy and compliance). Partial correlation analyses were performed to determine the relationships between each hippocampal subfield volume and both socio-emotional subscales while controlling for GA at birth and sex. Correction for multiple comparisons was performed using the False Discovery Rate (FDR).

Results: In this ongoing study, the hippocampi and subfields of 40 VPT infants were successfully segmented using Hippunfold (Table 1 and Fig. 2). Of those, 17 (43%) infants had an available BITSEA at 12 months corrected age. The results of the BITSEA showed that 29% of VPT infants had deficits on the Problem and 41% on the Competence subscales. The left CA4/DG volume at TEA was significantly negatively associated with the Problem score (r=-0.55; p=0.03) and positively associated with the Competence score (r=0.53, p=0.04) at 12 months corrected age. However, these associations did not remain significant after FDR correction. No other significant associations were found.
Table 1. Mean volumes of the bilateral hippocampal subfields for the 40 VPT participants with successful Hippunfold segmentations.

<table>
<thead>
<tr>
<th>Hippocampal region</th>
<th>Left mean volumes (mm³)</th>
<th>Right mean volumes (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subiculum</td>
<td>285.11</td>
<td>292.06</td>
</tr>
<tr>
<td>CA1</td>
<td>321.02</td>
<td>335.82</td>
</tr>
<tr>
<td>CA2/CA3</td>
<td>207.13</td>
<td>180.52</td>
</tr>
<tr>
<td>CA4/DG</td>
<td>135.51</td>
<td>164.63</td>
</tr>
<tr>
<td>SRLM</td>
<td>255.67</td>
<td>270.31</td>
</tr>
<tr>
<td>Total</td>
<td>1204.45</td>
<td>1423.82</td>
</tr>
</tbody>
</table>

Figure 1. Left hippocampus and subfields segmentation of a VPT infant at TEA.

Conclusions: In this study, we found significant associations between left CA4/DG volumes at TEA and socio-emotional development at 12 months in VPT infants. Upcoming analyses in a larger sample size will allow the addition of more clinical variables in our models to better understand these complex associations. We hope that these results will enhance our comprehension of the role of hippocampal subfield development in the socio-emotional well-being of VPT infants.

References
High-resolution 3D Mapping of the Human Hypothalamus: Towards a Comprehensive Cytoarchitectonic Atlas

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Introduction: The hypothalamus plays a central role in maintaining homeostasis and coordinating various physiological and behavioural processes including sleep-wake cycles, appetite, circadian rhythm and thermal regulation (Nieuwenhuys et al., 2008). It encompasses distinct nuclei with a specific microstructure, connectivity, molecular organisation. Despite its importance, the structural organization and precise boundaries of the human hypothalamus, and the functional differentiation of its nuclei, are still not fully understood. Existing anatomical maps of the hypothalamus do not reflect interindividual variability in 3D space; they often lack the spatial resolution and morphological detail to provide a comprehensive understanding of this complex region and to inform neuroimaging studies about the brain's microstructure. Therefore, here we aimed to develop probabilistic cytoarchitectonic maps to address inter-subject variability and to provide a high-resolution 3D reference map for informing studies in the living human brain.

Methods: We delineated the hypothalamus and its nuclei on every 15th cell-body stained brain section in 10 brains (5 female, 5 male) including the BigBrain (Amunts et al., 2013). For creating maps in the high-resolution BigBrain model, we used a deep-learning based tool (Schiffer et al., 2021). The ten brains were used to create probability maps that capture intersubject variability in space and location of areas. To do this, brains were 3D reconstructed and superimposed in standard reference space (Amunts et al., 2020). Quantitative tools, including texture analysis (Devakuruparan, 2022) and object instance segmentation (Upschulte et al., 2021), were applied to characterize subdivisions in more detail.

Results: We generated high-resolution 3D maps of 20 nuclei of the human hypothalamus (Figure 1), that show their shapes and neighbourhood relationships with high precision. They were associated to four rostro-caudal zones: preoptic, anterior, tuberal, and mammillary. In the preoptic zone, we found the periventricular and median preoptic nuclei, lining the third ventricle. The uncinate and intermediate nuclei form a compact cluster around the medial preoptic nucleus. In the anterior hypothalamic area, we observed the paraventricular nucleus housing magnocellular neurons in its ventrolateral region and parvocellular neurons medially. Also, we identified the supraoptic nucleus with densely packed magnocellular neurons, and the suprachiasmatic and anterior periventricular nuclei. In the tuberal region, we located the ventromedial nucleus exhibiting high peripheral cell density. Adjacent, the posteriormedial nucleus, smaller in size, fills the space between the ventromedial nucleus and mammillary body. The dorsomedial nucleus holds densely packed small neurons at its center. The arcuate nucleus consists of densely packed neurons within the tuber cinerium. In the mammillary region, we found the medial and lateral mammillary nuclei. The tuberomammillary and supramammillary nuclei contain large dark magnocellular neurons. Finally, the lateral tuberal nucleus in the basolateral mammillary zone houses three subnuclei of medium-sized neurons, positioned closer to the periphery than the nucleus center. The mean hypothalamic volume was 1688 ± 48 mm³. The lateral (446 ± 49 mm³) and posterior hypothalamic areas (248 ± 50 mm³) showed the highest volumes, whereas the uncinate and lateral mammillary nuclei exhibited the lowest values (1.2 ± 0.3 mm³; 1.35 ± 0.2 mm³). Permutation tests found no significant effects of hemisphere, sex, or their interaction on the shrinkage-corrected volumes for each nucleus. Intersubject variability was also reflected in the probabilistic maps that will be part of the Julich-Brain Atlas (Amunts, 2020).
Conclusions: In sum, we provide a detailed microstructural map of the hypothalamus, serving as a comprehensive anatomical basis for interpreting and comparing neuroimaging data helping to refine the functional organization of the hypothalamus.

References

Poster No 2152

Mild Traumatic Brain Injury Associated with Greater Bilateral Medial Thalamic Nuclei Volume

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Introduction: Evidence points to the vulnerability of the thalamus in mild traumatic brain injury (mTBI), due to its anatomical position at the brains’ centre of mass and abundant cortical connectivity profile. Few studies have systematically investigated the possibility of structural change in the thalamus, nor have they adequately assessed its constituent subnuclei. The treatment of the thalamus as a unitary structure may mask subtle structural changes, which is problematic considering the variable functional contributions of thalamic subnuclei to cognitive, sensory, and motoric functions. Therefore, we aimed to investigate whole and thalamic subnuclei volume following mTBI, using a joint structural MRI (sMRI) and diffusion MRI (dMRI) Bayesian segmentation algorithm to segment the thalamus into subregions.

Methods: 39 mTBI patients and 29 trauma control (TC) patients aged 18 – 60 were recruited as inpatients. Participants were classified into the mTBI group if they fulfilled the World Health Organisation criteria for definition of mTBI, and into the TC group if they sustained a traumatic injury in the absence of a head strike. Participants completed an MRI neuroimaging protocol including both sMRI (MPRAGE) and dMRI (b = 0, b = 1000, b = 3000s/mm2) sequences at 6 – 10 weeks (m = 57 days, sd = 11) following injury. Lateralisated whole and regional thalamic volumes were estimated using a Bayesian joint structural and diffusion segmentation method, yielding 25 labels per hemisphere which were merged to create nuclei groups. Bayesian linear models were fitted, with age and estimated intracranial volume (ICV) as covariates. Firstly, the median and 95% Highest Density Interval (HDI) are reported. There is a 95% probability the effect is within this confidence interval. Additionally, three sequential probabilities are reported: of direction, of significance (effect is of sufficient size to be considered non-negligible), and of being large. The thresholds for significant and large effects are 0.05*SDy and 0.3*SDy respectively.

Results: Analysis revealed some evidence for greater whole thalamic volume and thalamic subnuclei between the groups, although the magnitude of effect varied. Briefly, the effect of Group [TC] on right whole thalamus volume (median = -0.34, 95% CI [-0.64, -0.03]) has a 98.46% probability of being negative, 96.83% of being significant, and 59.33% of being large. The effect of Group [TC] on left whole thalamus volume (median = -0.21, 95% CI [-0.51, 0.09]) has a 92.42% probability of being negative, 86.41% of being significant, and 28.77% of being large. The effect of Group [TC] on right medial thalamus volume (median = -0.58, 95% CI [-0.90, -0.25]) has a 99.95% probability of being negative, 99.8% of being significant, and 95.16% of being large. The effect of Group [TC] on left medial thalamus volume (median = -0.47, 95% CI [-0.81, -0.15]) has a 99.74% probability of being negative, 99.4% of being significant, and 85.00% of being large. Other subnuclei groups with a high probability of being significant were the left anterior thalamic nuclei and the right anterior thalamic nuclei, however the probability of being large was small, which indicates posterior is mostly contained between the significance and large thresholds.

Conclusions: Our findings suggest mTBI is associated with thalamic and thalamic subnuclei abnormality toward the end of what is frequently considered the end of the typical recovery period. Whilst our data suggest bilateral whole thalamus and bilateral anterior thalamus are also larger in the mTBI group, the largest effect was identified in the medial thalamic group. Given the medial thalamus sits closest to the midline of the brain, it may be more vulnerable to injury effects in mTBI. Greater
volume may reflect thalamic inflammation, which could serve adaptative or maladaptive mechanisms. Further work should investigate the possible mechanisms underpinning increased volume by applying techniques that can probe additional microstructural metrics.

References

Poster No 2153
Simultaneous cortical, subcortical, and brainstem mapping of sensory activation
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Introduction: Whole-brain fMRI allows for complete mapping of neural systems that have key subcortical and brainstem components, such as sensorimotor pathways. However, subcortical and brainstem fMRI has historically been challenged by high physiological noise and small nuclei sizes, leading many studies to use a restricted field of view or move to 7T². To address these challenges at 3T, we implemented a targeted scan protocol that provides a whole-brain field of view, sufficient in-plane spatial resolution in the brainstem, and multi-echo denoising for improved data quality. Here, we demonstrate our simultaneous cortical-subcortical-brainstem protocol to map sensory activation across the brain and test its ability to differentiate adjacent sensory nuclei in the brainstem: cuneate (upper extremity sensation) and gracile (lower extremity sensation).

Methods: Data Collection: fMRI scans were collected in a Siemens 3T Prisma MRI system with a 32-channel head coil, using a multi-band multi-echo GRE EPI sequence: TR=2.2s, TEs=13.4/39.5/65.6ms, FA=90°, MB factor=2, voxel size=1.731x1.731x4mm3. Axial slices were aligned perpendicular to the base of the 4th ventricle. During each scan, a hand or foot was brushed at a rate of 1Hz: 20s on/20s off x 12 repeats. 10 healthy participants (4M,26±2y) underwent brushing of the right and left palm/fingers for 2 scans each, and 10 participants (5M,25±3y) underwent brushing of the right sole/toes for 2 scans. A T1-weighted structural image and field map were acquired to aid with registration and distortion correction. Data Analysis⁴,⁷: The first 10 volumes of each fMRI scan were removed to allow for steady-state magnetization, then scans were distortion-corrected. Head-motion realignment parameters were computed for the first echo with reference to the initial Single Band reference image, then applied to all echoes. Optimally combined (OC) data were calculated, then converted to signal percentage change. Multi-echo ICA was performed (tedana⁵) and components were manually accepted or rejected as noise⁴. Subject-level activation was modeled with a sensory task regressor, motion parameters, Legendre polynomials up to 4th order, and rejected ICA components. Subject-level beta parameter and t-statistic maps were transformed to MNI space and averaged across sessions. Group-level activation was identified across the whole brain using AFNI 3dMEMA, and within a mask of the medulla using FSL randomise with threshold-free cluster enhancement.

Results: For all stimuli, activation was detected in the sensorimotor cortices, putamen, and cerebellum. Thalamus activity was detected for hand stimuli (Fig1). With brainstem-specific analyses, activation was detected in the ipsilateral cuneate nuclei for hands and gracile nucleus for the foot; clusters did not overlap (Fig2).
Conclusions: Cortical, subcortical, and brainstem activation findings for hand and foot stimuli aligned with expectations and previous findings. The lack of thalamus findings for the right foot suggests that greater sample size may be needed, as foot sensory fibers are fewer than in the hand. Sensory and motor systems are linked, demonstrated by activation detected in motor-related areas, such as the putamen and motor cortex, in addition to expected sensory areas. A similar single-echo acquisition protocol has been used previously to aid in full brain fMRI analyses. We incorporated multi-echo denoising, shown to improve data quality, to enhance sensitivity to activation (particularly in the brainstem) with a small sample size. Importantly, our protocol allowed for the lateralization of activity in the medulla for right vs left hand stimuli and, for the first time, differentiation between adjacent cuneate and gracile nuclei using fMRI. Our results demonstrate the feasibility of
simultaneous whole-brain task-fMRI at 3T, with potential applications in investigating sensorimotor changes in clinical cohorts, such as stroke and Parkinson’s, that have brainstem involvement.

References

Poster No 2154
Investigating the neuromodulatory potential of the caudal zona incerta across species: a review
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Introduction: The zona incerta (ZI), situated between the subthalamic nucleus and ventral thalamus, has emerged as a promising neuromodulatory target for Parkinson’s Disease (PD) and essential tremor (ET). Its role as a therapeutic target has been investigated in both animal models and clinical studies of deep brain stimulation (DBS; Plaha et al. 2006; Ossowska 2020; Plaha et al. 2011). Notably, the caudal region of ZI (cZI) is uniquely enriched in glutamatergic neurons, characterized by its extensive projection to the motor cortex and other subcortical regions implicated in motor control (Yang et al. 2022; Ossowska 2020). This intricate pattern of connectivity underscores its role in modulating postural and locomotion (Ossowska 2020; Wang et al. 2020), which is similarly reflected in a clinical setting, as DBS targeting of the cZI shows significant alleviation of motor symptoms in PD patients (Plaha et al. 2006; 2011; Blomstedt et al. 2018). Although rodent studies offer valuable insights into cZI organization, the neuroanatomical, cytoarchitectural, and genetic disparities between rodent and primate brains are substantial (Belmonte et al. 2015; Herculano-Houzel 2009; Molnár and Clowry 2012). The extent of neurochemical cross-species conservation of this structure remains poorly understood, insights into which could help to reveal the mechanism of action of cZI neuromodulation.

Methods: Articles published in English were identified using PubMed. Keywords included combinations of “zona incerta” with “non-human primate”, “marmoset”, “rhesus monkey”, “macaque”, “rodent”, “mouse”, “rat”, “human”. Inclusion criteria were: 1) studies investigating the connectivity, cyto- or chemo-architecture of the ZI; 2) animal models of rodents, non-human primates, PD or ET patients; 3) direct visualization of the ZI for the treatment of neurological disorders.

Results: This review summarizes and compares the anatomical, cellular, and molecular landscapes of the ZI between rodents, non-human primates, and humans, exploring their implications for the treatment of neurological disorders. Briefly, rodents have a larger ZI to brain ratio than primates, potentially driven by differential expansion patterns during brain development across species. The primate ZI also expresses different immunomarkers in its caudal region comparing to rodents, suggesting potential difference in cellular composition (Figure 1). Although connectivity patterns and molecular composition are largely conserved, rodents have an additional intermediolateral region of connectivity that has not been observed in primates (Figure 2). Key projection areas, such as the thalamus and motor cortex, of the primate cZI also demonstrate distinct genetic profiles when compared to rodents, indicating functional differences.
ABSTRACTS

Figure 1. Neuronal populations in the cZI of rodents and primates. (A) Dense Pdx1/GABA1 protein expression throughout the ZI, but becomes sparser in medial cZI. Ptx2/GluT2 expression is sparse throughout the ZI, but is concentrated in medial cZI, representing the glutamatergic subtype implicated in symptom manifestation of PD mouse models; Allen Cell Atlas12. (B) GABAergic and glutamatergic gradients are less prominent in human cZI, as demonstrated by Gad2 (exp: 1000985256) and Sticklefinger (exp: 100995288) expression from ISH experiments of Allen Human Brain Atlas11. Th, thalamus; STN, subthalamic nucleus; ZI, zona incerta; cZI, caudal zona incerta.

Figure 2. Connectivity of the rodent and primate cZI. Rodent cZI demonstrates unique connectivity in the medial and lateral regions13 and exhibits a rostral-caudal gradient, whereas mammals demonstrate a dorsal (yellow)-ventral (red) pattern14. Rodent cZI projects glutamatergic efferent fibres to basal ganglia structures (globus pallidus, pedunculopontine tegmental nucleus, and entopeduncular nucleus) and receives GABAergic input from striatum, which is absent in primates15,16. BG, basal ganglia; STN, subthalamic nucleus; Sm, substantia nigra; Hy, hypothalamus.
Conclusions: We found the cZI is a highly conserved structure across rodents and primates, with subtle yet important molecular, connectomic, and anatomical inter-species differences. Improving our understanding of the neurochemical architecture of the cZI across species is critical for neuromodulatory advancements. An understanding of both electrode placement and molecular variations in cZI organization has the potential to impact treatment, enhance accurate interpretation of animal study findings in a clinical context, and ultimately improve patient outcome.

References

Poster No 2155
Cortico-hippocampal wave interaction: Insights from neural mass models
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Introduction: Dynamic interactions between subcortical structures and cortical regions are essential to the execution of cognitive functions. In particular, the relationship between the hippocampus and cortex is vital for memory encoding and retrieval (Ren et al., 2018), with both structures demonstrating oscillatory activity marked by propagation of traveling waves (Roberts et al., 2019; Zhang & Jacobs, 2015). As the understanding of wave-wave interactions underlying the integration of these two brain areas is limited, this study focuses on investigating hippocampal waves and their interactions with the cortex computationally, aiming to develop models of these interactions that yield testable predictions.

Methods: Biophysically informed non-linear neural mass models (i.e., Jansen-Rit columns) were used to simulate neural activity on a hippocampal mesh and a cortical representation. The coupled models of both brain areas were subjected to parameter sweeps and perturbation analyses to characterize global coherence, phase velocity and to identify preferred wave propagation patterns in the models. Different coupling mechanism between the hippocampus and cortex were then investigated.

Results: A small gradient in external input is crucial for the emergence of traveling waves in the hippocampus, yielding a clear preference for wave directions following the antero-posterior spatial gradient. The nodal phase velocity can be adjusted by tuning the magnitude of the gradient of the external input, i.e. the difference between minimum and maximum of external input; yielding velocities between 0.5 and 2 m/s. Intricate wave interactions, with phase-phase relationships, arose through coupling the hippocampal to the cortex. The nature of these interactions was substantially impacted by the chosen inter-system coupling configuration, including one-to-one, sparse, or clustered coupling schemes. Furthermore, the ratio of inter-system to intra-system coupling strength plays a crucial role in shaping these interactions.
Conclusions: These computational analyses offer detailed mechanistic insights into how traveling waves of neural activity form in the hippocampus and how wave-wave interactions can contribute to cortico-hippocampal functioning. Notably, the hippocampal model fits the wave velocity for slow theta oscillations, aligning with detailed neurophysiological recordings (Zhang & Jacobs, 2015). In sum, the models provide hypotheses that can be directly tested using neuroimaging data from intracranial EEG, such as in epilepsy patients performing cognitive tasks, thereby contributing to a translational neuroscience approach. By providing testable computational models, our study builds a robust framework for understanding cortico-hippocampal interactions and has significant implications for future research in cognitive neuroscience and neurodegenerative disorders associated with memory dysfunctions.

References

Mapping Surface Area Regionalization of Hippocampal Formation in Early Development
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Introduction: The hippocampal formation, which is a convoluted, thin subcortical structure, involves multiple crucial cognitive functions relating to specific hippocampal subregions (Hunsaker and Kesner, 2013). Current research indicates the hippocampal formation exhibits a distinct functional connectivity-based parcellation, which differs from traditional histology-based partition along the medial-lateral axis (Genon, et al., 2021). However, a paucity of studies delves into hippocampal internal organization in terms of early dynamic development, which is essentially related to both the underlying microstructure and functional connectivity. We thus aim to explore the development-based surface area regionalization of hippocampal formation by using high-resolution longitudinal MRI scans covering the first two postnatal years.

Methods: We used 513 longitudinal T1w and T2w brain MR images (resolution = 0.8*0.8*0.8 mm3) from 231 healthy subjects during the first two postnatal years from Baby Connectome Project dataset (Howell et al., 2019). All scans were processed with the infant brain extraction and analysis toolbox, iBEAT V2.0 (Wang et al., 2023). To map the surface area regionalization of the hippocampal formation, we utilized our created 4D infant brain volumetric atlases (Chen et al., 2022), which provide manually delineated hippocampal labels. When building 4D infant atlases, we obtained the deformations between age-specific atlases and between each age-specific atlas and the age-matched scans (Avants et al., 2011; Chen et al., 2023). To obtain the vertex-to-vertex correspondences of hippocampal surfaces across subjects and ages, we reconstructed the hippocampal surface mesh representation in 0-month atlas and then warped it to each scan at each age by combining the corresponding deformations between age-specific atlases and between each age-specific atlas and the age-matched scans. For example, for a 2-month individual scan, we concatenated the deformation fields in the following order: 0-month atlas to 1-month atlas,
1-month atlas to 2-month atlas, 2-month atlas to 2-month scan. Finally, the local surface area of each vertex was calculated on each surface and a matrix was formed with each column denoting the local areas of all vertices of a hippocampal surface and each row denoting the local areas of all scans at the same vertex. Then, a data-driven and hypothesis-free method, non-negative matrix factorization (NMF) (Lee and Seung, 1999), was adopted to partition hippocampal surface into a set of developmentally heterogeneous regions by clustering co-developing vertices into same regions (Wang et al., 2019; Sotiras et al., 2017).

Results: Silhouette coefficient and reconstruction error were jointly used to ascertain the optimal subregion number. Fig. 1 shows the values of silhouette coefficient and reconstruction error across different numbers of hippocampal subregions separately for bilateral hippocampi using NMF method. We opted for 7 as the proper hippocampal subregion number, considering the high local maximum of silhouette coefficient, relatively low reconstruction error, and more symmetric patterns in bilateral hippocampal subregions. The hippocampal surface partition and its spatial position relative to the brain were shown in Fig. 2. Two distinct developmental patterns of hippocampal surface area were discerned, with one pattern adhering to the tripartite subdivision, including hippocampal head (regions 1 and 5), body (regions 2, 4, 6, and 7), and tail (region 3). Another pattern followed a medial-lateral partition, with the medial portion consisting of regions 4, 5, and 6, while the lateral portion comprising regions 1, 2, and 7. Of note, there is no specific medial-lateral division for region 3.

Conclusions: This work firstly explores the surface area regionalization of hippocampal formation from developmental view and proposes important means for exploring the development of hippocampus-related cognition during early postnatal years.
ABSTRACTS

References

Poster No 2157

Age and Sex Dependent Hippocampal Normalization After Pain Relief in Trigeminal Neuralgia

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Introduction: Chronic pain is a silent epidemic. Individuals with trigeminal neuralgia (TN), the most common form of chronic neuropathic facial pain, show evidence of abnormalities within the hippocampus. Microvascular decompression (MVD) is a highly effective surgery to treat TN pain and patients who undergo the procedure are generally young. Thus, it serves as a valuable platform to investigate the dynamics of grey matter alterations and provides insight into how the brain recovers from chronic pain. Previously, we found that reduced hippocampal volume in TN was reversed upon pain relief following successful surgery. However, the roles of age and sex in hippocampal normalization remain unclear. We hypothesized that hippocampal recovery would be biased towards females of younger age.

Methods: Magnetic resonance imaging (MRI) scans of 50 MVD patients (14 males, 36 females) were collected before and 6-months after surgery. Subjects were age- and sex-matched with healthy controls from the Cambridge Centre for Neuroscience and Ageing (Cam-CAN). TN subjects rated their pain pre- and post-surgery on a numeric rating scale from 0 (no pain) to 10 (worst pain imaginable). 41 (82%) responded to the surgery, with a post-surgical decrease in pain rating of at least 75%. FreeSurfer 7.0 was used to segment the hippocampus into 10 bilateral regions. Head size differences were adjusted for using a generalized linear model of the form “ROI ~ Group + Age + Sex + SGV”, where ROI is the hippocampal region of interest, group is one of healthy controls, pre- or post-surgery, age is continuous, sex is binary-coded, and SGV is the subcortical grey matter volume or covariate. Models with lower AIC and BIC were selected and checked for goodness-of-fit. Hippocampal volumes were compared using independent and paired t-tests and checked for a relationship with age using Spearman correlation tests. All relevant p-values were corrected for multiple comparisons using the false discovery rate to become q-values, with α = 0.05. All data were analyzed in R 4.3.2 and validated in Python 3.11.5.
Results: At both pre- and post-surgical time points, males had larger bilateral hippocampi than females (q = 0.029). Notably, following MVD, females 50 years and younger (n = 12) had significant increases in total left-hemispheric hippocampal volume (q = 0.02) to a level comparable to controls. This included 6/9 of its subregions (dentate gyrus, CA3 and CA4, molecular layer, hippocampal head and body), and the right hippocampal head. Furthermore, a gradient of normalization was observed, in that younger females had a greater degree of normalization compared to females closer to the age of 50 (p = -0.62, p = 0.032). Similarly, in females with right-sided facial pain (n = 18), normalization was overwhelmingly (5/10 regions) in the contralateral hemisphere, including the whole left hippocampus (q = 0.038), while no regions in the right hemisphere significantly increased. No significant changes were observed in male responders nor in female responders over 50 years of age.

Conclusions: These results are another instance of sex-related effects in neuropathic pain, with an inflection point at the age of 50 in females, beyond which hippocampal normalization was no longer observed. Traditionally known for its role in memory, cognition, and emotions, we provide further evidence that the hippocampus may be a key structure of interest in chronic pain conditions. These findings support a pressing need to expedite clinical timelines for females with TN, as they experience significantly greater delays in receiving surgical treatment than males. Additionally, non-invasive measures like age, sex, and hippocampal volume may have predictive value for grey matter recovery following MVD. Ultimately, knowing that brain abnormalities in chronic pain can be reversed with pain relief presents promising new avenues for future pain research, with a focus on equitable patient treatment.

References
Neuroanatomical differences in Australian rules footballers following mild traumatic brain injury

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Introduction: Australian rules football is a full-contact sport played with intensity, in which players are exposed to one of the highest rates of concussion (a type of mild traumatic brain injury (mTBI)), across sporting codes in Australia¹. The wellbeing of athletes exposed to repeated mTBI and sub-concussive impacts is of growing concern given the association with long-term neurodegenerative consequences²-³. Previous work has highlighted changes in white matter microstructure and functional connectivity in professional Australian rules footballers following mTBI⁴-⁵; however, these footballers may also exhibit observable changes in standard structural brain measures. Here, we explored differences in structural brain measures in professional Australian rules footballers with a recent mTBI. We hypothesised that footballers would exhibit differences in volume and thickness measures, particularly in the hippocampus, which has well-documented vulnerability to mTBI⁶-⁷.

Methods: Professional male footballers from the Australian Football League (AFL), who had sustained an mTBI within 3 months prior to MRI acquisition, were included and categorised into either an acute mTBI group (n=17, ≤12 days since mTBI), or a subacute mTBI group (n=14, >12 days since mTBI). Healthy male age-matched controls with no history of head trauma were also included (n=37). T1-weighted MRI data were acquired at 3T on either a Siemens Trio or Skyra using an MPRAGE sequence (0.9mm isotropic voxels, inversion time=900ms, flip angle=9°, TR/TE=1900/2.5ms). All T1-weighted MRI scans were processed using FreeSurfer (v7.3.2). Estimated total intracranial volume (eICV), whole brain volume, hippocampal and amygdala volumes, and cortical thickness were quantified using FreeSurfer’s hippocampus and amygdala nuclei subfield recon-all pipeline⁶. Hippocampal subfield volumes were obtained using FreeSurfer’s hippocampus and amygdala nuclei subregion segmentation pipeline⁵. All outputs were manually inspected and edited where necessary using FreeView, and group-level comparisons made using multiple linear regression (adjusting for age and eICV). For subfield and thickness analyses, False Discovery Rate (FDR) correction was performed to correct for multiple comparisons. In a subset of mTBI participants (n=26), cognitive screening was performed using the CogSport computerised battery⁹. Normalised scores from the one-back and continuous learning tests (which assess working memory and learning, respectively) were used to examine the relationship between hippocampal volume and cognitive function post-mTBI using Pearson’s correlation.

Results: Compared to controls, both mTBI groups exhibited significantly smaller whole brain volume (acute: p=0.013; subacute: p=0.008) and right hippocampal volumes (acute: p=0.031; sub-acute mTBI: p=0.012). The acute mTBI cohort also exhibited significantly smaller right amygdala volume (p=0.018) and thinner right rostral anterior cingulate thickness compared to controls (FDR-corrected p=0.010). At the hippocampal subfields, the sub-acute mTBI group exhibited significantly smaller right subicular complex volume compared to controls (FDR-corrected p=0.035). A similar trend was seen in the acute mTBI group at the right subicular complex; however, this did not survive FDR correction (FDR-corrected p=0.063). There was a significant positive correlation between footballers’ cognitive learning scores, and hippocampal volume bilaterally (left: r(23)=0.44, p=0.030; right: r(23)=0.40, p=0.046).
Conclusions: Here, we provide evidence of subtle structural brain differences in Australian rules footballers following a recent mTBI, namely at the whole brain level, and at the hippocampus and amygdala (right more than left). Longitudinal research is needed to assess if these subtle differences may be early signatures of long-term neurodegenerative changes, and whether quantifying these structural MRI changes in individuals may be a clinically viable tool in future.

References

Poster No 2159
Multimodal Analysis of Brain Alterations in Bipolar Disorder and Relationship to Clinical Covariates
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Introduction: Bipolar disorder (BD) is a chronic and severe mental illness with no validated biomarkers to guide diagnosis or treatment. Altered cortical and subcortical volumes (Hibar et al., 2016, Ching et al., 2022), as well as functional dysconnectivity of the default mode network (DMN), have been reported in BD (Nabulsi et al., 2020, McPhilemy et al., 2020). However, differences in processing and analysis methods challenge the consistency of study findings, calling for large-scale, standardized analyses to improve replication and generalizability. In addition, the impact of illness severity and common treatments on brain measures in BD remains unclear. We aimed to evaluate both structural and functional brain alterations in
BD using standard protocols from the ENIGMA Consortium and map alterations associated with both symptom severity and medication use.

**Methods:** Structural T1-weighted and resting-state functional MRI data were acquired from one pilot ENIGMA-BD site, with 100 participants (44 BD, 56 controls (CN); age range 19-65, 54% female). Subcortical volumes of lateral ventricles, thalamus, caudate, putamen, pallidum, hippocampus, amygdala, and nucleus accumbens were derived using an ENIGMA-standardized protocol (based on FreeSurfer v5.3). ENIGMA-HALFpipe (v1.2.1) (Waller et al., 2022), a standardized pipeline based on fMRIPrep (Esteban et al., 2019), was used to derive overall within-network connectivity (N=94) of the DMN as well as 3 subnetworks ('core', dorsal medial, and medial temporal), using individual Pearson's correlation matrices (Schaefer et al., 2018). Multiple linear regression was used to test subcortical volumes for the effect of diagnosis, treatments (lithium, antipsychotics, antidepressants) and symptom severity (number of mood episodes). Any significant associations were also evaluated in DMN network connectivity. Models were covaried for age, sex, intracranial volume (structural), motion parameters (functional) and adjusted for multiple comparisons (FDR q<0.05).

**Results:** No subcortical volume differences were detected between BD and CN. In those with BD, antidepressant treatment (primarily targeting serotonin; SSRIs) was associated with smaller pallidum volumes (pFDR=0.035, R²=0.35). Greater number of (hypo)manic episodes was associated with larger putamen (pFDR=0.04, R²=0.46) and pallidum volumes (pFDR=0.001, R²=0.56) even when adjusting for medication use and duration of illness. Number of depressive episodes was not associated with subcortical volume. Neither antidepressant treatment or (hypomanic episodes) was associated with DMN functional connectivity measures derived from the current implementation of the ENIGMA-HALFpipe protocol.

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**Fig 1.** A) Subcortical volumes represent average volumes between L and R hemispheres. Models were adjusted for age, sex, and intracranial volume. B) Antidepressant treatment primarily targeting serotonin (Category 4) was associated with smaller pallidum volumes (n=7), even when adjusting for other medication use. Antidepressants targeting serotonin + other monoamines (Category 5) was not associated with subcortical volume alterations (N=8). A greater number of (hypo)manic episodes (total number of manic and hypomanic episodes) associated with C) larger pallidum and D) putamen volumes.
Conclusions: In this pilot sample, we found no subcortical volume differences between BD and CN, highlighting the challenge of detecting subtle BD-related structural brain alterations without large-scale samples (Hibar et al., 2016). Whereas serotonergic antidepressant treatment was related to smaller basal ganglia volumes, greater number of hypo- and manic episodes was related to larger volumes. The differential effects between medication and illness severity are intriguing and merits further evaluation in the larger ENIGMA-BD sample. The ENIGMA Schizophrenia working group found larger pallidum volumes associated in patients (van Erp et al., 2016), and the ENIGMA obsessive-compulsive disorder working group has also shown smaller striatal volumes associated with antidepressant treatment (Ivanov et al., 2022). Neither antidepressant use or number of (hypo)manic episodes was related to alterations in DMN connectivity in this current implementation of the ENIGMA-HALFpipe protocol. However, prior findings from the team have highlighted BD-related functional alterations in this sample (Quirke et al., 2023). Ongoing work is focused on assessing the downstream effects of variable rsfMRI processing streams in large, multisite samples to improve detection of the subtle functional brain alterations in BD.

References

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Thalamic nuclei in trigeminal neuralgia: gray matter volume reduction and its reversal after surgery

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Introduction: Trigeminal neuralgia (TN) is a prevalent chronic pain disorder characterized by recurrent, intense, and sharp pain. Prior research has established that biomarkers derived from MRI imaging hold promise in aiding clinicians to tailor personalized treatment schedules ( Hung et al., 2021 ). However, most of these studies have focused exclusively on the trigeminal system, overlooking the fact that chronic pain leads to widespread neural reorganization throughout the brain ( Liu et al., 2022 ). Among the brain regions affected by prolonged pain, the thalamus stands out for its prominent role in sensory processing, including the processing of nociceptive signals. Several recent publications have shown significant reductions in gray matter volume (GMV) in the thalamus of patients with trigeminal neuralgia ( Wu et al., 2020 ; Danyluk et al., 2021 ). However, previous studies investigating thalamic GMV alterations have often treated the thalamus as a single entity, without examining structural changes at the level of individual nuclei. In this study, we aimed to provide a more detailed analysis of pain-induced remodeling in the thalamus by parcellating it into 25 distinct nuclei.

Methods: The total number of participants involved in the study was ninety one: patients with trigeminal neuralgia ( n = 62 ) and age- and gender-matched healthy participants ( n = 29 ). MR imaging data were acquired using a 3T system (Ingenia, Philips Healthcare, The Netherlands) equipped with a 16-channel receiver head coil. Fully automatic surface-based MR morphometry of high-resolution T1-WI was performed with FreeSurfer v7.2.0 software. Segmentation of the thalamic nuclei was done following the approach described in (Iglesias et al., 2018). One-way ANCOVA with post hoc Tukey tests was employed to compare mean values of grey matter volumes between groups while controlling for age, gender and intracranial volume variables. The follow-up data was collected 6 months post-surgery.

Results: We revealed three clusters of nuclei showing significant differences between groups. First cluster consisted of intralaminar nuclei such as centromedial (CM), parafascicular (Pf) and paratenial (Pt) nuclei. Second cluster included lateral (LGN) and medial geniculate bodies (MGN) as well as thalamic nuclei belonging to the ventral group, mainly related to sensory processing. Third cluster was composed of so-called associative thalamic nuclei, namely, medial dorsal lateral (MDL), lateral dorsal (LD) and pulvinar nuclei. The most pronounced differences were shown in LGN (right LGN - right-sided pain vs controls: t(82) = 3.94, p < 0.001; left LGN - right-sided pain vs controls: t(82) = 4.63, p < 0.001) and medial pulvinar nucleus (right PuM - left-sided pain vs controls: t(82) = 3.9, p < 0.001). Furthermore, we were able to provide evidence that the Pf nucleus was the sole nucleus to experience an increase in GMV following the surgical intervention. As a result, its median volume became comparable to that of the control group, and there was a significant difference observed between the pre- and post-surgery conditions ( W = 585, p = 0.2 and W = 397, p = 0.037, respectively).

Conclusions: In this study, we have demonstrated that thalamic nuclei underwent significant changes in gray matter volume in patients with trigeminal neuralgia. Particularly noteworthy are the significant alterations occurring in the intralaminar nuclei and nuclei associated with the processing of visual and auditory signals, as opposed to the ventral group nuclei involved in nociceptive processing. Moreover, our findings indicate that only the right parafascicular nucleus exhibited a substantial increase in volume subsequent to successful surgical intervention. Our results are consistent with previous studies, which have shown that stimulating the CM-Pf complex in patients with chronic pain unresponsive to other treatments may provide a viable alternative therapeutic approach (Weigel et al., 2004; Abdallat et al., 2021).

References
**Poster No 2162**

**The Human Globus Pallidus: Parcellation, Connectivity Pattern, and Behavioral Function**

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**Introduction:** The human globus pallidus (GP) is regarded as an important role in the motor circuits¹, and an effective target in deep brain stimulation (DBS) for patients with motor conditions, such as Parkinson's disease (PD)². However, as the motor symptoms reduce, cognitive function in PD patients can deteriorate mildly³ while stimulating the GP internus in DBS treatment. This suggests the need to obtain the function-separated parcellation of GP to separate the cognitive and motor circuits in GP for precision treatment. This study used diffusion MRI and functional MRI to obtain the parcellation of GP, explore the structural and functional specificity of GP subregions, and describe the relationship between GP subregions and various behavioral measures. This manuscript provides a new perspective on the organization and function of GP.

**Methods:** 7T resting state fMRI data and 3T diffusion data of 170 participants (age: 22-36, 68 male) were used from the Human Connectome Project, which was randomly split into dataset 1 (n = 80) for parcellation and dataset 2 (n = 90) for validation. Besides the standard pipeline in the HCP preprocessing, diffusion images were further processed with nonlinear co-registered and probabilistic tractography to obtain structural similarity. Functional images were processed with the first 15 frames removed, 4-mm FWHM smoothed⁴, band-pass filtered (0.01~0.08 Hz)⁵ and $\eta^2$-coefficient calculated to obtain the functional similarity. Shared-nearest-neighbor-based density peak clustering (SNN-based DPC) algorithm⁶,⁷ was used to avoid round parcels, spatially disconnected and unstable one-step allocation strategy. There were three kinds of feature input for the SNN-based DPC algorithm: the similarity of diffusion images, the similarity of functional images, and the concatenated similarity of the first two kinds. Then, the connectivity patterns were defined to compare the specificity of GP subregions by diffusion MRI and functional MRI⁸. Finally, kernel ridge regression (KRR)⁹ was used to predict each behavioral phenotype in individuals by functional connectivity to evaluate the function of GP subregions¹⁰.

**Results:** First, the three parcellations of GP by diffusion images, functional images, and the concatenated similarity matrices were compared by the dice coefficient of reliability (diffusion-based: 0.91, function-based: 0.93, fusion-based: 0.95). Then, the parcellation based on the hybrid similarity was chosen, which divided the GP into 3 subregions (see Fig. 1A) in each hemisphere. It was significantly more homogeneous than random parcellations (homogeneity: 24.44%, p<0.01). Second, connectivity profiles and fingerprints were analyzed in structure and function (see Fig. 1B, C, D, E and Fig. 2A, B, C). Results showed that aGP (anterior) had stronger connectivity to the limbic network. mGP (medial) was extensively connected to cortical networks, and more relevant to higher cognitive networks (such as DMN and FPN). pGP (posterior) was connected to the salience network and sensorimotor network. Finally, the prediction accuracy for each behavioral phenotype is illustrated in Figure 2D. aGP showed stronger correlations with emotion-related behaviors, mGP was more relevant to cognitive tasks, while pGP was more correlated with motor and personality.
Conclusions: This study obtained the organization of the GP according to the structural and functional connectivity and explored the difference in structure and function between different subregions. Results showed that the GP parcellation obtained by fusing structural and functional information is more stable between participants. Furthermore, from posterior to anterior, GP showed a trend from low-level networks to high-level networks, and from motor and personality to cognition to emotion tasks. This study will help to reveal the multiple roles of GP in complex circuits and provide convincing support for DBS at GP in PD patients.

References

**Poster No 2163**

**Mesoscopic functional connectivity between cortex and globus pallidus nuclei**

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**Introduction:** The globus pallidus/pallidum (GP) receives cortical feedback from deeper layer V via the striatum and connects with the thalamus and other subcortical nuclei¹⁄². The GP connected thalamus further engages in feedforward input to the medial layer 4 of the cortex³. With such a connectivity scheme within the cortico-basal ganglia-thalamo-cortical loop, GP engages in a broad array of brain functions, including motor control and cognitive functions. However, the GP’s functional connectivity concerning cortical laminar organization has not been investigated in the human brain. To address this gap, our study employed high-resolution fMRI to map the functional connectivity of the GP with respect to the cortical depth in the human brain.

**Methods:** Subjects: 16 healthy subjects (Age 23-39 Y, Mean age: 27 Y, 9 F, 7 M) participated in the study with written informed consent before participation. The local research ethics committee approved the study. Data acquisition: MRI was performed at 9.4 Tesla (Magnetom, Siemens) using a custom-built 16 transmit and 31 receive channel head coil. We acquired structural MP2RAGE (0.6 mm isotropic) and rsfMRI data (SMS EPI, FLEET pre-scan, MB 3, 1mm isotropic, TR 2200 ms, TE 27 ms, 117 slices, 300-360 scans, 10 scans with reversed phase encoding⁴. Data Analysis: i). Laminar Delineation: The MP2RAGE was reconstructed using raw data with in-house Matlab code The uniform contrast was analyzed using presurfer (https://github.com/srikash/presurfer⁵). The layer delineation in 11 equidistance bins was performed after the freesurfer segmentation and manual quality control using LAYNII⁶. ii). rs-fMRI analysis: The thermal noise correction of the fMRI data was performed using the NORDIC Matlab toolbox⁷. The fMRI preprocessing was performed in native subject space using AFNI with despiking, slice time correction, distortion correction, coregistration, motion correction, anaticor (noise correction), and without smoothing⁸. The correlations between the GP and cortex were computed using AFNI⁹. Subsequently, smoothing within layers (0.7 FWHM was performed using LAYNII (Figure 1). The computed correlation maps (2) were then corrected for multiple comparisons (FDR p 0.05) with AFNI. iii). Group Profile Tracking Analysis: The depth profile of the functional connectivity of the GP with each cortical area was determined using non-linear modeling⁹,10. In the next step, the predicted similar depth profiles with the peak connectivity in the medial and deeper cortical depth were segregated and visualized (Figure 2).

![Figure 1: Left Pallidum Functional Connectivity with cortical depth: a-b) An axial slice depicts the pallidum's uncorrected and multiple comparison corrected (FDR p 0.05) correlations with the cortex. b-c) The cortical gray matter ribbon is divided into four layers for visualization, and corresponding correlations of the left pallidum in a single subject from superficial to deeper cortical depth are visualized for the right and left brain hemispheres. Note: Functional connectivity of the pallidum shows depth-specific correlations with the cortex](image-url)

**Results:** The majority of cortical areas show association with GP in the medial and deeper cortical depth (Figure 2). The GP connectivity with medial depth in cortical regions covers mainly the default mode, visual, fronto-parietal, and salience networks, suggesting the GP is more involved in the feedforward flow of information to these cortical networks during rest (Figure 2). In contrast, deeper depth-specific highly correlated cortical regions cover mainly somatosensory, visual, cingulate, temporal, and frontal areas, suggesting the GP is more involved in the feedback flow of information from these cortical areas during rest. The left and right pallidum show similar depth preferences with cortical areas, with slight laterality differences.
Conclusions: The analysis reveals a depth-specific spatial precision of the functional connectivity between cortical areas and pallidum. The depth-specificity with different cortical regions hints a feedforward and feedback communication at rest. The study allows a coarser interpretation concerning cortical laminar profiles, as individual layers may vary with size and density in different cortical areas. GRE BOLD fMRI has limitations to the spatial specificity of the signal and can be biased by cortical orientation; therefore, depth-specificity may be enhanced with other imaging functional contrasts, i.e., VASO and bSSFP.

References

Poster No 2164

Segmentation and quantification of mesoscopic subcortical vessels using post mortem MRI at 50 micron

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**Introduction:** Recent work has mapped human neurovasculature in neocortex using anatomical MRI (Bollman et al., 2022; Gulban et al., 2022), but such work has not yet investigated subcortical vessels comprehensively (see Fig. 5 from Sitek & Gulban et al., 2019, for a preliminary investigation). While subcortical vessels were laboriously delineated by Duvernoy (Duvernoy, 1978), no quantitative characterisation of the whole three-dimensional vasculature in human subcortex has been performed at this point. Subcortical vascular mapping is important within the context of fMRI because T2*-weighted images-including BOLD functional MRI—are sensitive to blood vessels and distort the immediate vicinity of vessels, causing activation patterns to spatially shift (e.g. “draining veins” (Havlicek et al., 2020)). However, currently it is difficult to directly image the subcortical vessels at mesoscopic scale in vivo (e.g., below 250 μm). Therefore, here we use high contrast post mortem MRI at 50 μm isotropic resolution to segment vasculature in a portion of the human brainstem-dorsal midbrain, including superior and inferior colliculus-and quantify the radius, length, and tortuosity of these subcortical vessels.

**Methods:** T2*-weighted anatomical MRI was collected with 50 μm isotropic resolution from a post mortem human brainstem (65-year-old male, no neurological conditions) using a small-bore 7 Tesla MRI (Calabrese et al., 2015). To segment the vasculature, we first created a binary mask of the midbrain with fslnmaths, which required thresholding the image, eroding the mask to remove “islands” in the mask, dilating the mask to return boundaries for most parts of the image, and filling holes. We next inverted the T2*–weighted image such that low intensity parts of the original image (such as blood vessels) were now high intensity and vice versa. To return the non-brain parts of the image back to 0, we then masked the inverted image using the binary mask in step 1. Vessels were extracted using a self-learning algorithm (Bollman, 2023 ISMRM), which used a manually cleaned thresholding segmentation as the training label. Vessel statistics were quantified using VesselVio, which reports the Number of Segments per Radius Bin, Mean Length of Segments per Radius Bin, and Mean Segment Tortuosity per Radius Bin.

**Results:** Using VesselVio (Bumgarner and Nelson, 2022), we identified 8368 segments corresponding to vasculature in the dorsal midbrain of our T2*-weighted sample. These segments had a mean radius of 59.4 μm and a mean length of 440.5 μm. The smallest vessels identified had a radius between 20–30 μm (corresponding to the 50μm spatial resolution of our data), while over 50% of the vessels were between 40–70 μm. In terms of segment length, vessels with a radius between 60–90 μm had the highest estimated length (>500 μm; over 10 voxels). Tortuosity generally decreased as a function of segment length, with highest tortuosity in vessels with a 30–50 μm radius.

**Conclusions:** Using 50 μm isotropic T2*-weighted MRI in a post mortem sample, we provide the first characterization of key properties of vasculature in human dorsal midbrain. By using uniquely high resolution anatomical MRI, we found vessels as small as 20–30 μm in radius. Smaller radius vessels generally had shorter trajectories similar to class 1-3 intracortical arteries and class 1 veins based on Duvernoy's classification (Duvernoy, 1981; see also Gulban et al., 2022, Sup. Fig. 9), with the longest vessels having radii that correspond to class 5 and 6 arteries and class 5 veins. Future work will expand this analysis to all of the human brainstem and thalamus.
References
Mapping Terra Incognita: Exploring Subcortical Structures in Major Depressive Disorder with 7T MRI

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Introduction: Despite significant advances in recent years, our understanding of the neuropathological mechanisms underlying major depressive disorder (MDD) remains limited. This restriction is particularly evident in subcortical regions, where neuroimaging techniques at lower magnetic field strengths encounter challenges related to resolution and detail. Animal and theoretical models of affective psychopathology propose the involvement of specific subcortical regions and their subnuclei. Moreover, recent research has highlighted the importance of detailed subcortical investigations in MDD. However, current neuroimaging techniques lack the necessary precision to thoroughly investigate the structural integrity of these areas. Consequently, our understanding of subcortical brain systems in the context of MDD is constrained, significantly hindering the practical application and translation of research findings in this field. Nevertheless, the introduction of ultra-high-resolution MRI protocols, specifically those acquiring data at 7 Tesla (7T), holds significant potential in addressing these limitations and facilitating a more comprehensive understanding of the neurobiological foundations of MDD. Aligned with this objective, we conducted a cutting-edge 7T imaging study to unravel the pathophysiology of MDD by investigating subcortical structures.

Methods: We acquired T1-weighted MP2RAGE images and T2-weighted quantitative images at ultra high-field (7T MRI) from a cohort of 71 individuals, including 57 MDD patients and 14 healthy controls. The segmentation of subcortical regions was performed using Nighres, a novel open-source parcellation algorithm designed for processing high-resolution neuroimaging data. Thirty-one subcortical structures were sampled onto each subject’s volumetric space, and the T1-/T2*-data corresponding to these structures were processed using Nighres’ profile sampling module. Statistical analysis included Bayesian ANCOVA and Bayesian correlation analysis implemented in JASP, aiming to elucidate effects observed across groups and within the MDD patient group. Segmentations of subcortical regions, lateral ventricles, and total volume were compared between patients and controls using Bayesian ANCOVA, controlling for age and sex. We also explored the effects of symptom severity, medication (antidepressants/psychotropics), childhood trauma, and comorbid anxiety using a between-patients dimensional approach.

Results: Both Bayesian ANCOVA and regression analyses yielded anecdotal to moderate evidence in favor of the absence of a group effect of major depressive disorder across all thirty-one subcortical regions (1<Bayes Factor (BF)<10). Bayesian ANCOVA demonstrated anecdotal to moderate evidence for the effects of medication, childhood trauma, and comorbid anxiety on major depressive disorder across all thirty-one subcortical subnuclei (1<Bayes Factor (BF)<10). Bayesian regression identified no association between the symptom severity of major depressive disorder and subcortical brain volumes (1<Bayes Factor (BF)<10). Additionally, sample characteristics such as mean age, gender, and medication use did not moderate the alterations in subcortical volumes, and the T1-/T2* metrics.

Conclusions: Our study stands as one of the scarce pioneering efforts delving into the exploration of subcortical nuclei in major depressive disorder through the application of ultra-high field imaging. Despite the Bayesian framework offering evidence of weak strengths in identifying depression biomarkers in our study, the utilization of ultra-high field imaging persists as a compelling avenue for unraveling the neuropathology of Major Depressive Disorder (MDD). A future direction involving extensive mapping of the subcortex using ultra-high field imaging holds the promise of yielding profound insights into the potential role of these subcortical regions as prominent biomarkers in the neurobiological modeling of MDD.

References
Multi-receptor analysis of the macaque lateral geniculate nucleus

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Introduction: The lateral geniculate nucleus (LGN) is one of the thalamic nuclei which process visual information from the retina and transmit visual signals to the cortex. The LGN is composed of three subdivisions: the magnocellular, parvocellular and koniocellular (Figure 1A). Although the structure and function of LGN has been extensively studied through various methods (Hubel & Livingstone, 1990; Denison et al., 2014; Oishi et al., 2023), its receptor architecture has not yet been fully understood so far. As the regional and laminar distribution patterns of different receptors in the cerebral cortex has been shown to be a powerful tool for understanding the potential functional segregation as well as hierarchical organization among different brain areas (Rapan et al., 2022), here we aim to elucidate the receptor architecture of the LGN by analyzing receptor autoradiographs obtained from macaque monkey brains for better understanding underlying relationship between receptor architecture and function of the LGN (Palomero-Gallagher & Zilles, 2018).

Methods: We analyzed coronal sections from four hemispheres of three adult male Macaca fascicularis (Rapan et al., 2022). We quantified the densities of 15 receptors visualized by in vitro receptor autoradiography using previously established protocols (Palomero-Gallagher & Zilles, 2018; Zilles et al., 2002). We delineated LGN sublayers as regions-of-interest (ROIs) in both cell-body stained sections and the adjacent receptor autoradiographs and extracted the density of each receptor type in each, the borders between each layer were charted on the pseudocolor-coded autoradiographs (Figure 1B). The magnocellular, parvocellular, and koniocellular layers were defined as ROIs, the densities of each ROI were measured by calculating the average receptor densities from their component sublayers, respectively. Finally, the mean densities of all receptors were visualized for each ROI separately in a polar plot as a ‘receptor fingerprint’. To evaluate differences in receptor architecture between the LGN and visual cortex, we compared the receptor fingerprints with those of primary visual areas published by Rapan et al., 2021.
Results: The color-coded autoradiographs of representative sections in Figure 1B show the exemplary receptor distribution patterns of the LGN. We found a considerably higher concentration of acetylcholine M2 and α4β2 receptors in the LGN than in the cortex. Furthermore, the distinct cytoarchitectonic layers in the LGN are clearly reflected by the receptor architecture. The receptor fingerprints of all three ROIs were similar in shape, but differ in size (Figure 2A): magnocellular part exhibited the highest densities, while the koniocellular ones exhibited the lowest densities, whereby M2 receptors presented the highest overall receptor densities, followed by the M3, α4β2. Lowest densities were measured for the AMPA and M1 receptors. This balance resulted in fingerprints that differed considerably in both size and shape from those of the dorsal and ventral parts of V1 (Figure 2B), where the highest densities are reached by the GABAergic and glutamate receptors.

Conclusions: The present study showed that the LGN presents considerably higher M2, and α4β2 receptor densities than does V1 and its three subdivisions differ in their averaged densities. The high density of LGN in M2 and α4β2 receptors may be related to the functional roles of acetylcholine during sensory information processing, such as involvement with improving signal-to-noise ratio of neural response to sensory stimuli, by decreasing noise correlation among neurons and improving encoding efficiency (Minces et al., 2017). Our results suggest that the receptor architecture of the LGN may be geared towards improving the encoding efficiency of visual information before it is forwarded to cortical visual areas.

References

Poster No 2167
Locus coeruleus non-REM sleep signatures in human fMRI
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Introduction: The locus coeruleus (LC) gives rise to highly diffuse noradrenergic projections targeting most brain regions, modulating brain states and arousal. Mammalian sleep studies have established an integral role for the LC in sleep: precise timing of LC firing during non-REM sleep is required for the coupling of spindles to slow wave oscillations and hippocampal sharp wave ripples (Eschenko et al., 2012; Osorio-Forero et al., 2021; Swift et al., 2018). In humans, these diverse rhythms
and temporal couplings involving the LC remain relatively unexplored. Here we aim to uncover LC specific signatures during human non-REM sleep and how its activity modulates the coupling between sleep oscillations and transitions between brain states.

**Methods:** Simultaneous electroencephalogram (EEG) and functional MRI (fMRI) were collected in thirty-three individuals (mean age = 22.1) at resting-state and across several sleep sessions (Gu et al., 2023, 2022). fMRI scans were pre-processed using FMRIprep. In addition, regression of head motion artifacts, the average combined signal of CSF and white matter, and low-pass filtering (0.1) was carried out. Time-series signal was extracted and z-scored from a parcellation of 456 regions (400 cortical regions (Schaefer et al., 2018), 54 subcortical regions (Tian et al., 2020), the noradrenergic LC (Ye et al., 2021) and the cholinergic nucleus basalis of Meynert (Zaborszky et al., 2008)). Individual sleep scans were time locked to 30-sec epochs of sleep stage scoring from EEG which was completed by registered polysomnographic technicians. Activity and complexity patterns of the LC was measured and compared across sleep stages.

**Results:** We used simultaneous EEG and fMRI to identify patterns in subcortical and cortical activity, and their coupling, across wake and non-REM sleep stages 1 and 2. We found significant differences in activation patterns of the LC across the states of sleep, with activity during stage 2 significantly different to stage 1 sleep and more closely resembling awake activity (p = 0.03). Increased LC activity in stage 2 sleep, relative to stage 1 was associated with decreased recruitment of the default mode and frontoparietal control networks (p <0.05).

**Conclusions:** Our results demonstrate a prominent difference in LC activity patterns between wake and non-REM sleep stages in human simultaneous EEG-fMRI analysis. These results substantiate a role for noradrenergic modulation of large-scale brain state organisation and oscillations during sleep. Ongoing analyses will calculate time-varying functional connectivity dynamics between the LC and other regions of interest across states and explore transitions between wake and sleep states in relation to LC phasic activity using low-dimensional energy landscapes (Munn et al., 2021). Given that non-REM sleep rhythms, as well as the LC itself, undergo profound alterations across neurodegenerative diseases of ageing, understanding the intricacies and specific profiles of sleep-wake circuitry in healthy humans is crucial for improving sleep treatment and probing the bidirectional relationships between altered sleep and neurodegenerative diseases of ageing.

**References**


**Poster No 2168**

**White matter microstructural aging depends on developmental order, fibre calibre and vascularization**

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**Introduction:** To understand the consistently observed spatial distribution of white-matter (WM) aging, developmentally driven theories of retrogenesis have gained traction, positing that the order WM development predicts declines⁴,⁵,⁶. The validity of such theories remains uncertain, in part due to lack of clarity on the definition of developmental order⁶,⁷,⁸. An alternative theory is termed “gain-predicts-loss”⁸, which posits that the rate of development predicts rate of declines, likewise for which
several definitions may apply\textsuperscript{9}. Our recent findings also suggest that WM degeneration may vary by physiological parameters such as perfusion\textsuperscript{7}. Here, using the HCP-A data, we address the question of whether WM degeneration is determined by development trajectory or physiological state.

**Methods:** 535 data sets from healthy subjects (300 female, aged 36-100) were drawn from the HCP-A study (OMB Control# 0925-0667)(2), including diffusion-weighted MRI (93 directions at $b=1500s/mm^2$) at 1.5mm isotropic resolution. We corrected for eddy-current and susceptibility-related distortions via EDDY, and kurtosis-corrected fractional anisotropy (FA) and mean diffusivity (MD) maps were derived using Dipy’s DKI tool. FreeSurfer TRACULA (v 7.2.0)\textsuperscript{10} was used to provide 10 bilateral tract segmentations in subject space. All DTI values were normalized to the youngest 50 subjects to produce FAperc and MDperc values. We defined 6 models to help explain DTI age effects: Last-in-first-out models; (1) “Last-appearing-first-out” (LAFO): ordered by time of prenatal emergence\textsuperscript{6} (2) “Last-myelinated-first-out” (LMFO): ordered by time of peak R1 (“myelination”) at birth\textsuperscript{3} Gain-predicts-loss models; (3) “Slowest-peak-first-out” (SPFO-MD): ordered by rate of MD change from adolescence to adult peak\textsuperscript{8} (4) “Slowest-myelinated-first-out (SMFO): ordered by rate of R1 change from adolescence to adult peak\textsuperscript{8} Physiological models: (5) “Axon-diameter-determined” (ADD): ordered by mean axon diameter at birth\textsuperscript{4} (6) “Vascular-diameter-determined” (VDD): ordered by mean macrovascular density\textsuperscript{1} The predictiveness of these models was assessed using multivariate regression in R (version 4.1.1), with sex as a covariate of no interest.

**Results:** Age-related declines were observed in MDperc for all ten tracts, and in FAperc for seven of ten tracts (Fmajor, Fminor, ATR, CAB, CCG, ILF, and SLFP). Both last-in-first-out models demonstrated significant associations with at least one measure of microstructural integrity (Fig. 1). In the LAFO model, tract development order was positively associated with mean FAperc but not MDperc. In LMFO, R1 order was inversely associated with FAperc, while MDperc was positively associated. In rate-of-decline comparisons, significant interactions by tract order on association between FAperc and age were observed in the LMFO ordering significantly associated with FAperc rate of decline (Fig. 2). No significant contributions were identified by the gain-predicts-loss models (SPFO-MD and SMFO). Both physiological determinant models demonstrated significant associations with both FAperc and MDperc (Fig. 1). FAperc was positively associated with axon diameter and inversely related to macro-vascular density order. Inversely, MDperc was positively associated with vascular density and negatively associated with axonal diameter. In rate-of-decline comparisons, the rate of FAperc decline correlated positively with axonal diameter and negatively with vascular density (Fig. 2). The reverse was true for MDperc.
Conclusions: Of the many alternative definitions of “last-in-first-out”, order of myelination seems most promising, i.e. fastest loss in tracts last to reach peak myelination. Importantly, our results also suggest that tracts with the largest fibre diameters and lowest vascular densities to be more preserved in aging. This also implies that larger fibre diameters are associated with lower vascular density, a finding to be further investigated.

References

Poster No 2169
Pregnancy alters the organization of the structural brain network
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Introduction: Pregnancy is a monumental phase in many women's lives, which is orchestrated by unparalleled endocrine and physiological changes. We have previously shown that this period is also characterized by unique brain plasticity, with volumetric reductions in gray matter structures (Hoekzema et al., 2017, 2022). However, to fully understand the organization and plasticity of the brain during this period, we also have to consider the connections between gray matter regions and study the brain from a network perspective (Bassett & Sporns, 2017). Therefore, in this study we aimed to investigate whether pregnancy induces alterations in the organization of the structural brain network, as measured with diffusion-weighted imaging.

Methods: We used a pre-conceptive prospective cohort study to investigate the influence of pregnancy on the organization of the structural brain network. We followed first-time mothers (n=40) and nulliparous control women (n=40) longitudinally: from pre-conception (PRE) to the early (POST) and late postpartum period (POST+1). Anatomical T1-weighted imaging and diffusion-weighted imaging were performed at every time point. The T1-weighted image was parcellated with FreeSurfer to identify 82 brain regions (34 cortical and 7 subcortical per hemisphere) for each subject based on the Desikan-Killiany atlas. We reconstructed the structural brain network with whole-brain single shell constrained spherical deconvolution tractography in MTrix3. The streamline count between brain regions was corrected for underlying white matter density and used as a measure of structural connectivity. For each participant, we removed the 5% weakest connections to reduce the influence of spurious connections. To study the organization of the brain network, we determined several global network measures, including the normalized weighted shortest pathlength (l), normalized weighted clustering coefficient (C), small-worldness (s = l / C) and density (d) for the PRE and POST timepoints.

Results: Each group contained two outliers in the network density which were excluded from the analyses. An example of whole brain tractography and a subsequently reconstructed structural brain network are shown in Figure 1A. Mixed linear models, corrected for age, education and time between the PRE and POST scan, showed statistically significant group (pregnant vs. control) * time (PRE vs. POST) interaction effects for clustering (F(73) = 5.47; p = 0.022), small-worldliness (F(73) = 6.09; p = 0.016) and density (F(73) = 5.36; p = 0.023). Subsequent paired t-tests only showed significant effects from PRE to POST in the pregnancy group, who showed increased clustering (PRE: C=1.78 ± 0.13; POST: 1.84 ± 0.15; t(37) = -2.98; p = 0.005) and small-worldness (PRE: s = 2.43 ± 0.21; POST: 2.52 ± 0.24; t(37) = -2.67; p = 0.011) and decreased density across pregnancy (PRE: d = 0.61 ± 0.03; POST: 0.60 ± 0.03; t(37) = 3.23; p = 0.003) (Figure 1B). To check whether the density difference across
pregnancy was influencing the results, we performed all analyses again with a set density (d = 0.3), which yielded highly similar results.

Conclusions: In this study, we present, for the first time, changes in the organization of the structural brain network across pregnancy in first-time mothers. These changes are characterized by an increase in global clustering and, as a result, small-worldness (calculated by dividing the weighted shortest pathlength by the clustering coefficient). As the clustering coefficient represents how neighboring regions cluster together (Bullmore & Sporns, 2009), an increase in the global clustering represents more segregation of the network. This indicates that in first-time mothers information may be processed more locally. Since previous studies have shown that changes in global clustering may relate to cognitive abilities (Chen et al., 2021), we aim to further investigate relationships between structural brain network organization and behavioral measures in first-time mothers.

References
Spatiotemporal Characterization of White Matter Hyperintensity Pathophysiology

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Introduction: The sparse vascularization of the deep white matter makes it particularly vulnerable to vascular dysfunction, resulting in areas of ischemia/hypoxia and blood-brain barrier leakage frequently seen in elderly individuals. These events are detectable with magnetic resonance imaging (MRI) and appear as white matter hyperintensities (WMHs) on Fluid-Attenuated Inversion Recovery (FLAIR) T2-weighted images. Numerous studies have demonstrated that the pathophysiology underlying WMHs is highly heterogeneous, with edema, demyelination, axonal loss, oligodendrocyte loss, and inflammation being present at various degrees or even absent. It remains unclear if WMHs in different spatial locations all represent similar pathophysiology and etiology. Here, we demonstrate a framework developed to estimate WMH pathophysiology in vivo using microstructural MRI and normative models, which allowed us to precisely characterize spatiotemporal patterns of WMH tissue alterations and assess the added value of that information in predicting cognitive function.

Methods: We used data from 32,014 UK Biobank (UKB) participants. T1-weighted (T1w) and FLAIR images were used for identifying WMH and normal-appearing white matter (NAWM) regions using the Brain tISsue segmentatiON (BISON) pipeline. Diffusion-weighted and susceptibility-weighted images were used to derive fluid-sensitive, fiber-sensitive, and myelin- and iron-sensitive microstructural markers. Diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI) were used to model the diffusion MRI signal. Multispectral registration to a custom unbiased UKB template was performed using T1w and fractional anisotropy (FA) maps as inputs. In this common space, we calculated voxel-wise normative models of NAWM using Bayesian linear regression with sex and age modelled with 4th-order B-splines with the PCN toolkit. We then normalized WMH microstructural maps using these age- and sex-specific atlases of expected NAWM microstructure, resulting in subject-wise estimates of WMH pathophysiology (i.e., change in microstructure as the tissue transitioned from NAWM to WMH).

ABSTRACTS

Poster No 2170

Spatiotemporal Characterization of White Matter Hyperintensity Pathophysiology

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Results: First, from between-subject averages of WMH microstructural abnormality (Fig. 2A), we used spectral clustering to derive spatial patterns of WMHs that share similar pathophysiological properties (Fig. 2B). The first cluster (periventricular) has low abnormality on all metrics. The second (posterior) and third (anterior) clusters both show fluid accumulation, fiber alterations, and myelin and iron loss, while the anterior cluster shows higher abnormality on most metrics. Second, we calculated the subject-wise median WMH microstructural abnormality value within each spatial cluster. Using the Subtype and Stage Inference (SuStaIn) algorithm, we determined the temporal sequence at which these markers become abnormal in each WMH location (Fig. 2C) and assigned a stage of WMH pathophysiological progression for each subject in each WMH region. We did not find evidence for sub-trajectories. Third, using random forest models, we assessed the predictive power of different combinations of predictors (WMH volumes, WMH sustain stages, median WMH abnormality for all metrics, and their combinations) on cognitive function (Fig. 2D).

Conclusions: Using a novel framework to assess WMH pathophysiological processes in vivo, we uncovered spatiotemporal patterns of WMH tissue alterations. Our results separating anterior and posterior WMHs are consistent with accumulating evidence showing that posterior WMHs may be linked to Alzheimer’s pathology, whereas anterior WMHs are more associated with vascular pathologies. We further demonstrated that the pathophysiological severity of WMH can be adequately summarized into one stage of disease with SuStaIn and that this information increased the predictive power of WMHs on cognitive tests, particularly those sensitive to processing speed.

References

Poster No 2171

Geometric deep learning for language prediction via pointwise tract microstructure analysis
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Introduction: The brain’s white matter connections (fiber tracts) and their tissue microstructure can be quantitatively mapped using diffusion magnetic resonance imaging (dMRI) tractography1, enabling the study of the brain’s structural connectivity. To better understand how brain structure relates to function, recent research explores the prediction of individual cognitive performance based on structural neuroimaging data (such as dMRI)2,3. A critical challenge is how to represent white matter tracts to utilize their detailed microstructure and positional information instead of averaging or binning data along the streamline3,4. Another challenge is the improvement of performance in regression-based prediction and a potential direction is to utilize the intrinsic continuity in regression scores. In addition, the identification of predictive brain regions is a notable challenge drawing substantial attention5. Therefore, we propose a novel geometric deep learning framework, which includes a point cloud representation of tracts, a novel regression loss, and a critical region localization algorithm to predict language performance and identify predictive brain regions within tracts.

Methods: The overview of our method is shown in Figure 1. Our method was evaluated on dMRI data and two language assessment scores, the NIH Toolbox Picture Vocabulary Test (TPVT) and the Toolbox Oral Reading Recognition Test (TORRT)6, from 809 subjects of the Human Connectome Project7. Whole brain tractography was generated from dMRI using a two-tensor unscented Kalman filter method8, followed by the identification of white matter tracts. The left arcuate fasciculus (AF) and inferior longitudinal fasciculus (ILF) were selected for prediction due to their relationship to language. Each white matter tract was represented as a point cloud (Figure 1). Each point was characterized by three spatial coordinates and two additional measurements (fractional anisotropy and number of streamlines). During each training iteration, the input of the network was formed by randomly sampling points from the cloud. We designed a Siamese network9 that contains two PointNet-based10 subnetworks with shared weights. To utilize the information of continuous language scores, we propose a novel regression loss that constrains the difference between the predicted scores of the input pair to be the same as the difference between the ground truth scores. We propose a Critical Region Localization algorithm to identify critical regions within fiber tracts for language score prediction. First, the subject-wise contributing points are identified as point sets that contribute to the max-pooled features. Then group-wise analysis is performed to localize critical regions that are consistently important for prediction across testing subjects.
Results: The popular Pearson correlation coefficient (r) was adopted as the evaluation metric of prediction performance\(^2,3\). We compared our proposed method with several baseline methods that use different tract representations (mean value and AFQ\(^4\)). For TPVT, the r values of our method, mean value and AFQ are 0.33, 0.15 and 0.16 for left AF, and 0.33, 0.25, 0.09 for left ILF. For TORRT, the r values are 0.36, 0.14 and 0.17 for left AF, and 0.33, 0.25 and 0.15 for left ILF. Therefore, our approach consistently outperformed baseline methods across both fiber tracts for both prediction tasks, as demonstrated by higher r values. Critical predictive regions, as shown in Figure 2, were distributed across the left hemisphere and all cerebral lobes for both assessments.

Conclusions: In this work, we propose a novel geometric deep learning framework for the prediction of language scores using white matter tracts represented as point clouds. Evaluated on a large-scale public dataset, our method showed superior prediction performance and successfully identified brain regions highly predictive of language scores.

References
Sex-related variability of white matter tracts in the whole HCP cohort

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Introduction: Behavioral studies have shown that men and women have many similarities, but also some specificities. Whether these are due to biological or social differences, or a combination of both, remains unclear. Many studies have examined sex differences in cortical gray matter, but few have done so for white matter tracts. We therefore conducted a sex comparison of all deep white matter tracts in a large cohort of 1065 subjects.

Methods: Cohort and imaging protocol We used the dataset from the HCP cohort4 of 1065 healthy subjects aged 22-35 years old. Each subject had a series of diffusion-weighted MRI (dMRI) sequences performed on a 3T Siemens MRI system using a 2D spin-echo single-shot multiband EPI sequence (1.25mm isotropic spatial resolution) over 3 shells along 90 diffusion sampling directions for each. Data processing For dMRI data processing, we used the Ginkgo toolbox developed by the CEA/NeuroSpin team, available at https://framagit.org/coupon/gkg. Our pipeline performed several successive steps: diffeomorphic registration to a common atlas space (the MNI ICBM 2009c nonlinear asymmetric template) with the Advanced Normalization Tools (ANTS); computation of the Orientation Distribution Functions (ODF) with the analytical Q-ball model; computation of a whole-brain probabilistic tractography; and intra-subject fiber clustering which groups fibers according to their geometric properties. Group analysis Cross-subject fiber clustering was performed on the entire cohort using the HDBscan algorithm. Deep white matter tracts were independently identified by two neuroanatomists using manual ROI selection. This allowed the construction of a deep white matter atlas of 79 tracts. Statistical analysis We measured the total brain volume (TBV) from the Freesurfer brain mask, and tract volumes from their density masks, which were then normalized to the subject’s TBV. We computed several microstructural parameters: fractional anisotropy FA, mean diffusivity MD, parallel and transverse diffusivity (from the DTI model); generalized fractional anisotropy GFA (from the Q-ball model); neurite density index NDI, isotropic water volume fraction ISOVF, and orientation dispersion index ODI (from the NODDI model). We applied Bonferroni correction for multiple comparisons (corrected threshold: p=7.0225*10^-5), and estimated effect size with Cohen’s d-test.

Results: Volumetric analysis Total brain volume was significantly different between men and women (mean +/- standard deviation: 1128 +/- 90 cm3 in women, 1290 +/- 102 cm3 in men; relative difference: 12.62%; p=3.87*10^-76, d=1.7). 19 white matter tracts had a significant difference in normalized volume between men and women, two having a Cohen’s d greater than 0.8: the corpus callosum genu and the parallel fibers (Fig 1), both larger in women (12.54% and 6.1%, respectively). Linear regression and ANCOVA confirmed a significant interaction between the normalized volume of these two tracts and sex (corpus callosum genu: p=3.49*10^-65; parallel fibers: p=3.87*10^-75). Microstructural analysis Many significant microstructural differences between sexes were found in several tracts with moderate or large effect sizes, from which a composite score was calculated (Fig 2). The most different tracts were associated with the motor system, most of which showed higher ODI, MD, parallel and transverse diffusivity in men; or with the limbic system, most of which showed higher FA, GFA, MD, and parallel diffusivity, and lower ODI in women.

Conclusions: Our study revealed some differences in white matter tracts between men and women, both in their normalized volume and in their microstructure. Future research can build on our findings to further explore the complex relationship between brain connectivity and the cognitive and behavioral traits that differ between men and women.
Fig 1. Comparisons for total brain volume (top), normalized volume of white matter tracts (middle) and linear regression for the two most different tracts (bottom).

Fig 2. Composite score of microstructural sex differences from the various parameters, keeping only significant differences with a $d$ greater than 0.8 (2 points) or between 0.5-0.8 (1 point).
Introduction: Around 50% of patients undergoing frontal lobe surgery for focal drug-resistant epilepsy become seizure free post-operatively, however, only about 30% of patients remain seizure free in the long-term. Early seizure recurrence is likely to be caused by partial resection of the epileptogenic lesion, whilst delayed seizure recurrence can occur even if the epileptogenic lesion has been completely excised. This suggests a coexistent epileptogenic network facilitating ictogenesis in close or distant dormant epileptic foci. As thalamic and striatal dysregulation can support epileptogenesis and disconnection of cortico-thalamostriatral pathways through hemispherotomy or neuromodulation can improve seizure outcome regardless of focality, we hypothesise that projections from the striatum and the thalamus to the cortex may contribute to this common epileptogenic network.

Methods: To this end, we retrospectively reviewed a series of 47 consecutive individuals who underwent surgery for drug-resistant frontal lobe epilepsy. We performed voxel-based and tractography disconnectome analyses to investigate shared patterns of disconnection associated with long-term seizure freedom.

Results: Seizure freedom after 3 and 5 years was independently associated with disconnection of the anterior thalamic radiation and anterior cortico-striatal projections. This was also confirmed in a subgroup of 29 patients with complete resections, suggesting these pathways may play a critical role in supporting the development of novel epileptogenic networks.

Conclusions: Our study indicates that network dysfunction in frontal lobe epilepsy may extend beyond the resection and putative epileptogenic zone. This may be critical in the pathogenesis of delayed seizure recurrence as thalamic and striatal networks may promote epileptogenesis and disconnection may underpin long-term seizure freedom.
References
Reliability of Fiber Quantification for DTI and NODDI Metrics: A Comparison of Segmentation Methods

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**Introduction:** In recent years, fiber quantification has gained popularity as a method for accurately characterizing microstructural information along fiber tracts in the individual brain (Colby et al., 2012; Yeatman et al., 2012). The fiber quantification pipeline typically involves three steps: fiber segmentation, metric estimation, and quantification. Among these steps, fiber segmentation is crucial for obtaining reliable results. In this study, we compared the reliability of quantification for microstructural metrics derived from DTI and NODDI using three established fiber segmentation methods: AFQ (Kruper et al., 2021), TractSeg (Wasserthal et al., 2018), and RecoBundle (Garyfallidis et al., 2018). Additionally, we investigated the effects of within-subject and between-subject variance. These analyses demonstrate the specificity of different segmentation strategies across different fibers and measurement metrics, highlighting the complexity of existing fiber quantification methods.

**Methods:** We used the HCP test-retest dataset (Van Essen et al., 2013) with a subset of 15 participants. T1-weighted MRI data and multi-shell (b = 1000, 2000, 3000 s/mm\(^2\)) diffusion MRI data with 270 directions were acquired. All participants underwent test-retest measurements in the LR and RL phase-encoding directions for reliability research. The Multi-shell multi-tissue constrained spherical deconvolution (MSMT-CSD) model was utilized to reconstruct fiber orientation distributions (FODs) using MRtrix3. Fiber segmentation was performed using three strategies: TractSeg, AFQ, and RecoBundle. Ten tracts in common were finally reconstructed, including the bilateral arcuate tracts (AF), the bilateral corticospinal tracts (CST), the bilateral inferior fronto-occipital fasciculus (IFO), the bilateral inferior longitudinal fasciculus (ILF), and the bilateral uncinate fasciculus (UF). Fractional anisotropy (FA) and neurite density index (NDI) were estimated using DIPY 1.7.0 and dmri-amico. Profiles with 100 nodes were generated between pairs of waypoints for each metric and tract by applying the AFQ algorithm using pyAFQ. The two-way mixed effects model intraclass correlation coefficient (ICC) was calculated to assess the reliability of each position of profiles. The between-subject variance (Vb) and within-subject variance (Vw) were calculated.

**Results:** As shown in Figure 1, the overall reliability of quantification was higher for FA compared to NDI. For NDI, the ICC was consistently below 0.6, indicating low reliability for most fiber quantification results. The analysis of Vb and Vw also revealed that, for FA, the inter-subject variability (Vb) was higher than the variability between different trials (Vw), whereas for NODDI, the advantage of Vb over Vw was not significant. In terms of the FA, TractSeg demonstrates superior reliability on fiber bundles such as CST, AF, and ILF, while RecoBundle performs similarly to TractSeg on CST and AF. AFQ is more suitable for IFO and UF. Regarding the NDI, TractSeg shows superior reliability on fiber bundles like CST, AF, IFO, and ILF, while RecoBundle is more suitable for UF. The optimal fiber segmentation scheme for different tracts and different metrics was summarized in Table 1.
Conclusions: This study compared the reliability of fiber quantification in fiber segmentation and further analyzed the between-subject and within-subject variance in a more detailed manner. Ultimately, we obtained strategies for selecting tract-specific and metric-specific fiber segmentation methods. However, it should be noted that the reliability of NDI was generally lower than that of FA, which could be attributed to the difference in model complexity. The limited sample size of the participants may also be an important underlying factor. Overall, our findings provide evidence for the specificity of different segmentation strategies across various fibers and measurement metrics, thereby emphasizing the intricate nature of current fiber quantification methods.

References

Poster No 2175

Myelin packing marker through in vivo water gap mapping

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Introduction: Multiple sclerosis (MS) is characterized by loss of membrane adhesion, swelling across the water gaps, vesiculation, and eventual disintegration of the myelin structure1. Myelin water imaging (MWI) methods are sensitive to MS demyelination processes2. This T2-based quantitative magnetic resonance imaging (qMRI) method is sensitive to myelin content and its integrity. MWI is a multieponential T2 model that estimates the fraction of the signal that arises from the water trapped between the myelin membranes and that arises from other tissue water3,4. The macromolecular and lipid tissue volume (MTV), defined as 1-water fraction (WF), was shown to approximate the total myelin fraction5. MWI and MTV are sensitive to the reduction of myelin in MS but not to the changes in myelin organization, such as the size of the water gap between the myelin membranes. We hypothesize that combining the MWI technique with myelin content fraction from other qMRI measurements will allow characterizing the size of the water gap between the myelin.

Methods: Our model describes the T2 exponential decay as the sum of the myelin water (MW) and any other tissue water (TW) contributions. Our modeling relies on multi-echo spin-echo or gradient multi-echo data. In the dependency of the T2 multi-compartment model on the myelin water gap ratio equation there are three unknown parameters: T2MW, T2TW, and the ratio (dw/dm). We used a novel lipid phantom to characterize and validate the water gap model. Our specifically designed in vitro biological systems6,7 mimic the biological assembly of myelin and are well-designed multi-lamellar vesicles (like the myelin sheaths) with well-characterized water gap thickness. We suspended the membranes in NaCl solutions at different concentrations (0-500 mM) to change the water gap between the membranes (dw). We used cryo-TEM to measure the water gap and the membrane thicknesses in the phantom system. Next, we tested our biophysical model on healthy young adults (N=25) in four white matter regions (lateral-occipital, superior-temporal, superior-frontal, and superior-parietal). The phantoms and human subjects were scanned in a 3T Skyra Siemens scanner with a 32-channel receive head-coil for R27, R15, and WF5 mapping.

Results: The lipids’ membrane thickness is measured to be 4.5-5 nm, which is about the same size as the myelin membrane. The water gap between the membranes decreased from ~15 nm to ~4 nm (Fig. 1a) depending on the salt concentration. Our in vitro measurements validate our biophysical model and the water gap thickness fits very well with the cryo-TEM measured
The ratio between the water gap thickness to the membrane thickness (dw/dm) is a measure of the membrane packing. The model-fitted ratio correlates well with the cryo-TEM measured ratio (r=0.99, p<10^{-2}; Fig. 1b). In healthy young adults, the model estimates of the TW T2 was ~90 msec and the MW T2 values ranged between 20-40 msec (Fig. 2a) across subjects and regions. Importantly, these values agree with the myelin water T2 previously estimated using the MWI technique. All the areas yielded similar membrane packing ratios between 0.7-1 across all subjects and regions. Assuming a constant membrane thickness (4.5 nm), the estimated water gap thickness is between 3-4.5 nm, which agrees with ex vivo and animal models estimation. (Fig. 2b).

Conclusions: We developed a new model to study the myelination packing status in vivo using clinical multi-echo sequences and simple WF estimates. Until now, the water gap could only be calculated in postmortem axonal analysis. We established this approach with a biophysical model and validated it with a specifically designed in vitro phantom system and in vivo human data. Our phantom in vitro system and in vivo human data showed high agreement for the predicted signal and the extracted parameters.

References


**Poster No 2176**

**Establishing the Spatial and Cognitive Specificity of Cerebrovascular Burden: A UK Biobank Study**

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**Introduction:** Cerebrovascular (CV) risk factors are shown to have a detrimental impact on cognitive function and are likely to do so through the disruption of key white matter (WM) networks. Identifying early neurocognitive indicators of poor CV health may be critical in preventing later-life cognitive dysfunction. The heightened sensitivity of WM to CV insult is well established (Iadecola, 2013), but increasing evidence shows this effect may be region-specific within WM. For example, hypertension, a known CV risk factor, is associated with greater change in anterior CV function, such as reduced blood flow, relative to posterior regions (Kandil et al., 2022; Beason-Held et al., 2007). This shows the unique CV aetiological processes between regions and highlights an anterior-specific vulnerability to ill CV health, which is likely also reflected by anterior WM change. Given the proposed region-specific impact of CV burden, it’s likely that the cognitive impact of this is also specific to certain cognitive domains. Processing speed (PS) is a likely candidate given its links to WM (Kerchner et al., 2012), CV health (Cox et al., 2019) and anterior degeneration (Kochunov et al., 2010). As such, our current work aims to establish the relationship between CV burden, WM and cognition and to assess the regional and cognitive specificity of this effect.

**Methods:** The sample of 35,000 from the UK Biobank contained both males and females aged between 45-70, with complete data. A baseline SEM was built whereby CV burden acted as the predictor variable, loaded with 7 known CV risk factors. A latent construct of anterior WM integrity was the mediator variable, loaded with averages of 7 anterior tracts with separate models made for FA & MD (figure 1a). We ran a PCA on cognitive data from the UK Biobank to derive two principal components. One which represented general cognitive performance and a second which separately captured PS. The PS principal component was used as the outcome variable for the baseline SEM. To establish spatial specificity, a new SEM was built, identical to the baseline model, but the anterior WM integrity was replaced with posterior WM integrity (Figure 1b) as a mediator. To establish cognitive specificity, a third SEM was built, here PS was replaced with cognitive performance as an outcome variable. Models were then statistically compared.
**Results:** All measured variables loaded significantly onto each latent construct. The baseline SEM illustrated that increased CVB is associated with slowed cognitive PS. This is mediated by anterior WM integrity loss. All pathways in the baseline model were significant and the model fit well (Figure 2a). Replacing anterior WM integrity with posterior WM integrity either reduced the mediation effect (FA) or it became no longer significant (MD) (Figure 2b). The model also fit significantly worse, when compared with the baseline model (p < .001). When the outcome measure was replaced with general cognitive performance, the direct effect remained significant. However, the mediation either reduced (FA) or became no longer significant (MD) (Figure 2c). Model fit indices demonstrated good fit, with no significant change from baseline.

**Conclusions:** The findings demonstrate increased CV burden was associated with slowed PS. This effect was at least partly mediated by diffusion changes in anterior WM, which was shown to be stronger and more consistent than posterior WM, in line with previous work. While CV burden was associated with both cognitive measures, changes in anterior WM integrity best explained the relationship between CV burden and PS, as opposed to cognitive performance. The next empirical steps will focus on addressing why this regional vulnerability exists through the use of multimodal imaging techniques, establishing the timeline of CV-driven decline associated with each cognitive domain and finally, identifying the networks which underpin CV-driven cognitive decline in other domains using a graph theory approach.

**References**

**Poster No 2177**

**Analyzing Brain Topography Via Directional Derivatives of Connectivity**

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**Introduction:** Topographic organization stands as an important characteristic of the brain6,10. Tractography studies have highlighted this principle in the sensory and motor systems4,4. Gradients have been used to describe spatial changes in connectivity patterns6. Since gradients are rooted in dimensionality reduction9, these informative methods may not comprehensively encapsulate the complexity of the brain’s structural organization. Here, we introduce a novel approach...
founded on the mathematical concept of directional derivatives. This method effectively quantifies variations in structural connectivity across multiple directions, presenting a robust tool for the detailed exploration of the brain’s topography.

**Methods:** Figure 1 illustrates how we compute the structural connectivity and its derivatives starting from dMRI-based tractography. Consider the tractogram T composed of streamlines si. We define TS(x, r) as the subset of streamlines in T that intersect a sphere S(x, r), centered at x ∈ R³, with radius r. Each streamline in TS(x, r) contributes to structural connectivity at x, and the contribution is determined by a weighted sum w(x, i). This weight is calculated by integrating over the segments of si that intersect S(x, r). For each segment, we consider its length as well as its distance to point x. Each streamline is connected to the brain surface, Ω, that can be obtained through FreeSurfer³. This surface is composed of cells and vertices. We then assign the weight of each streamline to the vertices surrounding the intersecting cell to obtain f(x) ∈ R² that is our metric of structural connectivity. We can evaluate the same function at slightly shifted position around x, with a displacement h. Finally, the numerical approximation of the directional derivative of structural connectivity along a direction d on the unit sphere can be obtained with finite difference as in ∇d f(x) = (f(x+hd) − f(x))/h. The sum of ∇d f(x) over the surface is the scalar that encapsulates the structural changes along the specified direction, and is stored in the output image at position x.

**Results:** To test our method, we conducted experiments with subject 100307 from the Human Connectome Project⁸. The entire brain tractogram comprised 100 million streamlines, generated through parallel transport tractography² with anatomically constrained tractography⁷, so to ensure streamline termination on Ω. Figure 2A depicts the gradual changes in connectivity on the surface due to small displacements in the neighborhood of a point in the corpus callosum. It highlights how our metric of structural connectivity f(x) provides insights into the topographic organization of connections along various directions. Figure 2B displays RGB-encoded directional derivatives. The image is formed by using the absolute values of the derivatives along the directions [1 0 0], [0 1 0], and [0 0 1], represented by red, green, and blue colors, respectively. The images are computed on a 0.5 mm isotropic image grid, employing h=0.0125 mm.
Conclusions: This study proposes an innovative computational tool for investigating the brain and its topographic organization. While our present focus is on structural connectivity, the concept of directional derivatives in connectivity stands for other types of connectivity and could be extended to functional measurements such as fMRI and EEG. Beyond contributing to our understanding of the brain’s organization principles, we anticipate the relevance of our method in all contexts where precision and personalization are crucial, including surgical planning and brain stimulation studies.

References
Fibre-specific white matter differences: preliminary findings from the Australian Epilepsy project

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Introduction: Epilepsy is one of the most common chronic neurological conditions and is understood to be characterised by disruption to large-scale brain networks\textsuperscript{1,2}. Diffusion-weighted imaging (DWI) has enabled investigation of structural brain network changes in the epilepsies. Here, we applied advanced DWI analyses to investigate fibre-specific abnormalities in participants from the Australian Epilepsy Project (AEP). We hypothesised that epilepsy patients, particularly those with drug-resistant epilepsy, would exhibit large-scale changes in brain white matter pathways when compared to neurologically healthy controls. We also explored individual variability in large-scale white matter differences across the clinical cohorts when compared to the normative cohort.

Methods: Adult participants (aged 18 to 65) who have been recruited to date into the AEP in three clinical categories were included: (i) First unprovoked seizure (FUS) but with no diagnosis of epilepsy (n=42) (ii) New diagnosis of epilepsy (NDE) made in the past 6 months (n=68) (iii) Drug-resistant epilepsy (DRE) despite trial of 2 or more medications (n=56) Neurologically healthy adult control participants recruited to date into the AEP (HC; n=74) were also included. Multi-shell DWI data were acquired at 3T on a Siemens Prisma with the following parameters: TE/TR = 83/3065 ms; voxel size = 1.8 mm\textsuperscript{3}; b-values = 0, 300, 1000, 3000 s/mm\textsuperscript{3}. DWI data were preprocessed using MRtrix3\textsuperscript{3}, and fibre orientation distribution (FOD) functions were extracted using multi-shell multi-tissue constrained spherical deconvolution (MSMT-CSD)\textsuperscript{4}. Spatial correspondence was achieved using an unbiased study specific template. A measure of fibre density and cross-section (FDC) was computed, and whole-brain fixel-based analysis (FBA)\textsuperscript{5} performed to compare across groups, and between each clinical group and controls. Age and log-transformed estimated intracranial volume (eICV\textsuperscript{6}; based on FreeSurfer estimate from structural T1-weighted images) were used as nuisance covariates. Post-hoc analyses were performed to explore individual variability in widespread white matter abnormalities. Mean FDC values across the ‘fixels’ (fibre populations within a voxel) that exhibited significant differences on the F-test (affected fixel mask) were extracted for each participant, and a linear model computed for mean FDC as a function of eICV in the HC group only. Individuals were identified as outliers if standardised residuals were > 3.

Results: Whole-brain FBA revealed significant (family-wise error (FWE) corrected $p < 0.05$) group differences on an F-test across extensive white matter fixels (Figure 1A). These significant group differences appeared to be driven predominantly by significantly decreased FDC in the DRE cohort when compared to controls, while no significant differences were observed in the FUS or NDE cohorts compared to controls (Figure 1B-D). Figure 2A shows the density distribution of mean FDC values within the affected fixel mask across individuals by cohort. The DRE cohort exhibited a distribution shift in these mean FDC values when compared to controls (as expected given the whole-brain result), but there were also individuals in the NDE and FUS cohorts who appeared to exhibit widespread white matter abnormality (Figure 2B).
Conclusions: In this study, we demonstrated fibre tract-specific white matter changes in fibre density and cross-section (FDC) in epilepsy patients from the Australian Epilepsy Project. Group comparisons demonstrated significant and widespread
changes only in the drug-resistant epilepsy cohort when compared to controls; however, post-hoc exploration identified individual outliers with substantial white matter abnormality across all 3 clinical cohorts. Future work that examines individual differences from the normative cohort in fibre-specific measures, and their association with clinical parameters will be valuable.

References

Poster No 2179
Brain Cortical Surface Can Predict Fiber Trajectories
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Introduction: The brain primarily consists of gray matter and white matter, which interact with each other to form the complex functions of the brain. Research concerning the interplay between gray and white matter structures have offered some evidences support a link between the formation of cortical convolutions and the connectivity of underlying white matter. Moreover, studies of brain diseases have found white matter network reconfiguration is a response to deep gray matter pathology in clinically isolated syndrome and early-stage relapsing-remitting multiple sclerosis patients. These studies have revealed a clear correlation between gray matter and white matter. This work tries to explore their close relationships from a novel perspective, which directly utilizes brain cortical surface information to predict the fiber trajectories. Previous research focused on predicting the presence of fiber connections between two points on the brain surface. In contrast, this work advances this understanding by predicting the coordinate information of fiber trajectory between two points on the brain surface.

Methods: The overall framework of this work is depicted in Fig.1. The T1 MRI images and diffusion MRI (dMRI) images from 20 healthy subjects in the publicly available HCP S900 dataset were used, the probabilistic fiber tracking were performed by MRtrix3, thus 10^6 fiber streamlines were obtained for each subject and the inner cortical surfaces were reconstructed by FreeSurfer. Then we need to prepare sample data from actual data to train model parameters. Firstly, we selected those fibers with both endpoints located within the gray matter cortex. Then, we sampled fiber streamlines to standardize their length to 100 points for the purpose of simplifying the training process and facilitating evaluation. We selected the first and last points of each fiber streamline as part1 of training samples, which are also two cortical surface points. The remaining 98 points on the fiber which are to be predicted is part3 of training samples. The uppermost, lowermost, leftmost, rightmost, frontmost, rearmost points on the brain surface, as well as the geometric center point of the entire brain surface is part2 of training samples. We used part1 and part2 to predict part3. We improved the BiLSTM model for the regression task of predicting fiber coordinates. To gauge the proximity of the predicted fiber coordinates to the true fiber coordinates, we utilized evaluation metrics including Mean Squared Distance (MSD), Cosine Similarity, and Hausdorff distance. Among them, the MSD loss and cosine similarity loss function were also used in the training process.
Results: We performed a K (K=5) folds cross-validation on a set of 20 individuals. We select the true representative fibers and their prediction results to show in Figure 2. The true representative fibers are selected from the TractSeg fiber tract atlas for each subject because we used the same subjects as the TractSeg dataset. It can be seen that the predicted fiber streamlines is very close to the true fiber streamlines. Additionally, we conducted quantitative evaluation experiments using data from different individuals, and computed the above three metrics. The average MSD, cosine similarity and Hausdorff distance are 21.5518, 0.9982 and 9.8085, respectively. Both qualitative analysis and extensive quantitative experiments confirm that information derived from the brain's cortical surface can be employed to predict fiber trajectories.

Conclusions: This study tried to use the cortical information to predict the trajectories of white matter fiber, which provides a new perspective for further study of the close relationship between gray matter cortex and nerve fibers.

References

Poster No 2180
Can Personality be Predicted from the Structural Connectome?
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Introduction: Personality neuroscience aims to explore the neurobiological basis of personality as it strongly affects interindividual differences of human behavior. We investigate if the structural connectome (SC) derived from diffusion weighted images can be utilized to predict the big five personality traits. As previous work in the field showed mixed results (e.g.,) and prediction from the SC itself is a comparably new field, we systematically evaluated different design choices of the SC and feature selection processes, illustrate a large spectrum of possible results and suggest a few conditions for improved predictions.

Methods: This study used pre-processed structural and diffusion data from unrelated subjects of the Human Connectome Young Adult dataset. We analyzed the effect of the following different settings on prediction performance: • 19 different cortical parcellations • Three SC weightings: Streamline count, mean diffusivity (MD), fractional anisotropy (FA) • Four feature selections methods: Upper triangle of the SC (whole-brain), k first principal components (PC) of the SC, k SC edges most correlated with the target across subjects, regional connectivity profiles (RCP, separate rows of the SC) • Three subject groups: Mixed males and females (n=426), only males (n=272), only females (n=272) • Five personality traits This leads to a total of 3,420 different pipelines. The SC for each subject was calculated using probabilistic tractography for all parcellations and weightings. When feature selection was used, we investigated further options, i.e., different k’s for PCs and correlated edges and different rows of the SC for RCPs. Ridge regression was used to make all predictions using a nested 5-fold cross-validation for hyperparameter tuning. Selection of most correlated edges and PCA fitting was performed on the training set to prevent data leakage. Predictions for all settings were repeated 100 times for random data splits. We additionally predicted cognition (CogTotalComp_AgeAdj) of individuals using the mixed sex dataset and the whole-brain features to give context to the prediction performance of the personality traits.

Results: With only a few exceptions, the prediction results over all different settings yielded low correlations. The mean of the distribution of average prediction correlations was around zero at r≈-0.003 (Fig. 1A). Predicting cognition led to slightly higher test set correlations compared to personality traits (Fig. 1B). Despite the overall zero-centered prediction accuracies, some differences between the distinct settings could be observed: For the different feature selection methods, the highest correlations could be reached by applying the RCPs (Fig. 2A). Within the same parcellation strategy, there was a tendency towards better performance with higher granularity (Fig. 2B). Overall, there was no clear best SC weighting. When deriving maps of the average test correlations across 19 parcellations using the RCP feature selection, one can see higher similarity (correlation) in prediction results between the microstructural weightings MD and FA and distinct prediction patterns for streamline count (Fig. 2C).
Conclusions: By systematically evaluating many different pipelines for predicting personality traits from the SC, we find only a few cases of promising prediction performance ($r \geq 0.2$) which are similar to values reported in the literature for personality prediction from the FC (6,7). Most results, however, are centered around a correlation of zero indicating no generalizable linear relationship between personality traits and SC. However, we did find some methodological differences between distinct settings and suggest considering RCPs for feature selection. The improved but still limited performance when predicting cognition indicates that the results for personality prediction might be influenced by both known limitations of the standard SC and the target itself, which requires additional investigations.

References

Poster No 2181
Mapping White Matter Tracts to NeuroSynth Cognitive Functions
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Introduction: White matter tracts efficiently support the relay of information between distant brain regions and thus facilitate integrative cognition (Fields, 2008; Goddings et al., 2021). However, no systematic mapping exists that links tracts to specific...
cognitive functions in humans. Here, we capitalize on NeuroSynth (Yarkoni et al., 2011) and a recently developed white matter atlas of probabilistic tract-to-region mappings (Yeh, 2022) to systematically delineate the core cognitive functions of canonical white matter tracts. We hypothesized that white matter tract architecture is linked to the spatial organization of cognitive functions.

Methods: Probabilistic estimates of white matter tract-to-surface connections derived from 1,065 young adults in the Human Connectome Project were used to link cognitive function maps and canonical white matter tracts. Specifically, the probability that each of 50 tracts (Yeh et al., 2018) reconstructed with DSI Studio (http://dsi-studio.labsolver.org) connected to each of 360 cortical regions (Glasser atlas) was determined at the population-level (Yeh, 2022). Next, we leveraged coordinate-based cognitive maps from NeuroSynth (Yarkoni et al., 2011) to annotate white matter tracts using a subset of 12 core cognitive functions from the Cognitive Atlas (Poldrack et al., 2011), including attention, cognitive control, inhibition, decision making, planning, imagery, language, memory, working memory, movement, emotion, and social cognition. We used two different approaches to determine whether the spatial organization of core functional activation maps reflect the architecture of underlying structural connections. First, for each cognitive activation map, we used mass-univariate t-tests in each cognitive map and tract to assess whether the distribution of cognitive activations differed between regions that are connected to the tract vs. other unconnected regions within the same hemisphere. Second, we fit multiple linear regression models to evaluate if tract-to-region probability maps (i.e., independent variables) were associated with each cognitive map (i.e., dependent variable). To account for the inherent spatial autocorrelation in the covariance structure of the cortical surface, 10,000 spin-based spatial permutations were used for significance testing in both independent t-tests and regressions (Alexander-Bloch et al., 2018).

Results: Half (25 out of 50) of the white matter tracts were enriched for specific cognitive functions (Figure 1A; p spin<0.05). We found some expected tract-to-function relationships, such as a specialization for language in the arcuate fasciculus, for memory in cingulum tracts, and for emotion in uncinate tracts (Figure 1B; p spin<0.05). Results also uncovered lesser-known tract functions, including an enrichment for imagery in the middle longitudinal fasciculus, and a specific involvement of attention in the posterior thalamic radiation (p spin<0.05). White matter tracts explained the spatial organization of attention, cognitive control, and working memory maps (Figure 2; p spin<0.05; R²:0.5 to 0.8). The frontal aslant, superior longitudinal and corticostraital tracts were particularly strongly associated with working memory.
Conclusions: We introduced a novel framework for ascribing cognitive functions to white matter tracts. This allowed us to both validate expected tract-to-function relationships and suggest new links. Moreover, structural connectivity patterns of white matter tracts explained the topographical organization of several cognitive functions. Taken together, this work bridges the gap between the functional neuroimaging-based literature of cognitive functions and white matter architecture, providing a systematic mapping of tract-to-function relationships. This framework may be used in future studies to help annotate tracts using contemporary representations of cognitive functions.

References
Deep Learning disconnectomes to accelerate & improve long-term predictions for post-stroke symptoms

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Introduction: White matter connections are recognized as fundamental building blocks of behavior and cognition, and their disconnections can be quantified to facilitate personalized prediction. This is particularly relevant in the context of stroke that is going to damage a specific brain region but also disconnect several remote areas. Being able to anticipate the risk of developing motor, cognitive, and emotional impairments following stroke could help to refer the patients to dedicated training to improve their outcomes. With the rise of Artificial Intelligence applications in healthcare, we explored and evaluated the potential of deep-learning models to accurately generate disconnectomes in a population of stroke survivors in order to speed up and accelerate the individualized prediction of neuropsychological scores one year post-stroke.

Methods: We implemented a 3D U-Net network for predicting individual deep-disconnectomes from binary masks of infarcts that was trained on N=1333 synthetic lesions and their corresponding disconnectomes, and tested on N=1333 real stroke lesions. The level of similarities between deep-disconnectome and conventional disconnectomes was assessed by the percentage of the variance of disconnection reproduced by the 3D U-Net. To explore any systematic differences in terms of disconnected voxels, we contrasted frequency maps of disconnected voxels. To predict clinical scores, we embedded the deep-learning-based disconnection pattern of each of the 1333 patients within a 2D morphospace using UMAP dimensionality reduction. With the achieved association between location within the morphospace and neuropsychological scores, we were able to predict scores for an out-of-sample population. We tested this on 139 new stroke patients using multiple regression and validated out-of-sample on 20 patients. Finally, we compared the accuracy of prediction between the two methods.

Results: The trained 3D U-Net algorithm was able to capture most information obtained in conventional disconnectomes, i.e., statistical maps filtering normative white-matter networks, but outputed a deep-disconnectome 720 times faster – compared to disconnectome computation with the state-of-the-art software. Moreover, through the morphospace, the deep-disconnectomes predicted neuropsychological outcome at 1 year with an average accuracy of 85.2% \( (R^2=0.208) \) which was significantly better \( (p=0.009) \) than prediction from the conventional disconnectome approach and confirmed out-of-sample. In order to understand why the score prediction of the deep-disconnectome outperforms the conventional disconnectome, a systematic comparison across the embedding coordinates was performed for each patient. To find explanations for this, we assessed the structure of the morphospace by means of the average Euclidean distance between each embedding set of coordinates against the rest of the embedding points. This calculation suggests a greater differentiation for deep-disconnectomes derived from similar stroke lesions. This may have improved the segregation between similar profiles of white-matter damage and, accordingly, could have led to better modeling of fine differences within the same neuropsychological assessment.
Fig. Visual comparison of the deep-disconnectomes with the conventional disconnectomes

**Fig. UMAP morphospace embedding of N=1333; R^2** for the predictions with the two disconnectome types; Bland Altman plot with differences in the average Euclidean distances between the disconnectomes

**Conclusions:** Our 3D U-Net algorithm is able to accurately resemble the ground truth and produce an accurate deep-disconnectome from a binary lesion mask that captures statistical maps filtering normative white-matter networks, just as the conventional disconnectome, but 720 times faster. For long-term stroke outcome predictions, the deep-disconnectome’s predictive power outperformed the conventional disconnectome predictions for neuropsychological scores. This work demonstrates the potential of practical application of AI-driven models for clinical settings related to stroke outcome predictions and stroke management, which might enhance efficiency within healthcare systems, and ultimately contribute to an improved quality of life for stroke survivors.

**References**

**Poster No 2183**

**Association between exposure to childhood maltreatment and brain structure in adults: a DTI study**

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**Introduction:** Childhood maltreatment represents a strong psychological stressor which can lead to development of later psychopathology as well as a heightened risk of health and social problems\(^1\)\(^2\). Previous studies have utilized voxel-wise and ROI-wise mean diffusivity to detect brain white matter (WM) abnormalities in individuals of childhood maltreatment\(^3\)\(^4\). However, these methods may be not sensitive to represent the diffusivity in a long-range WM fiber tract distributions within a voxel and to reveal the WM microstructure changes due to diseases\(^5\)\(^6\). The automated fiber quantification (AFQ)\(^7\) method provides a more sensitive and specific tool for detecting developmental and clinical changes, and identifying the precise locations of such changes within fiber tracts, making it appropriately suited for exploring WM abnormalities in cases of childhood maltreatment.

**Methods:** Participants We enrolled 43 healthy adult individuals, including 21 with childhood maltreatment (CM) and 22 healthy controls (HC). The participants were recruited from the campus of South China Normal University (SCNU). The study was approved by the Institutional Research Board of SCNU. Each participant gave the written informed consent prior to the study. Data acquisition All the MRI data were acquired on a 3T Siemens Trio MRI scanner with a 32-channel phased array head coil. The DTI data were obtained with the following parameters: TR = 9,800ms, TE = 85ms, FOV = 224×224mm\(^2\); matrix = 112×112, slice thickness = 2mm and without an interslice gap, 64 non-linear directions with b = 1,000s/ mm\(^2\) and one volume with b = 0, and 75 interleaved transversal slices. High-resolution brain images were obtained using the T1-weighted MP-RAGE 3D sequence: TR = 2,300ms, TE = 3.24ms, FOV = 256×256mm\(^2\), voxel size = 1mm\(^3\). Data processing The DTI and T1w data were preprocessed using FSL. The DTI preprocessing included the following steps: the b0 images extraction, the head motion estimation, eddy current correction, imaging segmentation, tensor fitting to obtain the voxel-wise eigenvalues, and the calculation of fractional anisotropy (FA). The T1w images were used for brain extraction and were averaged to align with the AC-PC plane. The preprocessed DTI images and T1w images were fed into the AFQ software. The AFQ procedure steps were summarized as follow: performance of the whole-brain tractography, segmentation of a whole brain fiber group into 20 fascicles groups, definition of the tract core and filtering out of stray fibers, and quantification of the diffusion measures at 100 equidistant nodes along each fiber tract. A non-parametric permutation test (10,000 times) was used to detect between-group difference in FA along the tracts. Potential confounding variables (age and gender) were selected as covariates in the group comparison. Significance level was set at \(p < 0.01\)\(^8\)\(^9\) with a family-wise error (FWE) correction. Only the FA differences that included three or more adjacent nodes along a tract were reported\(^10\).

**Results:** Fig. 1 shows the node-wise comparison of 2 identified white matter fractional anisotropy profiles among the CM and the HC. The CM showed significantly lower mean FA than the HC in the right inferior fronto-occipital fasciculus (nodes 11-14) and the left uncinate fasciculus (nodes 69-73).

**Fig. 1** Node-wise and mean FA along the 2 identified white matter tract profiles between the CM and the HC. The FA tract profiles are presented in mean ± standard error (SE). The solid curves stand for the mean values across each white matter tract and the area between dotted curves stand for SE. The horizontal axis indicates the location between the beginning and termination waypoint region of interest along the given tract, while the vertical axis indicates FA value. The regional difference of the tract profiles of these two fiber tracts and the specific segments showing significant between-group differences in FA are also showed. The non-white color means significant group difference. Abbreviation: FA, fractional anisotropy; IFOF, inferior fronto-occipital fasciculus; UF, uncinate fasciculus; L (R), left (right) hemisphere.
Conclusions: The CM had a significant lower mean FA than the HC in the right inferior fronto-occipital fasciculus (IFOF_R, nodes 11-14) and the left uncinate fasciculus (UF_L, nodes 69-73). These results revealed the neurodevelopmental alterations associated with the progression of childhood maltreatment. The findings can provide new insights into the microstructural change of psychopathology.

References

Poster No 2184

Fractional Anisotropy Varies with Age, Cognition, and Depression in Patients with Sickle Cell

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Introduction: Sickle cell disease (SCD) is a genetic condition causing abnormal hemoglobin formation, chronic hemolysis, anemia, poor perfusion, and decreased oxygen delivery. As neurological function relies on adequate blood and oxygen, SCD patients often experience neurological complications from tissue damage1. These complications may lead to cognitive deficits experienced by patients with SCD starting at a young age2. Diffusion tensor imaging (DTI) characterizes white matter microstructure and connectivity in the brain. The sensitivity of this imaging technique may help predict SCD disease progression. The fractional anisotropy (FA) metric from DTI measures tissue organization and directional coherence and has been associated with cognitive function3 and depression4, which is highly prevalent in SCD. However, the association between FA metrics and mental health outcomes has not been examined in this population. This study examines the associations between FA values, age, cognitive performance, and depressive symptoms in adults with SCD patients and healthy controls.

Methods: 24 healthy controls (aged 38±15, F=16) and 24 patients with SCD (aged 35±13, F=15) were included. Patient subtypes include HbSS, HbSC, and HbSβ+ thalassemia. DTI data was acquired with a 7T MRI scanner (MAGNETOM, Siemens) and a customized 16Tx/32Rx head coil5,6. The sequence parameters were: 64 directions with a b-value of 1ms/μm², 2 acquisitions without diffusion gradients (with and without reversed phase encoding direction), TE/TR=80/10031 ms, and total acquisition time 11:33 min. Preprocessing of the data was conducted with the softwares MRtrix7 and FSL8. Tract-based spatial statistics9 was used to compare diffusion metrics. The average FA value for each participant was calculated over the JHU ICBM-DTI-81 white-matter labels atlas. On the day of their MRI scans, participants self-reported depression (Center for Epidemiological Studies-Depression (CES-D)) and anxiety (Generalized Anxiety Disorder-7). They also completed cognitive tests, including the digit symbol substitution test (DSST). Pearson correlations tested associations between FA values, age, cognition, and depression/anxiety for all participants and patients/controls separately. Correlations with absolute values 0.3-0.49 were considered moderate, ≥0.5 were strong. P<0.05 indicated significant moderate/strong correlations.

Results: Overall correlations were found between FA values and age, DSST scores, and the CES-D. Across both groups, higher age was associated with lower FA values (r(46)=−0.52, p<0.01; Figure 1), while higher FA was associated with higher DSST scores, indicating faster processing speed (r(45)=0.49, p<0.01; Figure 2a). Increasing CES-D scores, indicating worse depressive symptoms, were also associated with lower FA values (r(45)=−0.41, p<0.01; Figure 2b). For patients with SCD, the
correlation between age and FA was stronger, r(22)=-0.64, p<0.01, compared to controls, r(22)=-0.54, p<0.01. Correlations between DSST scores and FA values were similar between patients (r(21)=0.46, p=0.03) and controls (r(22)=0.48, p=0.02). For correlations with the CES-D, only patients had a moderate negative correlation (r(21)=-0.46, p=0.03).

**Conclusions:** Prior research suggests adults with SCD show accelerated white matter aging compared to non-SCD counterparts. This is supported by data from this study showing stronger correlations between lower FA and age in the SCD participants compared to controls. This study also identified correlations between FA, cognitive function, and depressive symptoms. To our knowledge, this is the first 7T MRI study to examine correlations between FA, age, DSST performance, and depression severity in SCD patients and controls. Next, we will explore correlations between specific cognition and depression-related brain regions and FA in SCD. This can provide further insights into SCD’s neurological effects.

**References**

**Poster No 2185**

**Assessment of U-Net in the segmentation of short tracts: transferring to clinical MRI routine**

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**Introduction:** Accurately studying structural connectivity requires precise tract segmentation strategies (Zhang, 2021). The U-Net network has been widely recognized for its exceptional capacity in image segmentation tasks (Ronenberg, 2015). It has demonstrated remarkable results in segmenting large tracts using high-quality diffusion-weighted imaging (DWI) data (Wasserthal, 2018). However, short tracts, which are associated with various neurological diseases, pose specific challenges, particularly when considering the DWI data acquisition within clinical settings. The objective of this work was to evaluate the capability of the U-Net network in segmenting short tracts using DWI data acquired in different experimental conditions.

**Methods:** To accomplish this, we conducted three different types of training experiments with a total of 350 healthy subjects and 11 white matter tracts, including anterior, posterior, and hippocampal commissure, fornix, and uncinate fasciculus. In the first experiment, the model was exclusively trained using high-quality data from the Human Connectome Project (HCP) dataset, presenting 270 gradient directions and 3 bvalues (1000, 2000, 3000 s/mm²). The second experiment focused on images of healthy subjects acquired from a local hospital dataset (CAAE - 08219712.7.0000.5407), representing a typical clinical routine acquisition with 32 gradient directions and b = 1000 s/mm². In the third experiment, a hybrid training approach was employed, combining images from the HCP and local hospital datasets. The utilized architecture for this study was the 2D U-Net, originally proposed by Wasserthal et al. (2018). In this case, the input consisted of a 2D image with dimensions of 144x144 voxels and 9 channels representing the orientation information of the fiber. To achieve this, the images were sliced into three different orientations: axial, coronal, and sagittal. Consequently, three separate networks were trained, with one dedicated to each orientation. Reference labels were created using pre-defined regions of interest based on existing literature (Pinto, 2020). The individual tracts were transformed into binary masks to establish the ground truth. To evaluate the performance of the trained model in each experiment, we conducted tests on two separate sets of subjects. The first test was performed on 60 unseen subjects from the HCP dataset and the second on 60 unseen subjects from the local hospital dataset, ensuring that the model was evaluated on data that it had not been trained on. Dice score was used to evaluate the accuracy prediction.

**Results:** The third experiment showcased significant visual improvement compared to prior trials (Figure 1). Training exclusively on the public dataset posed challenges for tract reconstruction in the local hospital dataset, but the third experiment delivered the most promising results. Particularly, short tracts within the local hospital data achieved dice scores ranging from 0.60 to 0.75 (Figure 2). Additionally, substantial enhancement was observed for the HCP dataset compared to training solely with high-quality data.

![Figure 1 - Results of one random subject from local hospital dataset test for different networks (Dice score).](image)

Figure 1 - Results of one random subject from local hospital dataset test for different networks (Dice score).
Figure 2 – Test in unseen public dataset and local hospital dataset for hybrid approach training. (+) Mean Dice score obtained training and predicting with Public Dataset.

**Conclusions:** This outcome strongly indicates that the fusion of datasets from various sources, coupled with resolution standardization, significantly fortifies the neural network’s capacity to generalize predictions across a spectrum of datasets. It’s crucial, however, to recognize that the performance of short tract segmentation is intricately linked to the composition of the training, validation, and testing data. Moreover, the segmentation of shorter and intricately curved tracts introduces added complexities due to their intricate structural nature. Although this approach has shown promising results, caution is essential when extrapolating its application to datasets acquired under distinct experimental conditions, even when dealing with higher-quality data or analyzing long or short tracts.

**References**

**Poster No 2186**

**Mapping the connectivity of the zona incerta with diffusion MRI: replicability and reproducibility**

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**Introduction:** The zona incerta (ZI) is a poorly understood deep brain region with growing evidence suggesting that it plays a crucial role across a wide range of brain functions, and is considered a candidate region for neuromodulatory therapies. Advancements in MRI at ultra-high magnetic field strength (7 Tesla; 7T) have enabled direct visualization and differentiation of the human ZI and surrounding structures. We previously demonstrated the feasibility of using diffusion MRI (dMRI) to map the structural connectivity (SC) of the ZI in vivo. In this work, we investigate the replicability and reproducibility of identifying the internal organization of the ZI using 7T and 3T dMRI data from the Human Connectome Project (HCP).

**Methods:** SC between the ZI and the cortex was investigated using the minimally preprocessed HCP 7T (n=169), 3T (same subjects as 7T) and 3T test-retest (n=42) dMRI datasets. Cortical regions were defined in each subject’s native space using volumetric HCP-MMP1.0 parcellations, while the ZI was previously derived from probabilistic parcellations. Probabilistic tractography was performed using FSL’s probtrackx2 (default parameters unless otherwise indicated - 10000 samples per voxel, sampling in proportion along a set of fibre orientations, with distributions obtained with FSL’s bedpostx). Tractography was seeded from the ZI (thresholded at 50% and a 3 voxel radius dilation) to the target cortical regions, followed by transformation to the MN152Lin6Asym template space. Spectral clustering (n=6 clusters) was performed by cosine-similarity based on connectivity patterns of the ZI to the cortex. Additionally, ZI connectivity gradients were extracted using BrainSpace. Reliability was evaluated through comparisons between 7T and 3T (i.e. replicability), and test and retest 3T.
datasets (i.e. reproducibility). Centroid distances and Dice similarity from clustering-defined regions, as well as Procrustes disparity, comparing the connectivity patterns based on the first two gradients, were assessed.

**Results:** Figure 1 exhibits the identified clusters in the (A) ZI and (B) their associated cortical regions. Evaluation results in C show good replicability (7T vs 3T), with an average centroid distance of 0.82 ± 0.47 mm and 1.00 ± 0.50 mm for left and right hemispheres, respectively. Similarly, good reproducibility (test vs retest) was shown with an average centroid distance of 0.37 ± 0.18 mm and 0.94 ± 0.46 mm. Dice similarity measures indicate good replicable overlap (0.78 ± 0.086 and 0.74 ± 0.14) and great reproducible overlap (0.83 ± 0.018 and 0.73 ± 0.079). Figure 2 shows the two SC gradients explaining most of the variance (average eigenvalue of G1: 0.15 and G2: 0.08), in the (A) 3D MRI and (B) 2D gradient space. Procrustes analysis for left and right hemispheres, quantifying the similarity based on the 2D gradient distributions in C, revealed reproducible distributions among the 3T datasets. Notably in both analyses, the 7T dataset demonstrated the greatest difference relative to the various 3T datasets (Fig. 1C and Fig. 2D).
Conclusions: Reliable SC mapping of the ZI is crucial for furthering our understanding of ZI organization and to support its use for stereotactic neurosurgical planning. From both the cluster- and the gradient-based analyses, the largest differences were observed between the 7T dataset and the various 3T datasets. This can likely be attributed to dMRI acquisition as well as field strength related differences, and their impact on image and tractography quality\(^\text{10}\). Nonetheless, the high reproducibility among the 3T datasets supports the potential of SC-driven identification of the optimal ZI location for neuromodulatory therapies. Future analyses are required to validate these data-driven in vivo connections as well as to link these results to surgical outcomes.

References
Towards in-vivo quantification of the optic nerves' microstructure with diffusion MRI

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Introduction: Diffusion MRI (dMRI) enables in-vivo quantification of the central nervous system microstructure; however, the accuracy of this approach varies in different anatomical locations\textsuperscript{1}. Probing the microstructure of optic nerves (ONs) is particularly challenging due to involuntary eye movements during dMRI acquisition\textsuperscript{2} and Echo Planar Imaging (EPI) artifacts at the air-tissue interface near sinuses\textsuperscript{3}. The goal of this preliminary study was to estimate the intra-axonal volume fraction, diffusivity coefficients, and the diameter of axons inside the ONs from Radial Diffusion Spectrum Imaging (RDSI).\textsuperscript{4} To assess the reproducibility of our results, we scanned each subject twice. During the second scan, we asked the participants to watch a video aiming to minimize the involuntary eye movements. Our results show that in-vivo quantification of ONs can be feasible and reproducible. This approach could be applied in tracking progression of ON tissue degeneration in injuries, glaucoma, or acquired blindness\textsuperscript{5}.

Methods: We acquired dMRI of 4 healthy subjects (1 female, 32±5 y.o.) at 2mm isotropic resolution, single-shot EPI, TE/TR=74/5800ms, 60 diffusion encoding directions sampled at RDSI radial lines\textsuperscript{4} with b=250,1000,2250,4000s/mm\textsuperscript{2}, interleaved with 17 images at b=0. Each scanning session comprised two identical parts, i.e., test and retest, separated with a 15-min. break. During the retest, the participants were watching a video of their choice. Our postprocessing in MRtrix3\textsuperscript{3} included denoising, Gibbs ringing removal, correction of B1 field inhomogeneity and eddy currents. Next, we virtually dissected the optic pathways in DSI-Studio\textsuperscript{1} (Fig. 1) and fitted the dMRI signal along the streamlines to the Ball&Cylinder\textsuperscript{6} microstructure model in dmipy\textsuperscript{7}. For the latter, we employed the Van Gelderen axonal model\textsuperscript{10} due to its realistic assumption of Gaussian diffusion during the dMRI gradient pulse. We assessed the plausibility of our estimated microstructure parameters through comparison with earlier studies in the brain white matter. Also, we computed the two-sided statistical t-test with the significance level α=0.05 between the aggregated test and retest measurements to verify the reproducibility of our procedure and potential motion reduction due to video watching during acquisition.

Results: The intra-axonal volume fraction p1 oscillated around 0.27-0.29, dropping below 0.20 on both ends of the ONs – in proximity to the globe and near the optic chiasm, respectively (Fig. 1&2). Consequently, the extra-axonal volume fraction piso demonstrated the exact opposite behavior. The intra-axonal diffusivity Da remained at the stable yet relatively low average level 0.52–0.65 ×10-9m\textsuperscript{2}/s, whereas the extra-axonal diffusivity Diso=2.6×10-9m\textsuperscript{2}/s was close to the values reported for the brain white matter\textsuperscript{11}. The estimated axon diameter of approx. 10-20μm was an order of magnitude higher than the values reported in histology\textsuperscript{12}, which conforms with the systemic overestimation observed in dMRI-based methods [13,14]. Finally, the t-test showed no significant differences between the test and retest measurements regardless of the video watching during acquisition (p≈0.05, Fig. 2).
**Conclusions:** Our RDSI acquisition protocol and the assumed Ball&Cylinder diffusion model were sufficient for reproducible quantification of the human ON microstructure parameters in vivo. The observed variability of the intra-axonal fraction was likely attributed to the partial volume effect at the extremities of the ONs. Another limitation of our study was the simplicity of the diffusion model which led to underestimation of the intra-axonal diffusivity. Nonetheless, the numerical stability of our estimates suggests that dMRI-based microstructure quantification may be considered for probing the integrity of ONs. Future work should include disease controls and potential extensions of the diffusion model.

**References**
ABSTRACTS


Poster No 2188

The Diffusion Visualization Explorer (DiVE) Tool

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Introduction: Diffusion MRI based tractography reconstructs the white matter (WM) pathways in the brain, allowing for a 3D assessment of structural brain connectivity. Visualization tools for tractography are important for displaying complexities of WM pathways. These tools help researchers and clinicians understand the individual brain’s structural connectivity and display population based findings related to neurological and psychiatric conditions. While classical tools like Trackvis, MRView, MI-Brain, DSI-studio analyze and visualize dMRI data to different degrees there is a need for a tool with a seamless integration of tracts, masks, and mesh structures for displaying individual tracts and population level statistical findings. Our tool, Diffusion Visualization and Explorer (DiVE) was developed out of necessity for our novel Medial Tractography Analysis (MeTA) toolbox to complement existing toolboxes, offering enhancements such as statistics-based visualization, creating and saving high-quality images, and simultaneous visualization of bundle specific meshes, volumes or masks, and streamlines or tracts. We distribute DiVE as a stand alone package for wider use.

Methods: DiVE uses the Free Unified Rendering library in pYthon (FURY) a high-performance scientific visualization library. FURY can visualize diverse components, including streamlines, brain masks, and meshes, coexisting within the same spatial context. We leverage OpenGL, a versatile cross-platform application that renders both 2D and 3D surfaces. DiVE takes a 3D region of interest label image in NIFTI format and renders it as a set of 3D contours. It applies either the color specified by the user or a random color for single labels and chooses a set of distinct colors for multi-labeled masks using “distinctipy”s if a colormap is not provided. Tract rendering can be conducted across all common formats (trk, tck, trx, vtk), with user defined coloring options, as well as available defaults. A mesh (vtk) is rendered as a surface mesh using pyVista polydata inherited from Python VTK representing the geometry of 3D objects using a combination of points, vertices, lines, and polygons. DiVE’s 3D visualization feature allows users to render complex fiber structures in 3D space, enabling viewing of fiber bundles from different angles and perspectives, providing a comprehensive understanding of their spatial distribution. Each fiber is displayed as tubes with a user-defined width. DiVE also allows for the overlay of NIFTI masks and surface meshes on the fiber tracts, which can map scalar values to color or opacity, providing insights into tissue microstructure. Users can also add as a background 3D or 2D slices from the full brain NIFTI images to understand how fibers interact with specific brain regions. The GUI and examples of different visualization options can be found in Figure 1.

Results: DiVE is a dynamic open-source initiative, operating across multiple platforms, and we anticipate continuous development and active community engagement. Python integration allows for easy scripting, a high degree of flexibility and automation. The software provides an extensive array of visualization capabilities encompassing both 2D and 3D rendering for streamline and bundle tractography visualization, and more. Visualizations are enhanced by the inclusion of user-defined statistical metrics, along the trajectories of white matter bundles. We showcase results from, wherein the t-value derived from MeTA_25% core volume is mapped in association with the corresponding p-value Figure 1. DiVE is compatible with various neuroimaging file formats, ensuring seamless integration of existing data.

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Conclusions: DiVE is available for the wider diffusion tractography and visualization community https://github.com/USC-LoBeS/DiVE to complement existing toolboxes with a range of customization options to fine tune the visualization of tracts, meshes and masks and create custom visualizations.

References

Acknowledgements
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Vertical Orbitofrontal Fascicles in the Brain: A Preliminary Confirmation via Diffusion Tractography

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Introduction: The vertical orbitofrontal fascicles (VOFF) is a critical association pathway in white matter (WM)¹⁻⁴ for coordinating sense, emotion, and memory, which connects the lateral orbitofrontal cortex (LOF) and the superior frontal cortex (SF). It is related to multifunctional coordination processing and is the only vertical white matter pathway connecting lateral orbitofrontal and superior frontal cortices. While the WM pathways that involve LOF (e.g., superior occipitofrontal fascicles) or SF (e.g., uncinate fascicles (UF)) have been well investigated in previous studies, detailed delineation of the anatomical pathway connecting the two cortices is non-existent. In this work, we investigate the organization and structure of the connection between LOF and SF via diffusion tractography⁵⁻⁷ and confirm for the first time the existence of a vertical connection, i.e., VOFF. To date, VOFF is a poorly understood anatomical structure that potentially involves high-order cognition, such as decision-making⁸. The VOFF is one of the three vertical pathways in the human brain⁹ and extends between the superior and inferior frontal cortices (Fig. 1a), discovered by Lamendella and Geschwind¹⁰⁻¹². Understanding the anatomical structure of vertical VOFF will improve our knowledge of the prefrontal lobe’s role in executive functions.

Methods: We investigated the vertical VOFF using the anatomical MRI and diffusion MRI (dMRI) data of 100 unrelated subjects from HCP Young Adults¹³. All diffusion-weighted images were corrected for eddy-current and susceptibility distortions. We performed whole-brain tractography using asymmetric fiber orientation distribution functions (AFODFs) to capture better complex axonal configurations, such as bending, fanning, and crossing, and to mitigate gyral bias for better cortico-cortical connectivity⁵⁻⁷. Generated by successively following the local directions determined by the AFODFs, whole-brain tractography performed with 64 random seeds per voxel resulted in approximately 10 million streamlines. The fiber streamlines connections between (i) SF and medial-orbitofrontal cortex (MOF) and (ii) SF and LOF were retained for subsequent processing. We removed standard false-positive bundles and commissural bundles. An unsupervised bilateral fiber clustering was then implemented to group the streamlines into K fiber clusters (we set K=30)¹⁴. We semi-automatically extracted the vertical VOFF and similar structures (Fig. 2b) from these fiber clusters based on the Kahle Human Anatomy Atlas³.

Results: The vertical VOFF and five similar structures near the vertical VOFF were detected in all subjects (100%). Fig. 1c confirms the existence of VOFF and indicates that it is orthogonal to the superior occipitofrontal fascicles (SOFF) and UF. Fig. 1d suggests that the vertical VOFF is approximately tangent to the cingulate bundle (CB). These observations form guidance for the identification of the vertical VOFF from among the whole-brain streamlines. Fig. 2 (b-2 to b-6) shows some WM pathways adjacent to the vertical VOFF, indicating that the geometries of WM pathways connecting the SF to the different parts of the orbitofrontal cortex are different. The vertical VOFF is more likely to connect the SF and the LOF, but not the MOF.

Figure 1. The vertical VOFF pathway. (a) Position of the vertical VOFF in the human brain[1]–[3]. (b) Fiber configuration near the vertical VOFF shown for a young adult subject. (c) Orthogonal relationship between the vertical VOFF and SOFF/UF. (d) Tangential relationship between the vertical VOFF and CB.
Conclusions: We unveiled an association pathway called vertical orbitofrontal fascicles (VOFF), which is likely to subserve the communication between the lateral orbitofrontal and superior frontal cortices. Using diffusion tractography, we showed that the VOFF can be identified consistently across the population. The preliminary shape analysis revealed distinctive tissue properties in the vertical VOFF compared to neighboring pathways, indicating potential cytoarchitectonic and functional transitions in the lateral orbitofrontal cortex. Future research needs to identify the underlying changes in VOFF across lifespans further.

References

Poster No 2190

Associations between prenatal lead DNA methylation scores and white matter connectome in adolescence

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Introduction: Lead is a neurotoxic substance that has been shown to significantly affect the developing brain through multiple mechanisms. Lead exposure can have broad, long-lasting effects on a variety of physiological processes including epigenetic modification and myelination. Early exposure to lead can occur in-utero leaving an epigenetic signature of exposure and posing lasting health issues. The relationship between epigenetics and in-utero lead exposure may provide insight into the molecular mechanisms of lead’s toxic effects and serve as a proxy of measured in-utero lead exposure.
**Methods:** 181 adolescents from the Study in Adolescent Neural Development (SAND) were included in the analyses. SAND is a subset of participants from the Future of Families and Child Wellbeing Study, a population-based longitudinal cohort study with substantial representation of marginalized youths. Participants provided DNA methylation (DNAm) via saliva samples at ages 9 and 15 as well as diffusion MRI scans at 15. DNAm scores of prenatal lead exposure in umbilical cord blood were quantified using weights derived by (Wu et al., 2017) and applied to age 9 and 15 DNAm samples, which were then residualized for known confounders (immune cell and fibroblast proportion, batch, and maternal smoking at birth). Diffusion MRI was processed using the MRtrix pipeline that generated 94x94 individualized matrices representing whole-brain structural connectivity connectomes. Graph analysis was then applied to the resulting matrices to generate metrics of network architecture: global efficiency, modularity, and transitivity. All measures were z-score standardized. All analyses controlled for participant age, gender, birth city, race, mother’s education at birth, poverty ratio at birth, and current poverty ratio. All results are corrected with false discovery rate correction.

**Results:** A higher prenatal DNA methylation lead score measured at age 9 was associated with decreased structural global network efficiency ($\beta = -0.185$, $q = .025$). No association was found between prenatal lead score and modularity or transitivity using methylation measured at 9 or all three brain metrics at 15.

**Conclusions:** The present findings suggest that greater prenatal DNAm scores of lead derived from children at age 9 may contribute to differences in white matter connectivity organization across development. Lack of an association between prenatal DNAm scores of lead at age 15 and brain metrics may reflect a decay in lead methylation signal between 9 and 15, possibly as a result of in utero and early life lead exposures being deposited in bone rather than immune cells. Future analyses will investigate the impact of lead scores on subnetworks.

**References**


**Poster No 2191**

**Tract Profile Analysis Reveals Focal White Matter Changes in Individuals with HIV**

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**Introduction:** Individuals with chronic HIV suffer from HIV-associated neuroinflammation. Chronic neuroinflammation compromises white matter (WM) integrity, which can be evaluated using diffusion-weighted imaging (DWI) within regions of interest (ROI). Yet, recent work has shown that tissue properties vary along individual tracts due to differentially vulnerable axonal populations. Thus, tract profiles can reveal subtle differences between distinct locations along a tract. We performed tract-profile analysis using automated fiber quantification (AFQ) to investigate susceptible sites along WM bundles affected by HIV-associated neuroinflammation. DWI metrics exhibited differential variability and sensitivity to cognition along tracts and between groups, providing complementary information to understand disease processes better.

**Methods:** 80 individuals without HIV (mean age: 52.03 +/- 17.1 [SD], M/F: 51/29) and 85 individuals with HIV (mean age: 53.5 +/- 10.3 [SD]; M/F: 61/24) were evaluated using DWI. Images were acquired using a 3T Siemens MAGNETOM PrismaFit (Erlangen, Germany), using a 64-channel head coil. DWI was performed using a single shot SE-EPI sequence along 64 directions with two non-zero b-values (1,000 and 2,000 s/mm²; TR/TE = 4300/69 ms; FOV: 172x172, 1.5x1.5x1.5 mm3). Preprocessing of multi-shell DWI data is described previously. Free-water, fractional anisotropy (FA), radial diffusivity (RD), axial diffusivity (AD), and mean diffusivity (MD) were estimated using diffusion tensor imaging. Axial kurtosis (AK), mean kurtosis (MK), and radial kurtosis (RK) were obtained using diffusion kurtosis imaging. The orientation dispersion index (ODI), isotropic volume fraction (fiso) and the intracellular volume fraction (icvf) using neurite orientation dispersion and density imaging (ODDF). Whole brain probabilistic tractography was performed in MRtrix36 following estimation of fiber orientation distribution functions (fODF). RecoBundles was used to extract 80 WM bundles from tractograms based on similarity with template streamlines using an atlas. Tract-profile analysis was performed using AFQ, splitting each tract profile into 100 nodes and sampling ODI, FA, MD, and RK at each node. Neurocognitive evaluations were performed to evaluate six cognitive domains, and a composite total cognitive z-score was determined. Independent t-tests were performed to compare tract profiles and mean tract values between groups. Pearson correlation test was used to test associations between two continuous variables.

**Results:** Figure 1A shows mean tract profiles for the left and right superior longitudinal fasciculus (SLF), and the left and right middle longitudinal fasciculus (MoLF), selected for clarity. Similar changes were observed in other tracts. Differential sensitivity...
to neuroinflammation is observed along the tract, compared to mean tract values between groups (Figure 1B). Figure 2A shows the correlation coefficient between ODI, FA, MD, and AK at each node along a tract with the composite total cognitive z-score for individuals with and without HIV. Along each tract, we observed high variability of the correlation coefficient, illustrating which areas are associated with cognitive changes, not discernable with conventional analysis (Figure 2B).

Conclusions: Tract profile analysis revealed WM bundles are differentially affected by HIV-associated neuroinflammation. We observed differential sensitivity to cognitive measures using tract profile analysis, suggesting more nuanced manifestations of HIV-associated neuroinflammation are appreciated at specific locations compared to conventional tract-averaged measurements. This work is consistent with prior results implicating the SLF in cognitive impairment in individuals infected with HIV3, and associates the MdLF as a distinct entity involved in HIV-associated cognitive decline.

References
Can shape be as informative as microstructure for cognitive performance assessment?

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Introduction: The connectivity and microstructure of the brain's connections are known to relate to individual cognitive performance, including language performance (Zekelman et al., 2022). Deep learning methods have shown that the connectivity of fiber tracts is predictive of language proficiency in children with epilepsy (Jeong et al., 2021). However, the potential of shape as a feature for predicting individual cognitive performance remains largely unexplored. Shape is an important descriptor of fiber tracts (Corouge, Gouttard and Gerig, 2004) and is known to change with aging (Schilling et al., 2022). This study investigates the relevance of fiber tract shape in predicting neurocognitive language performance.

Methods: We employed measures of fiber tract shape and individual language performance in 1065 subjects from the Human Connectome Project Young Adult (HCP-YA) dataset. Whole brain tractography was generated from HCP-YA diffusion MRI (dMRI) using a two-tensor unscented Kalman filter method (Malcolm, Shenton and Rathi, 2010), followed by the parcellation of tractography into 953 fiber clusters using an anatomically curated atlas (Zhang et al., 2018). We studied 12 fiber tract shape features, including cluster length, diameter, elongation, span, curl, volume, trunk volume, branch volume, total surface area, total radius of end regions, total area of end regions, and irregularity (Yeh, 2020). For comparison, we extracted traditional fiber tract microstructure features of fractional anisotropy (FA), mean diffusivity (MD), and the traditional connectivity feature of the number of streamlines (NoS). In total, 15 features were computed for each fiber cluster. We utilized a convolutional neural network (CNN) (Liu et al., 2023) to predict subject-specific language performance given each input feature. We predicted two neurocognitive language assessments: the NIH-TB Oral Reading Recognition Test (TORRT), and the NIH-TB Picture Vocabulary Test (TPVT) (Weintraub et al., 2013). The Pearson correlation coefficient (r) was employed to assess the prediction performance of each CNN model.

Results: Certain shape features demonstrated equivalent or higher performance in comparison to microstructure features (Figure 1). For example, the total surface area shape feature outperformed all microstructure and connectivity features for both TORRT and TPVT language performance prediction. The total surface area feature measures the surface area of the 3D volume occupied by a fiber cluster. In the TORRT evaluation, 7 out of 12 shape features surpassed the performance of either FA, MD, or NoS. Similarly, in the TPVT evaluation, the same proportion of shape features-7 out of 12-exceeded the effectiveness of either FA, MD, or NoS.

<table>
<thead>
<tr>
<th>Input Features</th>
<th>TORRT (correlation coefficient r)</th>
<th>TPVT (correlation coefficient r)</th>
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<td>Microstructure features</td>
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<tr>
<td>FA</td>
<td>0.332±0.055</td>
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<td>MD</td>
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<td>0.260±0.041</td>
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<td>Connectivity feature</td>
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<tr>
<td>Number of Streamlines</td>
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<td>Shape features</td>
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<tr>
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<tr>
<td>Elongation</td>
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<td>0.313±0.070</td>
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<tr>
<td>Total surface area</td>
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<td>0.395±0.060</td>
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<tr>
<td>Radius of end regions</td>
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<td>0.235±0.045</td>
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<tr>
<td>Surface area of end regions</td>
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<td>0.406±0.089</td>
</tr>
<tr>
<td>Irregularity</td>
<td>0.341±0.021</td>
<td>0.322±0.041</td>
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</table>

Table. Comparative Analysis of TORRT and TPVT Prediction Across Microstructure, Connectivity, and Shape Features

Conclusions: Our experimental results show that measures of the shape of fiber tract connections are informative for the prediction of individual, subject-specific language performance. This suggests that shape-related features can serve as an alternative and potentially superior source of features for predicting and evaluating various cognitive abilities, potentially...
outperforming microstructural and connectivity features in certain scenarios. This also indicates that the shape of the white matter fiber tracts may relate to important functions of the human brain.

References

Poster No 2193
The Effect of Cerebral Microbleeds on Surrounding White Matter Integrity in Patients with CADASIL
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Introduction: Cerebral microbleed (CMB) is considered as a potential marker of neurovascular impairment, which corresponds histologically to perivascular hemosiderin deposit from leakage through cerebral small vessels (Pétrault et al., 2019). CMBs are recognized as neuroimaging findings in patients with dementia, small vessel disease, stroke, and traumatic brain injury (Haller et al., 2018). CMBs located in disparate brain regions may have different clinical influences (Chung et al., 2020). Previous studies showed that CMBs are associated with loss of white matter integrity and damage to the surrounding microstructure through a streamline-based analysis (Irimia et al., 2022; Liu et al., 2020). However, little is known about the effect of CMBs on the white matter in patients with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). In this study, we aimed to investigate the spatial impacts of cerebral microbleeds on the surrounding white matter integrity in patients with CADASIL. We hypothesized that loss of white matter integrity is associated with the distance to CMBs in CADASIL patients.

Methods: Sixty-five CADASIL patients were recruited and their multimodal MR images were collected, including T1-weighted structure images, diffusion tensor images (DTI) and susceptibility-weighted angiography (SWAN) images, from Taipei Veterans General Hospital. CMBs were manually specified on SWAN images using a homemade program with semi-automated instance segmentation for each patient. Twenty-three patients were excluded due to the absence of CMB. Fractional anisotropy (FA) values were calculated from DTI images, which represent the white matter integrity. The mean FA values of the voxels located within certain distance, ranging from 1 to 5 voxels away from the CMB, were calculated (Figure 1). Paired t-tests were conducted to characterize the difference between microbleed-affected foci and surrounding areas. Moreover, nine brain areas from the Talairach Daemon lobe atlas were adopted to further investigate the impact of CMBs on microstructure among different brain regions. The significance was set at p < 0.05 with Bonferroni correction for multiple comparison.
Results: Our findings exhibited significant differences of the mean FA values between the CMB site and its surrounding areas. The results showed an upward trend as the distance from the CMB extended outward, indicating a more severe damage to white matter integrity closer to CMB site. Such phenomenon was observed in almost all brain regions, especially prominent in the limbic and sub-lobar areas.

Conclusions: The study demonstrated that CMBs impair the surrounding white matter integrity in CADASIL patients through a voxel-based analysis. White matter damage extends around the CMBs in a diminishing pattern. This study highlights the potential role of CMBs on neurological system pathologies and should be carefully considered in the future studies related to cerebral small vessel diseases.

References

Poster No 2194
Exploring the macaque precentral intragyral white matter using ultra-high field 11.7T dMRI
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Introduction: Within the gyral white matter, three types of fibers converge: association, projection, and commissural. Currently, models of gyral white matter structural organization based on autoradiographic studies conducted in non-human primates (Schmahmann and Pandya, 2010; Dannhoff et al. 2023) describe their trajectory until the fibers arrive near the grey matter. However, there is little information characterizing their organization within the gyrus. The development of ultra-high field ex vivo MRI and advances in tractography algorithms, at the mesoscopic resolution, now allow us access to this intermingled fibers’ organization. We sought to investigate the structural organization of white matter in the precentral gyrus (PrCG) of the macaque brain, using an ultra-high field 11.7T diffusion MRI dataset.

Methods: The post-mortem brain of a healthy adult male cynomolgus macaque (Macaca Fascicularis) was scanned on a preclinical Bruker BioSpec MRI 11.7T with an MSME sequence (TR=350ms, TE=20ms, 100μm isotropic resolution, total scan duration=30h) for the anatomical dataset and with a 3D-segmented EPI PGSE sequence (32 segments; 3-shells q-space
sampling at b=1500/4500/8000 s/mm$^2$ along 25/60/90 diffusion directions; TE=24.33ms; TR=250ms; 250μm$^3$ isotropic resolution; total scan duration=99h) for the diffusion dataset. Regularized streamline probabilistic tractography was performed using Ginkgo, seeding within a mask corresponding to the white matter plus the grey/white matter interface (27 seeds per voxel, forward step=62.5um, maximum aperture angle of 15$^\circ$), stopping streamlining at the mask boundary or when the GFA falls below 0.02. Regions of interest (ROIs) were manually segmented, by 2 independent observers: PrCG, cortical grey matter, basal ganglia as one ROI, brainstem and cerebellum as one ROI, several slices of the internal capsules, anterior commissure, and the corpus callosum. They were used to filter the tractogram into projection, association, and commissural fibers. We used the virtual dissection tools in DSI Studio to further filter the resulting tracts and remove artifactual fibers.

**Results:** Among the fibers ending in the PrCG, 65% were association fibers mostly short and strongly curved, corresponding to intergyral fibers poorly described in the literature. Projection fibers accounted for 17% of the fibers and commissural fibers for 16% (Fig. 1). Fibers converged towards the gyrus in partially intermingled strata and then crossed extensively as they reached the grey/white matter interface. Association fibers, traveling mostly at the extremities of the gyrus were then found along the gyrus convexity. Projection fibers approached the gyrus at its center but then projected to the superior border and anteroinferior extremity with low density in the middle of the gyrus convexity. Commissural fibers were also found at its center but then projected at the gyrus's dorsomedial end and its posterior border (Fig. 2).

**Conclusions:** Using ultra-high resolution MRI data and tractography, we depicted the intra-gyral organization of white matter of the PrCG. We observed a basal arrangement in partially intermingled strata, transitioning to numerous crossings at the grey/white matter interface. The distribution of each type of fibers highlights the predominance of associative fibers in the PrCG and its functional heterogeneity. Our results are consistent with recent functional MRI studies in humans showing regions of body/action somato-cognitive functions interrupt and intermingle with regions specialized for motor function (Gordon et al., 2023). Thus, we showed that the PrCG, often simplified as the primary motor gyrus, has a strong associative component that intermingles with motor regions. The ability of ultra-high resolution MRI to reconstruct fiber pathways in and around the gyrus demonstrates the potential of this technique to bridge data acquired from macaque studies to human neuroanatomy.
References
5. Ginkgo Toolbox repository: https://framagit.org/cpoignon/gkg

Poster No 2195
The inside-out technique: tailoring fiber dissection for the study of the superficial white matter
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1UMR 1253, iBrain, Université de Tours, Inserm, Tours, France, 2CHRU de Strasbourg, Strasbourg, France, 3BAOBAB, NeuroSpin, Paris-Saclay University, CNRS, CEA, Gif-Sur-Yvette, France, 4CHRU de Tours, Tours, France

Introduction: Despite major methodological advances in the exploration of the cerebral white matter (Axer et al., 2011; Beaujoin et al., 2019) and growing interest in short association fibers (SAF) (Guevara et al., 2020), the latter remain underexplored. The examination of these connections through the classical fiber dissection (Ludwig and Klingler, 1956) is significantly impeded by the fact that the procedure involves the removal of the cerebral cortex, leading to a smooth surface where the bundles are scarcely visible, and causing the loss of a substantial portion of the sulco-gyral anatomy. To address the methodological renewal necessary for the accurate analysis of these delicate and superficial structures, we present the
A novel technique for inside-out fiber dissection of the post-mortem human brain that approaches subcortical fibers from their deep aspect with the preservation of the cortex.

**Methods:** Six cerebral hemispheres were obtained from a body donation program and fixed in 10% formalin. After two cycles of freezing and thawing (Klingler, 1935), a standardized fiber dissection protocol was carried out, consisting of peeling fibers from deep structures towards the cortex. In the end, it allowed the isolation of intergyral fibers in the subcortical white matter. The following elements were assessed: quality of the dissection plane containing the deeper fasciculi; visibility of fiber crossings, as well as neighboring, intergyral, and intragyral association fibers; and capability of the method to enable the evaluation of thickness of an isolated layer of the subcortical white matter.

**Results:** Inside-out fiber dissection enabled the selective isolation of the outermost layer of the superficial white matter in the lateral and medial aspects of the human telencephalon. SAF were easily cleaved from deeper fibers, as their deeper aspect was less adherent to underlying fibers than their outer aspect was to the cortex. Characterization of the SAF layer thickness and fiber orientation was performed without significant difficulty. The increased contrast between gray and white matter caused by the tissue preparation enabled the assessment of SAF layer thickness through direct observation and T2-weighted ex vivo MRI.

**Conclusions:** The inside-out fiber dissection technique effectively demonstrates intergyral association fibers in the post-mortem human brain. This technique completes the neuroscientist’s armamentarium, circumventing a severe methodological obstacle and providing the anatomical substrate necessary for modeling neural circuits and validating diffusion imaging of the superficial white matter.
ABSTRACTS

References

Poster No 2196
Cytoarchitecture and brain-wide connectivity reveal topographic organization of insula networks

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Introduction: One of the major challenges to carrying out in vivo neuroanatomical analyses is that regional cytoarchitectural variation is difficult to capture by MRI. As a result, parcellation of brain regions is often limited to a scale too coarse for the understanding of their functions. While this presents a challenge for many regions of the brain, the insula is comprised of distinct laminar cyto-archetypes that form the basis of highly integrative whole brain networks. These subregions have been linked to an astonishing number of functional roles, and may ultimately be targets for future development of interventions in physical and mental health1–4. In order to capture the heterogeneity of these subregions and networks, it is necessary to improve the specificity of neuroanatomical data and analyses using resolutions across disparate spatial scales and contrasting modalities from within the same subjects. We present our first integrated (Mic)ro to (Mac)ro Macaque brain dataset, here called MicMac (Fig. 1). MicMac is an extendable workflow, represented by a within-subject whole brain dataset that integrates aligned multi-parametric in vivo MRI, high resolution ex vivo MRI, and histology within a single, standardized template space. We then translate this workflow to perform a group level network analysis to identify network features in an in vivo cohort of n=16 middle to older aged macaques (7-20 years, 3M, 13F).

Methods: The MicMac dataset was obtained from a 10.3 year old healthy female rhesus macaque. In vivo MRI scans were performed on a Siemens 3T equipped with an 8-channel monkey head coil. Ex vivo MRI were conducted on a Bruker 7T using a 72mm volume coil. Both in vivo and ex vivo imaging protocols were harmonized, and optimized for experimental factors such as tissue fixation. Multi-shell diffusion MRI (dMRI) was acquired for structural connectivity analysis using constrained spherical deconvolution probabilistic tractography5. Complete 3D histological volumes were reconstructed from a stack of cell-body (Nissl) and myelin-stained (Gallyas) 2D microscopy sections (2x2 micron in plane, 40 micron slice thickness, 400 micron

Poster No 2196
Cytoarchitecture and brain-wide connectivity reveal topographic organization of insula networks

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interslice spacing) with optical-balancing to account for histological staining variations. All processed data were spatially aligned in a common in vivo reference space using an adapted image registration framework that was previously established for the human BigBrain project. The group level analysis was performed using matched protocols, preprocessing and analysis steps to the in vivo MicMac data. The 15 cytoarchitectonically-defined insula subregions were specified on the histological images, rendered in MicMac template space, and used as seed-regions for tractography to reconstruct the connections between these subregions with other cortical regions. For the group comparison, insula subregions were transformed to native space for each subject to perform tractography. The projection endpoints of tractography results are rendered on cortical surfaces defined by CIVET-Macaque.

Results: Results demonstrate correspondence of insula connectivity that aligns with macaque histological tract tracing studies and previous human structural and functional connectivity studies. The specificity of these projections, even for small subregions, was well-defined and occupied distinct patterns across the cortex. These results were repeatable for the in vivo cohort of n=16 adult macaques.

Fig. (Mic)ro-to-(Mac)ro Macaque: Aligned whole brain MRI and histology volumes are resampled in a template space to allow for analysis across scale and translation to group studies.

Conclusions: Mapping insula subregions and their connectivity throughout the brain is an important target in both humans and nonhuman primates. The MicMac workflow allows for the combination of noninvasive imaging with invasive histology markers that is impossible in humans. We demonstrated macaque insula subnetworks follow discrete organizational principles, and that the workflow shown here is translatable to a group level analysis.

References

Poster No 2197

White matter correlates of face recognition impairments in cerebral visual impairment

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Introduction: Children with early brain injury are at increased risk for cerebral visual impairment (CVI). CVI is a leading cause of pediatric visual impairment, with heterogeneous manifestations that may include impaired visual function (i.e., reduced visual acuity) and higher order visual perceptual dysfunctions. Previous research from our lab indicates that face recognition may also be impaired in those with CVI (Bauer et al., Vision 2023). However, the neural correlates remain unclear. In this work, we investigated the white matter structural changes of key white matter tracts associated with the ventral visual stream, specifically the optic radiations (OR), inferior longitudinal fasciculus (ILF), and the interior fronto-occipital fasciculus (IFOF). As a secondary analysis, we investigated the relationship between tract volume and face recognition impairments in individuals with CVI.

Methods: Multishell diffusion data (97 direction, b = 500, 1000, 2000, 3000 s/mm² was acquired for seven participants with CVI (22.5 years, 3.53 s.d., 3 females) and seven controls (20.67 years, 4.92 s.d, 4 females) on a 3T Phillips Ingenia Elition X. Preprocessing of diffusion data included top-up, brain extraction, motion, and eddy correction using FSL functions. Whole brain tractograms were reconstructed using MRTRIX3 default parameters (Tournier et al., 2019). Tract segmentation of individual tracts was done with TractSeg (Wasserthal et al., 2018), which segments white matter tracts using constrained spherical deconvolution (CSD) to extract three dominant diffusion directions in each voxel. Tract volumes were calculated and visualized in TrackVis. The face recognition task was completed by each of the seven CVI and a subset of the control participants (n=2) (Bauer et al., Vision, 2023). We used partial Spearman correlations to investigate the relationship between volume of the three tracts and performance on the face recognition task (threshold and proportion correct), while adjusting the potential effects of age. Bonferroni correction for multiple comparisons was used (critical p = 0.0042).

Results: Volume of the left ILF was significantly reduced in CVI compared to controls after adjusting for age and intracranial volume (F(2,13) = 14.13, p = 0.0032). Significant correlations were observed between threshold and volume of the right IFOF (r = -0.95, p = 0.0042), whereby smaller volumes were associated with worse performance (i.e., increased threshold). There was a trend for a negative relationship with volume of the left ILF (r = -0.96, p = 0.0059) and right OR (r = -0.90, p = 0.014), but these did not survive correction for multiple comparisons. Similarly, proportion correct was significantly correlated with volume of the right IFOF (r = 0.99, p = 0.0001), whereby smaller volumes were associated with fewer correct responses. Trends were observed for the left ILF (r = 0.93, p = 0.0072) and right OR (r = 0.84, p = 0.038), however these did not survive multiple comparisons correction.

Conclusions: These results indicate that there are specific changes in volume of key tracts involved with face processing in individuals with CVI. Further, these reduced volumes may be associated with impairments in face recognition frequently observed in this population. Additional analyses are warranted in a larger sample to verify the findings.

References
White matter integrity and peripheral inflammatory markers in obsessive-compulsive disorder

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Introduction: Diffusion-weighted imaging (DWI) is widely used to study white matter (WM) structural integrity in neuropsychiatric disorders. Despite the increasing number of DWI models and metrics, the most studied index of WM integrity continues to be fractional anisotropy (FA), which can be used as a proxy for WM fiber injury. Obsessive-compulsive disorder (OCD), a common and chronic neuropsychiatric disorder, has been extensively studied using DWI techniques. Indeed, DWI studies report widespread WM abnormalities mainly in the corpus callosum and the left inferior frontal gyrus. However, the pathophysiology of such WM structural changes in OCD is not clearly understood. In other conditions, abnormal DWI-derived indexes of WM integrity have been associated with increased concentration of inflammatory markers in peripheral blood, such as C Reactive Protein (CRP) and several cytokines. In OCD, inflammation may have a relevant role, given the well-known contributions of childhood adversity and early-life infections in the etiology and neurobiology of OCD. Here we tested if changes in WM integrity, as assessed with DWI, are associated with peripheral inflammatory markers in patients with OCD. Specifically, we aimed to 1) identify WM abnormalities in patients with OCD compared to healthy controls; and 2) test if these WM abnormalities are associated with CRP levels in peripheral blood.

Methods: Patients with OCD (n=70) and age- and sex-matched healthy controls (n=69) were assessed for sociodemographic and clinical variables. Participants underwent multisHELL DWI acquisition in a 3.0Tesla scanner. Diffusion data were preprocessed, and scalar maps of FA were estimated using DSI Studio. Additionally, a peripheral blood sample was collected from all participants, and serum was processed and stored. For aim 1, we used tract-based spatial statistics (TBSS) from FMRI Software Library to map between-groups FA differences in a group-derived skeleton. Voxel-wise significant differences were assessed with permutation-based (5000 permutations) two-sample t-test (one-tailed and α<0.05) with threshold-free cluster enhancement (TFCE), and voxels were labelled using the JHU ICBM-DTI-81 WM atlas. Mean FA values were extracted, for each participant, from clusters of voxels with significant group-differences and used for correlation analysis with clinical variables in patients with OCD, corrected for multiple comparisons. For aim 2, high sensitivity CRP (hsCRP) concentration was determined in serum using enzyme-linked immunosorbent assay. Mean FA values, as obtained in the previous aim, were used for correlation analysis with hsCRP. All statistical analyses were adjusted for age and sex.

Results: Patients with OCD had significantly lower FA in the corpus callosum, anterior corona radiata and superior corona radiata. Also, among patients, mean FA values were not significantly correlated with OCD symptom severity or depression symptoms. While patients with OCD and healthy controls did not differ in peripheral blood hsCRP concentration (z=0.2; p=0.9), mean FA values correlated negatively with hsCRP in patients with OCD (β-coefficient=-0.3; p=0.006) but not in healthy controls (β-coefficient=-0.1; p=0.6).

Conclusions: Our results confirm that patients with OCD have significant WM abnormalities compared to healthy controls, and that such changes do not correlate with disease-related clinical variables. Although we have found no differences regarding hsCRP between the two groups, this marker of immune function was negatively correlated with FA in those brain regions that showed WM abnormalities in patients. This raises the hypothesis that patients with OCD may have an innate or acquired vulnerability to the effects of peripheral inflammation in the WM structure.

References

Multiparametric Mapping of Superficial White Matter Architecture Using 7T Quantitative MRI

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Introduction: The superficial white matter (SWM) is a layer of white matter (WM) located immediately underneath the cortex. This SWM contains subcortical U-fibers interconnecting adjacent brain gyri, which remain incompletely myelinated until later in life (Parazzini, 2002). Due to the key role of U-fibers in brain plasticity and aging, alterations in their density are observed in various disorders (Zikopoulos, 2010; Liu, 2016). Particularly noteworthy is the report that this WM aspect is more advanced in humans compared to other mammals, making the SWM study an area of significant interest. Despite its importance, the SWM has been understudied, primarily due to technical difficulties and limitations (Kirilina, 2020). Recent advances in ultra-high field 7 Tesla magnetic resonance imaging (MRI) technology have enabled precise imaging and mapping of brain microstructure, leading to reliable research on the SWM. Specifically, quantitative MRI (qMRI) could unravel complex microstructural properties by measuring diffusion MRI parameters and by quantifying changes in myelin-sensitive contrasts. This study focuses on standardizing qMRIs on the SWM, validating the reliability of SWM mapping, and contributing to a more comprehensive understanding of its microstructural features.

Methods: This study utilized data acquired at the Montreal Neurological Institute on a 7T Siemens Terra system. The dataset included ten healthy participants with a mean±SD age of 26.8±4.61 years (5 females). For each MRI protocol parameters were as follows: (i) T1 relaxation time maps (T1 map) and T1-weighted images (MP2RAGE; 0.5mm isovoxels; TR=5170ms; TE=2.44ms; T1=1000ms; T12=3200ms), (ii) apparent diffusion coefficient (ADC) and fractional anisotropy (FA) derived from diffusion-weighted MRI (1.1mm isovoxels; TR=7383ms; TE=70.60ms; b-values=0, 300, 700, and 2,000 s/mm²; 10, 40, and 90 diffusion directions) (iii) Myelin-sensitive magnetization transfer (MT) ratio maps computed from gradient echo data with and without MT (0.7mm isovoxels; TR=95ms; TE=3.8ms, 50ms, shaped off-resonance MT pulse with a custom offset frequency of -2.0 kHz) MT saturation (MTsat) maps were generated using qMRLab based on MT and T1w images. (iv) iron-sensitive T2* relaxation time maps derived from multi-echo gradient echo (0.7mm isovoxels; TR=43ms, TEs=6.46-11.89-17.33-22.76-28.19-33.62ms). We preprocessed all MRI data using micapipe (Cruces, 2022). To examine the SWM, we solved the Laplace equation over the WM domain. This was achieved by initially computing a Laplace field across the WM and subsequently shifting an existing WM surface along that gradient. Stopping conditions were set by the geodesic distance traveled.

Results: SWM surfaces were sampled at six depths, each separated by 0.5 mm, beneath the gray and WM interface (Fig. 1A). The microstructure intensity profiles, depicting the intensity values of qMRI features, are presented in Fig. 1B. The matrix illustrates the subject mean value of the profile on each SWM surface, and this mean value was subsequently mapped onto the brain mask. This mapping allows for the examination of variations in qMRI feature intensity concerning alterations in SWM depth. Fig. 2A presents a matrix illustrating the average microstructure intensity profile across all SWM surfaces for each qMRI. The Spearman correlation coefficient between MTsat and FA intensity profiles was found to be the highest, and there were high negative correlation coefficients between T1 map and MTsat, as well as T1 map and FA. Fig. 2B demonstrates vertex-wise similarities among highly correlated qMRI pairs, showing high correlations for each feature pair across all SWM depths.

Figure 1. Depth-wise microstructural intensity variation in SWM construction. (A) SWM surface sampling. (B) Alterations in qMRI feature intensity according to the SWM depth.
Conclusions: In this study, we investigate the microstructural intensity profile of the SWM using 7T qMRI. By establishing quantitative relationships between qMRI features and standardizing microstructural profiles, our work will contribute to a deeper understanding of the SWM, potentially enhancing abnormal connectivity estimation.

References

Poster No 2200

Multi-modal, multi-scale imaging shows that long-association systems are made of short relay fibers

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Introduction: Obtaining accurate connectional neuroanatomy across scales and modalities ex vivo is crucial to inform the interpretation of in-vivo diffusion MRI (dMRI) findings and advance our understanding of brain circuitry. Here we combine data across multiple modalities, scales, and species to show that low spatial resolution may result in artifactual long-range connections. We focus on the dorsal superior longitudinal fasciculus (SLF-I), a major fiber association system running within the superior frontal gyrus (SFG). Tracing studies in monkeys describe the SLF-I as connecting the postero-medial parietal regions (PGm, PE, PEC) to different frontal regions (6D, 8B, 9). Due to the complexity of the SFG, with shorter, superficial fibers running parallel to longer, association fibers, the morphology of the human SLF-I remains controversial. Tractography and post-mortem dissections have yielded conflicting results, some supporting direct, long connections, and others supporting
shorter or no SLF-I fibers\textsuperscript{2,3}. Here, we combine multi-scale, multi-species, multi-modality data to investigate the mesoscopic organization within the SLF-I fiber system.

**Methods:** The datasets used in this work are presented in Figure 1A and acquisition details are listed below. Human data: 1) In vivo 1.5 mm dMRI: 3T, 2D EPI, 552 volumes (40 b=0, 64 b=1000, 64 b=3000; 128 b=5000; 256 b=10000 s/mm\textsuperscript{2})\textsuperscript{4}. 2) In vivo 760 μm dMRI: 3T, gSlider-SMS, 2808 volumes (144 b=0, 420 b=1000, 840 b=2500 s/mm\textsuperscript{2})\textsuperscript{5}. 3) Ex vivo 750 μm dMRI: 3T, 3D DW SSFP, 68 volumes (TR=30.21 ms, TE=25.12 ms, 8 b=0, 60 b=4,000 s/mm\textsuperscript{2}). 4) Ex vivo 250 μm dMRI: 4 small blocks (roughly 2x2x1cm) cut from dataset 3 (9.4T, 3D EPI, 515 volumes, TR=75ms, TE=43ms, max b=40,000 s/mm\textsuperscript{2}). 5) Ex vivo 10 μm polarization-sensitive optical coherence tomography (PS-OCT)\textsuperscript{6}. Macaque data: 6) Ex vivo 700 μm dMRI: 4.7T, 3D EPI, 514 volumes (max b=40,000 s/mm\textsuperscript{2}). 7) Tracer data: 3 male macaques received an injection in the frontal pole, in 9M, and in 6A (cases 1, 2, 3 respectively)\textsuperscript{7}. Pre-processing: All dMRI data were denoised and corrected for motion/eddy current distortions. For each dataset, fiber orientation distributions were estimated using constrained spherical deconvolution and connectivity matrices were generated in MRtrix3. PS-OCT data were processed as described in\textsuperscript{8} and tractography was performed using an in-house algorithm developed in Julia. Datasets 2, 3 and 6 were downsampling to 1.5 mm to investigate the effect of spatial resolution.

**Results:** Higher resolution tractography in humans (<750 μm) shows that the medial SFG white matter mainly comprises short-range connections that come in and out the cortex, rather than long-range direct connections as observed in in vivo lower resolution dMRI (Figure 1B, top row). Anatomic tracing and dMRI tractography in macaques support these findings, showing direct connections only between 6M and Pe/Pec and shorter relay fibers rostral to 6M (Figure 1B, bottom row). Most of the longer, direct connections between parietal and frontal regions course within the cingulum bundle (Figure 2B), in accordance with the literature\textsuperscript{9}. White-matter fibers originating in parietal regions and coursing within the SFG white matter mainly terminate in areas 4, 6, and 8B, as previously reported\textsuperscript{2}. The number of direct, long connections coursing within the SFG white matter is greater at 1.5 mm resolution than at higher resolutions (Figure 2C-D).
Conclusions: By comparing data across multiple modalities, scales, and species, we provide preliminary novel evidence that the SLF-I is composed of a succession of shorter relay fibers, which, in lower-resolution dMRI tractography result in a long, direct association bundle. These results point to the fact that each large white matter pathways like the SLF should not be thought of as monolithic structures, connecting a pair of remote cortical regions, but as conduits for connections between multiple pairs of regions.

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The impact of COVID-19 on the integrity of deep and superficial white matter bundles

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Introduction: The recent coronavirus disease (COVID-19) has significantly impacted public health, affecting not only the respiratory system but also other organs such as the brain [Spudich et al., 2022]. Studies have shown that recovered patients may experience neuropsychiatric alterations and thinning of certain cerebral cortex areas, especially those connected to the primary olfactory cortex. It has also been suggested that patients who have anosmia could present affection of orbitofrontal regions [Douaud et al., 2022]. This study aims to detect changes in the integrity of specific fiber bundles using two brain fiber atlases: the first composed of known deep white matter (DWM) bundles and the second composed of short association bundles of the superficial white matter (SWM).

Methods: A total of 101 subjects participated in this study: 72 patients recovered from COVID-19 and 29 healthy controls. Images were acquired with a 3T Siemens Skyra scanner. A diffusion-weighted scan sequence (DTI) was acquired (voxel size: 1.8x1.8x2.4 mm, slices: 64, b-value: 1000s/mm², directions: 70, FoV: 240mm, TR = 10.0s, TE = 95 ms). Fig. 1 shows a general outline of the processing pipeline to identify bundles with significant differences between groups. The DTI model was computed using DSI Studio software (http://dsi-studio.labsolver.org/), which extracted diffusion measures such as fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). Deterministic tractography algorithm [Yeh et al., 2013] was applied using the following parameters: angular threshold=60°, step size= 1mm, minimum length= 30mm, maximum length= 250mm, smoothing= 0.5, and QA threshold=0. The fiber segmentation was performed using both a DWM bundle atlas [Guevara et al., 2012], which consists of 36 known bundles, and a SWM bundle atlas [Román et al., 2022], composed of 525 short bundles, from which the 209 most stable bundles for deterministic tractography were selected. An automatic segmentation algorithm based on the maximum Euclidean distance between the corresponding points of two fibers was used [Vázquez et al., 2019]. For each segmented bundle, a binary mask was computed to calculate the average of each diffusion measure. Then, a t-test was computed to compare the patient and control groups, where statistical significance was considered when p-value<0.05.
Results: For the fiber segmentation, we used the predefined thresholds, between 6 and 8mm for SWM bundles and between 10 and 20mm for DWM bundles. After applying the t-test, 3 bundles with significant differences were found in some of the diffusion measures for the DWM atlas, and 29 bundles for the SWM atlas. Fig. 2 shows the bundles with significant differences between COVID-19 recovered subjects and controls. The AD is the diffusion measure that showed significant differences between groups in a greater number of bundles (DWM: 3 bundles, SWM: 21 bundles). To complement the quantification of differences between groups, the effect size was calculated using Cohen’s d. For the bundles with significant differences, an average Cohen’s d of 0.64 was obtained, while the average Cohen’s d considering all the bundles was 0.27.

Conclusions: In this study, the difference in bundle integrity between COVID-19 recovered subjects and controls who have not had the disease was analyzed. For this, metrics obtained from DTI in bundles of the DWM and SWM were compared. Among the known bundles of the DWM with significant differences are the fornix, thalamic radiations, and the corticospinal tract of the right hemisphere. In the case of the SWM bundles, the region that presented the highest number of bundles is the precentral region with 10 bundles. The bundles with significant differences between groups also showed a higher Cohen’s d compared to the other bundles. We aim to continue this study complementing it with functional magnetic resonance data to determine both structural and functional consequences due to the disease.
References

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Poster No 2202
Deep Learning Approach for Automated White Matter Fiber Bundle Segmentation
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Introduction: The segmentation of white matter (WM) tracts based on Diffusion magnetic resonance imaging, known as virtual dissection, is crucial for studying brain structural connectivity and analyzing neurodegenerative diseases (d’Albis et al., 2018), as well as planning brain surgeries to minimize harm (Essayed et al., 2017), among other applications. Manual segmentation, the gold standard, involves the selection regions of interest and fibers by an expert. This method is time-consuming and presents variability among experts (Rheault et al., 2022). Automatic WM bundle segmentation methods use anatomical information such as an anatomical atlas (Wassermann et al., 2016) or a WM bundle atlas (Guevara et al. 2012b) and, in general, can label massive tractography datasets quickly with reproducibly results. The method (Vázquez et al. 2019, Guevara et al., 2012b), uses centroids from a WM bundle atlas as reference fibers to identify those fibers from a new subject with a shape and location similar to the atlas fibers. This method has proven its efficacy in several clinical studies [Buyukturkoglu et al., 2022]. It uses a pairwise fiber distance, which is sensitive to differences in fiber shape and length that can lead to the loss of bundle fibers. In recent years, emerging deep learning methods based on autoencoder like FINTA (Legarreta et al., 2021), TractoFormer (Zhang et al., 2022) and GESTA (Legarreta et al., 2023) aim to enhance tractography data processing. But still, there is a research gap on applying these find of models for automatic WM bundle segmentation. We propose a new method based on a WM bundle atlas to process tractography data in the latent space of an autoencoder trained with a HARDI database.

Methods: Our method employs a convolutional autoencoder to project data into the latent space. We adopt the FINTA autoencoder structure (Legarreta et al., 2021) with minor modifications: replacing ReLU layers with Leaky ReLU layers for processing Talairach space data and increasing the latent space size from 32 to 128 values for better fiber description. The autoencoder was trained with 5 tractography datasets from the HARDI ARCHI database (Poupon et al., 2012), in Talairach space (~ 1 million fibers per subject). We used the Adam optimizer with a mean squared error loss. Hyperparameters were tuned using Bayesian search, with fixed values of learning rate of 2.88e-04 and a weight decay of 4.61e-05. For segmentation, we utilize a deep WM (DWM) bundle atlas (Guevara et al., 2012b) in Talairach space, composed of 36 fiber fascicles, transformed to the latent space. A radius neighbors classifier was trained with different search distances for each fascicle to identify the atlas bundles from new tractography datasets by comparing radial distance with reference data. The proposed segmentation method was applied to a clinical database of 37 male subjects, with 19 high-functioning Autism Spectrum Disorder (ASD) patients, and 18 controls (d’Albis et al., 2018). Mean WM microstructural measures (ADC, FA, and GFA) for each bundle served as input for an SVM classification algorithm (Fig. 1).
**Results:** To evaluate the proposed segmentation method (S2), the results were compared with the segmentation method (Vázquez et al., 2019) (S1). This comparison was conducted using the 37 subjects from the ASD database. The proposed segmentation algorithm (S2), on average, achieved a better recovery for most of the 36 fascicles compared to S1, and visually reveals a clear improvement in the coverage of segmentations, especially for the thalamic radiations as shown in Fig. 2a. Results from the classification of ASD show an improvement of the accuracy from 73% to 87%.

![Fig. 2 a) Segmented fiber for each fascicle of the left hemisphere. b) Visualization of the left hemisphere fascicle. c) Results for ASD classification using SVM over the WM microstructural features.](image-url)
Conclusions: The proposed algorithm improves the quality of WM bundle segmentation in terms of the number of fibers and coverage. Also, a positive impact of the methods was observed for the classification of patients with ASD. Future work will improve the method parameter setting and validation.

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Poster No 2203

The Development of White Matter Tract Functional Segregation during Adolescence

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Introduction: Due to the advancement of diffusion MRI technology, there are a large number of studies investigating the development of white matter (WM) microstructure during adolescence. However, limited by the unclear physiological significance of WM functional signals, few research has reported on WM functional development. In recent years, more and more studies have demonstrated that WM functional signals reflect the functional activity of specific tracts. In human brain functional connectomes, functional segregation is a fundamental organizational principles, which has been observed to strengthen with age in distinct cortical networks during adolescence. To understand the development of WM tracts functional segregation during adolescence, we characterized the normative development trajectories of functional segregation of WM tracts during adolescence by utilizing the HCP-D dataset and GAMLLSS model, and explore whether gender affects the development trajectories of different WM tracts.

Methods: 608 healthy subjects from HCP-development (HCP-D) datasets were included, including structural MRI and resting state fMRI (ages: 8-21). Data post-processing were performed by xcp_abcd. To quantify the segregation of WM tracts, we calculated a segregation index at WM tract-level. More specifically, the WM tracts were defined by the rICBM_DTI_81_WMPM_90p_FMRIB58 WM atlas. The segregation index was defined as (FCSw - FCSb) / FCSw, where FCSw (within-tract functional connectivity strength) was defined as the averaged FCS among all voxels within tract and FCSb (between-tract functional connectivity strength) was the averaged FCS between this tract and all other tracts. To estimate the normative age-dependent curves for functional segregation of tracts during adolescence, we implemented the GAMLLSS using gamlss package in R. Specifically, we constructed the GAMLLSS procedure with the segregation index as the dependent variable, age as a smooth term (B-spline basis function, df = 3), sex and mean frame displacement as other fixed effects, and Johnson’s SU (JSU) distribution as the data distribution. Finally, we added sex to form an interaction term with age to explore the sexual differences in development trajectories of functional segregation.

Results: After excluding tracts with less than 40 voxels and correcting for multiple comparisons, the segregation index of 27 tracts was found to be significantly correlated with age (FDR p < 0.05). Fig. 1A showed the averaged tract segregation value for each age group. The development trajectories and change rate of all the 27 tracts were characterized in Fig. 1B and 1D. After z-score normalization, we can find that the development trajectories present three different trends (Fig. 1E), that is (1) “decreased-increased-decreased” development pattern, (2) “U-shaped”development pattern, (3) continuing decreased
development pattern. However, in all the three development trajectories, the value of the segregation index was always greater than zero, indicating that between-tract functional connectivity was always stronger than within-tract functional connectivity. In addition, differentiated development of the WM functional segregation mainly appeared from 15 years old (Fig. 1F). Finally, sexual differences were not found in the functional segregation development trajectories of tracts (Fig. 2).

Conclusions: Our study revealed the development of WM tracts’ functional segregation with age in adolescence. Specifically, three different development trajectories were found and the differentiated development were mainly appeared in the ages of 15 to 20. Besides, there was no sexual differences in the development trajectory of tract functional segregation. These findings might provide new insights about the WM functional development.

References
Three-dimensional Subcortical Atlas of the Marmoset (“SAM”) based on MRI and histology

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Introduction: Despite its importance as a model for human brain development and neurological disorders, the marmoset lacks a comprehensive MRI-histology-based parcellation and 3D atlas of brain areas. Here, we first generated a Subcortical Atlas of the Marmoset, called the SAM, from 251 delineated subcortical regions derived from the ex vivo high-resolution multimodal MRIs¹² and matched histology with multiple stains derived from the same brain specimen. Tracing and validating atlas-based brain regions is imperative for neurosurgical planning, anatomical tract tracer injections, deep brain stimulation probes navigation, functional imaging (fMRI) studies, and establishing brain structure-function relationships.

Methods: We scanned one adult male perfusion-fixed marmoset brain on a 7T scanner using MAP-MRI with 150 μm resolution. We acquired 256 diffusion-weighted images with multiple b-values (bmax=10000s/mm²), pulse duration δ=6 ms, and diffusion time Δ=28 ms. In each voxel, we estimated the MAP and computed microstructural DTI/MAP parameters: fractional anisotropy (FA); mean, axial, and radial diffusivities (MD, AD, and RD, respectively); propagator anisotropy (PA), non-gaussianity (NG), return-to-origin probability (RTOP), return-to-axis probability (RTAP), and return-to-plane probability (RTPP), along with the fiber orientation distribution functions (fODFs)³. The MT ratio (MTR) was computed from images acquired with and without MT preparation. Following MRI acquisition, we prepared the brain specimens for histological processing with five different stains⁴⁵. An alternating series of 50 μm thick coronal sections were processed with Nissl, Acetylcholinesterase, or immunohistochemically with antibodies against parvalbumin, neurofilament protein, and choline acetyltransferase. The high-resolution images of these stained sections were manually registered to corresponding maps of MRI volumes to allow analysis in histologically defined subcortical regions.

Results: Using a combined ex vivo MAP-MRI with direction encoded color (DEC) map⁶ derived from the fiber orientation distribution (FOD) functions and histology, we identified and segmented 211 gray matter subregions in the deep brain structures, including the basal ganglia, thalamus, hypothalamus, brainstem (midbrain, pons, and medulla), amygdala, bed nucleus of stria terminalis, and the basal forebrain. In addition, we also distinguished and segmented 40 fiber tracts of different sizes and orientations associated with the basal ganglia, thalamus, brainstem, and cerebellum. The examples in Figure 1 illustrate the subcortical gray and white matter regions in MAP-MRI (DEC-FOD) that are segmented with reference to matched histological sections for the 3D atlas. This newly segmented volume is called ex vivo “SAM,” or the Subcortical Atlas of the Marmoset. The SAM atlas in Figure 2 shows the segmented subcortical regions on the 2D coronal, axial, and sagittal MRI and in 3D. This new digital atlas provides a practical standard template for neuroanatomical, functional (fMRI), clinical, and connectional imaging studies. The ex vivo digital template atlas is available as volume and surfaces in standard NIFTI and GIFTI formats. We estimated, confirmed, and validated the atlas-based areal boundaries of subcortical areas by registering this ex vivo atlas template to in vivo T1W MRI datasets of different age groups (single vs. multisubject population-based marmoset control adults) using a novel pipeline developed within AFNI and SUMA. These results demonstrate that affine and nonlinear warpings are sufficient to distinguish and provide atlas-based estimates of areal boundaries of marmoset subjects in vivo.

Conclusions: The combined multimodal MRI and histology enabled detailed noninvasive segmentation of gray and white matter regions and the generation of a 3D digital template atlas. This comprehensive MRI/histology-based atlas provides a readily usable standard for region definition for the marmoset brain.
ABSTRACTS

Fig. 1 Subcortical areas for the 3D atlas (SAM). Examples showing the basal ganglia, thalamus, hypothalamus, brainstem (pons), and basal forebrain that are identified and segmented on the MAP-MRI (DEC-FOD) with reference to matched histological sections stained with ChAT and SMI-32 (A-F). abbreviations: Avl-olfactory ventricle; 6th-olivary nucleus; 7th-facial nerve; 8th-acoustic ventricle; 8th-vestibule/semicircular nucleus; 9th-vestibule nerve; ac-anterior commissure; AM-anterior medial nucleus; Avc-arcuate hypothalamic nucleus; AV-anterior ventral nucleus; BST-bed nucleus of the accumbens; CB-corticothalamic tract; CC-corpus callosum; cl-amygdaloid nucleus; cla-claustro-nucleus; ist-internal capsule; MTT-corpus callosum; MS-medial septal nucleus; NBM-nucleus basalis of Meynert; ntr-nucleus raphe magnus; ntu-nucleus raphe obscurus; np nucleus raphe pallidus; oto-optic tract; Po-paraventricular nucleus; PPA-preoptic area; pr-preoptic nucleus; rPOA-posterior optic nucleus; RFc-refolution nucleus; VAmc-ventral anterior nucleus; VAmv-ventromedial nucleus; VMp-ventral posterior nucleus; VPL-ventral lateral nucleus; VPLv-ventral lateral ventral nucleus; SMI-32-32° anterior mean line (AML). Scale bar: 1.5 mm applies to A-F.
References


Poster No 2205

Personalized Functional Networks in ABCD Children: Linking Topography with Socioeconomic Status

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Introduction: Convergent evidence has demonstrated that there is remarkable inter-individual variability in the spatial topography of functional networks, even after alignment of brain structure (Wang, Buckner et al. 2015, Gordon, Laumann et al. 2017, Kong, Li et al. 2019, Cui, Li et al. 2020). More importantly, the variability of functional topography subserves higher-order executive functions and confers to diverse psychopathologies (Sydnor, Larsen et al. 2021, Tooley, Bassett et al. 2021). If individual differences are not accounted for, the estimation of topographic variations could be aliased into between-network connectivity, potentially biasing both inference and interpretation. Here, based on a larger-scale cohort, the adolescent brain cognitive development (ABCD) study (Volkow, Koob et al. 2018), we aim to delineated 17 personalized functional networks for ABCD children to accelerate the understanding of personalized functional topography with diverse environmental, cognitive, and psychopathological factors.

Methods: We delineated personalized functional topography for 3921 ABCD participants (9 and 10-year-olds) who had high-quality resting-state fMRI data with at least 20 minutes. Using an advanced machine learning technique, spatially regularized non-negative matrix factorization (NMF) (Li, Satterthwaite et al. 2017), we parcellated the cortex into 17 functional networks for each ABCD child based on their own fMRI data. As an exemplary usage, we further examining how individual variation in cortical structure of functional networks was related to childhood socioeconomic status (SES). We used partial least square regression (PLS-R) and nested two-fold cross validation (2F-CV) to evaluate whether the multivariate pattern of functional topography could be used to predict unseen individuals’ SES.

Results: We parcellated the cortex into 17 networks based on previous studies (Yeo, Krienen et al. 2011, Kong, Li et al. 2019, Cui, Li et al. 2020) for each ABCD child and publicly shared this resource (https://zenodo.org/records/10200111). By comparing the overlap with priori canonical functional atlases (Yeo, Krienen et al. 2011, Cui, Li et al. 2020), our networks were named as two visual, three somatomotor, one auditory, three dorsal attention, one ventral attention, two fronto-parietal, three default mode, one temporal-parietal, and one limbic networks (Figure 1). These networks exhibited distinct spatial topography across individuals (Figure 2A), with maximum variability in higher-order association networks and lowest in sensorimotor networks, which is consistent with prior studies in adults (Wang, Buckner et al. 2015, Gordon, Laumann et al. 2017) and youths (Cui, Li et al. 2020) (Figure 2B). Compelling evidence suggest that lower SES in childhood impacts brain development and potentially increases risks for mental disorders (Luciana, Barch et al. 2023, Sydnor, Larsen et al. 2023). Therefore, we also evaluated brain-wide association between the multivariate pattern of functional topography with individuals’ SES. For 3,198 participants who have complete SES measures, we employed PLS-R and 2F-CV to predict individual’s SES and found that the personalized brain networks could significantly predict unseen individuals’ SES (median Pearson’s r=0.26, permutation p<0.001, Figure 2C). By examining the total contribution weights of each cortical vertex, we observed that the occipital-temporal, parietal, and prefrontal areas contributed most to the prediction (Figure 2E), and these multivariate patterns of feature weights were constrained by individual topographic variability (Spearman correlation, r=0.45, spin test p<0.001)(Figure 2F).
ABSTRACTS

Figure 1. Group atlas of 17 functional networks in ABCD children
The networks in the group atlas include two visual (3 and 9), one auditory (2), three somatomotor (10, 15, and 16), one ventral attention (13), three dorsal attention (5, 7, 17), one tempo-parietal (11), three default mode (4, 8, 11), one limbic (12), and two fronto-parietal networks (1, 14).
In this atlas, there are 17 loadings for each vertex that quantify the extent to which the vertex belongs to each network. Brighter colors indicate greater loadings. Discrete network parcellation (left upper side) was acquired by assigning a vertex to the network with the highest loading.

Figure 2. Personalized functional topography is associated with individual differences in SES
A. Vertex-level individual variability of functional network topography is maximum in the higher-order association cortex, including prefrontal and occipito-temporal cortices.
B. By ordering the median of network-level individual variability across the 17 networks based on the probabilistic atlas, a larger variability in the association networks and a lower variability in somatomotor networks were confirmed.
C. The multivariate pattern of functional network topography significantly predicted unseen individuals’ SES. Data was split into two halves, and a full 2-fold cross-validation (2F-CV) was applied. This process was repeated 101 times. The distribution of the 101 prediction accuracies was displayed. A permutation testing (1,000 times) that shuffles the order of participants in the training set indicates that the prediction accuracies were significant.
D. The screeplot of 2F-CV with the median prediction accuracy across the 101 repetitions. Data points depict the predicted SES in a model trained on independent data. Average prediction accuracy of two folds is displayed.
E. Summing the absolute contribution weights for each cortical vertex indicates that regions in the prefrontal, parietal, and occipito-temporal cortices contributed most to the SES prediction.
F. The cortical contribution map in panel E is hierarchically organized along the axis of vertex-level individual variability of functional network topography.
**Conclusions:** Overall, our results provide an open resource to improve the exploration of brain function for basic and clinical research that accounts for individual difference in functional network topography, with SES as an example to offer a potential explanation for how environmental factors impacts on later-life outcomes.

**References**

**Poster No 2206**

**Heterogeneous domain adaptation of connectomes across atlases using optimal transport**

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**Introduction:** Brain parcellations are crucial for analyzing fMRI and DWI datasets, reducing dimensionality, noise, and enhancing interpretability. Connectomes built from preprocessed parcellated data are the standard for data sharing in neuroimaging research. However, the lack of standardized brain atlases limits comparability and data aggregation across studies. In this paper, we propose a method using optimal transport to map between atlas domains and transform connectomes across domains.

**Methods:** We employ optimal transport to map between two domains. For fMRI data, we calculate transportation matrices for parcel-wise signals from two atlases, yielding the functional mapping through averaging across all time points and subjects\(^1\). For structural connectomes, we use a graph-matching method to minimize the Gromov-Wasserstein discrepancy\(^2\) and learn a transportation matrix, which is then averaged across all subjects. With the established mapping, we transform connectomes from the source to the target domain in three steps: 1. Decompose the connectome into its node representation. 2. Map this representation to the target domain. 3. Estimate the connectome in the target domain as the product of the transformed node representation. In our experiments, we employed five atlases (Shen\(^3\), Craddock\(^4\), Brainnetome\(^5\), Dosenbach\(^6\), and Schaefer\(^7\)). Functional mapping was learned from the Yale dataset\(^8\), while structural mapping was learned from the HCP datasets\(^9\). We assessed method accuracy by evaluating functional connectomes in the HCP dataset and structural connectomes in the HCP-D dataset, using Pearson’s correlation between the estimated connectomes and the “ground-truth” structural connectomes as the metric. To validate our domain adaptation approach, we applied it to predictive modeling tasks for fluid intelligence and age in cross-validation. The training and testing sets included connectomes from different atlases, with data in the training set transformed into the testing set’s domain for modeling. This process was repeated 100 times, and predictive performance was assessed using Pearson’s correlation between true and predicted values.

**Results:** Figure 1a illustrates the precision of connectome estimation. In most scenarios, we observe notable correlations between the transformed connectome and its corresponding target connectome for both functional and structural mapping. These correlations provide insights into the degree of similarity or overlap between atlases. Particularly, when transforming data from the Shen atlas to the Craddock atlas, we observe high correlations ($r = 0.744$ for FC and $r = 0.692$ for SC), as both atlases are derived from clustering time series using variations of the N-cut algorithm. In contrast, the correlation between data transformed from the Dosenbach atlas, constructed based on task activation analysis, and other atlases is significantly lower. Figure 1b displays the predictive performance, with diagonal values representing results using “ground-truth” data. Notably, predictive performance aligns closely with estimation accuracy, indicating that connectomes estimated with higher precision also yield better predictive performance. It’s worth noting that functional mapping demonstrates superior performance on both functional and structural data.
Conclusions: We devised a heterogeneous domain adaptation technique that utilizes optimal transport and matrix factorization to facilitate connectome transformation across different atlases. Our approach yielded substantial correlations between the estimated data and ground truth data, particularly when the atlases exhibited relatively high similarity. Furthermore, we found that predictive performance remained largely consistent when the estimation accuracy was high. Functional mapping, which leverages data from multiple timepoints, outperformed structural mapping. In cases where timeseries data was unavailable, structural mapping provided a viable alternative.

Fig 1. a) Correlation of estimated connectome and ground-truth connectomes between atlases. b) Predictive performance of models trained on ground-truth data (diagonal) and transformed data.

References

Poster No 2207
A human brain atlas of χ-separation (chi-separation) for normative iron and myelin distributions
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Introduction: Alterations in iron and myelin distribution in the human brain are associated with neurogenerative diseases such as Alzheimer’s disease, Parkinson’s disease, and multiple sclerosis (Möller, 2019). The imaging of paramagnetic iron and diamagnetic myelin can be achieved with magnetic resonance imaging (MRI) by quantitative susceptibility mapping (QSM) (de Rochefort, 2008). However, when iron and myelin are co-localized in a voxel, their contributions to QSM contrast are hardly separable. This limitation can be resolved with a susceptibility source separation method, χ-separation (chi-separation) (Shin, 2021), which utilizes phase and R2’ (or R2∗) to create para- and diamagnetic susceptibility (χpara and χdia) maps. In this...
study, we created a brain atlas of χ-separation from 106 healthy human brains as a reference for utilizing χ-separation in the neuroimaging field (https://github.com/SNU-LIST/chi-separation-atlas).

**Methods:** 106 healthy human volunteers (27-85 years old) were recruited from two hospitals and scanned using 3 T MRI (Ingenia CX or Ingenia Elition X) with multi-echo gradient-echo and magnetization-prepared rapid gradient-echo (MPRAGE) sequences. Fig. 1 shows the workflow for atlas construction. The phases of multi-echo gradient-echo images were combined (Wu, 2012) and unwrapped (Schofield, 2003). The background field was removed to generate a tissue field map. A R2* map was generated from the magnitudes of multi-echo gradient-echo images. χ\text{para} and χ\text{dia} maps were acquired with χ-sepnet (Kim, 2022) utilizing the tissue field and R2* maps as inputs. A QSM map was calculated by summing the χ\text{para} and χ\text{dia} maps. The QSM map and T1-weighted image were linearly combined to generate a hybrid image, which was nonlinearly registered (Avants, 2008) to the hybrid image atlas from MuSus-100 (He, 2023) in the MNI space. Using the resulting deformation field, the χ\text{para} and χ\text{dia} maps were registered to the MNI space. These maps were averaged across subjects to create a χ-separation atlas. The inter-subject variability of the atlas was evaluated by a relative standard deviation (rSD) map, which is standard deviation divided by mean. To conduct regions of interest (ROI)-based analysis on the χ-separation atlas, eight subcortical nuclei and three thalamic nuclei labels from MuSus-100 (He, 2023), twenty-eight white matter labels from ICBM-DTI-81 (Oishi, 2008), and a whole white matter ROI generated via intensity-based segmentation (Avants, 2011) were employed. The median χ\text{para}, χ\text{dia}, and QSM in ROIs were averaged across subjects and the population means and standard deviations were reported.

**Results:** In Fig. 2, representative slices of χ\text{para} atlas exhibit high values in iron-rich nuclei in basal ganglia, thalamus, and midbrain, while white matter fibers such as corpus callosum are clearly depicted as high |χ\text{dia}| value. The slices provide a comprehensive view in our χ-separation atlas, visualizing anatomical structures associated with iron and myelin distributions.
When the normative profile of $\chi_{\text{para}}$ and $\chi_{\text{dia}}$ across subcortical nuclei, thalamus, and white matter were examined, high $\chi_{\text{para}}$ values (45–145 ppb) are observed in subcortical nuclei and pulvinar, while white matter shows $\chi_{\text{para}}$ of 10–30 ppb. Contrarily, white matter shows high $|\chi_{\text{dia}}|$ of 25–50 ppb, while it is 10–25 ppb in subcortical and thalamic nuclei. In thalamus, nearly same levels of $\chi_{\text{para}}$ and $|\chi_{\text{dia}}|$ are observed in lateral thalamic nuclei.

**Fig. 2.** Ten axial slices of the $\chi_{\text{para}}$ and $\chi_{\text{dia}}$ atlases. Anatomical structures are marked with red dotted lines.

**Conclusions:** The $\chi$-separation atlas demonstrates exquisite details of anatomical structures associated with iron and myelin distribution. Moreover, it provides normative ranges of $\chi_{\text{para}}$ and $\chi_{\text{dia}}$ in the brain across subcortical nuclei, thalamic nuclei, and white matter fibers. Beyond its application in research, our atlas may be utilized in treatments targeting deep brain structures such as deep brain stimulation or high-power focused ultrasound.

**References**

Poster No 2208

An atlas of the functional specialization of the human brain’s white matter

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Introduction: Cognitive functions such as memory, attention and language are critical for our survival and success as a species. They rely on cortical networks connected by bundles of axons (i.e., white matter) which, when disconnected, can lead to different disorders. While tremendous progress in our anatomical description of white matter has been achieved in the last 20 years¹, the relationship between brain connections and the emergence of cognitive functions remains elusive. This proposal aims to unveil the functional specialization of the white matter in the brain in a data-driven way².

Methods: The data for 110 participants were derived from the HCP 7T release. This dataset comprises alternate fMRI sessions of resting and video-watching that have already undergone preprocessing and registration to the MNI152 reference space. The dataset was divided into two groups of 55 subjects each, with the first group designated as the discovery group and the second group as the replication group. The functionnectome method applied to naturalistic videos: Throughout each session, the variation in the activation for each participant and voxel over time was z-normalized. We estimated the contribution of the associative tracts of the white matter circuits to the cortical variation during the video-watching, by projecting the data onto a recently developed method called functionnectome (i.e., functionnectome time series)³. The functionnectome is generated by projecting the fMRI signal from grey matter voxels to the white matter and weighting the signal by the probability of structural connectivity between each grey matter voxel and the rest of the brain. Subsequently, for each group, each time point of the functionnectome time series underwent a one-sample t-test to reveal the significant variation of each voxel in the brain in response to the videos. White matter parcellation based on the functional organization: The profiles of the time course variation for each brain voxel were entered into a Uniform Manifold Approximation and Projection (UMAP) embedding design, where voxels with similar covariation clustered together, and voxels with different profiles were placed farther apart. Finally, clusters in that space were identified using the HDBscan clustering algorithm. Different parameters for the HDBscan clustering algorithm were evaluated, and we selected the algorithm with the highest Density Based Cluster Validity (DBCV;⁴) and projected it back onto the brain to provide the first division of white matter based on functional activations. Validation of the results: The UMAP analysis was also computed in the replication group. We computed the Euclidean distance matrix between 1000 random values in the UMAPs of the discovery and replication groups⁵. We calculated the Pearson correlation coefficient between these two distance matrices to validate the UMAP reproducibility.

Results: The UMAP analysis was replicated in the replication group, demonstrating consistency in the distribution of data points (see Figure 1). The Pearson correlation coefficient, quantifying the similarity in Euclidean distance between UMAP embeddings in both groups, was 0.98. The highest DBCV for the HDBscan clustering algorithms was 0.36 (see Figure 2A). This analysis yielded a robust parcellation comprising 83 parcels, covering a substantial 64% of the white matter voxels (see Figure 2B). These findings underscore the reproducibility of our UMAP design between groups, providing a reliable foundation for interpreting and generalizing the identified white matter functional organizations.

![Figure 1. Visualization of data into the two dimensional UMAP embedding. UMAP plots illustrating the distribution of data points for the discovery group (left), replication group (middle), and randomized data of the discovery group (right). Each point represents a voxel, and the UMAP algorithm is used for dimensionality reduction to visualize the underlying patterns in the data during naturalistic video-watching.](image)
Conclusions: By combining fMRI functional signals with white matter circuit anatomy, we linked brain activation to the structure of neural connections. This innovative methodology enabled us to create a comprehensive white matter parcellation tuned to brain activations and, accordingly, functional specialization.

References

Poster No 2209

Anatomical Connectivity Profile Development Constrains Medial-lateral Topography in the dIPFC

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Introduction: The prefrontal cortex (PFC) is a highly variable, evolutionarily expanded brain region that is engaged in multiple cognitive processes1-2. The subregions of the PFC mature relatively late compared with other brain regions3, and the maturation times vary between these subregions. Among these, the dorsomedial and dorsolateral prefrontal cortex (dmPFC and dIPFC) share a parallel topographic pattern of functional connectivity while participating in different types of complex behaviors4. However, the developmental trajectories of the two areas remain obscure. In this study, we uncovered differences in the developmental trends of the dmPFC and dIPFC. These differences were mainly caused by structural and functional changes in the medial area of the superior frontal gyrus (SFG). The developmentally different arealization patterns were verified using multiple parcellation approaches with multimodal data and a publicly available transcriptomic dataset. Human brain gene expression data was also used to perform downstream analyses, which could inform us about the potential biological mechanisms underlying the developmentally different arealizations. Furthermore, behavioral analyses hinted at the effects of regionalization on ontogeny. In brief, this study revealed a tendency toward a medial-lateral prefrontal division and can provide a fuller understanding of the potential underlying genetic underpinnings as well as of the potential effects on developmental behavior.

Methods: The data used in this article were from HCP-D5 and IMAGEN6. After preprocessing, the dMRI data were used for the parcellation, and multimodal data were used to verify the appropriate patterns (Fig. 1A). Differential gene analysis and gene
enrichment analysis were performed to further explore whether subregion division is associated with genetic mechanism and to discover its biological fundamentals (Fig. 1B). The relationship between gene expression and connections was explored using PLS regression (Fig. 1C). Finally, how the functional connections affect behavior was also investigated (Fig. 1D). The detailed description is as follows.

Figure 1. Summary of the analysis flowchart.

**Results:** Childhood and adolescence are two periods with extensive cortical maturation in the PFC, causing cortical patterning to be substantially dynamic across the developmental stages and shaped by the interplay of intrinsic and extrinsic mechanisms. In the present study, we delineated the human cortical parcellation trajectory of the SFG based on anatomical connectivity profiles. Specifically, we found that the A9 region separated into medial and lateral subregions with the advent of adulthood (Fig. 2A), as validated by several cohorts with multi-modal data that included cortical thickness, functional connectivity patterns, cytoarchitectonic maps, and transcriptional profiles. This separation revealed by connectivity contrasts may occur gradually with age, reaching a specific boundary at the transition from adolescence to young adulthood (Fig. 2B). Accordingly, we found that the differential gene expression patterns between the areas that showed a tendency to segregate originated in toddlers and widened increasingly distinctly during adolescence (Fig. 2C). These changes may be involved in the process of medial-lateral differentiation in the dorsal PFC (Fig. 2D). In addition, the transformation of connectivity patterns appears to influence development and behavior that is mostly concerned with a young person’s persistence and the degree to which they show non-impulsiveness (Fig. 2E).
Conclusions: In this study, we provided a detailed version of a developmental atlas that depicts the changes in the arealization pattern of the frontal lobe and focused on the different developmental trajectories for the dorsomedial and dorsolateral prefrontal cortices, which are mediated by genetically constrained structural and functional connectivity patterns and should have an impact on changes in children’s behavior.

References

Poster No 2210
Interconnections within the rrAD420 Functional Network Atlas for Older Adults
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Introduction: Risk Reduction for Alzheimer’s Disease (rrAD) is a recently completed randomized clinical trial designed to investigate effects of improved cardiovascular health on neurocognitive function, brain structure, and brain network functional connectivity (Szabo-Reed et al., 2019). rrAD enrolled 513 hypertensive older adults (60 to 84 years, 68.8±5.9) who had a family
history of dementia or subjective cognitive decline. Study participants underwent aerobic exercise training and/or intensive pharmacological interventions for 2 years. Of 513 participants, 420 completed anatomical and resting-state functional MRI (rs-fMRI) scans at baseline and after 2-years of interventions. MRI scans were performed on 5 different 3T scanners. Most of the currently used rs-fMRI atlases are based on young and healthy subjects which may not be applicable in older adults who had brain atrophy and/or changes in brain resting-state network (RSN) connectivity. The aim of this study was to use the rrAD baseline rs-fMRI data to create a robust rs-fMRI atlas, which is suitable for studying older adults, without the limitation of spatial independence, and allowing for spatially overlapping temporal configurations (modes) to facilitate the investigation of functional interconnections of RSNs.

**Methods:** Data acquisition protocols on all five 3T scanners were harmonized to ensure comparability across sites. Using SPM12’s DARTEL registration we created a cohort-specific MNI-adjacent anatomical template space, namely rrAD420. The fMRI data were preprocessed using slice-timing correction, T1 co-registration and motion correction, spatial blurring of 4mm, aggressive ICA-AROMA, and normalization into the rrAD420 space. Details on scanning and preprocessing parameters were presented in Scheel et al., 2022. After extensive manual quality assessment and control, we used a data-driven probabilistic functional mode decomposition (PROFUMO) approach (Farahibozorg et al., 2021; Harrison et al., 2015) to create a rs-fMRI atlas that includes different modes of major networks. With sampling multiple dimensions (30, 50, and 80) for the PROFUMO decomposition, we assessed RSN representation, splitting, grouping, reproducibility, and identifiability, through cross-referencing with diverse brain atlases and functional parcellations (Damoiseaux et al., 2006; Yeo et al., 2011; Shirer et al., 2012; Pruim et al., 2015), to determine which decomposition provides the best overall RSN fit.

**Results:** For network representation, we found that all PROFUMO decompositions captured the RSNs of the reference functional atlases. However, the 50-mode parcellation ranked highest for RSN splitting and grouping metrics. For the 50-dimensional PROFUMO, we found 42 functional modes attributed to neural activity and 8 components attributed to noise. Following consensus on RSN taxonomy (Uddin et al., 2023), we grouped the resulting 42 modes into 13 singular networks and 6 combinatory networks, and sorted these by their reproducibility (see Table 1).

**Conclusions:** Using PROFUMO decomposition, we created a rs-fMRI network atlas specifically for an older population. Additionally, we subdivided these networks into spatiotemporally overlapping modes, providing more insight into the temporal organization of resting-state networks in older subjects. The resulting combinatory networks of the salience and attention, as well as the language and default modes (see Figure 1), are especially interesting as they are consistent with recent findings (Gordon et al., 2020). Thus, this new atlas may be able to give more nuanced insights into cognitive processes leading to cognitive decline, previously difficult to disentangle using common Independent Component Analysis (ICA) approaches. We expect that the rrAD420 rs-fMRI atlas will be applicable to study the rs-fMRI connectivity and cognition of older populations in general, which could lead to more reliable biomarker development and implementation.
**References**


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**Poster No 2211**

**A High-Resolution In Vivo Atlas of the Human Brain’s Cyclooxygenase-2 (COX-2) System**

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**Introduction:** Cyclooxygenase-2 (COX-2) is one of the main enzymes activated by inflammatory stimuli and is a key target for anti-inflammatory drugs1. Here, we present a quantitative high-resolution in vivo atlas of the spatial distribution of COX-2 in the healthy human brain, obtained using Positron Emission Tomography (PET) data. The atlas will be made publicly available to the community as part of the OpenNeuroPET project (https://openneuropet.github.io/).

**Methods:** Twenty-seven healthy participants (12 males, 15 females; mean age: 36±10.36 years, range: 22-56) were scanned using a Siemens Biograph mCT PET scanner 120 min after a bolus injection of the radioligand [11C]MC1. Arterial sampling
was done to determine the input function. Ten of the participants also had a blocking scan to determine levels of receptor occupancy and non-displaceable distribution volume (VND). An isotropic 3D T1-weighted MRI was acquired for all participants using a Philips Achieva 3T MRI-scanner. The PET data were head motion corrected using the BIDS application PETPrep_hmc (v.0.0.7). The MR data were processed using FreeSurfer (v.7.4.1) and co-registered to the PET data using a rigid transformation and a normalized mutual information cost function. The PET data were quantified to estimate total distribution volume (VT) for each region using Logan graphical analysis in PETSurfer and the radiometabolite-corrected plasma curve as input function estimated via the bloodstream BIDS application. Occupancy and VND were estimated using the Lassen plot, from which the specific distribution volume (VS) was calculated. Parametric images of distribution volumes VT and VS were created in the MNI152 (CVS volume space from FreeSurfer) as well as in surface space (fsaverage), smoothed with a 6 mm and 10 mm smoothing kernel in the volume and surface, respectively.

Results: The main outcome of this work is the generation of a brain atlas of the COX-2 VT and VS (Figure 1). The regional VT estimates ranged from 1.05 to 3.43 mL/cm³ across participants and scans (average = 2.14 ± 0.4 mL/cm³) and were mostly expressed in the cortex (Figure 2). VS estimates (VS = VT - VND) were generally low in subcortical regions (Figure 2), whereas measures in cortical regions largely ranged between 0.25-0.75 mL/cm³. The estimated average occupancy across participants from the baseline-blocking condition was 72 ± 17% (range: 37% - 89%), and the average VND was 1.81 ± 0.15 mL/cm³ (range: 1.64 - 2.1 mL/cm³).

Conclusions: This quantitative in vivo brain atlas of the spatial organization of COX-2 distribution volumes in the healthy human brain provides a valuable tool for investigating the COX system; in particular, the atlas can be used as a reference to
patient groups with alterations in their inflammatory system or to understand the effects of pharmacological interventions that act on the COX-2 system.

References

Poster No 2212
A high definition anatomical brain template of one individual healthy subject
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Introduction: Brain templates aggregate averaged features across subjects in a normalized stereotactic space and are critical to formalize prior knowledge in neuroimaging analyses1. The most widespread templates have been developed by the Montreal Neurological Institute (MNI), yielding a number of templates referred to with the umbrella term of “MNI space”2. Recently, some attention shifted towards emphasizing depth rather than width in datasets with few subjects that have many images3. Such “dense sampling” protocols, coupled with modern neuroimaging tools, are effective at enhancing image resolution and provide more accurate surfaces4. With this in mind, we propose a high-definition template of a single healthy brain built from 70 MR images with multimodal registration.
Methods: 35 T1-weighted (T1w) and 35 T2-weighted (T2w) anatomical brain images of one individual healthy male (aged 40) were retrieved from the Human Connectome Phantom (HCPH) dataset, an ongoing Stage 1 Registered Report5. MRI scans were acquired on a 3T Siemens Magnetom PrismaFit. T1w images were acquired with a magnetization-prepared rapid acquisition gradient echo (MPRAGE) sequence with isotropic voxel size of 0.8x0.8x0.8 [mm3], TR=2.2s, TE=2.55ms, FA=8°. T2w images were acquired at the same spatial resolution with a Sampling Perfection with Application optimized Contrast (T2-SPACE), TR=3.2s, TE=413ms. The images were first corrected for distortion within the internal processing of the scanner (3D distortion correction). Then, correction for intensity non-uniformity and denoising were applied using N4BiasFieldCorrection6 and DenoiseImage7 from ANTs. Finally, the intensity of white matter voxels was normalized to values around a value of 110 using mri_normalize from FreeSurfer8. The template was estimated in a multivariate (T1w and T2w) approach using antsMultivariateTemplateConstruction2.sh script from ANTs9. To first create an initial template, all images are averaged to create a reference and each individual image is then registered to this reference using a rigid body transformation. Then, the initial template is refined in an iterative process where each image is registered to the template using affine transformations to maximize cross-correlation. An alternative, high-dimension template has been computed by creating a 3D grid of 504x576x384 voxels of size 0.4x0.4x0.4 [mm3] and projecting the center of each voxel to the individual maps for interpolation. The distance between the projected grid coordinates and the nearest image voxel was used as interpolation weight. The HCPH dataset will be publicly released at the end of Stage 2 of the corresponding registered report. In addition, the template and individual images will be released. The code used for template generation is publicly available at https://github.com/acionca/hcp-template.
Results: A high-SNR, multivariate template of a single-human brain’s anatomy. The template shows sharp boundaries between the different brain tissue and high definition of cortical structures. Furthermore, SNR within the whole brain, the white matter and the gray matter is increased when compared to the original images. Precise single-subject brain parcellation of the white matter and pial surfaces of the brain. Leveraging the high similarity between individual images resulted in sharper tissue probability coupled with precise surface definition without abnormality within the mesh. Distance-weighted interpolation of
the input images to build a super-resolution template. The approach to super-resolution interpolation, which considers the distance between projected coordinates, provided improved sharpness and contrast between the brain tissues.

Figure 1. Anatomical cut of the improved T1w Colin 27 template (top) along with our T1w (center) and T2w (bottom) templates. All brains were aligned to the same coordinate system.

Figure 2. Brain intensity histogram (left) for each individual T1w image (blue) and for the T1w template (orange) along with T1w (top-right) and T2w (bottom-right) tissue SNR comparisons.

Conclusions: We provide a high-definition template derived from a single healthy individual and generated from T1w and T2w contrasts at 3T. This initiative is an effort to grow interest in densely sampled datasets and to improve mapping of the individual human brain.

References
ABSTRACTS


Poster No 2213

MRI/DWI mini atlas of the Thalamus, in vivo Human Brain Atlas

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Introduction: Long considered as too challenging for most MRI, the thalamus has received increasing interests in recent years. However, in particular the segmentation of the thalamus based on in vivo MRI data is still challenging. The Human Brain Atlas project aims to provide an MRI atlas of the living human brain (Schira et al. 2023), but with the detail presently only provided from histology based atlases of about 1000 structures (Mai, Majtanik and Paxinos, 2015). Here we present a mini atlas of the thalamus, providing a guide to scientist investigating this crucial area of the human brain.

Methods: Multiple acquisitions were collected for each contrast for each participant (20 T1w, 12 T2w, 10 DWI scans), and were averaged using symmetric group-wise normalisation (Advanced Normalisation Tools). T1w and T2w data were acquired using a 7T human research scanner (Siemens MAGNETOM) at the Centre for Advanced Imaging, University of Queensland. T1w scans were recorded using a MP2RAGE sequence (WIP944) at 0.4 mm isotropic resolution, T2w scans were recorded using TSE sequence (WIP692) at 0.4 mm isotropic resolution with the parameters: DWI scans were recorded with a human 3T MRI (Philips Achieva CX) (NeuRA Imaging Centre) using an inverse blip corrected SPIR sequence at 1.25 mm isotropic resolution. Using ANTsMultivariateTemplate fitting these datasets were combined into a combined space at 0.25mm.

Results: The resulting image quality permits structural parcellations rivalling histology-based atlases, while maintaining the advantages of in vivo MRI. Our data are virtually distortion free, fully 3D, and compatible with existing in vivo Neuroimaging analysis tools. Our data is available for open access under https://osf.io/ckh5t/. Using manual, digitized pen and paper tracings we delineated the entire thalamus from the bed nucleus of the stria terminalis and the anterior commissure to the most anterior point at the pulvinar and the posterior commissure. The maps cover the entire thalamus and all in-between, detailing the mediodorsal and posterior thalamic nuclei to the centromedian and ventroanterior nuclei.

Fig. 1 shows a coronal section of our atlas through the anterior commissure (x=0 mm).
Conclusions: Our extensive scanning and image processing scripts resulted in exceptional image quality, the basis for the HBA project. In particular for the DWI data, combining effectively over 400 images resulted in remarkably improved detail and resolution. Our detailed segmentation resulted in the most comprehensive and detailed MRI map of the human in vivo thalamus and serves as and serves as a template. We argue that the dataset presented herein and made available for open access1 satisfies the new needs for a modern 3D atlas of the human brain. Importantly it uses contrast that is immediately familiar to the user of MRI. It can inform researchers, clinicians and educators.

References

Poster No 2214
Precision of template-based inter-subject spatial normalization of QSM of the older adult brains
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Introduction: Quantitative Susceptibility Mapping (QSM) holds significant potential for studying metal and iron homeostasis. It can serve as an important diagnostic tool for various pathologies1. However, there are no studies on the precision of QSM spatial normalization for older adults, which is contingent upon the quality and representativeness of the chosen template, as well as the type and quality of information utilized during image registration. This study aims to compare three available QSM templates in terms of their representativeness of the older adult brain, and in terms of the precision of inter-subject matching of older adult QSM data when they are used as references for spatial normalization.

Methods: Data: In this study, 3D T1-weighted MPRAGE and multi-echo 3D GRE data from 100 older adults (aged 67.8-97.2 years) were used. Recently introduced T1w and QSM2-4 templates of the MIITRA atlas were compared to the only two other sets of publicly available T1w and QSM templates from HybraPD5 and MuSus-1006, mainly based on younger adults. Process: Magnetic Susceptibility Map Generation: For each participant, magnetic susceptibility maps were generated using the Morphology Enabled Dipole Inversion (MEDI) software on multi-echo GRE data7. Image Registration: Five distinct registration pipelines were employed using the ANTS image registration toolbox8. - Single channel registration of T1-weighted images to T1-weighted templates. - Multi-channel registration of T1-weighted images and susceptibility maps to T1-weighted (75% weight) and QSM templates (25% weight). - Equal weight multi-channel registration of T1-weighted images and susceptibility maps to both T1-weighted and QSM templates. - Multi-channel registration of T1-weighted images and susceptibility maps to T1-weighted (25% weight) and QSM templates (75% weight). - Single channel registration of susceptibility maps to QSM templates. Deformation Calculation: Log-Jacobian maps of the nonlinear deformations were generated for each participant for registration to each space, and the average Log-Jacobian was calculated for each voxel in each space. Template Alignment: The transformations from the image registration step were used to align the participants’ susceptibility maps to the different atlases. Spatial Matching Precision: Inter-subject pairwise normalized cross-correlation was calculated for each registration approach and each atlas, considering all 100 participants (100x99/2=4950 pairs).

Results: Spatial normalization of older adult brains required less deformation when registering to the recently generated MIITRA templates compared to other templates (Fig.1). This was true for all five registration approaches tested here. Thus, the MIITRA templates were more representative of the older adult brain. Furthermore, pairwise normalized cross-correlation was higher when using single channel registration of susceptibility maps to QSM templates than other registration methods (Fig.2). Overall the highest spatial matching of magnetic susceptibility maps of older adults was achieved when using single channel registration of magnetic susceptibility maps to the MIITRA-QSM template.

Conclusions: This study provides insights into the role of different atlases and registration approaches in spatial alignment of magnetic susceptibility maps of the older adult brain. It demonstrates that the recently developed MIITRA atlas is more representative of the older adult brain, as evidenced by the lower amount of deformation required compared to other atlases. The present study also shows that the highest inter-subject spatial matching of magnetic susceptibility maps from older adult brains is achieved when using single channel registration of individual magnetic susceptibility maps to the MIITRA QSM
These findings underscore the importance of selecting appropriate templates and registration pipelines for QSM studies of the older adult brain.

References
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Neuromark v2: Spatiotemporal Templates to Search Reproducible Biomarkers in Hybrid ICA Framework

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Introduction: The most challenging topic in recent neuroscience is the reproducibility of population-based research (Poldrack et al., 2017). We previously developed a hybrid framework called Neuromark (Du et al., 2020), aiming to address the issue of reproducibility for biomarker development in data-driven methods. Neuromark has been successfully applied to many studies, capturing a bunch of robust brain markers across diseases (Fu et al., 2021; Dhamala, Yeo and Holmes, 2023; Vaidya et al., 2023). However, there is a limitation on the implicit assumption of invariant templates with age, which oversimplifies the changes in brain structure throughout the lifespan (Rieck et al., 2021). Therefore, in this study, we proposed to construct 4D (age \times 3D brain) templates using a total of more than 6000 fMRI scans from four datasets. We evaluated the reproducibility of independent components (ICs) across data and investigated the unique and shared patterns across templates. Our study is the first attempt to build spatiotemporal templates compatible with the adaptive ICA framework, which will be beneficial for precisely capturing well-replicated mapping of abilities to brain functions.

Methods: We adopted the resting-state dataset from the human connectome project development (HCP-D) (Somerville et al., 2018) including 652 subjects aged 5~21 years old to build the developmental template. We built the aging template using the dataset from the HCP aging (HCP-A) (Harms et al., 2018), including 725 subjects aged 36~100+ years old. To build the infant template, we used two infant datasets, including 143 infants collected at Emory University. Group ICA was performed on each data, resulting in multiple groups of ICs for building the template. We examined the replicability of ICs using a greedy spatial correlation analysis. We considered the reference IC replicable if it had the best-matched ICs with correlations > 0.4. The replicable ICs were labeled as intrinsic connectivity networks (ICNs) to construct the template if their peak activations fell in the meaningful gray matter areas. We also examined the similarities and uniqueness shared across the templates by evaluating their spatial correlations.

Results: Fig. 1A displays the results of ICs of sessional data from the HCP-D cohorts. Here, the first session is the reference, and the other sessions are the replication data. All 100 ICs have replicable ICs in the other sessions with a mean correlation > 0.4. Among the replicated ICs, 67 ICs were characterized as ICNs, which were used to construct the developmental template. For the HCP-A cohorts, 99 ICs from the reference data are replicable across sessions (r > 0.4). 56 of the 99 replicable ICs were identified as ICNs to construct the aging template (Fig. 1B). Fig. 1C displays the results of ICs from two infant datasets. 99 ICs from the reference data were replicated in the replication dataset, and we labeled 72 replicable ICs as ICNs to construct the infant template (Fig. 1C). These three templates share similarities and show unique patterns, whereas the older template tends to be more aggregated (Fig. 1D). Fig. 2 displays the composite maps of 4D templates. ICNs were arranged into 9 domains according to the prior functional information, including subcortical, hippocampal, auditory, sensorimotor, visual, cognitive-control, parietal, default-mode, and cerebellar domains.
Conclusions: The mixture of big data and algorithmic advances has propelled the neuroimaging field forward rapidly. Neuromark, combining priori neuroimaging with the data-driven approach, is a promising tool that provides a way forward here, continuously advancing the field. Neuromark v2 templates, which include spatiotemporal information, will have plenty of applications in future neuroimaging studies. They can capture features adaptable to the datasets and disorders in different age populations, which might boost accuracy in mental health research and advance our understanding of lifespan alterations.

References

Poster No 2216

Public nEUro: a european platform to share neuroimaging datasets publicly

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Introduction: Data sharing using a web-platform is becoming an integral part of the research life cycle. Not only data sharing allows reproducing analyses, a tenet of experimental research, but it also allows deepening analysis of existing datasets, combining data, meta-analysing and asking outright new question. Because neuroimaging data can be seen as personal data, this activity is challenging for EU-based researchers who have to comply with the General Data Protection regulation - the law that protects EU citizens from misusing their personal data. Here we introduce Public nEUro (https://public-neuro.github.io/index.html), a platform for EU-regulation-compliant data sharing.

Methods: (1) We constructed a legal framework allowing data providers to share their neuroimaging data using institution-specific data user agreements (figure 1) (2) We created a governance framework ensuring fair, legal and secure data sharing (3) Leveraging Denmark’s national life science super-computing facility (computerome) we can offer secured hosting of datasets (4) Using DataLad (Halchenko et al., 2021) data catalogue (https://docs.datalad.org/projects/catalog/en/latest/) we are developing tools to share openly metadata, making EU dataset findable. (5) Using verified user registration, we can make EU neuroimaging data accessible.

Results: (1) We have successfully established connections with several institutions whose legal teams agreed with the ‘terms and conditions’ - illustrating the generalizability of our concept to share EU data. (2) Datasets are being uploaded and processed for data sharing. Each dataset must be BIDS (Gorgolewski et al., 2016) compliant (https://bids.neuroimaging.io/) ensuring interoperability and reusability.

Conclusions: The sharing of EU protected neuroimaging data is possible, without the need of data lakes thereby bringing users to the data. Instead, by allowing data creator to use institution specific data user agreements, verifying users identities and controlling data access, one can bring data to users, a model we believe to be more relevant in many cases, as proven by the success of OpenNeuro. Public nEUro aims to achieve more than just providing data access, but to also make data public, that is create a public record of metadata to enhance findability.

Figure 1: shematic of data flow and responsabilities of different parties

References
Poster No 2217

Multimodal precision neuroimaging of the individual human brain at ultra-high field

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Introduction: Neuroimaging has advanced our understanding of the human brain by allowing non-invasive examination of brain structure and function. Nevertheless, human MRI research has predominantly centred around group-average data, which limits the specificity and clinical utility that MRI can offer¹. Precision neuroimaging facilitates individualized mapping of brain structure and function through the use of repeated and prolonged scans¹. A dense sampling of fMRI allows for detailed and reliable characterization of individual brain states and heteromodal networks². Structural MRI’s specificity can be augmented by using multiple quantitative MRI sequences, providing microstructural parameters characterizing inter-regional heterogeneity and inter-individual differences. Harnessing ultra-high field (UHF) neuroimaging at magnetic field strengths of 7 Tesla, can further enhance spatial and temporal resolution and is often imperative for precise mapping of highly susceptible and deep structures³,⁴. Several initiatives have generated open-source UHF datasets; however, these focused either on functional⁴ or structural sequences⁵. Here, we describe a multimodal precision neuroimaging dataset that capitalized on multiple sessions 7T MRI.

Methods: Our imaging protocol was implemented at the Montreal Neurological Institute and data were acquired on a 7T Terra Siemens scanner with the 8/32-channel transmit/receive Nova head coil. Ten healthy subjects (5M/5F, age=26.8±4.61, left/ right handed=2/8) underwent three imaging sessions, each consisting of five distinct structural and five functional imaging protocols (Fig. 1A,C). Our UHF MRI data were processed with micapipe_v0.2.2⁵, a surface-based processing software developed in my host lab, which introduced a standardized processing workflow for multiparametric UHF MRI acquisition. Structural scans included: (i) T1w and (ii) T1 relaxometry (T1) for examining intracortical microstructural organization, (iii) DWI for examining structural connectomes and fibre architectures, (iv) myelin-sensitive magnetization transfer, and, (v) iron-sensitive T2*-weighted multi-echo gradient echo. Each multi-echo fMRI scan lasted for 6 minutes and included, (i) rs-fMRI, (ii,iii,iv) multi-state task-based fMRI⁶ with episodic encoding/retrieval and semantic tasks (Fig. 2B left). We also collected fMRI data as subjects watched (v) movies to study brain activity during naturalistic conditions⁷. Finally, we used the multidimensional experience sampling questionnaire (MDES), to study patterns of ongoing thought⁷ (Fig. 2B right).
Results: Alongside anonymized raw data, we will release fully processed\(^5\) data for each modality, which provides surface-based neuroimaging features such as cortical thickness, quantitative MRI maps, and inter-regional structural and functional connectomes (Fig.1A,B). With this unprecedented dataset, we have generated upsampled data (i.e., from 0.5mm to 0.25mm isovoxels) from MRI acquisitions and averaged denoised data across sessions\(^4,9\). We have tested this method, particularly focusing on T1w images which substantially enhanced image contrast, and, with T1 maps which provided more granular intensity profiles than single-session data (Fig. 2A bottom left). The multi-session data also allows to assess test-retest reliability\(^10\) of various MRI features. Exemplary analysis of DMN connectivity derived from rs-functional connectomes demonstrated high intra-subject reliability and inter-subject DMN uniformity, with strong identifiability\(^10\) (d=1.95), indicating reliable and distinct DMN patterns from our UHF rs-fMRI data while preserving individual differences (Fig. 2A bottom right).
Conclusions: Our open-access precision UHF dataset promises to become a key resource for researchers aiming to advance our understanding of structure-function relationships in individual human brains and is instrumental in the development of novel image processing and analysis methodology.

References
Toward Open MRI Consistency Data for fMRI and dMRI scans

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Introduction: With a shift towards quantitative MRI, neuroimaging initiatives, clinical trials, and longitudinal studies are increasingly employing advanced MRI techniques like functional or diffusion MRI with quantitative analysis. Concerns about data consistency between software versions often discourage sites running longitudinal studies from availing of new features and enhancements. We investigated data consistency in fMRI and dMRI scans from version 29.1 to 30.1 software upgrades on two GEHC MR systems, as a needed and essential first step in ensuring that MR systems are able to keep up-to-date with new capabilities without compromising data consistency. We introduce the Open MRI consistency data publicly available on the OSF (https://osf.io/uh2jx/), as a way to enable researchers to check data consistency between different software upgrades (e.g. from 28 to 30.1) or between different hardware systems and to contribute to the database.

Methods: FUNSTAR fBIRN phantom (Gold Standard, Sheffield, UK) and five healthy subjects (age 19-71 years) were scanned under an IRB-approved protocol on a 3T Premier with 48 CH head coil (GE HealthCare, Waukesha, WI) and a 3T MR750 with Nova 32 CH head coil. For each software version and system, the phantom and three subjects were scanned, with test-retest performed on the phantom and 1 subject. Acquisitions include: Standard fBIRN QA protocol on the phantom, structural 3D T1/T2 images, rsfMRI, dMRI, B0 field map, two SE-EPI with opposite PE polarity (see details MRI protocol on the OSF page). Resting-state fMRI data were processed using SPM12 and homemade Matlab code. EPI data was slice-time corrected, motion corrected, registered to MNI via T1 and then scaled to the mean, detrended (2nd order) and nuisances were regressed-out (aCompCor) and smoothed (6 mm). The tSNR was evaluated to compare the data quality for 11 fMRI scans after removing 5 scans due to excessive motion. Diffusion MRI data were processed via MP-PCA denoising, removal of B1 inhomogeneities and Gibbs ringing using Mrtrix3, and then processed for eddy current and movement correction using FSL. FODs estimation, whole brain tractography and FA maps were then calculated using Mrtrix3. NODDI maps were generated using the NODDI Matlab toolbox.

Results: Open Data Sharing: The open MRI consistency data consists of detailed MRI protocol data, the raw DICOM data, and the BIDS data converted by dcm2niix (v1.0.20230807) and dcm2bids (v2.1.7) as well as the configuration file. We validated that DICOM to NIfTI/BIDS conversion were consistent across software versions with no issue. Data Consistency for fMRI scan: Phantom fMRI datasets were evaluated using GE fMRI QA tool available on console. The QA metrics (RMS, SFNR, SNR, RDC, Mean Ghost) were very similar between the two software releases (Fig 1a). For volunteer fMRI data, the tSNR in grey matter voxels was consistent across software release and no significant difference was found in the tSNR (Fig 1). Data Consistency for dMRI scan: No significant difference in b0 SNR was observed between two software versions for phantom data (paired t-test: t=0.856, df=3, p=0.45) and volunteer dMRI data (N=16)(Fig 2b,c). Qualitative comparison of noise maps, FA/FOD/CNR/NODDI maps (Fig 2a), tractography for all 16 scans was performed and results were consistent across software versions. An ANOVA analysis didn’t show significant differences in any metrics considered: MP-PCA noise (mean, SD, max), tractography FA (mean, median, SD), whole brain FA (mean, SD), FSL eddy QC metrics (Fig 2d).
ABSTRACTS

Figure 1. Consistency check for functional MRI scans

Figure 2. Consistency check for diffusion MRI scans
**Conclusions:** We present the Open MRI Consistency Data. While done in a small subject cohort, this is the first necessary step towards addressing concerns in discrepancies in fMRI and dMRI measurements between software versions. No statistically significant differences were observed in the comparisons between the software versions. We invite our collaborators to participate in this ongoing initiative by contributing data and results.

**References**

**Poster No 2219**

**Fetal developing Human Connectome Project functional MRI data release: methods and data structures**

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**Introduction:** Advances in fetal fMRI represent, for the first time, an opportunity for neuroscience to study functional brain connectivity at the time of its emergence¹². The unique challenges of in utero imaging require a community-wide effort to develop tailored methods for image preprocessing and analysis. The progress however has been hampered by the lack of openly available datasets that could be exploited by researchers across disciplines. The dHCP closes this gap by releasing the first open-access and largest-to-date fetal fMRI dataset at https://nda.nih.gov, processed using state-of-the-art methods.

**Methods:** 275 completed resting-state fetal fMRI scans (255 unique subjects, 137 male, 116 female, 2 unknown) were acquired with Philips Achieva 3T system and a 32-channel cardiac coil, using a single-shot EPI (TR/TE = 2200/60) sequence, with slice grid = 144 x 143, 48 slices, isotropic resolution = 2.2 mm, multi-band (MB) factor = 3, and SENSE factor = 1.4³. Each scan consists of 350 volumes. The data underwent 4 stages of preprocessing (Fig 1A): 1) image reconstruction based on soft SENSE ESPIRIT for considering motion or fat-shift induced model inconsistencies⁴⁵; 2) dynamic shot-by-shot B0 field correction based on phase unwrapping of complex data using weighted iterative least squares for solving the Poisson equation with iterative correction of residuals after rewrapping⁶; 3) rigid motion correction where volume-to-volume motion estimates are used to initialise slice-to-volume (SVR) corrections with motion states defined jointly for simultaneously excited slices, using a simplified version of⁷; 4) optimised temporal denoising. Specific artefacts were targeted with denoising: 1) failure of SVR corrections in the presence of large motion; 2) potential effects of residual leakages which could not be suppressed with SENSE reconstruction; 3) residual effects of distortion corrections; 4) motion-induced artefacts, including spin history artefacts, manifesting themselves as spatially non-stationary travelling waves. To address these, the pipeline utilises novel types of 4D (voxelwise) regressor maps, in addition to traditionally used volume censoring and data-derived white matter and CSF timecourse regressors. The dHCP data release also includes an advanced volumetric mapping infrastructure between native and template spaces using one interpolation step (Fig 1B), that enables group-level analyses and synthesis of the fMRI data with structural and diffusion data, acquired in the same cohort, and the wider neonatal cohort of the dHCP⁸.
**Results:** 263 scans were fully processed. Fig 2A-C shows the outputs of the dHCP fetal preprocessing steps for an exemplar subject following MB-SENSE reconstruction. Fig 2A shows the effect of distortion corrections on the brain geometry in comparison to the raw reconstructed image. Figure 2B shows the effect of slice-to-volume reconstruction on temporal signal-to-noise ratio compared to volume-to-volume alignment, the default approach in ex-utero image preprocessing. Fig 2C shows the effect of temporal denoising on the temporal evolution of the signal for the same subject. Finally, capabilities of the registration infrastructure are exemplified by the results of group-level ICA analysis, as shown in Fig 2D.
Conclusions: The dHCP fetal fMRI dataset is designed to promote fetal MRI from its current status as a niche research field to its deserved and timely place in the community-wide effort to build a life-long connectome of the human brain. By releasing the data at different pre-processing stages, we ensure that researchers with diverse scientific background can benefit from this dataset, starting from reconstruction and preprocessing method developers, who can utilise raw or partially pre-processed data to benchmark performance of their models, to modelers of neurodevelopment, who can use the fully pre-processed data and advanced registration infrastructure to probe key questions about early brain development.

References
Image processing in the Acute to Chronic Pain Signatures Project

Patrick Sadil, Brian Caffo, Vince Calhoun, James Ford, Xiaodong Guo, Micah Johnson, Heejeung Jung, Ari Kahn, Scott Peltier, Joshua Urrutia, Carol Vance, Tor Wager, David Zhu, The Acute to Chronic Pain Signatures Consortium A2CPS

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Introduction: Typically, the pain of an acute injury goes away after it heals. But sometimes, the pain of an injury, surgery, or disease can linger, eventually becoming chronic. Currently, a high proportion of people in the United States transition to chronic pain after an acute event, but the causes of this transition remain unknown. A new project aims to study the transition: the Acute to Chronic Pain Signatures (A2CPS) initiative (Berardi et al. 2022; Sluka et al. 2021). The study aims to collect neuroimaging data on over 1000 participants who will undergo an incident of acute pain—surgery for either total knee replacement or thoracic surgery. Information collected includes psychosocial, omics, quantitative sensory testing, and brain magnetic resonance imaging data. Participants are imaged both before and after their surgery. The multimodality and scale of these data will provide a unique opportunity to test candidate biomarkers for susceptibility to chronic pain and generate novel, putative, biomarkers and biosignatures. Here, we present the first release of the brain imaging data, quality control procedures, and analysis pipelines.

Methods: The A2CPS imaging protocol was designed to allow collection of several candidate biomarkers (Figure 1a), including volumetric and gray matter density differences in individual regions of interest, structural connectivity, fractional anisotropy, evoked responses, functional connectivity measures, graph theoretic measures, and multivariate signature responses. The scan protocols are based on those from the Adolescent Brain Cognitive Development study (Casey et al. 2018), and were tailored to the study and to the scanner hardware of participating collection sites. Analyses comprise three stages (Figure 1b). First, the data are indexed and organized according to the Brain Imaging Data Structure (Gorgolewski et al. 2016). Then, the data are sent through a series of pipelines, including both established (MRIQC, fMRIPrep, FreeSurfer, QSIprep, fsl_anat, CAT12; Esteban et al. 2017, Esteban et al. 2018, Fischl 2012, Cieslak et al. 2021, Jenkinson et al. 2012. Gaser et al. 2022) and bespoke pipelines. Finally, the outputs from these pipelines are aggregated, de-identified, and stored with data from other modalities. To ensure usability, the raw data have undergone quality control and assurance. The aim of this was a straightforward, three-tier quality rating assessing comparability: “no known defects”, “minor defects/issues, correctable”, and “major defects/issues, not expected to be comparable”. The quality rating is derived from a combination of automated metadata checks (e.g., adherence to acquisition parameters), standardized visual review (e.g., checks for eye spillover), and automated thresholds on measures extracted from the data (e.g., average framewise displacement).
**Results:** The initial data release comprises 595 participants with imaging data, with all images collected before the incident of acute pain. To facilitate analyses, the (deidentified) raw data are provided along with phenotypes derived from the images. This initial release includes outputs from structural, resting, and task MRI (Figure 2). These image-derived phenotypes provide one way to begin machine-learning studies immediately. Users wishing to run their own analysis pipelines have access to the raw data.

**Conclusions:** The A2CPS research initiative provides a unique opportunity to study the multimodality of the transition to chronic pain in a large dataset. This is the first of several planned releases. The dataset itself, analysis pipelines, and quality control procedures will be made available to researchers outside of the consortium. Future releases will include scans post-surgery, as well as refinements to the imaging derivatives. For neuroimagers, the data and associated pipelines provide a rich medium to study predictive biomarkers, and to contribute efforts to address the pressing health issue of chronic pain.

**References**
Poster No 2221

Transdiagnostic Connectome Project: A open dataset for brain-based models of behavior in psychiatry

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Introduction: A primary aim of computational psychiatry is to establish models that link individual differences in brain functioning to clinically relevant symptoms and behaviors. Progress in this field has been hindered by an overemphasis on discrete diagnostic categories and limited behavioral measures. Converging evidence from epidemiology, genetics, and neuroscience suggests that the boundaries between nominally distinct disorders are not phenotypically discontinuous, either between diagnoses or in comparison to healthy populations. Furthermore, behavior measures in clinical samples often consist of a narrow selection of self-report scales, constraining the ability to establish precise and reliable brain-behavior correlations. To advance the field of psychiatry, datasets that are richly phenotyped with a diverse range of both self-report and clinician-assessed behavioral measures, along with neuroimaging data, are essential.

Methods: We introduce a large, open repository containing behavioral and neuroimaging data from 244 individuals, including 150 meeting diagnostic criteria for a broad range of affective and/or psychotic illnesses (Fig1A), including major depressive disorder, bipolar disorder, post-traumatic stress disorder, generalized anxiety disorder, substance use disorder and schizophrenia, as well as a comparison group of 95 individuals without a mental health diagnosis. Participants were aged 18 to 70 and recruited from two sites (Fig1B-D): Yale University, New Haven, Connecticut and McLean Hospital, Boston, Massachusetts. Each participant underwent a neuroimaging session that included high-resolution anatomical scans (T1w and T2w), resting-state functional MRI (4 runs), and task-based fMRI (3 runs). Additionally, participants completed over 50 self-report, computerized, and clinician-assessed tests across multiple in-person and online sessions.
Results: Behavioral data, raw and processed MRI data will soon be made openly available via the National Institute of Mental Health Data Archive (NDA). MRI data were processed using Human Connectome Project pipelines (v4.3.0), with each functional neuroimaging run denoised using ICA-FIX. This processing significantly reduced the association between functional connectivity and quality control metrics, such as head motion (Fig2A). Processed data also displayed known characteristics, including inter-hemispheric connectivity and canonical functional network structure (Fig2B). Group-level analysis revealed similar correlation structures across 101 behavioral scales and subscales for both diagnosed and non-diagnosed individuals (Fig2C). Principal component analysis of the behavioral data revealed that the first component, accounting for 21% of the variance (Fig2D), represented a general functioning and wellbeing factor. The second, third, and fourth components were associated with internalizing, externalizing, and cognitive scales, respectively.

Conclusions: We provide a comprehensive, high-quality, and analysis-ready transdiagnostic dataset comprising individuals with a range of psychiatric diagnoses and a comparison group without diagnoses. This dataset can facilitate research for purposes such as identifying disease-relevant biotypes, predicting individual symptom profiles, establish brain-behavior associations and recommending personalized therapeutic interventions.
Can I have your data? Recommendations for sharing neuroimaging data upon a direct personal request

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Introduction: Sharing neuroimaging data through a direct request can be challenging both for researchers who request the data and those who agree to share their data. Unlike sharing through repositories that have standardized protocols and data sharing/use agreements, each party often needs to negotiate the terms of sharing and use of data case by case against the backdrop of complex ethical and regulatory requirements, not to mention the technical issues regarding data transfer and management. This study aims to help researchers navigate these challenges by examining what to consider during the process of data sharing and by offering recommendations and practical tips from a case study.

Methods: We first divided the process of sharing data upon a direct personal request into five stages: requesting data, negotiating terms for sharing and use of data, preparing and transferring data, managing and analyzing data, and sharing the outcome of secondary analysis of data. For each stage, we identified factors to consider through a review of 1) relevant literature; 2) ethical principles and guidelines for human subjects research, such as the Belmont Report in the US; 3) institutions' and funding agencies' policies, such as NIH's new data management and sharing policy; and 4) applicable regulations including HIPAA and Common Rule in the US and GDPR in the EU. Then we offer lessons learned from one of the authors' recent project on shared neuroimaging data as a case study. In this case study, a total of 782 subjects' PET/MRI data are collected from 7 sites through direct personal requests, spanning the countries USA, Canada, UK, Denmark, Germany, and Austria.

Results: Table 1 shows the preliminary results of the review of the literature and ethical/regulatory analysis on the factors to contemplate at each of the five stages of data sharing through a direct request. The main takeaways from the case study are: 1) start contacting the research team that owns data ahead of time, 2) offer co-authorship on work coming out of the sharing, 3) consider proposing multiple projects on shared data to make your collaborators more invested in efforts, 4) make sure to address the redistribution of secondary and derived data when negotiating terms of data sharing, 5) have a good local contact who will be actually involved with preparing and transferring data, 6) offer your help facilitate the preparation and sharing of data and be patient, 7) keep your collaborators updated with your progress and send them intermediate results, and 8) make sure to have legal support from both the receiving site and transferring site. On average, it took 7.8 months (range 2-12 months) per site to share the data (Table 2), and for several sites, additional requests were required in order to fix inconsistencies and/or errors in the data found during processing (average of 7 requests across 4 sites), extending the sharing time up to 24 months in some cases.

<table>
<thead>
<tr>
<th>Stages</th>
<th>Data Requester</th>
<th>Data Provider</th>
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<tbody>
<tr>
<td>Stages 1: Requesting Data</td>
<td>- Utilize personal contact to request data</td>
<td>- Check whether the proposed secondary analysis on shared data is consistent with the original study's informed consent form</td>
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<td>- Check data availability statement, if any, in a published target study</td>
<td>- Review whether the proposed secondary analysis on shared data may cause harms to data subjects</td>
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<td>- Determine what type of data is available (raw data/derived data/metadata/code)</td>
<td>- Check the data requestor's credentials</td>
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<td>- Start contacting the research team that owns data ahead of time</td>
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<td>Stages 2: Negotiating Terms for Sharing and Use of Data</td>
<td>- Define the institution(s) and individual(s) who will provide the data and who will receive and use the data</td>
<td>- Review the data recipient, their institutional oversight desired by the data provider(s)</td>
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<td>- Define the permitted/prohibited uses and disclosures of data</td>
<td>- Clarify whether data provided(s) will be used as an author of publications or presentations coming out of the shared data</td>
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<td>- Include requirements under applicable laws and regulations, particularly in the context of international data sharing</td>
<td>- Describe data breach reporting, and incident mitigation requirements</td>
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<td>- Confirm institutional oversight and review on the risks of data sharing</td>
<td>- Describe data disposition requirements</td>
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<td>- Confirm data security safeguards to prevent unauthorized use or disclosure of data</td>
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<td>- Enforce flow-down restrictions, terms, as well as responsibilities regarding privacy and confidentiality, applicable to all parties who have access to the data</td>
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<td>- Explain the challenges and any relevant risk assessments</td>
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<td>- Include prohibitions against reidentification of or recontacting with study participants</td>
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<td>Stages 3: Transferring Data</td>
<td>- Clarify the types of data and a specific list of data elements to be shared</td>
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<td>- Clarify preprocessing steps and format for data to be shared</td>
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<td>- Clarify the method that the data provider(s) will use to transfer the data and how the data requestor will receive or get access to the data</td>
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<td>Stages 4: Managing and Analyzing Data</td>
<td>- Check whether data are deidentified as agreed</td>
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<td>- Report any incidents of unauthorized (intentional or inadvertent) disclosure or misuse of data</td>
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<tr>
<td>Stages 5: Sharing the outcome of secondary analysis of data</td>
<td>- Acknowledge the data provider(s) in the publication(s) resulting from research on shared data</td>
<td>- Confirm any further disclosure of (derived) data alongside with the publication(s) complex with the terms in the agreement between the parties</td>
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<tr>
<td></td>
<td>- If allowed under the agreement with data provider(s), share derived data</td>
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**Conclusions:** In this study, we proposed best practices for sharing data upon direct personal request by summarizing crucial factors to consider at each stage of the data sharing through a review of relevant literature and ethical, policy, and regulatory requirements. In addition, we provided practical tips from a case study on how to facilitate this process while minimizing friction and frustrations. Our case study also showed that researchers should on average expect to spend 8 months on data sharing efforts by direct personal requests, which could be extended up to 24 months due to additional requests. The current state of direct personal requests to share data is far from ideal and standardized and will be particularly risky for early career scientists, often working on projects with a 2-3 year time frame.

**References**

The BIDS connectivity project - A practical standard to report and share brain connectivity data


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Introduction: Historically, neuroimaging data have been stored in a variety of unique file formats and directory structures, presenting obstacles in data sharing, scientific clarity, and rigor. The introduction of the Brain Imaging Data Structure (BIDS)1 has been pivotal in addressing these issues by standardizing file system structures and metadata for raw neuroimaging data, leading to its widespread adoption2. Over time, BIDS has evolved beyond its original scope of MRI data, encompassing a broader range of imaging modalities, thanks to contributions from the community3. However, due to this evolution being mostly centered around raw data, BIDS currently lacks detailed descriptions for advanced data derivatives, particularly in brain connectivity research. To address this gap, the BIDS connectivity project (https://pestillilab.github.io/bids-connectivity) is expanding the scope of BIDS derivatives. This extension includes both raw and minimally processed data, as well as more sophisticated derivatives from brain connectivity experiments. The project aims to establish standard descriptions for connectivity derivatives across six key data modalities: anatomical, diffusion-weighted, and functional MRI, along with PET, M/EEG, and iEEG. This initiative will significantly bolster research capabilities in terms of data generation, sharing, and replication of studies using published data derivatives. Additionally, it will streamline neuroimaging pipelines and processing, thereby accelerating research and development.

Methods: The development of the BIDS Connectivity standard was community-driven, involving several stages: (1) A stakeholders’ meeting held in September 2022, (2) Beginning drafts of new BIDS Extension Proposals (BEPs) with input from experts present at the meeting, (3) Feedback on these BEPs from the broader neuroimaging community was solicited in Spring 2023, (4) a workshop was conducted during OHBM 2023, (5) Community feedback obtained during this time period was incorporated into the BEPs, and (6) Integration of the Connectivity BEPs into BIDS.

Results: Together, the BIDS Connectivity workshops in September 2022 and during OHBM 2023 saw the participation of over thirty expert investigators, who advanced five BEPs. These initial drafts, in line with BIDS BEP guidelines, represent the first comprehensive community-driven effort to standardize descriptions of brain connectivity data derivatives across six major neuroimaging modalities. The five BEPs in development cover: (1) diffusion voxel-wise models, (2) diffusion tractography, (3) connectivity matrix schema, including seed-based connectivity methods, (4) dimensionality reduction-based networks, and (5) brain atlas specification. These BEPs have been open for feedback from the neuroimaging community since spring 2023.

Conclusions: The establishment of a data-sharing standard for brain connectivity metrics is a crucial step toward enhancing best practices, scientific stringency, and transparency in the field of neuroimaging4. Following this process, the BEPs are expected to be merged into the main BIDS specification by summer 2024. Further meetings are scheduled for Spring 2024 to finalize community feedback integration and revise the BEPs. This framework will facilitate the integration of results from various datasets and processing pipelines, boosting interoperability among diverse brain connectivity projects. This, in turn,
will create opportunities for synergy across different levels of analysis of neuroimaging data, as network neuroscience can help combine data across modalities, spatial and temporal scales.

References

Poster No 2225
Extensions to EEGNet open data discovery, analysis and collaborative annotation EEG-BIDS ecosystem
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Introduction: The global reach and accessibility of neuroelectrophysiology provides unique opportunities for collaboration and translation to applications in health and research. Fundamental to these outcomes is a common basis of data sharing, interpretation and analytics, supported by community-driven standards such as EEG-BIDS and HED tags (Pernet 2019, Robbins 2021). EEGNet is an online open platform (eegnet.loris.ca) which launched in November 2023 designed for open collaboration in building gold-standard annotated datasets for exploitation in machine learning and early biomarker detection. Its pilot release includes 7 datasets and test datasets for research community members to log on, annotate, download, query and provide input on workflows. EEGNet further drives data sharing and open tool deployment as well as implementation of the emerging BIDS derivative standard through community engagement and active participation in global working groups, and contributes to open EEG data preparation tools. Through these efforts and in partnership with the Global Brain Consortium (globalbrainconsortium.org) and the Canadian Open Neuroscience Platform (CONP.ca, Harding 2022) EEGNet’s combined data and analytics hub removes adoption barriers to open EEG research collaboration.

Methods: EEGNet’s core infrastructure builds on the open-source LORIS data system and CBRAIN processing portal (Das 2012, Sherif 2014), and leverages ethics and governance groundwork by the Canadian Open Neuroscience Platform (CONP.ca, Harding 2022), supporting interoperability, scalability, and transparency in sharing and processing standardized EEG data. Layered on this technology, EEGNet has embedded tagging with the HED and SCORE (Beniczy 2017) clinical ontologies to provide standardized annotation capacity in a unified platform. Extensions to the code developed for EEGNet are anticipated to be deployed in initiatives including NEMAR (Delorme 2022), Born in Bradford (F.Mushtaq) and other Global Brain Consortium projects. EEGNet has also supported additional tool development empowering researchers to convert EDF or .SET data to EEG-BIDS on any operating system with enhanced metadata checks and customization. The EEG2BIDS open-source tool (github.com/aces/eeg2bids) is undergoing final testing for re-release in late 2023 with added capacity developed by the HBCD (Human Brain Cognitive Development) consortium.

Figure 1: Dashboard for open data discovery on EEGNet with Analytics activity
Results: All members of the clinical and scientific research community are welcome to log into EEGNet.loris.ca - begin by requesting an account to access, navigate, visualize, query, and download or export all data on the platform. At the pilot launch EEGNet data and analytics hub included 7 open datasets, 200+ recordings, and 4 open analytics tools on CBRAIN (portal.cbrain.mcgill.ca, Li 2022). A portal listing all EEGNet community-contributed datasets and tools is also published at EEGNET.net.org. Additional formats are expected with a growing collection of datasets. Further workflows in 2024 should include granular controls for collaborative data annotation and validation, advanced metadata querying, and enhanced visualization utilities. Spanning over 35 Canadian researchers across 10 sites, EEGNet’s scientific and clinical partners will continue to provide guidance to optimize platform utility for the research, informatics and clinical EEG community.

Figure 2: Interactive EEG annotation workflow for collaborative online open data knowledge-building

Conclusions: Community-driven EEG-BIDS and HED frameworks are implemented by platforms driving data sharing and knowledge-building in collaborative hubs. New workflows and open tools have been added by EEGNet since mid-2023 to reduce barriers to adoption, also serving as an open data and analytics hub. This work is currently being extended by the EEGNet technical team at McGill University as well as global collaborators, to further the reach and application of these emerging standards and accelerate the scientific and clinical impact of EEG research.

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ABSTRACTS


Acknowledgements
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Poster No 2226

Announcement of the Oxytocin Brain Imaging Data Exchange (OBIDE) Initiative
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Introduction: Initial studies have started to unravel the neural mechanisms that underlie the clinical-behavioral effects of exogenous oxytocin administration in human (patient) populations. Effects of intranasal oxytocin have been identified on brain connectivity among different regions of the central oxytocinergic system e.g., amygdala-centered circuits, reward circuits, salience network. However, variability across studies in design and person-dependent characteristics have made it challenging to precisely characterize oxytocin’s neural mechanisms. To facilitate the implementation of oxytocin as a therapeutic approach, it is crucial to gain a deeper understanding of the neural substrates that underlie its behavioral effects. There is a growing emphasis on promoting the sharing of open data to gather large-scale datasets, which are valuable to address sample variability, enhance transparency and facilitate the validation of research findings. In an effort to implement the concept of open data sharing in the oxytocin pharmac-neuroimaging field, we here introduce the Oxytocin Brain Imaging Data Exchange (OBIDE) Initiative, a grassroots consortium for the harmonization and open sharing of oxytocin pharmac-neuroimaging data. The specific aim of OBIDE lies in enhancing and accelerating the pace of exploration and identification of the neural correlates of oxytocin through aggregating pharmac-neuroimaging data in an unprecedentedly large repository size.

Methods: OBIDE will encompass existing resting-state functional magnetic resonance imaging (fMRI) data sets with corresponding structural MRI and phenotypic information from human participants receiving a single-dose of oxytocin or placebo nasal spray. Here, initial sample descriptors regarding aggregated phenotypic data are presented across contributing sites. Also design-related information regarding administration regimen (dose) and adopted resting-state protocols are provided (scan duration, eye open/closed).

Results: Twelve data sets are contributed from five sites (Beijing Normal University, University of Electronic Science and Technology of China, University of Florida, University of Leiden, University of Leuven), including resting-state and structural MRI data from a total of 1,013 individuals, acquired after intranasal oxytocin (n= 541) or placebo (n= 472). All included data sets adopted a randomized, placebo-controlled, between-subject design, with fMRI scanning performed 30 to 120 min post-nasal spray administration. Across sites, resting-state fMRI scanning was performed for an average of 7.6 min (5 to 8.5min), either with eyes open (65.6%) or eyes closed (34.4%). Administered doses ranged from 16–40 IU, with the majority of sites adopting a dose of 24 IU. Scans were predominantly taken from neurotypical individuals, except for a subsample of individuals with autism (n= 38). Three sites included hormonal collections of oxytocin or cortisol through salivary or blood sampling (n= 185 samples). The aggregated sample displayed variation in age across sites with a mean age of 24.6 years in the oxytocin (range: 18–80 years) and 25.1 years in the placebo (range: 17–81 years) group. The aggregated sample also displayed a predominance of male (75.9%), compared to female subjects (24.1%), with several data sets excluding females by design.

Conclusions: The open sharing of resting-state fMRI scans from intranasal oxytocin studies among international sites will significantly promote collaboration, enhance sample sizes, and allow for more robust and generalizable findings. Specifically, the harmonized data set emerging from OBIDE will advance research discovery in oxytocin pharmac-neuroimaging, i.e. regarding the impact of design-related (e.g., dose, scan paradigm) and person-dependent (e.g., age, sex) factors on oxytocin-brain effects. Gaining robust insights into the underlying neural correlates of exogenous oxytocin administration constitutes an essential step towards evaluating the therapeutic potential of oxytocin.
Multi-site Diffusion MRI Data Harmonization of Human Connectome Project Lifespan and Disease Studies

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Introduction: The Human Connectome Project (HCP) is a multi-site neuroimaging initiative that aims to study the connections of the human brain1–3. The HCP lifespan project explores how brain connectivity changes during typical development and aging, while the HCP disease projects explore how brain connectivity changes in various neurological and psychiatric disorders. However, combining neuroimaging data from multiple sites requires careful handling of scanner-related measurement bias before further analysis. Despite consistent imaging protocols across sites in the HCP, intrinsic hardware variabilities and software versions can introduce scanner-related bias4,5. This bias is particularly significant in diffusion MRI (dMRI), reducing statistical power and reliability of multi-site dMRI data analysis. Harmonization is an image processing technique that standardizes dMRI datasets from different sources, enabling pooling of data for joint analysis4,5. This is especially important for neuroimaging studies of psychiatric disorders, where effect sizes associated with psychiatric disorders are often small6. This study summarizes our harmonization efforts for the HCP lifespan and disease projects.

Methods: a) Dataset and dMRI data preprocessing: We sourced unprocessed dMRI data from the NIMH Data Archive (NDA), which included HCP lifespan and disease datasets. Figure 1 provides a participant overview by study. Diffusion MRI data was acquired on 11 scanners: 3T Siemens Prisma or Prisma fit scanners with similar acquisition parameters. We applied the same dMRI data preprocessing steps in all datasets using FSL’s eddy and topup tools, along with a deep learning-based brain masking tool7, to prepare the data for harmonization. b) dMRI data harmonization: We applied our retrospective harmonization algorithm, which aligns dMRI data from different scanners directly on the dMRI data by leveraging unique tissue properties using Rotation-Invariant-Spherical-Harmonics (RISH) features4,9. We selected 30 healthy subjects from each scanner, matched by age, sex, and IQ, to one reference dataset to which all other scanner data were harmonized. We chose the reference device based on its wide range of characteristics (e.g., age, sex) and sample size, which allowed us to obtain representative samples across all the different scanners. We used the RISH features of these subjects to create templates representing scanner differences. After determining these mappings, we applied these templates to the full dMRI dataset for harmonization. More details of these steps can be found in16. c) Harmonization Performance: Various dMRI measures, such as Return To Origin Probability (RTOP) and Fractional-Anisotropy (FA), were calculated pre- and post-harmonization and compared with the reference dataset as a baseline. We assessed the harmonization performance in 30 matched subjects. Averages of the measures were calculated over the whole brain white matter skeleton and 42 white matter regions of interest10. We first compared the original and harmonized datasets to the reference dataset using unpaired t-tests. To further verify the harmonization, we conducted unpaired t-tests using 30 newly matched subjects, which were not part of creating templates.

Results: We selected the scanner with deviceid=166007 as the reference due to its extensive collection of healthy controls and diverse age distribution (N=30) in the template creation process. The harmonization’s effectiveness for all datasets was evidenced by the elimination of any existing statistical differences across datasets during harmonization (before harmonization: p<0.01; after harmonization: p>0.3).

Conclusions: The harmonized HCP dMRI data of 2545 subjects will be available in the NDA for large-scale analysis. The enhancement in statistical power will aid in better characterizing connectomes in individuals with specific disorders compared to healthy controls and in identifying neuroanatomical changes related to each disease.
**Abstracts**

Figure 1. Overview of the number of healthy controls (N=1822) and non-healthy individuals (N=803) in each Human Connectome Project (HCP) dataset available in the NIMH Data Archive: HCP Aging (HCPA), HCP Development (HCPD), Perturbation of the Treatment of Resistant Depression Connectome by Fast-Acting Therapies (PDC), HCP for Early Psychosis (HCPEP), Dimensional Connectomics of Anxious Misey (DCAM), and Boston Adolescent Neuroimaging of Depression and Anxiety (BANDA). Controls were selected to span age range of non-healthy individuals.

Figure 2. Diffusion MRI data processing pipeline applied to the HCP study as part of this study, including harmonization.

**References**


Poster No 2228

Harmony: generating a large-scale connectome dataset for mental health research

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Introduction: Following the success of the initial Human Connectome Project (HCP) dataset, the NIH has funded several follow-up Connectomes Related to Human Disease (CRHD) studies. These CRHD studies were intended to adopt high-quality HCP data acquisition and processing techniques in disease-specific cohorts. Four CRHD studies collected data from mental health cohorts suffering from mood and anxiety disorders (Tozzi et al., 2021), namely: Dimensional Connectomics of Anxious Misery (HCP-ANXPE; PI Sheline), Human Connectome Project for Disordered Emotional States (HCP-DES; PI Williams; Tozzi et al., 2020), Perturbation of the treatment resistant depression connectome by fast-acting therapies (HCP-MDD; PI Narr), and Connectomes related to anxiety and depression in adolescents (HCP-BANDA; PI Whitfield-Gabrieli). However, recent work has shown that larger sample sizes than each of these individual studies (Ncases<250) contain might be required to identify robust brain-behavior associations (Marek et al., 2022). The goal of the Harmony project is to combine these studies and supplement controls from other cohorts to generate a harmonized large-scale connectome dataset for mental health research.

Methods: The combined Harmony sample will include N=1,540 participants, covering 770 cases and 770 matched controls (Table 1). 1,736 non-imaging variables spanning 52 instruments in 7 domains were harmonized and centrally annotated. Quality control based on the systematic inspection of variable distributions was performed to identify and correct source harmonization errors. All harmonization steps are publicly available, version controlled, and annotated to track provenance to maximize reproducibility. Preprocessing of neuroimaging datasets consists of the HCP minimal processing pipeline (Glasser et al., 2013) with MSMAII surface-based alignment (Robinson et al., 2018) and ICA-FIX cleanup (Salimi-Khorshidi et al., 2014) as implemented in Qunex (Ji et al., 2022). The resulting processed data are in CIFTI format using a 32k mesh matching HCP-YA data. Preprocessed neuroimaging data will be shared through the NIH Data Archive (NDA). Multimodal Imaging Derived Phenotypes (IDPs) will be extracted from common pipelines inspired by HCP-YA and UK Biobank datasets. Resting state IDPs will include amplitudes, full correlation matrices, and partial correlation matrices from the following parcellations: HCP-MMP1.0 (Glasser et al., 2016), Independent Component Analysis combined with dual regression, and PROFUMO (Harrison et al., 2020). Diffusion IDPs will include fractional anisotropy (FA), mean diffusivity (MD), and NODDI indices of neurite density index (ICVF), orientation dispersion index (ODI), and isotropic volume fraction (IsoVF) (Zhang et al., 2012). Structural IDPs will include cortical area, thickness, volume, and myelination (T1/T2) from HCP-MMP1.0 and DKT cortical parcellations and from ASEG and Harvard-Oxford subcortical segmentations. All IDPs will be harmonized using longitudinal COMBAT to account for site effects. Harmonized IDPs will be shared.
Results: At the time of abstract submission, non-imaging instruments and variables released through the NDA were cleaned and their metadata standardized. Furthermore preprocessing of neuroimaging data for MDD and BANDA has been completed and ANXPE data have been staged for preprocessing. See Figure 1 for a timeline overview. Community feedback on the Harmony processing and data sharing plans is encouraged. Feedback promoting the use of annotation standards which facilitate the steady transition to community use of persistent ontological identifiers is also encouraged.

Conclusions: The large-scale connectome-quality Harmony dataset will be a valuable community data resource for research into mental health. In particular, the Harmony dataset will facilitate the clinical translation of advances in methodological development and brain organization insights that have and continue to result from healthy cohorts such as the HCP-YA.

References
Manual Segmentation of Pituitary Gland and Surrounding Structures from T1-Weighed MR Images

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Introduction: The pituitary gland, often termed the master gland, plays a crucial role in controlling other endocrine glands. Diseases of the pituitary gland not only disrupt the activities of other endocrine glands but can also affect neighboring structures, including compression of the optic chiasm. Pituitary adenomas are recognized as the primary pathology, ranking as the third most prevalent intracranial tumor. Magnetic Resonance Imaging (MRI) serves as the gold standard diagnostic tool for pituitary disease. The recent increase in automatic segmentation of medical images relies on manually annotated images as ground truth data, yet there are no established guidelines for such data concerning the pituitary gland and its surrounding structures. This work intends to: 1) develop a comprehensive and validated methodology for manually delineating the normal pituitary gland and its surrounding structures, 2) generate ground truth data through the established approach to facilitate the training of automatic segmentation models, and 3) Lay the groundwork for the segmentation of pituitary disorders by establishing a foundational step based on the developed methodology and ground truth data.

Methods: Two independent annotators utilized T1-Weighted MR images from the Hammers atlas database and Lyon database to manually annotate the pituitary gland, pituitary stalk, and optic apparatus (optic nerve, optic chiasm, and optic tract). A novel illustrated segmentation protocol (which is available at https://acrobat.adobe.com/id/urn:aaid:sc:EUF70f80d26-0e5b-4cce-89b2-0641072290e5) was developed and used as a guide for manual delineation of the region of interest by the annotators (Figure 1). ITK-SNAP software was used as the segmentation tool. Both Inter-rater and Intra-rater reliability tests were conducted. Results for Jaccard Index and Dice similarity coefficient were considered crucial in the evaluation of the performance of the segmentation. Other metrics such as false negative (FN) and false positive (FP) predictions and Hausdorff distance were also obtained.

Results: Table 1 presents the Inter-rater reliability test scores for the two annotators; each having segmented at least 15 images. The intra-rater reliability test scores for annotator 1, based on 10 images, exhibited Jaccard index and Dice similarity coefficients of 0.82 and 0.90 for the pituitary gland, 0.71 and 0.82 for the pituitary stalk, and 0.75 and 0.85 for the optic apparatus, respectively. Annotator 2, working with 5 images, demonstrated Jaccard index and Dice similarity coefficients of 0.80 and 0.89 for the pituitary gland, 0.85 and 0.92 for the pituitary stalk, and 0.74 and 0.85 for the optic apparatus, respectively.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|}
\hline
\textbf{Label} & \textbf{Jacard} & \textbf{Dice} & \textbf{FP Predictions} & \textbf{FP Predictions} & \textbf{Hausdorff Distance} \\
\hline
Background & 1.00 & 1.00 & 0.00 & 0.11 & 2.15 \\
Pituitary Gland & 0.73 & 0.84 & 0.14 & 0.00 & 3.30 \\
Pituitary Stalk & 0.62 & 0.76 & 0.18 & 0.00 & 2.02 \\
Optic Apparatus & 0.61 & 0.75 & 0.10 & 0.00 & 12.08 \\
\hline
\end{tabular}
\caption{Table 1: Inter-rater reliability test scores}
\end{table}
Conclusions: The pituitary gland is relatively small when compared to other brain structures, and the pituitary stalk is notably smaller. This makes it difficult to obtain remarkable similarity scores between the annotators. Despite this, the final scores obtained fall within acceptable range. The novel illustrated replicable protocol has potential to aid in segmenting T1-weighted MR images from different publicly available and local database which can enrich the available ground truth data for pituitary glands and its surrounding structures.

References

Poster No 2230

Digging Deeper into the Pervasive Problem of Non-Compliance in MR datasets

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Introduction: Large-scale neuroimaging datasets are vital for brain-behavior studies, but the reliability of statistical results depends on its data quality. Therefore, protocol compliance becomes indispensable, emphasizing the need for accurate data acquisition for each subject across sites and scanners. Manual protocol compliance is impractical especially for massive datasets, necessitating an automated approach for minimizing non-compliance. We have demonstrated the pervasive lack of compliance in large-scale datasets¹ using our open-source tool mrQA, revealing a substantial non-compliance rate of up to 60%, even though the initial exploration focused on a limited subset of parameters. mrQA can now inspect many more parameters to generate a comprehensive compliance report. Apart from ensuring that all subjects were acquired accurately for each sequence (horizontal audit), mrQA also checks if related sequences acquired within a session are compatible with each other (vertical audit) as shown in Figure 1. With the integration of deeper checks with additional parameters, it becomes apparent that more issues may emerge, emphasizing the need for rigorous monitoring practices. We also explore patterns of non-compliance across scanner vendors, models, and sites such that appropriate strategies can be adopted to minimize such issues at MR imaging centers.

Methods: mrQA parses DICOM files from the input dataset to store the most comprehensive acquisition information, and then summarizes issues of non-compliance in a user-friendly report. We assess the protocol compliance and patterns of non-compliance, in the large open Adolescent Brain Cognitive Development (ABCD) dataset². For the vertical audit, we focus on field maps for DWI as they play a crucial role in distortion correction³.
**Results:** The results demonstrate a lack of compliance in coil and pixel spacing as shown in Table 1. We also observe significant differences in non-compliance rates across vendors, scanner models & sites. We observed that scans in the ABCD dataset have been acquired with different coils as the choice of using either a 32-ch (HEA, HEP) or a 64-ch coil (HC) was determined by their availability at respective sites. A few subjects were also scanned using body coil (BC) and spine coil (SP). Identifying scans with 32-ch/64-ch coils is important, so that appropriate measures are taken to adjust for coil differences. A total of 217 subjects had a non-compliant shim setting, meaning that the shim values were not identical for the field map and the corresponding DWI, which can lead to suboptimal distortion correction. Some subjects had a non-compliant PED for both the field map and the DWI, which we speculate may have been due to manual propagation of the acquisition information from prior sequences (field map) to the latter ones (DWI) at scanning interface. Although, this doesn't impede distortion correction, it may cause differences in fractional anisotropy estimates. Certain scanner models (Figure 2) and acquisition sites (Figure 3) exhibited higher levels of non-compliance rates, indicating the influence of scanner & site-specific factors. These patterns highlight the need for automated tools that can identify non-compliance across vendors and sites. mrQA can be used as a continuous monitoring tool e.g., hourly or daily, to promptly catch non-compliance and minimize the number of non-compliant sessions for a given project.

**Table 1:** For each sequence, the table shows the acquisition matrix, rows, columns, field of view (FOV) and pixel spacing. We observed that the pixel spacing for Philips scans (1.66 mm x 1.66 mm) does not match with the published image resolution (1.71 mm x 1.71 mm) by Hagler et al. [2]. The acquisition matrix and pixel spacing was consistent for Siemens and GE scanners.

**Figure 1:** Overview of the relationship between different various levels relevant to protocol compliance checks such as subject, sequence, site, etc. We define a horizontal audit to be across all subjects for a given sequence whereas a vertical audit checks if all the sequences are compatible for a subject in each session.
Conclusions: We have demonstrated that the problem of non-compliance is pervasive in MR imaging and report deeper patterns of non-compliance through vertical audits. Automated tools (such as mrQA) are required to minimize non-compliance that can directly interface with DICOM files from a scanner and conduct comprehensive horizontal and vertical audits. Furthermore, acquired images should be monitored for compliance on a daily basis, rather than the current practice of producing years’ worth of non-compliant data, that is a very costly reacquire.

References
Wrapping up the IBC project: Neuroimaging for precision mapping

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Introduction: The Individual Brain Charting (IBC) project was initiated in 2015, with the aim of constructing an extensive neuroimaging dataset, primarily focused on functional Magnetic Resonance Imaging (fMRI) data, that would capture core functional organization across individual brains by spanning a wide array of cognitive domains. This would enable detailed characterization of individual topographies and a more comprehensive understanding of factors influencing cognitive processes.

Methods: Here we present the final release of the IBC dataset, which comprises 1.5mm-resolution fMRI data from 8 to 12 participants, each undergoing 50 hours of fMRI data collection (with 12 participants completing 40 hours, and subsequently, some dropouts). Throughout these hours, participants engaged in over 80 different cognitive tasks. Additionally, we provide a glance of the broad spectrum of stimuli and tasks featured throughout all the IBC data collection years, aiming to offer a comprehensive view of the intensive and cumulative coverage of various cognitive domains. Prior releases have laid the groundwork for a very wide range of tasks and explored several domains: mathematical calculations, language, social reasoning, gambling, mental time traveling, spatial navigation, emotional memory, risk evaluation, motor planning, response inhibition, to mention some. This ultimate release builds upon these domains and introduces new exciting paradigms:

- Color effects in motion perception and working memory
- Motion detection and visual awareness
- Optimism bias for future projection and past recall
- Gender and emotion interaction
- Effect of face perception on gender and emotion perception
- Working memory related to orientation
- Outline and form recognition
- Movie watching and resting state
- Semantics processing and prediction
- Action observation and retrieval
- Motor execution
- Negative scenarios impact on emotional state
- Tactile stimulation and tactile working memory
- Video-game playing

Results: The collected data underwent preprocessing and statistical analysis, resulting in over 700 contrasts, described based on more than 200 cognitive atoms sourced from the Cognitive Atlas. Additionally, the IBC dataset includes resting-state fMRI and diffusion-weighted imaging data, a series of anatomical images acquired repeatedly over the years and the subjects’ behavioral performance results on each task. With this, and thanks to the consistent environment throughout all acquisitions, we have completed a years-long effort to acquire a high resolution dataset, free from inter-subject and inter-site variability, to characterize individual responses to a broad range of stimuli and assignments.
Conclusions: All data, at every processing stage (raw data and derivatives), are accessible through open-data platforms, with EBRAINS serving as the primary repository. The IBC project is committed to reproducibility and open science, openly sharing all routines and scripts used for protocol implementation and data analysis. This makes IBC a vast resource of ready-to-run tasks. Additionally, we develop and maintain tools to facilitate easy data or task fetching with just a few lines of code, with the aim of enabling convenient reuse by the community.
ABSTRACTS

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Poster No 2232

Cohort-creator: access and evaluate only the data you need from open BIDS datasets

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Introduction: The landscape of open neuroimaging datasets is expanding rapidly, with a notable increase in the availability of BIDS (Brain Imaging Data Structure) datasets. Many of these datasets have open derivatives data, (fMRIPrep preprocessed data2 or MRIC2 quality control reports). While platforms like OpenNeuro host a significant portion of these datasets and their derivatives, some are scattered across various platforms, necessitating users to navigate different sources. The introduction of a tool like Neurobagel6 addresses some of these challenges by enabling users to conduct searches across multiple datasets, providing a comprehensive list of participants that match specific queries. However users interested in a particular subset of data currently face difficulties accessing it seamlessly. In the current state, users encounter the following issues: - lack of monitoring for growing open data: there is no easy way for users to obtain regularly updated overviews of the content within these datasets. - absence of tools facilitating access: users looking to access specific subsets of datasets across various sources encounter a significant challenge. - no tools for summary reports on content and quality of the accessed data. This deficiency makes it challenging for users to assess the suitability and reliability of the data they intend to use.
**Methods:** The goal is to create a command line tool with the following functionalities. 1. Monitoring BIDS Datasets: - Periodically check specified BIDS datasets for updates. - Extract metadata about the datasets, such as available modalities, tasks, and participants. - Generate reports summarizing changes and additions to the datasets. 2. Aggregating synthetic cohort: - Take a neurobagel query results as input to define a cohort of participants to download from several datasets. - Access multiple BIDS datasets and their derivatives to aggregate participants. - Parametrize the cohort creation to only include the data necessary for certain analysis: for example only download functional MRI or diffusion MRI data. - Create a synthetic cohort based on the defined criteria and organize this new dataset following the recommendations from the BIDS extension proposal 35 for mega-analysis. 3. Generating reports on Cohort Content: - Create summary TSV file to report on the status of derivatives availability that can be viewed and browsed with the neurobagel digest dashboard. - Create MRIQC group summary reports for the subset of participants included in the cohort. - Produce reports detailing the number of subjects, basic demographics, imaging modalities, and other relevant information for each datasets included in the cohort.

**Results:** At the time of this writing the cohort-creator package (https://pypi.org/project/cohort-creator/) allows access to 1113 datasets containing 48579 subjects representing over 69 terabytes of data. 1018 of those datasets are on openneuro from which 781 datasets contain MRI data with the following available derivatives: - with fMRIPrep output: 97 (4179 subjects) - with freesurfer output: 38 (3342 subjects) - with MRIQC output: 333 (14829 subjects) Following a query on neurobagel providing the user a listing of datasets (dataset.tsv) and participants (participants.tsv), a user can easily get and reorganize the corresponding data and available derivatives with 3 commands. The output will include a TSV file summarizing the availability of derivative data for each participant and visualization of for each dataset (for example: number of subject, gender ratio) or for the entire cohort (age distribution for each gender).

```bash
# clone the relevant data/label datasets and derivatives
cohort_creator install
  -d datasets.tsv
  --dataset_types raw mriqc fmrilep

# get only data for participants, datatype in a specific MRI space
cohort_creator get
  -d datasets.tsv
  --participants.tsv
  --dataset_types raw mriqc fmrilep
  --datatype anat func
  --space T1w MNI152NLin2009cAsym

# reorganize the data into a cohort
cohort_creator copy
  -d datasets.tsv
  --participants.tsv
  --dataset_types raw mriqc fmrilep
  --datatype anat func
  --space T1w MNI152NLin2009cAsym
```

*Figure 1: example of the cohort creator API*

![Graph](image1)

**Figure 2:** TOP - size (number of participants and amount of data per participant) of open BIDS dataset; BOTTOM - age distribution of the participants aggregated from several dataset from openneuro queried with neurobagel.
Conclusions: The cohort-creator allows users to get an overview of available open BIDS datasets and access a subset of them. At the moment, one of the main limitations of this tool is that it only monitors and allows access to datasets curated with datalad and hence may be missing datasets hosted on other platforms (zenodo, openscience framework...).

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Poster No 2233

The Human Connectome Phantom (HCPPh) dataset
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Introduction: Network-based approaches are widely adopted to model functional and structural ‘connectivity’ of the living brain, extracted noninvasively with magnetic resonance imaging (MRI). However, these analyses -on functional and structural networks- render unreliable at the finer temporal, spatial, and brain-parcellation scales. Here, we introduce the Human Connectome PHantom (HCPPh) dataset as part of our recent Stage 1 Registered Report1 (Fig. 1).

Methods: Data. One healthy participant (author OE), left-handed, aged 40 at the onset of the study underwent 50 sessions (14 of which were piloting sessions or sessions excluded for insufficient quality of the data or circumstantial impediments to finalizing the protocol) with a comprehensive MRI protocol on a single, 3T Siemens PrismaFit scanner. The protocol includes anatomical (T1-weighted, T2-weighted), high-angular-resolution multi-shell diffusion-weighted imaging, three blood-oxygen-level-dependent (BOLD) functional MRI runs (including a quality control task, QCT, of 2 m 38 s, a breath-holding task, BHT, of 5 m 41 s, and a naturalistic timelapse watching akin to resting-state of 20min 3s). The MRI protocol was acquired while simultaneously recording eye-tracking, electrocardiogram (ECG), respiratory motion with a pneumatic belt, and gas concentration collection through a nasal cannula (O2 and CO2). A second wave of data is scheduled to start the collection of 12 sessions on each of three different 3T scanners using a single protocol (36 additional sessions). Standard Operating Procedures (SOPs). All the data collection and methodological implementation details are comprehensively specified in the SOPs document5, which is openly available at www.axonlab.org/hcph-sops under a CC-BY license. Data management plan. Data are converted into BIDS3 and version-controlled with DataLad4 as described in the SOPs. Quality assessment and control of unprocessed data will be implemented with MRIQC5. Data will be preprocessed with NeuroImaging PREProcessing toolS (NiPreps; www.nipreps.org) -particularly fMRIPrep5 and dMRIPrep5. The original BIDS dataset, as well as all derivatives, will be openly shared upon culmination of Stage 2 of the Registered Report.
Figure 1. Characterizing the reliability of nodes in connectivity matrices extracted from a single human phantom. Leveraging three 3 T scanners available at Los Angeles University Hospital, a single human subject will undergo 72 MRI sessions to evaluate the variability of structural and functional connectivity (SC, FC, respectively). One scanner will accommodate a reliability MRI acquisition protocol, including a number of physiological signals and eye-tracker information that will allow for sophisticated denoising and a more reliable identification of signal with non-neural origins. Data will then undergo standardized and pre-registered management, preprocessing (with MRIQC, Armitage et al., 2017, and FreeSurfer, Joseph et al., 2012), and connectivity extraction. Each of these steps will be correlated with data releases using the BIDS (Brain Imaging Data Structure; Gorgolewski et al., 2016) specifications to maximize reusability. A total of 36 pairs of SC and FC matrices will then be fed into analyses of variance to identify and characterize the reliability of edges. An additional set of 36 sessions (12 per scanner) of an adapted MRI protocol suitable for clinical practice will allow to investigate scanner effects and to estimate generalization of the results on data from other scanners. Abbreviations are spelled out at the bottom of Table 4.

Table 2. ‘The HCP database’ will fill a number of gaps within currently available ‘dense imaging’ datasets. A number of datasets have focused on acquiring large amounts of MRI data on a limited number of individuals. However, these datasets have typically been acquired with the advance of our understanding of the human brain as a goal. Conversely, the HCP is designed to fully understand and characterize the reliability of functional and structural connectivity analyses, from the acquisition of MRI data to the extraction of network information. Therefore, the HCP focuses on the assessment and optimization of our research instruments, henceforth contributing to making currently existing datasets more valuable and to increasing the trustworthiness of neuroimaging results. Several openly accessible datasets are not included in this table, because they only contain FMRI (e.g., Noble et al., 2017; Choe et al., 2015; Gordon et al., 2017; Seddiger et al., 2019) or fMRI (e.g., Cal et al., 2023; Forgel et al., 2016; Seiler et al., 2022) data, and therefore they cannot be used in multi-modal (SC and FC) analyses.
Results: A dataset to address hypotheses about the instruments as opposed to the brain. By very densely collecting data on a single individual, we aim to investigate questions about the MRI imaging device and interactions with physiological and instrumental sources of variability. While this dataset will not provide any new insights into behavior or white matter microstructure, it is the first dataset to ‘calibrate’ functional and structural connectivity neuroimaging pipelines, enabling their comparison and isolating the different sources of variability throughout the workflow. Table 1 (reproduced from the corresponding Registered Report) highlights the potential contribution of the HCPh in the landscape of open or at least reportedly accessible dense MRI datasets. A comprehensive, version-controlled experimental reporting. Our SOPs have been created using the NIPreps’ ‘SOPs-cookiecutter’ project (nipreps.org/sops-cookiecutter/), which maximizes the shareability of the SOPs documentation, keeps version control leveraging Git and may employ GitHub’s features for code review, automated actions (e.g., to check spelling errors or normalize the style of the Markdown code), and publishing while protecting sensitive information (e.g., usernames and passwords) by a design that keeps secrets inaccessible from the public repository. A resource to harmonize data across scanners. With the collection of a wealth of multi-scanner data (n=12 sessions per scanner), this dataset will help develop new harmonization techniques without introducing individual differences in models.

Conclusions: The HCPh dataset will be openly released to be used as calibration data on network analyses, as exploratory data, or for educational purposes.

References

Poster No 2234

Alright then, keep your secrets – federated cohort search at the participant level with Neurobagel

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Introduction: Sharing and combining neuroimaging datasets is impactful1, mandated by funders and journals2, and essential for obtaining the increasingly large samples needed to identify and validate robust brain-behaviour markers3. However, the growing amount and detail of participant information in datasets also raises questions on data governance4 and legal constraints to data sharing5 that can differ across institutions. These constraints hamper the pooling of data in centrally curated data platforms and the open sharing of data. Federated data governance is an alternative approach that stores and curates data locally under the control of the collecting institution (data owner), and connects and integrates data in a decentralised manner through the adoption of common technical standards and protocols. Recent efforts in genomics show the promise of this federated model6 but also the greater need for coordination on terminologies and the often prohibitive technical complexity. Neurobagel provides user-friendly tools for a research group to 1) annotate their own data using existing, standardised vocabularies and 2) create harmonised representations of the subject data in a local Neurobagel node, in turn 3) enabling cross-dataset subject search based on specific attributes. Here we introduce a federation architecture that builds on existing Neurobagel tools to provide participant-level search across decentralised nodes, which remain under the control of their local data owners, while respecting site-specific data visibility constraints.
**Methods:** The federation API (or f-API) is a Dockerized API built on existing local Neurobagel node architecture. Each Neurobagel node exposes a node API (or n-API) for querying data within, and the node owner can choose the restrictiveness of query results (Fig. 1). The f-API and n-API are designed so tools can be developed that can consume either API. The f-API supports two use cases: 1) deployed to the public internet as the federation engine for openly accessible Neurobagel nodes, 2) deployed intra-institute to enable internal federated queries across nodes managed by different local data owners (e.g., research groups). The node-specific control over query result granularity helps ensure that regardless of federation scope, individual dataset sharing constraints can be satisfied. The f-API reads an index of known nodes it can federate over, that by default includes all public Neurobagel nodes so that they will be readily searchable even by an internally deployed f-API. When a query is received, the f-API forwards it asynchronously to all known nodes and combines the responses, including complete or aggregated information about matching participants, into a single set of results to the user (Fig. 2). The f-API also exposes the list of nodes it federates over, allowing a user to query only a specific subset of nodes. Adding a new node to the f-API simply requires updating the local index of nodes and restarting the f-API service.

![Diagram](image1.png)

**Figure 1.** Architecture of a Neurobagel "node": a local graph store of harmonised dataset representations accessible to users via a dedicated API. Neurobagel-guided annotations of subject data for local datasets are processed into the local graph that can be queried using a Neurobagel node API. A node API can be configured with varying levels of detail for query matches depending on sharing restrictions for participant-level attributes.

![Diagram](image2.png)

**Figure 2.** Neurobagel architecture for federation subject queries across local and publicly accessible sites (nodes). The Neurobagel federation API allows querying of multiple nodes simultaneously. Through one-way federation, public Neurobagel nodes can be included in a federation network together with nodes only accessible within a local institute, allowing institutional researchers to query subjects in locally restricted datasets together with publicly available ones.

**Results:** Our public f-API searches over 23500 participants and 342 datasets from 3 public Neurobagel nodes, 2 of which provide only aggregated results. The index of public Neurobagel nodes is available on GitHub, making it easy to update. The graphical Neurobagel query tool (query.neurobagel.org) has been updated to be compatible with the federation API and lets...
users choose which nodes to include in a query. An internal f-API was tested at the Douglas Research Centre, where internal users can now search harmonised local data alongside those from the publicly available Neurobagel nodes.

**Conclusions:** The Neurobagel federation architecture will allow local data owners to participate in a federated data governance system by adopting existing Neurobagel tools for annotation and deployment of local nodes. We will expand this architecture by aligning with existing protocols for federated authentication, granting data owners finer grained control over what users can query about their data.

**References**


**Poster No 2235**

**NeuroSynth Compose: A Web-Based Platform for Reproducible Meta-Analyses**

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**Introduction:** The advent of fMRI has resulted in a deluge of over 20,000 studies mapping function to neuroanatomy. Meta-analysis is essential for gleaning insights into human brain function; however, the painstaking process of collecting, extracting, and synthesizing data is a major bottleneck limiting its routine application in scientific practice. We present a powerful and easy-to-use platform for meta-analysis, leveraging text mining, artificial intelligence and streamlined curation workflows to enable researchers to perform precise meta-analyses in a fraction of the time without leaving their browser.

**Methods:** Neurosynth Compose is a modular ecosystem of tools to curate, ingest, and annotate data, and execute meta-analyses. We index over 20,000 neuroimaging studies, featuring pre-extracted imaging data from a diverse range of journals. We automatically annotate studies with ontological labels from Cognitive Atlas and Disease Ontology and extract structured meta-data such as participant count using OpenAI’s GPT-3.5. We implement a web-based PRISMA curation workflow, enabling users to systematically include studies into a final set for meta-analysis, and annotate studies with custom meta-data. Finally, users can specify a reproducible meta-analysis specification, which is executed in the cloud and automatically uploads results for easy sharing.

**Results:** We replicated Witt (2008) meta-analysis of 38 studies investigating finger tapping using the ALE algorithm, resulting in a quantitatively similar result to the original study. The specification and results are accessible in the unique meta-analysis page (https://bit.ly/ns-meta-analysis).

**Conclusions:** Neurosynth Compose removes major barriers to meta-analysis democratizing quantitative syntheses of the vast and diverse neuroimaging literature for a wide range of researchers.
Fig. Components of the meta-analysis workflow from curation to execution of the meta-analysis

References

Poster No 2236

FMRIPrep preprocessing of the UK Biobank using CBRAIN for NeuroHub

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Introduction: NeuroHub (https://neurohub.ca) is a core platform of McGill University’s Healthy Brains, Healthy Lives initiative (https://www.mcgill.ca/hbhl/). NeuroHub offers researchers an overarching data and computational platform to store and analyze data, collaborate with colleagues and work with computational infrastructure. In particular, NeuroHub provides a unifying and efficient access to the UK Biobank (Miller et al., 2016) to the McGill research community. CBRAIN (Sherif et al., 2014) allows scientists to launch large-scale big data analyses using advanced scientific tools through an easy to use web-based user interface. CBRAIN has been used to perform large-scale preprocessing of the UK Biobank imaging data.

Methods: All UK Biobank data is downloaded and packaged into a single, access controlled instance. This instance is maintained on the Digital Research Alliance of Canada’s Beluga system through a large-scale, multi-year data storage allocation. The downloaded images are arranged together with the associated tabular participant entries into a BIDS structure (see Figure 1). The imaging data is then pre-processed by the NeuroHub team using tools such as CIVET (Kim et al., 2005), TractoFlow (Theaud et al., 2020) and fMRIPrep (Esteban et al., 2018). Derived data is shared back with other application members and avoids unnecessary duplication of computational effort. Since November 2023, preprocessing of the UKBiobank subjects with fMRIPrep has been completed using CBRAIN and the outputs have been packaged for user-level access. The outputs of the fMRIPrep pipeline run over 37,732 subjects from the UK Biobank dataset with neuroimaging data have been generated and are available on both the CBRAIN portal and directly on Beluga. The dataset is voluminous, containing 16,935,185 files and uses 117 terabytes of disk space. It took nearly 5 months for the HPC systems to produce the files, and over 103 years of computing time. During processing, over two billion intermediate files were produced. The
fMRIPrep task parameters include different output spaces offering multiple options to the users depending on their area of interest.

Results: Authorized users can access the fMRIPrep outputs through the NeuroHub portal and the command-line on the host HPC system. All modes of access adhere to the data use agreement with the UK Biobank. The portal offers a secure and friendly Graphical User Interface to the 37,732 fMRIPrep outputs. By selecting the file(s) of interest, users can open, expand and visualize the file(s) directly in the browser without the need of downloading (see Figure 2). On the Beluga system, the outputs of the fMRIPrep pipeline are available through a series of SquashFS files and need to be mounted via an Apptainer container. They are packed in 189 SquashFS files named as fmriprep_000_1000011-1025826.sqfs, for example. In this first file, the subject IDs 1000011 to 1025826 are present. Each SquashFS file contains about 200 subjects. Because the amount of data and the number of files are so large, users are not recommended to copy any of the SquashFS files. Instead, we offer multiple ways to directly access the contents. Detailed documentation is provided on how to browse the fMRIPrep outputs interactively and how to use tools and scripts for processing non-interactively.

Conclusions: NeuroHub provides McGill researchers with a unifying and efficient point of access to the UK Biobank. Users are able to access the UK Biobank fMRIPrep output through HPC resources via the NeuroHub and CBRAIN portals as well as the command-line. The coordinated preprocessing of UK Biobank data efficiently leverages available compute resources and avoids costly duplication of storage and effort. By doing so, NeuroHub offers a wide spectrum of preprocessed data (Diffusion-weighted imaging, Civet Output and now fMRIPrep output) available for users without the need of running pipelines so they can focus on advancing their research.

References


Poster No 2237

Image Quality Variation and Cortical Volume Estimation in a Multisite Study of Low Back Pain

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Introduction: Chronic low back pain (cLBP) is one of the leading causes of disability in the world and one of the top non-cancer reasons for opioid prescription in the United States (Ferreira 2023; Ringwald 2014). The Back Pain Consortium (BACPAC) Research Program is an interdiscipliary effort to better understand the biopsychosocial factors contributing to cLBP (Mauck 2023). Within the Consortium, the Brain Imaging Working Group conducts neuroimaging studies aimed at elucidating brain structural and functional biomarkers associated with pain perception and treatment efficacy. To collect a large, diverse participant sample, a protocol was developed to standardize image acquisition parameters across the different hardware and software configurations at participating sites. This work presents preliminary results comparing image quality control (QC) metrics and morphometric measures derived from structural MR images collected on 10 MR scanners within the BACPAC network.

Methods: Overview of Participants Participants were recruited as part of each institution’s BACPAC study. Common inclusion criteria include the presence of low back pain. Here we report results from the first 8-16 subjects per site. In addition, a traveling subject (healthy volunteer, male, age 28-29, BMI = 27.9) was scanned on at least one scanner at each site between July 2021 and September 2022. Image Acquisition Neuroimaging was performed on a total of 10 different scanners across 6 sites. The scan protocol outlined sequences for three MRI techniques: T1-weighted and T2-weighted structural imaging and functional MRI using single shot echo planar imaging. Here we report results using T1-weighted images only (MP-RAGE, TR/TE 2500/2.88 (Siemens), 2500/2 (GE); voxel size 1.0 mm isotropic; matrix 256x256; flip angle 8 deg). All sites used 3T MR Siemens or GE scanners. Quality Control Image quality metrics were extracted using MRIQC v23.1.0 (Esteban, 2017). Here we report 4 summary metrics: the signal-to-noise ratio calculated within the tissue mask (SNR_Total); the contrast-to-noise ratio representing the separation of gray and white matter signals (CNR); the average full width at half maximum, a measure of image smoothness (FWHM_AVG); and a ratio of the SNR to FWHM (SNR/FWHM). All metrics and formulas are described in further detail in MRIQC’s documentation. One-way ANOVA was performed to test for site differences in each of the QC metrics. Tests with a p-value less than 0.05 are reported. Brain Volume Analysis Brain volume measurements were derived from traveling subject data using FreeSurfer v1.201 (Dale 1999). Here we report total brain volume and insula volume, an ROI involved in pain processing (Labrakakis, 2023).

Results: Image quality metrics for all subject data are shown in Figure 1. There is a statistically significant difference between the sites for all four QC metrics, as follows: SNR_Total: F= 13.17, p-value= 6.13e-10, with an overall large effect (ω2) = 0.36. CNR: F= 11.22, p-value= 1.15e-8, with an overall large effect (ω2) = 0.32. FWHM_AVG: F= 13.00, p-value= 7.92e-10, with an overall large effect (ω2) = 0.22. Results of the brain volume analysis are shown in Figure 2. Whole brain volume estimations for the traveling subject = 1289874.43 ± 13209.57 mm3; Insula volume estimations = 7094.86 ± 271.21 mm3.
Fig. 1. Each subject is represented by a black point and where available, corresponding traveling subject data (ts) is represented in yellow. Boxes are colored according to the scanner manufacturer.

Fig. 2. Brain volume measurements derived from traveling subject data. Each point represents the same subject’s acquisition at a different scanner and is colored according to the legend on the right.

**Conclusions:** We show that group level image quality measures vary significantly between sites despite harmonization of the imaging protocol. We also show variation of several hundred mm3 in brain volume estimation on the traveling subject when scanned at different sites. Future directions will include a deeper investigation into the causes of these variations, such as image artifacts, coil or software differences, as well as the impacts and considerations when pooling the data for analysis.

**All authors besides Jennifer Cummings, Jagan Jimmy, and Scott Peltier are listed in alphabetical order**

**References**

Open Science Collection of Clinical, Biological, Imaging, and Genetic (C-BIG) Data and Samples

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Introduction: The Open Science Clinical, Biological, Imaging, and Genetic (C-BIG) collection at the Montreal Neurological Institute (The Neuro) has successfully recruited nearly 4000 participants, encompassing individuals with neurological conditions and healthy controls since 2016. Leveraging LORIS1 (Das et al., 2012), an open-source database developed at McGill University over two decades, this open biobank harmoniously integrates patient and sample data. The aim is to empower scientists globally, operating within an Open Science framework, to conduct cutting-edge research advancing our understanding of neurological diseases and exploring therapeutic interventions.

Methods: In the past year, LORIS introduced version 24.1, tailored as a biospecimen module for internal use by the C-BIG biobank. This module includes sample processing data and metadata for biological materials. A dedicated module collects de-identified patient information, such as phenotypic details, diagnoses, genetic reports, and participant enrollment details. The imaging module consolidates defaced scans (CT-scan, PET, MRI), linked via unique patient identifiers to the broader dataset. Within McGill's McConnell Brain Imaging Center, C-BIG serves as a pivotal database for storing scans from thousands of patients. On the patient-facing side, a new demographic data collection instrument was created, ensuring compliance with Equity, Diversity, and Inclusion guidelines. A patient portal bridges the gap between the patient-clinician database2 (OPAL) and the research database (LORIS), facilitating data analysis. Specifically for human induced pluripotent stem cells (iPSCs), a Data Query Tool captures historic data and Quality Control information for internal and external users. C-BIG’s genetic data is openly released worldwide, linked to C-BRAIN (cbrain.ca) for high performance computing. Additionally, C-BIG’s genetic data has leveraged the CBRAIN ecosystem to process and store large amounts of genetic information. Specifically, by breaking down each type of data available by cohorts using a data dictionary, harmonizing the different contents, uploading datasets using DataLad and creating metadata files to describe the data to the different users, C-BIG also uses the Canadian Open Neuroscience Platform to publish datasets and generate Archival Resource Key as a permanent identifiers on Amneal.

Results: The C-BIG repository utilizes an institutional version of LORIS for data access, featuring a Data Query Tool with three levels of access: Open, Registered, and Controlled. Open access allows browsing of insensitive metadata, including a data dictionary. Registered access includes low-risk data with aggregated clinical information, raw data, defaced images, and laboratory analyses. Controlled access necessitates researchers to submit project descriptions for review by a Tissue and Data Committee before signing a non-exclusive Open Transfer Agreement. Collaborating with over 90 partners, C-BIG emphasizes compliance with Open Science principles, requiring partners to provide summary data reports within a specified timeframe if no publication occurs.

Conclusions: The C-BIG Repository aspires to enhance material and data collection under Open Science principles, aiming for a comprehensive dataset on diverse neurological conditions. The overarching goal is to contribute to global translational neuroscience research by broadening participant recruitment, integrating extensive information into the multimodal database, and accelerating collaborative research efforts across diverse partners.

References

Poster No 2239

The NEMAR gateway to neuroelectromagnetic (NEM) brain imaging data

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Introduction: Although electroencephalography (EEG) was the first functional human brain monitoring modality (1926-), EEG data analysis long lagged in adapting new data analysis approaches – both in neurology, where visual pattern recognition applied to the raw scalp signal data is still the dominant approach, and in cognitive neuroscience where event-related potential (ERP) averages of individual scalp channel signals, collected from relatively small numbers of participants, long remained the predominant research measure. These methods, however, leave unrevealed much information about brain function contained in the data, and also cannot exploit consistencies in complex data that can only be identified in and extracted from large to very large data collections using new statistical and machine learning methods. Sharing neuroelectromagnetic (NEM) data is critical to leveraging public research investment and to supporting rigor and reproducibility in funded research. Several funding bodies require data sharing. Data sharing also allows researchers to use modern research tools to evaluate new data in a new way, by directly comparing it directly to ever accumulating stores of shared data collected in related or compatible paradigms. Here we report initial results of building NEMAR (nemar.org), a large, publicly available human neuroelectromagnetic (NEM) data, tools, and compute resource tightly linked to a freely available high-performance computing resource, the Neuroscience Gateway (NSG). Our goal is to build a widely used and scientifically productive open resource for archiving, sharing, and further analysis and meta-analysis of NEM data.

Methods: The OpenNeuro archive¹ currently offers more than 933 open neuroimaging datasets from more than 37,000 participants. The NEMAR project⁴ (Figure 1) is capitalizing on the ongoing achievements of the OpenNeuro, Neuroscience Gateway (NSG)², Open EEGLAB Portal³, and BIDS standards development projects by creating a community portal to a large and ever-growing archive of human neuroelectromagnetic (NEM: EEG, MEG, iEEG) brain imaging data, data analysis tools, and advanced computational resources. Our overall goal is to support the creation, maintenance, analysis, and cross-study mining of human neuroelectromagnetic (NEM) data by seeding and growing a ‘minable’ archive of NEM data deposited in the OpenNeuro resource. After users upload NEM data to OpenNeuro, those data are automatically copied to the San Diego Supercomputer Center (SDSC) storage using the DataLad cloning mechanism. New DataLad snapshots from OpenNeuro are synched daily. NEM relevant data measures are then automatically computed on the Neuroscience Gateway and made available for display to users through the NEMAR web interface.

Results: Since 2013, the Neuroscience Gateway (NSG)³ has been serving the neuroscience community by providing easy access to many software and pipelines running primarily on high-performance computing (HPC) resources provided by the Extreme Science and Engineering Discovery Environment (XSEDE) network that coordinates resources across the NSF-funded supercomputer centers. The NEMAR gateway project shares the same infrastructure as NSG, and NSG capabilities have been expanded to allow users to run data processing tools and pipelines on NEM data of their own or from the OpenNeuro archive. NEMAR already uses NSG for computing NEM data quality metrics and also allows users to run custom MATLAB and Python scripts on NSG (nsgportal.org) using NEMAR data.

Conclusions: The NEMAR (nemar.org) front-end portal to neuroelectromagnetic neuroimaging data allows users to search for and optionally explore data submitted to OpenNeuro (openneuro.org) by viewing precomputed data quality metrics and visualized dataset information, and then process selected data using the XSEDE high-performance resources in conjunction with The Neuroscience Gateway (nsgportal.org) without requiring a data download and subsequent re-upload.
LesionBank.org: An Open Source Platform for Brain Lesion Case Reports

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Introduction: Given the recent surge of methodological innovation using human brain lesion data, our objective is to create an open source, web-based platform for aggregating, viewing, and analyzing published case reports containing both brain imaging and clinical evaluation of the patient.

Methods: LesionBank.org offers a user-friendly interface for exploring a collection of curated brain lesion case reports. LesionBank enables users to search, visualize, and retrieve lesion images and related metadata. The application leverages the Django web-framework and a Postgres database to process user requests and handle the user interface. The application is deployed on a DigitalOcean droplet, and imaging data is stored in an S3-compatible DigitalOcean object space. Currently, the collection includes 163 lesion ROIs and associated lesion network maps that were found from previous published case reports.

Results: LesionBank.org has been launched with a viewer and search capabilities based on both textual search of case reports and image-based search of published brain lesion images. To date, the LesionBank.org platform has been used to successfully reproduce primary findings from an already-published study on amnesia (Ferguson, 2019). Additionally, LesionBank.org has been used to support training of several dozen undergraduate research assistants to identify brain lesion case reports of interest, create digital lesion tracings from published, catalog metadata, and relate brain lesions to their underlying functional connectivity.

Conclusions: Science: LesionBank, an open source platform for brain lesion case reports, is able to reproduce brain lesion mapping results from published literature. Education: LesionBank is able to power an asynchronous undergraduate semester research course on clinical neuroscience.

References

Poster No 2241

“TopUp Docker”, an SPM extension for EPI distortion correction

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Introduction: It is well known that EPI images, used in functional MRI, present geometric distortions due to the susceptibility distribution. These deformations prevent a good match with other non-affected modalities and accurate localisation of the brain activity recorded. To address this issue, two approaches have been proposed: the “field mapping” and “top-up” approaches¹². The former requires the acquisition of specific “field map” images, which allows the derivation of the field inhomogeneity and of the distortion through a physical model. On the other hand, the “top-up” approach only requires
the acquisition of a few EPI images with an opposite phase encoding direction thus leading to a distortion in the opposite direction. With these 2 sets of images, one then estimates the field that when applied to the two sets of volumes will maximise the similarity of the unwarped volumes. Both approaches are available in widely used open source packages, “field map” in SPM and “top-up” in FSL. Nevertheless either approaches cannot easily be integrated in the same processing pipeline, e.g. for a direct comparison of their performances, because of their respective eco-systems. For example SPM users are largely limited to the “field map” correction approach.

Methods: Here we propose a lightweight Docker containerized version of the FSL's topup tool directly interfaced in Matlab. On top of this, we provide the MatlabBatch GUI to integrate the “top-up” correction into SPM’s batching system. The Docker installation simply requires to 1/ install Docker Desktop, 2/ download the “TopUp_Docker” container [REF6], 3/ load it into Docker. Then the Matlab code has to be placed in a folder on Matlab’s path and the MatlabBatch “config” files in a folder named “TopUpDocker” in SPM’s “toolbox” subfolder, e.g. C:\SPM12\toolbox\TopUpDocker.

Results: The Matlab code, which will only work if Docker is installed and loaded with the right container, is organized in 3 levels: - “low level” functions talk directly to Docker and activate the container, through ‘system’ commands; - “intermediate level” functions deal with the images to parameters to perform the calculation, moving things around as necessary to work with Docker; - “high level” functions integrate the tool in SPM and provide a “wrapper” for the end user. We also provide a small function that tests if Docker and the TopUp container are behaving as expected when actioned from Matlab Since the core of the processing is FSL topup tool, the results of obtained on a dataset with an FSL installation or the Matlab-interfaced docker-ized version are exactly the same.

Conclusions: The code and container allow to fairly easily use FSL's topup correction in Matlab and SPM, without the need to install a full FSL distribution, which requires a macOS or Linux system. The approach proposed, interfacing Docker with Matlab, also opens the door to using other non-Matlab tools in Matlab. The container weights only about 350MB, compared to the “15GB of a full FSL distribution, and is available on ULiege's dataverse, while the Matlab code is openly available on GitHub.

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Poster No 2242

Integrating NiiVue into VS Code – A flexible image viewer for neuroimaging pipeline developers

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Introduction: For the development of new imaging and reconstruction methods, it is essential to have a convenient way to quickly view and compare images. While many professional viewers exist for medical images, they fail to streamline the workflow for developers. It is often inconvenient to transfer the files from the reconstruction computer to the device with the imaging software installed. Moreover, software is often limited to specific operating systems and supports only a small subset of image formats. Therefore, we developed a medical image viewer extension for Visual Studio Code (vscode) based on the NiiVue project1 for simple and fast viewing of local and remote files. This viewer is primarily targeted towards developers of reconstruction pipelines, but also supports a wide range of imaging workflows in vscode.

Methods: The niivue-vscode design prioritizes intuitive access to most commonly used features, aiming for minimal user clicks. While also incorporating advanced functionalities, the primary goal is to ensure a straightforward user experience, specifically tailored to developing workflows. Built upon the webGL-based NiiVue medical image viewer library5, the niivue-vscode extension integrates its capabilities into the vscode environment. This extension not only serves as an interface
to vscode but enhances its functionality especially for viewing multiple volumes in a synchronized view. This integration combines vscode’s robust remote capabilities with the seamless image viewing capability of NiiVue.

**Results:** More than 30 medical image formats are supported. The left side of Figure 1 shows the basic multiplanar layout with a 3D rendered image, and the right side of Figure 1 shows a mesh with curvature and a superimposed colored overlay. In the context of meshes, the extension further features saving and loading of the current view-angle. Comparison of multiple volumes is supported with synchronization of the selected voxel and of zoom settings between the volumes (Figure 2). After selecting the volumes in the vscode file explorer, they can be opened by right-clicking and selecting “NiiVue: Compare”. Contrast adjustments can be applied to all loaded images simultaneously. In addition to the images, basic metadata is presented and detailed header information can be accessed quickly. The vscode extension was developed to be compatible with remote environments and supports opening of images in a remote vscode session, e.g., through an ssh-connection to a cloud virtual machine or high-performance computing cluster, and it also supports vscode web and github.dev. Niivue-vscode uses web-based technologies and can be additionally accessed via the browser at https://korbinian90.github.io/niivue-vscode/. It supports progressive web application features and can be installed from chromium-based browsers as a local app on all major operating systems and integrates with local file associations. The code base is hosted open-source and feedback of the community is actively encouraged. The extension is in active development and a list of features planned to be integrated in future versions is posted as issues on the github repository.

![Figure 1: vscode window with two opened instances. Left: default multiplanar view with a 3D rendering. Right: mesh with curvature and superimposed overlay](image1)

![Figure 2: Synchronized view of multiple volumes in vscode. The pixel location, the selected slice as well as the zoom level are synchronized between all images](image2)
Conclusions: Niivue-vscode is a convenient tool to quickly view medical images for comparing and debugging during the development process of reconstruction and analysis pipelines. It supports over 30 medical imaging formats for voxel-based and mesh data assisting in image analysis and visualization across different contexts.

References
1. Niivue repository; https://github.com/niivue/niivue

Poster No 2243

Review of neuroimaging meta-analyses: Topics, methods, and authors
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Introduction: Researchers and clinicians increasingly rely on meta-analyses to make sense of the rapidly-growing literature. It is unclear whether we, like other fields, have over- or under-analyzed different topics. Further, in neuroimaging, researchers have invented novel methods for meta-analyzing image data, but we have not yet had a comprehensive review of the use of these methods. Finally, we do not know whether this field of meta-analysis is subject to the same gender biases as the larger neuroscience field. In this review, we aim to address these gaps in our knowledge about the topics, methods, and authors of neuroimaging meta-analyses.

Methods: For this project, we used the LitMining ecosystem of tools for meta-research. We used pubget to query PubMed Central and PubMed in order to find fMRI meta-analyses (n=849), as well as participant-level fMRI studies (n=4962). We further collected a set of papers associated with data on NeuroVault (n=1091). To extract topics, we applied non-negative matrix factorization on the matrix of term frequencies for fMRI papers. These terms were a subset of the terms from NeuroQuery, excluding anatomical terms. We then applied the topic weights to the term frequency matrices for a) the meta-analyses, and b) the papers associated with images on NeuroVault, in order to a) determine which topics have been more or less covered by previous meta-analyses, and b) to point to topics that have more image-based data on NeuroVault for potential future meta-analyses. Further, we used labelbuddy to manually label methodological details in meta-analyses, and present descriptive results to illustrate potential issues with methods. We store the annotations in a git repository hosted on Github: litmining/annotations. Finally, we used pubextract to automatically derive author genders from their names and author locations from their affiliations, for which we compare the subfield of meta-analyses and the larger fMRI field.

Results: We see an uneven coverage of topics by meta-analyses, with some topics receiving more attention than others (see Figure 1). Further, we point to topics, such as ‘risky decision making’, that potentially have enough image data on NeuroVault for future image-based meta-analyses. Image-based meta-analyses are the gold standard for meta-analyses, but are not common due to difficulty getting data. Regarding methods, we see that the most common methods are activation likelihood estimation, and Seed-based d Mapping, with very few image-based meta-analyses (see Figure 2C). The number of papers included in each meta-analysis approximately follows a power law, with many meta-analyses each examining relatively few papers. Indeed, many meta-analyses have fewer papers than the recommended minimums (17 or 30; see Figure 2D). Regarding authors, our results suggest that there is a higher proportion of meta-analyses with women as the first and last author, compared to participant-level fMRI studies (see Figure 2A). Further, there are not many meta-analyses done in low-income countries; this is a potential area for growth, since meta-analyses have relatively low cost compared to imaging studies (see Figure 2B).

Conclusions: This analysis of the neuroimaging meta-analyses is one example of the LitMining ecosystem, which comprises a set of tools and recommendations enabling faster, open, collaborative and more reproducible studies of the literature. These results have implications across many areas of neuroimaging, since meta-analyses are widely used across topics.
ABSTRACTS

References

Poster No 2244

Hyve, a compositional visualisation engine for neuroimaging data

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Introduction: By embedding data within geometric structures, visualisation provides a gateway to understanding and communicating complex information. In neuroimaging, embedding data in brain geometries improves the tractability of high-dimensional data; visualisation software (e.g.,¹³) is thus critical in brain mapping. However, the geometries that structure neuroimaging datasets can be highly heterogeneous. MR data, for example, are often reconstructed as image intensity values in a regularly sampled three-dimensional Euclidean volume. By contrast, the convoluted sheet of the mammalian cerebral cortex can be modeled as a two-dimensional Riemannian manifold, which software suites approximate as a polygon mesh⁴⁻⁵. Maps of brain connectivity have the intrinsic topology of a graph, with vertices that can be embedded either in physical coordinates or algorithmically in a low-dimensional space³⁻⁶. Measures of brain function further extend these geometries in the dimension of time. Existing software has often addressed this heterogeneity by implementing separate plotting routines for different geometries. Here, we introduce the software library hyve (the hypercoil⁷ visualization engine) to implement an alternative compositional approach. Under our approach, users construct a new visualisation protocol by composing an abstract base plotting routine with a chain of functional atoms called primitives (Fig 1). Each functional primitive imbues the base routine with a distinct functionality, forming the basis of a modular, flexible, and extensible system for building reusable plotting protocols.

Methods: hyve is an open-source Python library, based on PyVista⁸ and VTK⁹, for creating visualisations of neuroimaging data. The versatility of the hyve visualisation system comes from compositional functional programming. Under this programming paradigm, complex visualisation protocols are constructed by composing atomic functions, called primitives, in a combinatorial manner. Composition is performed under hyve.plotdef, the main function of hyve’s user interface, which transforms an abstract visualisation loop into a concrete protocol for creating a specific visualisation artefact. Users construct a reusable visualisation protocol by combining geometric primitives for representing data geometries, input primitives for common data formats and research objectives, and output primitives for producing interactive plots, configurable snapshots, or editable multi-panel figures. hyve also writes automatic documentation for user-constructed functions, maps over parameters to automate serial production of multiple visualisation artefacts, and includes a figure builder API and metadata system for semantically laying out scene representations.
Results: Input primitives specify transformations to be applied to data before they are passed to the core visualisation loop; these transformations include inter alia parcellation, coordinate detection, and archive queries. Output primitives determine the type of artefact that a visualisation protocol creates to represent a scene, which broadly fall into two categories: interactive and static. An interactive scene representation is characterised by a capacity to manipulate the view angle. Interactive scene representations include display windows and portable, persistent HTML files. hyve protocols that produce static scene representations (suitable for publication in legacy media) accept a “views” argument for specifying view angles on the scene. “Autocam” primitives use a heuristic or rule to automatically select a view or views. Each call to hyve’s core plotting loop returns both a visualisation artefact and a metadata dictionary; hyve can also use this metadata dictionary to semantically construct editable SVGs through its figure builder API (Fig 2).

Conclusions: In conclusion, we provide a tutorial notebook for hyve, available at https://github.com/hypercoil/notebooks/blob/main/nb/hyve/hyve-constructive.ipynb, to orient new users.

References
Latent Brain Age Predicts Mortality in Amyotrophic Lateral Sclerosis

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**Introduction:** The neuroanatomical changes associated with neurodegenerative disease progression appear to overlap with natural ageing. This suggests that changes akin to the ageing process might serve as indicators for predicting mortality in such diseases. In fast progressing neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), methods producing age related brain biomarkers must be particularly sensitive to the neuroanatomical effects of ageing. Generative models offer a solution to this problem as they have achieved state-of-the art representation learning capabilities. In this work, we leveraged a state-of-the art generative model called a diffusion autoencoder, in-order to produce age conditioned representations which are more effective than classic approaches for ALS prognostication.

**Methods:** Our approach combines a diffusion autoencoder model with a multilayer perceptron (MLP) which predicted survival time in days of ALS patients, based on their latent similarity to healthy individuals of the same age. The algorithm is visualised in Figure 1. First, the diffusion autoencoder is trained on MR images of healthy individuals, conditioned on their age, for N epochs. We then fix the weights of the diffusion autoencoder and begin to train the survival prediction MLP. To do so, we sample an individual with ALS of age = k. We then sample all MR images from healthy individuals of age = k, and place the healthy individuals and ALS patients through the encoder. Then the absolute difference between the mean latent representation of the healthy individuals and the latent representation of the ALS patient is computed. This quantity is the latent brain age. The latent age difference vector, then goes through the MLP to predict survival time. We trained our model on a dataset of, 4621 2D T1-weighted MR images (mean age = 56 years, std = 20.9 years) from 8 publicly available datasets. Our patient group consisted of 72 2D T1w MR images (mean age = 61 years, std = 10.9 years) from the San Raffaele Hospital in Milan. The diffusion based pre-training period lasted for 400 epochs, and our MLP was trained for another 400 epochs. The MLP was trained on 57 ALS patients, leaving 17 patients in the validation set. All training was performed on an Nvidia GeForce RTX 4090 graphics card, with the Adam optimizer in PyTorch lightning.

**Results:** We achieved a validation accuracy of 0.77(p<0.01) as measured by the Pearson’s r correlation between predicted survival and actual survival in days, with a mean absolute error (MAE) of 8.19 months. Table 1 displays how are method compares to other neural network based approaches to predicting survival with the same training data. The final column is a g score. The results demonstrate that we outperform them on our validation set. As the other approaches were not generative models, the pre-training task used was standard brain age prediction on the MR images derived from healthy controls. Table 2 displays results of a survival analysis via a cox proportional hazard regression using age, sex and brain predicted age differences (brain-PADs) of the ALS cohort. None of the covariates were significant predictor’s of survival, in contrast to our approach.

**Conclusions:** The present study was a preliminary exposition of the concept of latent brain age, in which its utility for the prognostication of ALS disease was demonstrated. Our results show that predictions using latent brain age outperform traditional cox proportional hazard analyses using standard brain age measures. Our approach also outperformed non-generative neural network approaches. However, given the small sample size of patient data (train size = 57, test size = 17), an analysis with more subjects is required to ensure the validity of the present findings. Future work should also apply the present approach in other diseases and on 3D MRI volumes.
**Abstracts**

Figure 1: Our model design. We compute the latent representation of the MR images derived from an ALS patient of age = $a$ and separately the latent representation of all individuals in ALS patient of age = $x$. We then average over the healthy latents and take the absolute difference between the average healthy latent and ALS latent to produce the latent age difference vector. This is vector is then used to predict the survival length in days of patients with ALS.

<table>
<thead>
<tr>
<th>OUR MODEL</th>
<th>MLP</th>
<th>CNN</th>
<th>ViT</th>
<th>LINEAR REG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PEARSON'S R</strong></td>
<td>0.77**($p&lt;0.01$)</td>
<td>0.48($p=0.68$)</td>
<td>0.41($p=0.13$)</td>
<td>0.40($p=0.13$)</td>
</tr>
<tr>
<td><strong>MAE</strong></td>
<td>8.19 MONTHS</td>
<td>16.63 MONTHS</td>
<td>17.05 MONTHS</td>
<td>15.11 MONTHS</td>
</tr>
</tbody>
</table>

Table 1: Results of the association between predicted and actual and survival time in months for the test set of 17 patients Amyotrophic lateral sclerosis. Significant relationships are displayed in **bold**.

Table 2: Results of a Cox Proportional Hazard Regression. The rows denote the machine learning model that was used to produce the brain-PADs featured in the hazard regression. All results are reported as Hazard Ratio (CI) $p$ value. Significant results are in **bold**.

**Post No 2246**

**Quantifying model suitability in the context of ultra-low-field MRI super-resolution**

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**Introduction:** Magnetic resonance imaging (MRI) is integral for assessment of paediatric neurodevelopment, but modern MRI systems are large and expensive. Recent ultra-low-field (ULF) MRI systems such as the 64mT Hyperfine Swoop (Deoni et al., 2021) show great promise in widening MRI accessibility and reducing cost. Imaging at low field strengths comes at the cost of lower spatial resolution and signal-to-noise ratio, although these can be mitigated by deep-learning super-resolution (SR). A difficulty with SR is that it is an ill-posed inverse problem (Dellanoy, 2020); for each low-resolution input there exist multiple viable high-resolution outputs. Even if a transformation is learned that reliably reproduces all target images in the training data, generation of artifacts is a consistent danger whenever a model runs inference on unseen input (Johnson, 2016). This reference is not identified, and it is unclear how these artifacts are generated or how they can be mitigated.

**References**

is a particular concern in medical applications, where outputs may inform diagnosis and treatment planning. We present a technique to quantify the suitability of new input to a pre-trained U-Net for SR of paediatric ULF MRI, to enable the a-priori identification of ‘unfit’ SR hallucinations.

**Methods:** We trained a 3D-U-NET using paired ULF (64mT Hyperfine Swoop T2; 1.5x1.5x5 mm) and high-field (Siemens 3T T2; 1x1x1 mm) MRI scans from 40 subjects aged 3-6 months. Our test data included 10 scans each from cohorts in the following age-groups: 6 months, 12 months, and 4 years, all scanned using the same protocol. We first fed all training and test scans into the encoding layers of the model and extracted activations from the bottleneck layer to obtain a ‘latent space representation’ (see Figure 1A). We then quantified the dissimilarity between latent features from the unseen test images and those of our training data using the Sinkhorn distance. To evaluate the utility of the Sinkhorn distance in predicting model suitability, we: 1) ran SR for ULF test scan using our model, 2) segmented each output using SynthSeg+ (Billot, 2023) to obtain grey matter (GM), white-matter (WM), and cerebrospinal fluid (CSF) measures, 3) quantified within-subject overlap between segmentations of SR outputs and high-field scans with Dice coefficients, 4) correlated the Sinkhorn distances and Dice scores across subjects.

**Results:** We found that the deviation of latent features from the training data, quantified using the Sinkhorn distance, was lower for unseen images of 6-month-old subjects was than 12-month-old subjects. The same trend was observed when comparing unseen scans from 6-month-olds to 4-year-olds, however in both cases the difference was insignificant (p=0.14 and p=0.10, respectively). The correlation between Dice scores of SR outputs and their Sinkhorn distances to the training data was not significant for 6-month-old or 12-month-old subjects, however a significant negative correlation between these variables was observed for 4-year-old subjects across GM (r=-0.86, p=0.0014), WM (r=-0.91, p=0.00027), CSF (r=-0.80, p=0.0058).
Conclusions: We aimed to quantify suitability of new, unseen input to a pre-trained SR model. We explored the Sinkhorn distance between latent space representations of images as a candidate for this metric and provide proof of concept analyses with subjects whose age deviates from those used in the training set. Although we did not find significant deviation in mean Sinkhorn distances across cohorts, we found that Sinkhorn distances obtained from 4-year-old scans are negatively correlated to Dice scores indexing SR quality, across tissue types. We speculate that a minimum threshold of deviation from the training set must be reached before the Sinkhorn distance bears sufficient informative potential for model suitability. Further analyses are required to validate this metric and assess its generalisability, including analyses of subjects across a wider range of ages and patients with neurological pathologies.

References
4. doi:https://doi.org/10.1016/j.neuroimage.2021.118273

Poster No 2247
Synthesizing DWI with high b-values from low b-value datasets using deep learning
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Introduction: Diffusion MRI (dMRI) has been widely applied in various fields. In comparison to the clinically common diffusion tensor imaging (DTI), high angular resolution diffusion imaging (HARDI) possesses the capability to resolve fiber crossings and provides more information about white matter neuroanatomy, such as fiber density. However, for various HARDI techniques, multi-shell diffusion weighted images (DWI) with higher b-values are required, leading to an increased imaging time. This may render it less suitable for clinical use. To address this issue, a previous study proposed computed DWI, synthesizing arbitrary

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Figure 2: Correlation between normalised Sinkhorn distances and Dice scores, investigating the relationship between I) dissimilarity of extracted features from test images compared to those of training images and II) final image quality.
A) Cortical grey matter, B) Cortical white matter, C) Cerebrospinal fluid
b-value DWI from a set of measured b-value images through voxel-wise fitting. In this study, deep learning techniques were employed using a model combining DenseNet and Generative Adversarial Network (GAN) to establish a model with low b-value DWI as input and high b-value DWI as output. The feasibility of the model was assessed by comparing the ground truth with the generated DWI, generalized Q-sampling image (GQI) indices mapping derived from generated DWI, and fiber density map derived from generated DWI.

**Methods:** All dMRI data were collected with a GE MR 750 scanner at Chang Gung Memorial Hospital, Linkou, Taiwan. Two-shell DWI with b-values of 1000 and 2000 s/mm², along with 60 non-collinear diffusion gradient directions on each shell, were conducted in 115 subjects. The data were partitioned into training, validation, and testing sets, with 89, 10, and 16 subjects, respectively. A multi-level densely connected network with GAN was employed as the data synthesis model. Paired DWI with b-value of 1000 s/mm² (DWI-b1000) and 2000 s/mm² (DWI-b2000) with the same diffusion direction were used as input and output for training, undergoing 200 epochs. For the evaluation of the model's feasibility, structural similarity index (SSIM), peak signal-to-noise ratio (PSNR) and mean squared error (MSE) were assessed between DWI-b1000, generated DWI-b2000 and ground truth DWI-b2000. Furthermore, the (GQI) indices mapping derived from generated DWI, and fiber density map derived from generated DWI were also assessed in comparing with DWI-b1000 only and ground truth DWI-b2000. The DSI Studio software and MRtrix 3 were utilized for GQI reconstruction and estimation of voxel-wise total fiber density.

**Results:** The results show that the SSIM/PSNR/MSE between the original DWI-b1000 and the ground truth (GT) DWI-b2000 are 0.82/35.68/0.00092, while the SSIM/PSNR/MSE between the generated DWI-b2000 and the GT DWI-b2000 are 0.862/36.83/0.0006. The differences between the two are statistically significant (p<0.001). This indicates that the generated DWI-b2000 is indeed more similar to the GT DWI-b2000 in image quality assessment. In GQI indices mapping, the SSIM/PSNR/MSE between the quantitative anisotropy (QA) estimation using original DWI-b1000 only and using original DWI-b1000 and GT DWI b-2000 are 0.97/57.57/0.00039 and the SSIM/PSNR/MSE between the QA estimation using original DWI-b1000 and generated DWI b-2000 and using original DWI-b1000 and GT DWI b-2000 are 0.965/57.11/0.00045. The mean angle error (the formula is shown in Figure 1) between using original DWI-b1000 only and using original DWI-b1000 and GT DWI b-2000, and using original DWI-b1000 and generated DWI b-2000 and using original DWI-b1000 and GT DWI b-2000 are 11.09 and 11.2, respectively. Based on voxel-wise total fiber density, in comparison with using only DWI-b1000 (SSIM/PSNR/MSE=0.985/60.75/0.000014), the estimation using DWI-b1000 and generated DWI-b2000 is significantly more similar to the ground truth data (SSIM/PSNR/MSE=0.998/65.79/0.000023) (p<0.001).
Figure 2 The results of image quality assessment

**Conclusions:** This study developed a deep learning-based method for generating high b-value DWI, and the generated images are quite similar to the ground truth images. In comparison to assessing fiber density using only lower b-value DWI, the inclusion of generated higher b-value DWI demonstrates significant improvement in effectiveness.

**References**

**Poster No 2248**

**Tools and platforms to investigate analytical variability in neuroimaging**

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**Introduction:** The reproducibility of neuroimaging studies is often limited by analytical variability. Researchers have access to a multitude of tools, many of which carry out the same tasks but yield different results when applied to the same data. Despite the neuroimaging community’s array of tools to investigate and address analytical variability, these resources are decentralized and scattered. Consequently, researchers often lack the necessary information and protocols to buttress the reliability of their findings. This review catalogs software tools neuroimaging researchers can use to address result variability arising from computational pipelines and environments. The aim of the review is to promote robust reproducibility practices by highlighting relevant strategies and reducing accessibility barriers.

**Methods:** The tools featured in the review were found through an assortment of queries in the NITRC and NIF databases, PubMed, Google Scholar, the background information sections of relevant papers, and suggestions and presentations from the neuroimaging reproducibility community. The inclusion criteria we use are: 1) At least one descriptive publication/DOI exists, 2) Open-source and publicly available, 3) At least one release or repository update in the past 5 years, and 4) At least one published neuroimaging study has used the tool. We found 30 tools fitting the criteria above and categorized them into four main sections: Tool variability stems from analytical choices regarding software-based algorithms, like data processing libraries and pipelines, along with parameters and versions. This section is divided into three subsections. The first subsection describes container technologies and tool repositories that facilitate the distribution and reproducible execution
of large collections of tools. It features subdivisions on container-solutions, integrated computational environments, and software collections. Another subsection describes Workflow Engines that provide machine-readable ways of encapsulating and automatically re-executing sequences of processings. The third subsection is about tools to leverage Continuous Integration by using it to frame a scientific result as an automated “test”, keeping track of how a result is affected by changes in the underlying computations. • ‘Environment variability’ is caused by the software infrastructure that is used to execute processings. It contains two subsections. One features tools to measure Numerical Stability in algorithms that occur due to varying implementations of floating-point arithmetic on different operating systems and hardware. The other features tools to facilitate running computations across multiple development environments and operating systems. • The ‘Data Provenance’ section describes tools that track transformations in data, providing an audit trail of processings. • The ‘Cloud Computing’ section features neuroimaging platforms that facilitate performing analyses across many workflows by providing access to computational resources and lowering the technical skill level required to access and execute tools. We also discuss Open Issues/Limitations of software-based approaches to analytical variability.

**Results:** The listing and categorization of the tools is summarized in Fig. 1. Fig. 2 depicts inter-category tool relationships in this study, based on data flow in a neuroimaging pipeline.

**Conclusions:** As the magnitude and ubiquity of the reproducibility issues posed by analytical flexibility become clearer, neuroscientists have the responsibility of adapting their computational methods to make sense of the multiverse of analytical approaches available. Despite difficulties in establishing consensus, available tools can aid in creating, organizing, and
executing processings that quantify and/or constrain analytical variability, fostering robust scientific conclusions. This study offers descriptions and guidance on the many tools enabling the study of analytical flexibility.

References

Poster No 2249

A novel approach to harmonize MRI-derived morphological features between different MRI scanners

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Introduction: There are increasing efforts to combine and share a huge neuroimaging dataset, especially across large-scale cohorts from multicenter1,2. Constructing the dataset is important because it allows the creation of analyzable datasets for more targeted study designs and enables multicenter collaborations3. However, when combining the dataset under various environment, we are inevitably faced with the challenge of dealing with various conditions, such as scanner, site, and acquisition parameters that can impact downstream analysis (i.e., extract cortical thickness, etc.).4 This effect, called the scanner (or site) effect in neuroimaging, must be removed for consistency and reproducibility of the analysis5. This study aims to test the comparability and calibrate the structural MRI-derived morphological features obtained from different MRI scanners.

Methods: T1-weigted (T1w) images were obtained from 48 participants (52.16±11.3 years old; age range: 31-75 years old; 24 men) who underwent 1.5T and 3T MRI scans within 2 weeks. The 1.5T T1w images were acquired on a 1.5T GE SIGNA scanner at Central Hospital, and the 3T T1w images were acquired on a 3T Siemens Skyra scanner at Korea University Ansan Hospital. The acquisition parameters of the 3D T1w images were as follows: 1) GE 1.5T MRI scanner with a fast spoiled gradient echo sequence (TR = 10.9ms, TE = 5.01ms, TI = 450ms, flip angle = 13°, voxel size = 0.47 x 0.47 x 1.2 mm3) and Siemens 3T one with a magnetization-prepared rapid gradient-echo sequence (TR = 1980ms, TE = 2.55ms, TI = 998ms, flip angle = 9°, voxel size = 0.54 x 0.54 x 0.9 mm3). Before the surface-based analysis using FreeSurfer 7.3.26,7, an automated segmentation software, all T1w images were processed using SynthSR that is one of the artificial intelligence techniques to turn heterogeneous MRI scans into high-resolution T1w images and convert to 1mm MPRA GE images8. The SynthSR-processed images were analyzed using the ‘recon-all’ pipeline of FreeSurfer. A visual inspection was performed through Freeview to ensure that the skull was properly removed with the cerebellum, that the pial surface and white matter surface were well defined, and that the brain regions were well segmented. Each cortical thickness (CTh) was extracted from 68 regions based on the Desikan-Killiany atlas9 using aparcstats2table function. ComBat4,5, which is an extended linear model for adjusting residuals based on the empirical Bayes to remove additive and multiplicative effects by scanners (or sites), was applied to harmonize the extracted CTHs of 1.5T and 3T preserving the interested covariates (i.e., age and gender). Paired t-test was used for comparison of each brain regions between 1.5T and 3T with Bonferroni correction and Bland–Altman plot was used in analyzing the agreement between two different data.

Results: Figure 1 and 2 show the results of paired t-test and Bland–Altman plot for areas that can be greatly affected in extracting morphological features among 68 regions in the brain before/after using ComBat. As shown in Figure 1, before using ComBat, there was a statistically significant difference in CTh between 1.5T and 3T in the 8 regions related to OSA, whereas after using ComBat, there was no statistically significant difference in the same regions. Figure 2 represents graphically little difference in average CTh after using ComBat compared to before using ComBat, demonstrating the
agreement of CTh between 1.5T and 3T. Additionally, the remaining 60 areas denoted the same results as above after using ComBat.

Conclusions: Our findings suggest that the proposed approach could minimize scanner-specific difference in the CTh of 1.5T and 3T in all segmented areas. It can be applied to horizontal analyses of big data obtained from multicenter studies.

References
All Quiet on the Clinical Front — Tales from Crossing the Great Divide

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Introduction: Integrating the results of research workflows into clinical systems can have many beneficial effects. For the most part, however, this final connection is rarely discussed or investigated in the literature and is almost left as an exercise for the reader. While most researchers might code complex computational workflows that provide meaningful scientific and clinical results, these same researchers rarely consider how to bridge the clinical / research divide. In this work, we summarize some reasons for this status quo, based on our own experiences as well as detailed interactions with clinicians at our Institution. Based on these insights, we importantly also present an open-source solution architecture that does bridge this divide. While aspects of this design are specific to our research back end, the solution itself is easily generalizable. We will discuss several workflows that we are integrating from research into clinical domains.

Methods: Most of our insights stem from an internally funded award tasked with providing the results of a research-based AI bone analysis tool to clinicians. This is a non-FDA approved tool that merely aids in clinical decision making by saving clinicians from having to make manual measurements on a bone image. We have conducted numerous interviews with clinicians to better understand their workflow and appetite for value added (AI) tools, similarly we have experience with fellow researchers and their approach to this problem. Based on these insights, we have determined two possible solutions: (1) a push solution where a clinical system “initiates” the integration; and (2) a pull solution in which a research system polls for data and self-initiates all processing. In this work we describe (1). The push solution has to be as simple as possible, see Figure 1. Since many clinical systems provide “user-configurable triggers” in their UI, we decided that the simplest possible connection is a single http POST request to a web address. This POST request contains information about the image to be analyzed (such as the SeriesInstanceUID). The return payload contains information on the progress of the analysis.

Results: From the clinical side, we determined there is little to no interest to changing or supplementing existing workflows, even if such a change could have benefits. Simply stated, we noted that clinicians are opposed to even opening a new browser and interacting with a new website. Any integration has to happen without as little friction as possible. From the
research side, coding complex infrastructural software is not seen as advancing the research enterprise. Moreover, there is a prevailing belief that integration between clinical and research is best left to commercial companies. In our experience, this belief is naive and has the practical effect of little to no integration ever happening. We believe that researchers can successfully lead and contribute to building practical solutions -- especially since researchers themselves are often times embedded in clinical hospitals. Our solution is “fire-and-forget”. The clinical system triggers an analysis by simply accessing a web URL. This is a server that based on the trigger event, further interacts with a more complex command and control center that in turn is able to pull data from a clinical system and pass to our research computing system, ChRIS, where a full analysis is managed. Importantly, one of the research nodules is able to itself connect back to the PACS and push resultant images to PACS. Each time the clinical system sends the same trigger event to the bridge server, it receives a status update (see Figure 2).

Conclusions: In conclusion, we believe this bridge solution is a viable concept for crossing the clinical/research divide and accelerating the ability to have research solutions provide value added benefit to clinical work.

References

Poster No 2251

Information retrieval using Large Language Models for automated neuroimaging meta-analysis

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Introduction: Over 5,000 neuroimaging articles are published yearly, representing a vast but unwieldy knowledge base. Meta-analysis can help make sense of this deluge, but annotating relevant information is painstaking and time consuming. Although there have been successful efforts to automate meta-analysis using text mining (e.g. Neurosynth), they were limited to frequency based features which are unable to differentiate fine-grained cognitive constructs or extract detailed methodological information. Breakthroughs in large language models (LLM), promise to enable high-quality information retrieval with little labeled training data (Labrak et al 2023). In two studies, we evaluate the performance of pre-trained LLMs for extracting information relevant for automated neuroimaging meta-analysis, such as methods and demographics.

Methods: We used Open AI’s GPT, a commercial LLM trained on a domain-general corpus, to extract information from the unstructured text of neuroimaging articles using prompt-based Zero Shot Learning (ZSL) and evaluated results against expert human annotations. In Study 1, we identified 751 studies from the NeuroVault database that were annotated by users for “task” using the Cognitive Atlas Ontology (Poldrack et al. 2011), providing a rare sample of annotated fMRI studies. Using only the abstracts, we used ZSL to predict task across 129 unique labels (e.g., ‘stroop’, ‘go/no-go task’, ‘monetary incentive delay task’). In Study 2, we evaluated GPT’s ability to extract demographic information from the full text of articles and compared it to a heuristic based on Poldrack et al. 2017. This consists of two steps: a semantic search to identify the most relevant section of each paper, and a zero-shot prompt to extract participant count. We separated each article into sections of <2000 characters and generated a latent embedding for each section using OpenAI’s Ada model. By computing the distance between a search query (“How many participants or subjects were recruited for this study?”) and each section, we ranked sections for relevancy, and used ZSL to “identify groups of participants”. We evaluated extracted data in 200 articles annotated for participant demographics, including number of participants for each group. We used the first half of annotated studies to prototype our approach and evaluated performance on a hold-out set of 103 studies. The methods used here are incorporated into an open-source package (publang) that simplifies the application of LLMs for information retrieval, and will be used to incorporate these features to the NeuroSynth ecosystem.

Results: In Study 1, GPT-3 matched abstracts to the correct task with 87% accuracy. Using GPT-4, the latest model with over 1 trillion parameters, we achieved 100% accuracy. In comparison, using tf-idf to vectorize abstracts into 7,006 features, SVC only achieved 34% accuracy on the test set (Fig 1) In Study 2, GPT-3 extracted sample size with an excellent 13.8% Mean Absolute Percentage Error (MAPE) and perfect recall, making a prediction for all studies. In contrast, the heuristic algorithm had a low error rate (15% MAPE), but had poor recall, only making a prediction for 58/103 studies (Fig 2). Upon inspection, we discovered
GPT’s accuracy was potentially high, as “errors” were often due to behavioral sample size being extracted in addition to final imaging sample, suggesting prompt engineering could improve performance. Preliminary qualitative analyses showed that GPT was also able to extract additional information such as age, gender and disease.

Figure 1. Predict task from article abstract

Figure 2. Accuracy of extracted sample size

**Conclusions:** Zero Shot Learning using general-purpose LLMs retrieves information from articles with high accuracy and recall without the need to train or develop domain-specific models. Extracted information is well suited to assist human-guided systematic literature synthesis. Paired with a flexible ecosystem for meta-analysis, such as Neurosynth, this technology can enable a powerful new class of automated fine-grained neuroimaging meta-analysis.

**References**


**Poster No 2252**

**Automated conversion of BIDS datasets to Linked Data using openMINDS**

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**Introduction:** BIDS¹ and openMINDS² are expert- and community-driven standards that facilitate FAIR data management in the field of neuroscience³. BIDS is a community-wide accepted data model that standardises the file organisation across multiple human neuroscience modalities. It includes restrictions for formatting data and metadata as well as strict naming conventions for folders and files⁴. Although the hierarchical structure is easy to read and interpret by humans, it lacks explicit links between data and metadata. As a result, tools have to hard code the implicit relations of data and metadata, indicated through the
naming convention and enumerated types. The openMINDS metadata framework provides an extendable set of (i) integrated metadata models for Linked Data and (ii) libraries of well-defined, ontology-based metadata instances. Both components enforce an explicit linkage between metadata, data, and external resources such as ontologies. The local file organisation is unconstrained by design, to guarantee maximum flexibility. BIDS and openMINDS are complementary. The former ensures that metadata are always available together with downloaded data files, while the latter supports rich search capabilities in data repositories based on Linked Data, such as E BRAINS. To facilitate the ingestion of BIDS-formatted datasets into such repositories, we have developed an easily-installable command-line tool bids2openminds.

**Methods:** bids2openminds is an open-source project on GitHub under the MIT License. Both standards, BIDS and openMINDS, are continuously extended to cover more areas of neuroscience. As a starting point bids2openminds supports the BIDS modalities structural and functional Magnetic Resonance Imaging (MRI), Electroencephalography (EEG), and Intracranial Electroencephalography (iEEG). The converter is provided as a Python package, building on the functionalities of two existing Python packages, pyBIDS and openMINDS_Python. pyBIDS allows handling of BIDS data and metadata while openMINDS_Python enables the creation and manipulation of openMINDS-compliant metadata collections. At present the semantic mapping from BIDS to openMINDS is hard coded, since BIDS does not currently provide unique identifiers for the schemata, properties, and enumerated types, but in future this could be auto-generated.

**Results:** With bids2openminds we present a command-line tool and Python package to the neuroscience community that converts the metadata from a BIDS compliant dataset into openMINDS (as a collection of JSON-LD documents), in order to represent BIDS data in graph databases. Note that openMINDS is a continuously growing metadata model, which does not yet provide extensions for all neuroscience modalities integrated in BIDS. We demonstrate the use of bids2openminds for data published on the bids-examples GitHub repository as outlined in Figure 1. We used the resulting openMINDS-compliant metadata collections to register these data in E BRAINS, providing insight into the advantages of Linked Data integrations: The registration enables users to search, filter and explore the data and metadata via the search user interface and via programmatic queries. Moreover, data are also linked to other databases by tagging research products with openMINDS ontology-driven controlled terminologies.

**Conclusions:** bids2openminds enables an easier registration of BIDS compliant datasets in openMINDS based graph databases, and thus further automates data curation workflows. Such explicitly linked graph databases offer advanced query options for heterogeneous neuroimaging data, promoting findability, and enable further annotations and cross-links going beyond the BIDS data model, to facilitate interoperability and reuse. Thus, bids2openminds promotes FAIR data sharing for neuroscience data.

**References**

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An Analysis of Performance Bottlenecks in MRI Pre-Processing

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Introduction: Computationally expensive pipelines have been one of the main bottlenecks in processing large subject cohorts in neuroimaging, and their execution time can hinder clinical applications where timely data analysis is needed. To leverage higher statistical power from larger cohorts and enable more applications, the community is constantly seeking for novel ways to speed up data processing with HPC, cloud computing, GPU accelerators, or Deep Learning models [Henschel et al., 2020; Hoffmann et al., 2022]. Optimizing a pipeline requires understanding and characterizing its different bottlenecks. We characterize the computational profile of several commonly-adopted MRI pre-processing pipelines. The results of our analysis can serve as a reference for future efforts to optimize MRI pre-processing workflows.

Methods: We focus on profiling fMRIPrep [Esteban et al., 2018], a commonly used pipeline for anatomical and functional MRI pre-processing and analysis. For finer granularity, we also profile the sub-pipelines of fMRIPrep which include tools widely used in the community (ANTS brainExtraction, ANTS registrationSyN, FSL FAST, FSL MCFLIRT, FSL FLIRT, FreeSurfer reconall). We used the OpenNeuro ds004513 v.1.0.2 dataset [Castrillon et al., 2023], with anatomical, functional, and diffusion data from 20 healthy individuals acquired from two cohorts: a cohort with nine participants (mean age=43 yrs, std=7 yrs; 4 females) and a replication cohort with eleven participants (mean age=27 yrs, std=5 yrs; 6 females). We measured CPU time, percent of memory boundness, and percent of floating point operations with the VTune profiler, which provides low overhead and varying levels of granularity, for the metrics collected. To collect human readable information from the profiler, we re-compiled each application with debug_info using Docker images. Then, we converted the Docker images to Singularity images using docker2singularity. We profiled the application with a single thread to simplify their analysis, but also with 32 threads to understand the performance of their multi-threaded implementation. For profiling, we used dedicated compute nodes with two 16-core Intel(R) Xeon(R) Gold 6130 CPUs, 250 GiB of RAM, Rocky8, and Linux 4.18.0-477.10.1.el8_lustre.x86_64. Data was transferred to compute nodes before profiling the applications.

Results: The average CPU time per function across all tested pipelines follows a long-tail distribution (Figure 1). Thus, future efforts can focus on a few functions to optimize the applications. A detailed analysis of the CPU time, contribution to total pipeline make span, and memory boundness of each application shows that interpolation is a primary bottleneck for all profiled applications (Figure 2 shows FreeSurfer reconall). We suggest future efforts to concentrate on optimizing interpolation techniques, using DL drop-in alternatives, or developing reduced precision techniques specialized for interpolation. Furthermore, we observed surprising slow-down for ANTS brainExtraction (1.14x) and registrationSyN (1.23x), while using the built-in single-precision option compared to the double-precision default. Both versions completed after a similar number of iterations. We speculate that the slow-down is due to less optimized implementations of single-precision in the ITK library. Finally, we observed underperforming multi-thread scaling for FreeSurfer, which we speculate results from an underperforming OpenMP scheduling policy. The code developed to conduct our benchmarks is available on GitHub: https://github.com/mathdugre/mri-bottleneck

Figure 1. Functions sorted by decreasing average CPU time (in second). Pipeline included: ANTS brainExtraction, ANTS registrationSyN, FSL FAST, FSL MCFLIRT, FSL FLIRT, FreeSurfer reconall.
Figure 2. Functions sorted by CPU time of their modules, then their own. Cumulative makespan percent showed with green dots. The function IDs using interpolation are 4, 8, 15, and 26.

Conclusions: We performed a detailed performance profiling of fMRIPrep and several of its sub-workflows. Overall, only a few functions contribute to a majority of the computation time and interpolation is the main bottleneck. ANTS applications were faster when using double-precision compared to single-precision, and FreeSurfer suffered from OpenMP bottlenecks while using multi-threading.

References

Poster No 2254

Fuzzy PyTorch: Rapid Numerical Uncertainty Quantification for Deep Learning Models

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Introduction: Numerical uncertainty – the quantification of errors in computer programs – is crucial for user confidence in application outputs. In neuroimaging, amidst a reproducibility crisis, ensuring research reliability is paramount for trusted decisions. Computational neuroimaging tools, including the ones relying on deep learning (DL), are prone to numerical uncertainty which can jeopardise the reliability of their results¹². However, in order to assess DL models, numerical uncertainty tools must be scalable, with minimal code modification and overhead. We present Fuzzy PyTorch (FP), a compiled framework for rapid evaluation of numerical uncertainty for DL methods in neuroimaging.

Methods: Numerical uncertainty originates in the numerical errors created by floating-point arithmetic models. We employ Monte Carlo Arithmetic (MCA⁴, a stochastic arithmetic technique that introduces randomness to assess numerical uncertainty. Verificarlo⁵, an MCA implementation, replaces floating-point operations using a clang-based compiler. Despite the overhead introduced by code instrumentation, Verificarlo’s multi-threading and parallelization capabilities enable efficient performance. FP is an application of Verificarlo to compile the PyTorch source code in order to obtain a MCA instrumented DL framework to measure numerical uncertainty. As we could not recompile the MKL library used by default in PyTorch, as it is closed source, we built PyTorch with the open source BLAS and LAPACK libraries⁶. We compare FP’s performance to that of Verrou⁷, another tool that implements MCA through dynamic binary instrumentation, albeit at a much higher computational cost than Verificarlo’s compilation approach. Verrou serves as the reference tool as it has already been used to analyse numerical uncertainty in DL models⁸⁹. FP allows standard model training and testing while enabling numerical uncertainty experiments. This provides insights into a model’s numerical properties at various stages.

Results: To assess FP, unit tests were designed to validate instrumentation and ensure random, unbiased error simulation. FP was then applied to a convolutional neural network (CNN) pre-trained on the MNIST digit dataset, a stable and well-solved DL problem. We observe slight uncertainty in class probabilities (Fig. 1) of the same magnitude for both FP and Verrou. However, given the small magnitude of the numerical noise, 10^-6, it does not filter past the argmax operation which determines the final
prediction of the model. This noise within the class probabilities, insignificant for final predictions, aligns with the assumption that MNIST classification is stable due to the quality of the dataset and the simplicity of the task. Table 1 compares FP’s slowdown which is half of that of Verrou. FP can be further sped up by employing multi-threading which is not supported by Verrou. Verificarlo also maintains alternative backends than the default one tested (common to both Verificarlo and Verrou) that speed up the instrumentation. DL models are notorious for their consumption of resources. so overhead optimizations ensure the feasibility of conducting numerical uncertainty investigations in a manner that aligns with the computational constraints imposed by DL models.

Figure 1: Standard Deviation of MNIST Class Probabilities. Left: Standard deviation across 10 MCA samples for Fuzzy PyTorch; Right: Standard deviation of across 10 MCA samples for Verrou PyTorch

Table 1: Comparison of Fuzzy PyTorch with Verrou PyTorch for Runtime and Slowdown Factor

<table>
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<th>Fuzzy PyTorch (mm:ss)</th>
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<td>21:14</td>
<td>47:45</td>
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<tr>
<td>Slowdown Factor</td>
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**Conclusions:** FP, an efficient tool for measuring numerical uncertainty in deep learning models, offers simplicity through a user-friendly Docker image. FP is faster than other MCA implementations, open source, and accessible here. Successfully tested on MNIST, it is adaptable to neuroimaging models like FastSurfer and SynthMorph. In brief, the analysis of numerical uncertainty in deep learning models is crucial for ensuring the reliability of neuroimaging results, contributing to the robustness and trustworthiness of diagnostic and treatment applications in healthcare. FP facilitates replication and analysis of DL uncertainty, providing a valuable resource for accelerating research in neuroimaging and beyond.

**References**

Thinking Inside the ChBOX -- Delivering Practical Computing Easily to Neuroimaging Researchers

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Introduction: ChBOX is a novel concept in research: make the setup of a computer suitable for research coding drop dead simple. Simply insert a USB, reboot, and research. Think of it as a Live Linux distribution for neuroscience. By booting off the USB, into “Live” mode, any existing computer can be simply repurposed as a ChRIS system -- without changing the existing OS. Alternatively, the USB can install ChRIS natively on the computer. ChRIS is an open source infrastructure allowing researchers an easy on ramp to cloud-based computing. Built on pervasive containerization, ChRIS is developer, not infrastructure, focused. In many cases need only a thin python wrapper to bring existing algorithms into ChRIS and the cloud. Neuroimaging researchers are fundamentally reliant on computing, not only as users but also as creators. As the computing needs of the field grow, the startup “cost” to doing research is more and complex. Contributing to research programming requires a fair amount of setup often including python, jupyter notebook, containerization, etc. Moreover, the ever increasing needs of AI requiring researchers to run their code on cloud clusters and to become familiar with cloud-computing concepts such as containerization and clusters such as kubernetes and Openshift. Unsurprisingly, many researchers are less interested in mastering these technologies, leaving a pressing need for simple turnkey solutions. This is especially pressing in developing communities where researchers might have little experience in configuring their own neuroimaging platforms.

Methods: In this work we present progress on “ChRIS in a Box” or simply, “ChBOX”. As the name suggests, “ChBOX” delivers the ChRIS Research Integration System to any computing device. ChRIS lets researchers work with folders and files when they code, not volumes and REST APIs. Behind the scenes, ChRIS interfaces with cloud technologies and translates down-to-earth workstation-based approaches to in the sky cloudiness without needing the developer to do so, thus greatly reducing the time to deployment and usage of research software. Once in ChRIS, the platform can interface with cloud backends seamlessly allowing researchers to run their applications on many environments without needing to learn new cloud or cluster technologies. “ChBOX” is a Linux-based bootstrapping system based off Ansible. When inserted into a new computer and booted, a user can choose to provision the machine with a ChRIS instance. ChBOX will install a basic Fedora Linux setup on the computer and then install ChRIS. The provisioning of the system is all performed using “software as a platform” with github as the default source provider. By simply using a CLI update command, the ChRIS on the Box will update to latest versions of all available research plugins (from a central ChRIS repository -- tools such as FreeSurfer, image anonymization, image conversions, etc).

Results: In addition to installing ChRIS and components, ChBOX will also provision the machine with basic developer tools such as the open source version of Visual Studio Code, latest python versions, and a system login account. Infrastructure such as podman and podman-desktop (for containerization) is also provided. Once prepared a user can easily add new analysis programs to their ChBOX by simply adding new information to a reference github and rerunning the ChBOX update, or they can connect to any other ChBOX via the web and synchronize applications. They can of course also develop new code on-box and register this to their ChBOX ChRIS, making it thus available to other ChBOX instances if desired.

Conclusions: We hope to demonstrate provisioning ChBOX on a new computer and then show how to further update and install neuroimaging tools live. We also hope to show how solutions such as ChBOX can enhance collaboration and also democratize research by affording simple, easy, and powerful infrastructure based on open source and open science principles to any party engaged in the field.

References

Nipoppy: a framework for the organization and decentralized processing of neuroimaging-clinical data

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Introduction: Many of the existing software platforms for reproducible neuroimaging data processing are centralized (i.e. requiring data to be uploaded to a third-party server)\textsuperscript{1,2}, which is not always possible due to concerns about data privacy and ownership. Moreover, processing of prospective studies with ongoing data collection is challenging: since different software tools and versions can produce different results\textsuperscript{3}, care needs to be taken to ensure that the new data are processed in the same way as the already processed data. We introduce Nipoppy, a collaborative and open framework that can help achieve decentralized processing of ongoing studies with neuroimaging and clinical data. Nipoppy aims to facilitate every stage of data organization and processing, be flexible and extensible to handle various types of datasets and pipelines, and promote methods transparency and reusability of neuroimaging-clinical data.

Methods: Nipoppy specifies a standardized workflow for dataset processing and organization, including a specification covering tabular as well as raw and derived imaging data (Fig. 1). The framework is based around two user-provided files: a configuration file for running analyses and a manifest file listing the participant IDs, visits, and imaging datatypes available in the dataset. A series of automatically-generated tabular files contain information about data availability and processing status for each participant-visit pair and each processing pipeline. These files are used to identify new participants and visits that have not been processed yet. Pipelines that were previously used for this dataset can then be run on the new data.

We provide tools for every step of a neuroimaging data processing workflow, including conversion of raw scanner output to the Brain Imaging Data Structure (BIDS) standard\textsuperscript{4}, processing of neuroimaging data, tracking of processing completion status, and extraction of imaging-derived phenotypes (IDPs) from pipeline outputs. The Boutiques framework\textsuperscript{5} is used to provide a harmonized interface for running pipelines on BIDS data. Users can add their own processing pipelines by creating appropriate Boutiques descriptor files for their software. Parameter values for each pipeline and version are stored in Boutiques invocation files, allowing for data provenance to be recorded. Information about processing status for each pipeline and version is combined into a single tabular file, which can be uploaded to a user-friendly web dashboard for interactive visualizations of processing progress (https://digest.neurobagel.org/).

Results: Nipoppy has been successfully used to process longitudinal Parkinson's disease cohorts from the Parkinson's Progression Markers Initiative (PPMI) and the Quebec Parkinson Network (QPN) (Fig. 2). Both datasets have been processed with fMRIPrep\textsuperscript{6} and MRIQC\textsuperscript{7} so far, with more pipelines such as TractoFlow\textsuperscript{8} and micapipe\textsuperscript{9} planned for the near future. Both datasets are longitudinal and actively releasing new data; Nipoppy is able to process newly added data with the same
pipelines and configurations as existing data. Outputs from each pipeline are organized into clearly labelled directories, allowing tracking to be performed automatically for each pipeline and version. Extractors for common IDPs (e.g., FreeSurfer statistics) are available for the currently integrated pipelines.

Conclusions: Nipopy can be used to establish a decentralized data processing network, where research centres or laboratories each process their own datasets following the same general workflow. Efficient data sharing within such a network can be achieved through Nipopy’s data organization standard. Nipopy also creates files compatible with the Neurobagel ecosystem for distributed dataset harmonization and search (https://neurobagel.org/).

References

Poster No 2257
FMRIPrep-next: Preprocessing as a fit-transform model
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**Introduction:** The value of publicly shared neuroimaging data depends on the level of processing applied to the data. While raw data provide the greatest opportunity for asking novel questions, each step of processing left to secondary researchers is a potential source of analytical variation that can lead to conflicting results from the same source data. A researcher wishing to share the data they have collected can reduce sources of variability in downstream analyses by providing a canonical set of preprocessed data for reuse. Publication of data that have been resampled into several spaces can enable different analyses while limiting analytical variability, but this requires significantly more storage and bandwidth. Generation of many derivatives may also be inefficient on shared, high-performance computing systems suited to computationally intensive tasks with relatively little storage use. It would thus be beneficial to calculate and distribute a compact set of preprocessing derivatives that permit the remaining derivatives to be generated cheaply and deterministically at the time of analysis. Here we present recent changes in the architecture of fMRIPrep, a preprocessing pipeline for functional MRI. These changes separate the typical processing pipeline into two discrete, user-accessible workflows. Firstly, a computationally expensive “fit” stage performs steps such as segmentation, registration, and surface reconstruction, the derivatives of which are small and therefore easy to distribute. A second “transform” workflow then utilizes the raw input data and the derivatives from the “fit” workflow to deterministically generate dense preprocessed fMRI data in any desired target space with minimal additional computational cost. We discuss the practical consequences of these software changes for fMRI data processing and distribution.

**Methods:** The fit-transform architecture has been published in version 23.2.0a2. To test the impact of the described changes, fMRIPrep 23.2.0a2 and the prior release, 23.1.4, were run on two subjects from two different datasets. Dataset A: 6 T1-weighted, 3 T2-weighted scans, 2 phase-difference fieldmaps, 4 single-echo BOLD runs with 195 volumes, and 1 single-band reference volume per BOLD series. Dataset B: 2 T1-weighted scans, 6 spin-echo fieldmaps, and 8 single-echo BOLD runs with varying lengths, for a total of 4274 volumes. The commands tested requested outputs registered to MNI152NLin2009cAsym volumetric template and the fsLR “grayordinate” template. All processes were run on a single, 20-core Intel i9-10900 2.8GHz processor.

**Results:** Table 1 compares runtimes and the storage usage in each version. Running fit-only workflows resulted in 34-66%, 94-98% and 84-92% reductions in runtime, data size and file counts, compared to the previous version. These reductions reflect the compute/storage utilization of the prior transform processes. Running fit and transform workflows resulted in 25-52%, 43-54% and 72-87% reductions in runtime, data size and file counts. Some efficiency was achieved through changes incidental to the structural changes described here. The increase in output sizes reflects additional outputs needed for resampling, present in the fit-only derivatives, as well as some unintended outputs which will be removed in future revisions.
Conclusions: Here we describe changes which result in a significant decrease in computational time and storage utilization for users of fMRIPrep. These changes particularly benefit researchers and data stewards interested in ensuring access to large scale data repositories. We also anticipate that these changes will simplify the process of resolving errors in preprocessing, as errors of fit and transformation can be addressed separately, and researchers will have the option of providing alternative fit results to be used in transformation. At the same time, the full workflow continues to provide the full range of derivatives that make fMRIPrep an attractive option.

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Poster No 2258
NeuroDOT: a Matlab and Python Toolbox for Optical Brain Mapping
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Introduction: Processing pipelines for functional near infrared spectroscopy (fNIRS) and diffuse optical tomography (DOT) data pose many challenges. Costly software licenses (e.g., Matlab) and a tendency to develop lab-specific pipelines prevent the adoption of standardized practices for data processing. Another challenge of fNIRS and DOT toolbox development is the need for compatibility with multiple data formats (e.g.,SNIRF, BIDS, NIRS, NIfTI, GIFTI, 4dfp, etc.) and a wide variety of commercially available systems (e.g., GowerLabs, NIRx, etc.). We are developing NeuroDOT as a Matlab and Python-based toolbox for fNIRS and DOT with functions and pipelines for data pre-processing, anatomical light modeling, image reconstruction, analysis, and visualization. Compatibility with various common data formats and the use of Python support community adoption of NeuroDOT alongside the modernization and expansion of NeuroDOT’s tools with best software practices.

Methods: NeuroDOT is a self-contained toolbox that contains individual functions and scripts for data processing. NeuroDOT provides tools for pre-processing, data quality analysis, head modeling, image reconstruction, and post processing with statistical analyses, removing the need to combine multiple packages to perform these tasks (Figure 1). NeuroDOT contains functions for the conversion between various data formats including volumetric data in the Neuroimaging Informatics Technology Initiative (NIfTI) and 4-dimensional floating point (4dfp) formats as well as converters between NeuroDOT’s format, the Shared Near Infrared Spectroscopy Format (SNIRF), the Near Infrared Spectroscopy (NIRS) format, and Brain Imaging Data Structure (BIDS) specifications. Individual functions are organized into categories based on shared functionality: Analysis, Reconstruction, Temporal Transforms, Visualizations, and others. Documentation for efficient training for the
novice and expert user is provided in the form of tutorial PowerPoints and Jupyter notebooks accompanying Matlab and Python scripts, respectively. XNAT, an open-source cloud-based platform, is utilized to develop containers for each of the NeuroDOT pipelines.

![Diagram of NeuroDOT Workflow](image)

**Figure 1 | NeuroDOT Workflow** The NeuroDOT analysis workflow includes multiple pipelines such as (a) Head Modeling (b) Light Modeling; (c) Pre-Processing; (d) Image Reconstruction, and (e) Tomographic Brain Mapping.

**Results:** NeuroDOT is available for download on GitHub (https://github.com/WUSTL-ORL/NeuroDOT) and NITRC (www.nitrc.org/projects/neurodot). All functions involved in the NeuroDOT pre-processing and reconstruction pipelines have been refactored to Python. Pre-processing, image reconstruction, and full data processing scripts have also been converted to Jupyter notebooks in Python and have been deployed as containers on XNAT. A guide for the use of the NeuroDOT pipelines on XNAT is also provided. Shared datasets including resting state DOT data, DOT data recorded during retinotopy, and common hierarchical language paradigms, and DOT data recorded during language tasks including silent reading of single words and covert and overt single verb production are available to download from NITRC.

**Conclusions:** Herein, NeuroDOT supplies the fNIRS community with a highly efficient and effective toolbox with shared extensible tools for fMRI-comparable high fidelity optical brain mapping. Functions are written as building blocks for workflows, so groups can build their own pipelines. We have aimed to promote modernization of the growing components of NeuroDOT by refactoring the toolbox in Python with enhanced development tools, shared data repositories, and data format standardization relevant to both optical and fMRI fields and have enhanced the support for our community of users and developers with expanded documentation and tutorials, detailed in Figure 2. Open-source software is essential for standardization of processing and accessibility of the NeuroDOT toolbox to new users. Next steps for this project include launching Optical-imaging XNAT-enabled Informatics (OXI) an XNAT-based platform for worldwide fNIRS and DOT data sharing and standardized or customized container-based processing on the cloud.
References

Poster No 2259

**NiCHART: A Software Suite to Translate Neuroimaging Big Data to Individualized Biomarkers in Disease**

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**Introduction:** Growing availability of open-access, large-scale neuroimaging data in healthy development and disease allows for rapid discovery of radiologic, neurologic, and psychiatric insights. This is especially true in the context of machine learning (ML), which promises improved prediction of diagnoses, prognoses, disease subtypes, and more. However, harnessing ML to pursue such precision medicine efforts remains a challenge for many neuroimaging scientists – barriers in coding skills, field-specific knowledge of state-of-the-art methodology, and access to large-scale neuroimaging data all limit the rate of biomarker discovery. We introduce niCHART (NeuroImaging Computational Harmonization and ARTifical intelligence Toolbox), a mutually-compatible ecosystem of state-of-the-art methods allowing for holistic processing of multi-modal MRI images as well as calculation of statistical and ML-based imaging-derived phenotypes (IDPs). Ultimately, niCHART will allow for improved
reproducibility and accessibility of neuroimaging analysis as well as allow end-users to contextualize their own data among open-access, curated neuroimaging big data.

**Methods:** niCHART integrates all-in-one software pipelines for pre-processing, harmonization, and statistical analysis of structural MRI, diffusion MRI, and functional MRI (Figure 1). Image pre-processing components consist of a validated structural MRI atlas-based segmentation pipeline, fMRIPrep, XCPEngine, QSIPrep (q-space image preprocessing), sopNMF (stochastic orthogonally projective non-negative matrix factorization), and pNet (personalized networks)\textsuperscript{1-7}. Post-processing components include generalized ComBat family harmonization methods, SPARE (Spatial Pattern of Abnormality for Recognition) IDP methods, smileGAN (SeMI-supervised cLustEr via Generative Adversarial Network), and more\textsuperscript{8-12}. Additionally, niCHART develops a statistical and ML-based dimensional system based on a large reference population and automatically projects end-user image data into this dimensional system. These niCHART dimensions capture multivariate imaging patterns of brain heterogeneity covering both normative aging and disease.

**Results:** niCHART reference data consists of pooled and harmonized multi-modal imaging data from 62,859 individuals across 24 studies (Figure 2). These reference individuals are demographically diverse with respect to age, sex, race, and underlying health conditions. Statistically-extracted IDPs include atlas-based anatomical and network segmentations, data-driven parcellations, structural covariance networks, and network metrics. In neurodegeneration, additional ML IDPs include deep learning metrics describing spatial patterns of atrophy related to normal aging, Alzheimer disease, and cardiovascular disease as well as metrics for subgroup identification within Alzheimer disease patients. In neuropsychiatry, ML IDPs include indices related to normal development, depression, autism spectrum disorder, and schizophrenia. Statistical harmonization models for IDPs have been pre-trained on this reference data and allow for automated harmonization of end-user data to the reference data, which allows for improved reproducibility and more valid inference.

**Conclusions:** niCHART offers an accessible and feature-rich software suite for processing and analysis of neuroimaging data to translate state-of-the-art methodology to the individual-subject level. niCHART’s panel of statistical and ML IDPs allow end-users to automatically extract high-level, individualized information from complex imaging data and contextualize their subjects among demographically and phenotypically diverse reference subjects. This machinery promises to accelerate research in precision medicine and dimensional phenomics.
Fig. Visualization of NiCHART general analysis pipeline, post-processing data visualization, and ML-based dimensional representation system for biomarker discovery with inclusion of a reference data.

References
(IDPs). The pipeline was optimised for UKB data and has been adapted for other studies with some effort\textsuperscript{2,3,4}. By 2023, 72k brain imaging datasets had been acquired and processed. 63k were usable data from the first imaging visit and 5k from the second. The goal is 100k first-visit and 60k repeat-visit scans. Fig 2 shows pairwise associations between 4k brain IDPs and 27k non-imaging variables.

Methods: The pipeline has maintained almost perfect backwards compatibility so that all outputs (for new scans) are compatible with existing outputs for previous subjects/scans. Therefore, changes have been limited to adding new processing (e.g., the recent addition of QSM processing). However, maintaining backwards compatibility limits the ability to incorporate improved algorithms and software, and we are now planning a complete rewrite of the pipeline, named BIP (Brain Imaging...
Pipeline. Improvements being considered include: Pipeline framework: fully Python-based and using three main components: - Fsipy®: Python library to perform FSL calls through wrappers - File-Tree®: Python library to abstract out filenames and folder structure - FSL-pipe®: Easy (to use and scale) declarative pipelining Python library Usage - The pipeline should be easy to configure (with as few configuration files as possible) for datasets with configurations different from UKB (but not too different) Registration - Multi-modal (T1, T2-FLAIR, dMRI) volumetric registration using MMORF and multi-modal UKB-derived OMM templates® - Surface registration using MSMAIR® Surface (“CIFTI” HCP processing (note that this has now been added to the pipeline) - fMRI projected onto the surface fMRI - PROFUMO as a complement/replacement for group-ICA+dual-regression® Diffusion - Better cleaning (Gibbs ringing correction, modelling Rician noise) - Improved Eddy-current correction (within-volume motion, long-time eddy currents) - Replace autoPtx with XTRACT (reference) - Improved NODDI model QC - Fully automated (if possible), improved QC

Results: We want to ask the neuroimaging community for their opinion on our plans and what else we can do with UKB data in BIP, starting with a set of surveys. We encourage suggestions for solidly established complementary/improved methods. We will engage experts in each area, with expert working groups to evaluate suggestions, including considering these criteria: - Feasible: Given the amount of data to process, the tools must be easy to implement (and free to use) and not too memory/disk/processing intensive - Testable: The method should be easily testable against similar methods with clear and measurable criteria to establish which is best for UKB (and other data). - Fit for framework: Once the framework has been decided, adding pieces that do not fit well with the framework would make the pipeline too complex. - Aligned with UKB data and goals: We will consider suggestions sufficiently close to the UKB brain imaging protocol.

Conclusions: UKB is an epidemiological study that needs a robust and fully automated pipeline to process all its data. Therefore, once BIP is considered “finalised”, backwards compatibility must be maintained. Thus, if you want to have your say on this processing pipeline, the moment to do that is now!

References

Poster No 2261

DPABI Harmonization: A Toolbox for Harmonizing Multi-site Brain Imaging for Big-data Era

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Introduction: Pooling multi-site datasets is the dominant trend to expand sample sizes in neuroimaging field, thereby enhancing statistical power and reproducibility of research findings. Nevertheless, the heterogeneity derived from aggregating data from various imaging sites obstruct efficient inferences. In particular, the removal of such site effects generally necessitates a certain level of programming expertise. In our effort to streamline the harmonization of site effects using advanced methodologies, we are pleased to introduce DPABI Harmonization module. This versatile tool, allowing agnostic to specific analysis methods, integrates a range of techniques, including linear models, ComBat/CovBat (Johnson 2007; Fortin 2017; Fortin 2018; Yu 2018; Chen 2022), subsampling maximum-mean-distance algorithms (SMA, Zhou 2018), and invariant conditional variational auto-encoder (ICVAE, Moyer 2020). It equips neuroscientists with an easy-to-use and transparent harmonization workflow, ensuring the feasibility of post-hoc analysis for multi-site studies.
Methods: DPABI Harmonization (Fig 1.A) is open-source and distributed under GNU/GPL, available at http://www.rfmri.org/dpabi. It supports Windows, macOS and Linux operating systems. We are continually updating the toolbox since its first release. Step1: Set computational environment. Timing: 1-5 minutes. Users can find the latest version of Harmonization in https://github.com/Chaogan-Yan/DPABI and downloaded it from website green “Code” button or git clone https://github.com/Chaogan-Yan/DPABI.git. Step2: Prepare brain and demographic data. Timing: 10-30 minutes. › Data preparation: i) Organize them into one .mat/.xlsx file and add it with “Add Image” button; ii) Use original .nii/.nii.gz/.gii/.gii.gz/.mat for individual, and organize them under one directory. Add this directory under “Parent Directory” within “Add Directory/Sites” and keep “Reference File for Sites” empty; iii) When arrange them based on their sites, it is required to name them by the same path. Add any one site directory to “Parent Directory” within “Add Directory/Sites” and choose any one .nii/.nii.gz/.gii/.gii.gz/.mat file of this site for “Reference File for Sites”. › Demographic file: All input choices require ensure the subjects align across covariates in demographic file (rows). For way i) this is the prerequisite. As for ii) and iii), an alternative way besides checking, is to add a column named “FileList” for voxel-based and network-based files/ two columns named “FileList_LH” and “FileList_RH” for vertex-based files in demographic file. Once input this file, no matter you have added images or not, it would load files by the order of provided “FileList”. Step 3: Methods setting. Timing: 10-15min. Fig1.B showcases four sub-GUIs of methods setting. The first step is to load demographic file. And next set corresponding parameters based on the specific application requirements (Fig 1.B). Step 4: Compute. Timing: Not sure. Based on the size of data to be harmonized, methodology option as well as hardware and software foundations, the runtime is uncertain.

Results: We showcase the runtime of all methods on example dataset with 41 subjects each scanned in three scanners once, and each image has 38810 features (Table 1). The parametric ComBat/CovBat is very fast. However, given to our evaluations, it is preferred to use nonparametric ComBat/CovBat over parametric. We illustrate our code structure in Fig.2.
Conclusions: We designed DPABI Harmonization to deliver a flexible, well-coordinated, and cohesive analysis experience. To achieve this, we commit to staying abreast of field developments and adapting to advancing technologies for continuous harmonization. Users have the option to share their needs, questions, or advice on our online forum at http://rfmri.org/ or can reach out directly through the authors’ emails ycg.yan@gmail.com or dwong6275@gmail.com. Let’s build DPABI Harmonization together!

References

Poster No 2262
Entense, a compositional data-to-tensor workflow assembler
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Introduction: Brain mapping and other data-intensive sciences have adopted data organization conventions that are formalised, structured, and principled (e.g.,). However, these conventions are often at odds with optimal practices for online training of large-scale machine learning models. For instance, volumetric brain image datasets often explicitly represent thousands of extraneous voxels. MRI datasets are usually scattered across many files that are non-contiguous on disk. One-size-fits-all workflows are not suitable in the setting of online training – even after preprocessing, data frequently require additional transformations before they are ready for consumption by a model, and different models have different input data demands. Together, these design limitations manifest in sluggish latency when naively loading data batches; because of the large size of fMRI data and limited memory bandwidth, data load operations can be a bottleneck in model training.

Methods: We introduce entense, a software library that transforms neuroimaging datasets into archive formats designed for downstream ingestion by widely used machine learning libraries like PyTorch² and JAX³. We do not introduce new data formats but instead leverage TensorFlow records⁴ and tar archives⁵ for interoperability with existing libraries. entense is built...
The Integrated Brain Analysis Toolbox for SPM (iBT)

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Introduction: The “Integrated Brain Analysis Toolbox for SPM” (iBT), also known as the “iBrain Analysis Toolbox for SPM” (iBrainTools)1, is a functional neuroimaging analysis toolbox that adds additional pre-processing, analysis, display and automation features to the Statistical Parametric Mapping software SPM2. iBT has been enhanced with many new features.

Methods: iBT is written in MATLAB and requires SPM2. Some optional features also make use of tools from FSL3 and/or iBrain4, or output from fMRIPrep5. iBT is designed to allow a complete a priori configuration of a computational pipeline that includes pre-processing, statistical analysis and display of functional Magnetic Resonance Imaging (fMRI) data. The toolbox is suitable for general linear model analysis of block and event-related designs, and functional connectivity. It allows easy access to features such as multi-session realignment to a single optimally auto-selected target volume, seed-timecourse regressor construction from regions of interest, configurable auto-generated motion-rejection regressors (to deal with excessive scan-
ABSTRACTS

to-scan motion), flexible regressor-orthogonalisation options, automated contrast generation taking into account nuisance regressors, adjustment of degrees of freedom for denoised input data, and automated generation of tiled output image montages in a print and display friendly format. The pipeline can be configured to automatically run for any number of subjects and sessions. iBT can be configured to analyse and/or display results from other neuroimaging software. iBT includes inbuilt support for analysis and display of fMRI data that has been pre-processed with fMRIPrep\textsuperscript{5}, including utilising any choice of confound regressors generated by fMRIPrep. One can also instruct iBT to call one's own custom MATLAB routine to undertake novel analyses. iBT includes tools to objectively assess relative laterality of activity in specified pairs of regions of interest\textsuperscript{6}. The toolbox plots curves of laterality as a function of activation volume, and it allows statistical comparison of an individual with a control group, in a manner largely independent of an activation map statistical threshold\textsuperscript{6,7}. New user-configurable display options are available to customise the output plots. In addition to conventional SPM toolbox deployment, iBT now also supports containerisation. The containerised version includes compiled SPM together with iBT to allow it to utilise Runtime MATLAB (no MATLAB end-user licence required).

Results: In a recent large-scale use case, the Australian Epilepsy Project (AEP)\textsuperscript{8} has been analysing functional MRI data at scale utilising fMRIPrep and iBT. The AEP has deployed containerised fMRIPrep and iBT on high-performance computing platforms at The University of Melbourne and Monash University, as well as on a Flywheel\textsuperscript{9} instance on AWS. Select iBT outputs, including functional MRI statistical maps (Figure 1) and Laterality Index (LI) results for a pseudoword language task (Figure 2), form part of an AEP Report for each participant that is returned to each participant's treating clinician.
Conclusions: iBT is a robust and flexible analysis toolbox for SPM that provides additional capabilities and facilitates advanced fully automated statistical parametric mapping. iBT is free and open-source software released under the GNU General Public License. iBT is available at https://florey.edu.au/imaging-software

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Poster No 2264
A robust, containerised workflow for processing multi-session, ultra high-field, high-res MRI data

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Introduction: With 7T MRI, we are able to image the human brain anatomy and function at a submillimetre scale. However, high spatial resolution (high-res) fMRI is often limited to partial brain coverage. For example, the majority of layer-fMRI
studies have focused on primary cortices due to well-established correspondence between cortical depths and the neuronal microcircuit. Recently, interest has grown to study non-primary brain areas and higher-level cognitive processes with layer-fMRI, e.g., using language processing, episodic and working memory tasks. An important challenge for this endeavour is the fact that there is a noticeable lack of readily-available and generalisable pipelines that can effectively preprocess 7T high-res fMRI data, particularly when small fields-of-view are involved and data are acquired over multiple sessions. Here, we present a workflow that has been developed for preprocessing of small field-of-view, multi-session, sub-millimetre resolution fMRI data of non-neocortical structures, such as the hippocampus. This workflow, building upon our previous work, is modular, containerised and BIDS-compliant, requiring only minimal input from the user. The workflow primarily uses ANTs for a majority of registration steps and integrates standard software, such as Freesurfer, SPM, AFNI and FSL for various intermediate steps.

Methods: We used four high-res fMRI datasets from an ongoing spatial navigation study acquired on Siemens Terra 7T at the ELH Institute, Essen, Germany. Data were acquired in 2 sessions: in ses-01, 0.75 mm iso MP2RAGE, hippocampus-aligned 2D-TSE (0.44 x 0.44 x 1.5 mm3, 3 reps), and 2 fMRI runs (func, 0.8 mm iso 3D-EPI) and 4 fMRI runs were acquired in ses-02 (6 fMRI runs per subject). Opposite phase-encoded (oPE) data were acquired after each fMRI run. Subjects performed a spatial navigation task. Briefly, our workflow (Fig1) realigns ‘func’ and ‘oPE’ data and performs distortion correction using ANTs (like 3dQwarp) for each run in each session. Inter-session alignment is done using the corrected runwise data and ‘func2anat’ is estimated using the boundary-based registration (BBR) algorithm in FSL, as it outperforms typical cost functions in data with the signal dropouts and artefacts (e.g., in ventral/medial temporal lobes). All matrices and warps are preserved and are concatenated and applied in a single resampling step to reduce interpolation errors. Motion and QC plots are generated using Python.

Results: For all subjects, both the structural similarity index (intra-session: 0.92 ± 0.023, inter-session: 0.873 ± 0.019; 1.0 being identical) and the normalised root mean squared error (intra-session: 0.041 ± 0.008, inter-session: 0.065 ± 0.027; 0 being identical) indicate a high degree of similarity between the reference and resampled images (both mean EPI, Fig. 2) after processing through our workflow.
Conclusions: Inter-session registration is more challenging than intra-session as different head positions and orientations have different distortions, and regions of dropouts and artefacts, and high-res fMRI is more sensitive to these. Improving on current state-of-the-art workflows, our approach combines optimal data acquisition (e.g., runwise oPE with fMRI) with automated, high-res optimised image processing (e.g., cost-function choice, ROI-confined registrations, image filtering to enhance boundaries) and one-step resampling, to ensure accurate intra- and inter-session results. Taking advantage of efficient, multi-threaded tools and evaluating on a system with just 32 Gb of RAM (typical University PC), the processing times were kept reasonable around 32 minutes per fMRI run (HPCs and servers will be faster) for high-res fMRI with partial brain coverage and large file sizes (900 MB, compressed). Containerisation using Docker takes care of software dependencies and helps easy adoption of our integrative workflow by the wider neuroscience community.

References

Poster No 2265
NiSpace: Neuroimaging Spatial Colocalization Environment
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Introduction: Most neuroimaging research focuses on brain-regional effect estimates. Spatial patterns across the whole brain or cortex may convey equally important information missed by regionally constrained analysis approaches. Such patterns are found in any brain map, from individual brain development over time1, to effect size maps reflecting case-control differences on the individual2 or group level3. By testing these maps for their colocalization with atlases of known biological entities (e.g., neurotransmitters, gene expression, or cortical microstructure), one can derive meaningful inferences from in-vivo human neuroimaging data. The most renowned spatial colocalization tools are JuSpace2 and neuromaps4. While JuSpace focuses on GUI-based evaluation of clinical case-control differences using univariate and multivariate colocalization statistics in MNI space, neuromaps’ core features include a multimodal atlas dataset, flexibility in regard to imaging spaces, and several spatial null models; with limited functionality in terms of colocalization statistics and analysis workflows. Here, we introduce NiSpace (“Neuroimaging SPAtial Colocalization Environment”), a user-friendly toolbox integrated in the Python neuroimaging ecosystem that allows for fast, flexible, and scalable colocalization analysis.
Methods: NiSpace employs a pipeline-style API (Fig. 1), extended by simplified command line and graphical interfaces for less experienced users. It advances available tools in that it (i) interfaces with existing multimodal human brain datasets, (ii) handles surface and volumetric imaging data types, (iii) allows for flexible and scalable analysis workflows, (iv) incorporates vectorized implementations of all currently used spatial colocalization statistics, (iv) provides permutation-based significance estimates, and (v) produces publication-ready visualizations. User-defined input brain maps are tested for colocalization with a set of multimodal brain atlases. All brain data is transformed to a common space, parcellated and, if required, group difference maps are calculated. Colocalizations are evaluated by treating individual parcels as “observations” and brain maps as “features”. In the univariate case, every input map is correlated with every multimodal atlas, with correlation coefficients as estimates of colocalization. In the multivariate setting, each input map is “predicted” from all multimodal atlases, resulting in R2 values that indicate how well a given map can be explained. All statistics are furthermore employed in gene set enrichment analyses based on the Allen Brain Atlas. To reduce false-positives, NiSpace provides exact p values based on permuted brain maps, subject groups, or gene sets.

Results: NiSpace’s core functions (Fig. 1) include: NiSpace.fit(): The user provides volumetric, surface, or parcellated neuroimaging data from a given number of subjects (Y) along with integrated or user-defined biological/functional maps of interest or gene sets (X), and a brain parcellation. NiSpace.transform(), .harmonize(), .compare(): If required, the parcellated data can be cleaned from covariates, harmonized across study sites, or parcel-wise compared between groups. NiSpace.colocalize(): Colocalization estimates are calculated. A focus is laid on regression-based approaches including dominance analysis, partial least squares, and regularized regression, using within-brain distance-dependent cross validation. NiSpace.
Improved Pipeline Development and Quality Control using File-tree and FSL-pipe

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Introduction: Neuroimaging pipelines typically produce a wide variety of different files (especially if one counts temporary, intermediate files). The need for different parts of the pipeline to correctly find these files on disk causes most pipelines to only work with a very specific file structure. This limits the interoperability between pipelines. To overcome this, one could either encourage a common file structure across all pipelines (e.g., BIDS) or make it easier to change the file structure used by an existing pipeline. We present two new tools to do the latter: file-tree2 and FSL-pipe3. In this abstract we illustrate the benefits of these new tools for running quality control across many subjects (even for output from pipelines not based on file-tree or FSL-pipe) and for pipeline developers.

Methods: File-tree is both a simple-to-write file format that defines a file structure and a python library to access that file structure (Figure 1A)2. Rather than directly including the file paths in the pipeline, the pipeline can refer to this file-tree to find the paths for any input, intermediate, or output files. FSL-pipe3 allows for the writing of declarative pipelines built on top of file-tree.

Results: Benefits for quality control Quality control (QC) across many subjects can be tedious. Such QC often relies on summary measures or 2D static images, which do not capture the full complexity of 3D neuroimaging data. Alternatively, one can open each subject’s data in an interactive viewer; however setting up a tool like FSLeyes4 (potentially with several complementary image/timeseries sub-views, each with their own display parameters), repeatedly for each subject can be very time-consuming. In FSLeyes, this has now been sped up. FSLeyes can load file-trees, which enables users to set up a plot to their liking for a single subject and then, with a single click, switch to the equivalent plot for any other subject (Figure 1B). In this example, the resulting image could be produced using either a file-tree describing the full HCP directory structure5 already included in FSL or by writing a file-tree describing the relevant part in Figure 1C. Benefits for pipeline development FSL-pipe is a new tool allowing one to write pipelines in a declarative manner. What this means is that, rather than describing what the computer must do and in what order, one instead provides the computer with a set of “recipes”. For example, in Figure 2A we define a multi-step registration6/7 pipeline with 3 recipes. By then providing a file-tree that defines where the input/output files are located (Figure 2B), FSL-pipe can put these recipes into a pipeline by inferring any dependencies between them (Figure 2C). FSL-pipe will also ensure that relevant output directories exist before any job is run. The code in Figure 2A is a fully functional pipeline with a command line interface allowing the user to: 1. Run only part of the pipeline (by requesting specific output files to be produced or selecting specific subject IDs) from the command line or using a GUI. By default, this pipeline will run for any subjects that have a T1-weighted image. 2. Overwrite any output files that already exist or...
to keep them. 3. Select whether jobs are run in sequence, in parallel using dask\(^8\), or submitted to a computing cluster. FSL-pipe will ensure that jobs run in the right order (and, where possible, in parallel).

Conclusions: File-tree and FSL-pipe are currently being adopted throughout FSL and in version 2 of the UK biobank pipeline. However, they are generic tools that would also benefit pipelines not based on FSL, even including non-neuroimaging pipelines. Documentation and tutorials: - File-tree (including movie on QC): https://open.win.ox.ac.uk/pages/fsl/file-tree/ - FSL-pipe: https://open.win.ox.ac.uk/pages/fsl/fsl-pipe/
Poster No 2267

Containerized pipeline for handling multi-echo fMRI data

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Introduction: Neuroimaging researchers have available a number of software tools and preprocessing options. Recently docker and singularity have facilitated the use and sharing of containers dedicated to processing neuroimaging data, most noticeably fMRIprep has been widely adopted as it provides a robust pipeline that can be evoked in a single command line argument (Esteban et al., 2019). However, there might be particular cases when it is desirable to have alternate pipelines available to researchers. Here we present a docker container that implements the pipeline described in (Lyn et al., 2020). This container aims to fill an existing gap. Although there are many processing software and pipelines available, there is no dedicated container for end-to-end processing and denoising of multi-echo fMRI. This pipeline previously showed good reliability with multi-echo fMRI data projected to the cortical surface.

Methods: The functional processing requires the anatomical processing of the HCP pipeline (Glasser et al., 2013). In short it consists of a pre-FreeSurfer step, which includes the alignment of the T1w and T2w scans, bias field correction and registration from subject to MNI space. This is followed by FreeSurfer processing, and lastly the final anatomical format in GIFTI or NIFTI is produced. The container allows for the researcher to run these steps, or to run only the functional processing if HCP style outputs are already available. The fMRI pipeline consist of i) preprocessing fieldmaps (averaging available fieldmap, TOPUP, aligning to subject space and brain extraction); ii) slice timing and head motion correction of the functional images; iii) signal decay based denoising and removal of spatially diffuse noise, using tedana. (DuPre et al., 2021; Kundu et al., 2012); iv) and mapping the denoised signal to surface space.

Results: We present a working docker container that is ready to run the aforementioned pipeline. The container entrypoint takes the pipeline (anatomical or functional), participant folder, path to the data (as mounted in the container), and number of cores to use as arguments. Currently the command line requires that the user specifies the correct mount point, FreeSurfer and MATLAB licenses. An example command is: """"Docker run --name test -v /PATH/TO/DATA://data -v /PATH/TO/OUTPUT:/out -v /PATH/TO/WORK:/work -v /Documents/licenses/license.txt:/opt/freesurfer-6.0.1/license.txt -v MLM_LICENSE_FILE=9999@your.license.server -v platform linux/amd64 listonpipeline <anat-func> -p [participant] -d [data/] -c [number of cores]"""" This container was tested on data now available online on openneuro (https://openneuro.org/datasets/ds004787/versions/1.1.0.). This data consists of 5 healthy volunteers, scanned in a GE MR750 3T scanner. Multi-band Multi-echo resting-state fMRI was acquired with the following parameters (2.5mm isotropic, TR=2.5 s; TEs=(12.9 ms, 32.2 ms, 51.6 ms, 70.9 ms); Flip Angle= 77 degrees; in-plane acceleration=3, multi-plane acceleration=2). High-resolution T1w and T2w scans were collected in the same session. All subjects gave informed consent and consented to data sharing (protocol 01-M-0192).

Conclusions: We provide a working container for preprocessing multi-echo fMRI and outputting fMRI signals in surface space. We intended to improve this container by removing the MATLAB license requirement and adding BIDS compatibility. The current version uses the automatic classification of noise components, tedana also allows for the manual classification of the components. Future versions should allow researchers to use manually selected components and re-run only the relevant steps of the pipeline.
Next Move in Movement Disorders (NEMO): Imaging protocols for hyperkinetic movement disorders

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Introduction: The Next Move in Movement Disorders (NEMO) project is dedicated to characterizing hyperkinetic movement disorders; i.e. including the phenotypes tremor, myoclonus, dystonia, and myoclonus-dystonia1. Precise phenotypic classification is essential for effective diagnosis and treatment planning. The project seeks to develop computer-aided tools to enhance diagnostic accuracy, assess disease progression, and individualize treatment approaches. For the NEMO project, we collected data from 140 patients using movement registration (as described in1) and neuroimaging measurements. These neuroimaging measurements include fMRI and 18F-fluorodeoxygluicos (FDG) PET scans to explore the relation between the phenotypes and brain function. Here, we outline our efforts from the past four years to improve data quality and to address challenges such as head movements, protocol design, and data preprocessing. Our standardized protocols enable comparative analyses between movement disorders, contributing to our understanding of each disorder’s distinctive attributes.

Methods: Hyperkinetic movement disorders, often mild at rest, intensify during tasks2. As body movements increase the risk of movement induced artifacts, we carefully selected neuroimaging protocol designs3. Two BOLD fMRI protocols were created: (1) a protocol with relatively high spatial precision and a short TR: Full brain T2*-weighted EPI with 2mm isotropic voxels, TR 1600ms, and (2) a multi-echo protocol that is more resilient to movement induced artifacts: Full brain T2*-weighted EPI with 3.5mm isotropic voxels, TR 1101ms. Preprocessing involved fmriPrep for single-echo data and a Nipype pipeline for multi-echo data, including fmriPrep, tedana, and ANTs for frame-based image-registration (FIR) methodology4. Spatial and temporal quality of the protocols were assessed using signal to noise ratios (sSNR/tSNR), framewise displacement (FD), and DVARs in 18 participants. 3 conditions were tested using these two protocols: a) resting-state (protocol 1,2), b) hand movement task (1,2), and a hand-posture task (2). For FDG PET imaging, dynamic acquisition of PET images was implemented to track head movements, and correction was performed using a frame-based image-registration (FIR) methodology5.

Results: fMRI Protocols Optimization: Task scans increased artifacts (FD +37%, p<0.001) and reduced tSNR (-22%, p=0.002), while protocol 1 had 189% higher sSNR (p<0.001). After preprocessing, tSNR increased by 39% for protocol 1 (p<0.001), with resting state surpassing movement task tSNR (+26%, p=0.003). Protocol 2 showed no tSNR differences across tasks (p=0.47), but tSNR was 287% greater (p<0.001) than protocol 1 after preprocessing. Little head movements during rest led to selecting protocol 1 for the rest scan. No distinct tSNR differences in multi-echo task scans led to choosing the kinetic hand movement task to evoke more movement disorders. PET Protocol: To address artifacts associated with motion, a dynamic acquisition protocol for FDG PET was implemented without restricting head movement. The FIR approach corrected motion in the dynamic images, providing a single static image for analysis. PET Preprocessing: An in-house preprocessing pipeline was developed, combining fmriPrep and Nipype. The robust procedure included HD-BET for brain extraction, two-step coregistration using ANTs, and transformation into subject and MNI spaces. The NEMO FDG PET preprocessing pipeline is accessible at https://github.com/jrdalenberg/PETBrainPreprocessing, offering an open-source, Nipype workflow for PET BIDS6 preprocessing.

Conclusions: The NEMO project represents one of the most extensive studies into rare movement disorders. Its distinctive contribution lies in the integration of PET and fMRI alongside movement registration measurements. Notably, this study is the first to systematically apply these modalities across multiple hyperkinetic movement disorders, contributing to a more standardized approach to compare these rare movement disorders in future studies.

References
References

Poster No 2269
XOANI: eXtensible Open-framework for Animal NeuroImaging
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Introduction: Neuroimaging is a rapidly evolving field that generates massive amounts of data from various sources and modalities. To harness the full potential of this data, researchers need to share and collaborate across different laboratories and institutions (Passerat-Palmbach et al., 2017; Poldrack et al., 2019). However, the lack of tools for data management and analysis are often insufficient, or unavailable, especially for animal studies. This contrasts with the growing interest in collaborative data harmonization for animal neuroimaging (Grandjean et al., 2020; Deruelle et al., 2022). To address this gap, we present XOANI (eXtensible Open-source Animal NeuroImaging Framework), a novel platform that enables standardized, reproducible, and collaborative neuroimaging research for animal models. XOANI is based on the Brain Imaging Data Structure (BIDS) standard (Gorgolewski et al., 2016), which provides a common framework for organizing and describing neuroimaging data. By adopting BIDS, XOANI ensures that datasets are consistent, predictable, and interoperable, which facilitates data sharing and reuse among researchers. In addition to data organization, XOANI also provides a solution for seamless data conversion and processing. XOANI leverages Docker Swarm technology (Cerin et al., 2017), which allows researchers to create and deploy reproducible workflows and analysis environments. This feature is particularly useful for animal neuroimaging, where novel and specialized methods are often required. By using Docker Swarm, researchers can ensure that their analysis pipelines are consistent, transparent, and portable, which enhances the reliability and reproducibility of their results (Gorgolewski et al., 2017).

Methods: XOANI introduces a structured project hierarchy that simplifies dataset organization into subject and session levels. Docker Swarm’s parallelization is harnessed for distributed computing, optimizing resource usage across cluster environments (Figure 1). The proposed framework includes: - A project structure that organizes comprehensive project data into a hierarchical manner, including BIDS data, subject-level derived data, group-summarized data, and code bases. - Data Conversion/Orgernizer Module: We developed a Python module to effortlessly transform raw data into the BIDS format, ensuring seamless BIDS-compliant data management. - DataFlow Module: Another Python module was created to simplify data retrieval and processing within the XOANI framework. - App Scheduler Module: To enhance task management and deployment, we utilized Docker Swarm. This feature proved invaluable for the development and testing of new pipelines in our preclinical research context.
Results: XOANI’s BIDS-Workflow enhances data preprocessing by offering a robust dataset parser, flexible output file configuration, and folder structure compliant with the extended BIDS format (Figure 2). The Docker Swarm integration enables efficient parallel processing, making XOANI suitable for laboratories aiming to leverage existing resources for cluster computing. This scalable solution aims to improve accessibility and efficiency in neuroimaging data analysis, particularly in resource-constrained research environments. The framework offers a multi-tiered organization system that neatly packages BIDS datasets, processed data, segmented images, and research outputs, enhancing clarity and accessibility. The Python module streamlines workflow from data conversion to analysis, reducing the complexity of dependencies and environment configurations. Docker Swarm's deployment aids in scalable and distributed computing, providing a user-friendly interface for managing imaging tasks.
Conclusions: XOANI presents a transformative open-source platform for preclinical neuroimaging, emphasizing standardized, scalable, and community-driven research. The integration of BIDS standards and Docker Swarm technology positions XOANI as a pivotal tool in advancing neuroimaging studies.

References
Rethinking How We Wrap Command Line Tools from Python

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Introduction: Given the increasing prominence of Python for brain imaging signal analysis, there is a common desire to also adopt Python for data preprocessing. However, a majority of fundamental brain imaging tools (e.g. FSL, AFNI, Freesurfer) are distributed as collections of executables, primarily written in C and GNU Bash, exposing heterogenous command line interfaces, making their integration with Python either cumbersome at best or clumsy and error-prone at worst. In the last decade, the Python library Nipype¹ has seen increased adoption², as it effectively bridges the interoperability gap by offering uniform Python interfaces for a variety of brain imaging software collections. However, this approach caters to the development of complex pipelines, and falls short in several key areas and simpler applications. It adds complexity in simpler applications, and manual management of these interfaces becomes burdensome and error-prone³, requiring extensive code modifications for even minor structural changes. Independent of Nipype, the process of reading and writing files to disk storage is challenging to implement robustly. Detecting errors and unexpected behaviours, such as tools accessing the wrong files, proves extremely difficult. In addition, large-scale processing in the cloud or across federated data centres necessitates separate handling of streaming data from remote file storage. These complexities result in unwieldy and user-unfriendly APIs, making the creation, expansion, and maintenance of brain imaging data pipelines a challenging endeavour. On the other end of the spectrum towards solving the problem of tool portability is Boutiques⁴. While Nipype provides a framework for describing and connecting complex workflows, Boutiques provides a descriptive framework through which individual tools can be defined. While this reduces the complexity of building simple pipelines, it does not overcome file-based data storage limitations.

Methods: To tackle these issues and increase the transparency between the use of Python programs and command line tools, we develop Styx. Styx is a compiler that automatically generates statically typed Python functions from Boutiques command line tool descriptors. This lets us create efficient and easy-to-inspect code for any tool. It provides users with the benefits of statically written code, specifically intellisense (i.e. in-editor type checking, auto1 completion, and documentation) and static code validation. Our code generation system maintains flexibility, allowing us to make structural changes in the compiler once, automatically propagating them to any number of generated interfaces. Styx also handles execution across different platforms (native, Singularity, Docker) and works closely with a FUSE-based virtual file system. This system helps sandbox⁵, stream, and monitor file-based inputs and outputs for command line tools, whether they're from local disk storage, Python-managed memory, or web file storage like S3.

Figure 1: Basic workflow of a command line tool Python wrapper generated from a Boutiques descriptor: ¹ The user specifies input and output data storage locations. These can be on a hard drive, Python memory, or web stores. ² Then the Python wrapper is called, with its primary role being the exposure of the sandbox file system through FUSE (Filesystem in Userspace) before proceeding to execute the command-line tool. ³ During the execution of the command-line tool, it exclusively interacts with the virtual sandbox file system. Data is streamed directly to and from the initially defined destinations, enhancing not only the speed of operations but also effectively reducing clutter. This architecture allows for more flexible data storage, ensures stringent data provenance, offers more fine-grained monitoring and facilitates robust interactions with third party command line tools.

Results: Developing Styx is an ongoing research experiment. Performance of different storage types (disk, memory, database) using Styx versus Nipype interfaces will be evaluated across a range of metrics such as processing speed, memory usage, and CPU usage. We expect Styx generated wrappers to be notably faster on distributed file systems that have a considerable overhead for individual file access, while showing comparable performance on low latency file systems.
Conclusions: In summary, the development of Styx offers a novel solution to the challenges of wrapping command line tools in Python for brain imaging data pipelines. By generating efficient and easy-to-inspect code, addressing performance issues, and simplifying file management, Styx represents a significant advancement in this field. With its ability to adapt to emerging technologies and streamline data processing, Styx is poised to make a substantial impact on the development and maintenance of such pipelines.

References

Poster No 2271
How C-PAC NodeBlocks and resource pool enable modular testing and cross-pipeline compatibility
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Introduction: C-PAC is a pipeline-builder for structural and functional MRI preprocessing and denoising that sits between researchers and core tool developers. We developed an engine built on NodeBlocks, an internal abstraction that wraps Nipype commands into interchangeable pipeline steps. A common challenge with highly configurable software is testing tool inter-compatibility and validating results, since there are many potential combinations. As tools are added and the length of possible pipelines increases, exhaustive testing becomes computationally intractable. Instead, we need to test individual components so that their composition results in high-quality pipelines. Complete integration tests are impossible, so we must turn to robust unit testing. In this abstract, we will focus on how the NodeBlock abstraction developed for C-PAC supports component-wise unit testing, and our proposal for a streamlined testing workflow to ensure pipeline quality as we issue new releases or integrate new algorithms. We will also highlight the various ways that researchers can compose pipelines across a variety of tools used commonly in the field, in particular, how they can ingress data derivatives from fMRIPrep and FreeSurfer.

Methods: Nodes in Nipype are objects that contain and execute one specific function. NodeBlocks are defined and implemented in C-PAC as groupings of Nipype nodes that comprise a pipeline step. By wrapping Nipype nodes into intuitive chunks, C-PAC NodeBlocks provide an interface between Nipype nodes and the processing pipeline as a whole, allowing users to create pipelines without having to interact with Nipype or the C-PAC engine. Users configure the pipeline file to switch on desired processing steps, each of which connects to a NodeBlock that encompasses all of the relevant processes. Due to the modular structure of the C-PAC NodeBlocks, the inputs and outputs of each NodeBlock remain identical regardless of internal modifications. This lends itself well to a NodeBlock testing suite of mock data where each pipeline step can be run and tested in isolation. In addition to the NodeBlocks architecture, C-PAC relies on a resource pool design where data are injected into the pool either after they are initially loaded, produced via processing, or pulled from another source. In the resource pool, each file has a strict definition, and NodeBlocks use this information to map inputs and outputs across each node of the pipelines.

Results: With the introduction of the NodeBlock infrastructure, it is now possible to set up a piecewise testing infrastructure. If there is an existing resource pool from prior runs, a NodeBlocks can be run and tested in isolation by developers. C-PAC gives users the opportunity to run community-standard processing pipelines, such as DCAN labs ABCD-HCP pipeline and fMRIPrep. These pre-built pipelines are modeled after and maintained to produce results that are maximally similar to their respective reference pipelines. Users can also build pipelines entirely from scratch. The modular NodeBlock structure allows for this seamless mixing and matching of tools and preprocessing steps. In addition, users can now import non-C-PAC output directories to carry out further processing and calculate derivatives in C-PAC. Currently, C-PAC is compatible with fMRIPrep and FreeSurfer output directories, and this function will be expanded to accept any BIDS-compliant directory. In an effort to maximally standardize the pipelines, we also now have an option to pre-process data in C-PAC to run through FreeSurfer according to the ABCD-HCP pipeline.
Conclusions: C-PAC is a highly configurable and flexible tool that supports researchers in not only processing their data in an end-to-end fashion, but extending the processing performed in other platforms. This configurability is due in large part to the NodeBlock infrastructure, and a testing suite for individual NodeBlocks further enables and demonstrates C-PAC’s stability and utility.

References

Poster No 2272
Snakebids: Flexible Input Interfaces for BIDS Apps
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Introduction: The increasing popularity of the Brain Imaging Data Structure (BIDS) specification for neuroimaging data (Gorgolewski et al., 2016) has led to a flourishing of workflows known as BIDS Apps (Gorgolewski et al., 2017). With a standardized data structure enforced by BIDS, a wide variety of workflows can be easily applied to neuroimaging datasets from any arbitrary source. This not only simplifies app development, but makes it easier to share generic analysis code for future replication. Nevertheless, even with the BIDS specification, a wide diversity of data formatting persists, especially for derived files. This makes it challenging to design BIDS Apps consuming derivative files with nonstandard naming conventions. To ensure workflows remain generic even in the absence of specific naming conventions, we present snakebids, a Python library leveraging pybids to create generic interfaces between BIDS Apps and datasets.

Methods: Snakebids defines a component as a set of files corresponding to the same type of data, for instance, a T1w image file, the bvec for a diffusion image, or a pial surface mesh. Each component is defined by a set of fixed and variable characteristics. For instance, all paths in a T1w component may have suffix of T1w, but vary across several subjects and session. In snakebids, fixed features are selected using filters, and variable features are defined using wildcards. In a snakebids app, these features are configured with sensible defaults by the developer. Within the app, snakebids provides
tools to derive new paths based on the input components. Wildcards can either be carried forward to the derived paths (e.g. for subject-specific analyses) or merged together (e.g. averaging across subjects in a group-wise analysis). Finally, snakebids automatically creates BIDS apps populated with options allowing users to set the filters and wildcards of each component. Thus, when running a snakebids app, users can provide specific filters to select the correct input files out of their dataset.

**Results:** Snakebids has been integrated into over a dozen workflows at various states of maturity. The most prominent example is hippunfold (DeKraker et al., 2022), which relies on snakebids to retrieve T1w, T2w, and diffusion weighted components, along with an optional segmentation. scatter, a snakebids app that identifies connections between specified ROIs (using methods introduced in (Kai, Khan, Haast, & Lau, 2022)), leverages snakebids’ flexible input interface to consume existing freesurfer outputs, avoiding redundant computations. Beyond this, our group has several unpublished snakebids apps to process MR and EEG data. These have been used in multi-dataset analyses (reports in preparation), applying the same methodology to multiple datasets despite differences in naming conventions.

**Conclusions:** The flexible interfaces from snakebids offer three advantages. First, it makes it easier to package methodologies as BIDS apps, reducing the barrier of effective code sharing. Second, it facilitates multi-dataset and mega-analysis by allowing the tuning of apps to different datasets without burdensome formatting requirements on dataset maintainers. Third, snakebids makes it easy to compose multiple BIDS apps together, freeing developers to produce smaller, more focused BIDS apps with
better reliability and maintainability. snakebids is under active development, but is mature enough for production use, with full documentation and near 100% test coverage. Thus far, snakebids has been developed around the snakemake workflow framework (Mölter et al., 2021), and all current snakebids apps are written in snakemake. However, the principles of snakebids are broadly applicable across all Python based workflows, and future releases will highlight it as a framework agnostic solution for generic BIDS workflows.

References

Poster No 2273

Advancing PET Surface-based Analysis - Integration in a Multimodal Imaging Pipeline

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Introduction: Investigating patient-specific differences remains a challenge when using neuroimaging approaches. Current studies have focused independently on pharmacological effects either using broad cortical network functional connectivity (i.e. resting state networks) acquired with fMRI or receptor quantification acquired with positron emission tomography (PET), but rarely integrating both modalities. PET analyses are traditionally implemented in a 3-dimensional volumetric space, which limits multi-modal comparisons across cortical areas that inherently follow a 2-dimensional geometry. We hypothesize superior alignment of modalities by representing the cerebral cortex as a two-dimensional geometry, i.e. surface-based analyses. Specifically, we aim to test the hypothesis that mapping PET data to single-subject cortical surfaces will reduce inter-subject variance in kinetic modeling as compared to a traditional volume-based workflow. This workflow will allow us to leverage state-of-the-art cortical and subcortical parcellations.

Methods: We set the framework to optimize the integration of PET with BOLD fMRI data across both cortex and subcortex to enable multi-modal comparisons of receptor distribution in relation to clinical dysconnectivity. All neuroimaging data was processed using the Quantitative Neuroimaging Environment and Toolbox (QuNex), which integrates HCP Pipeline workflows. PET data was analyzed using the novel surface-based workflow developed (Figure 1). We applied surface-based analytics either after (traditional volume-based workflow) or before (surface-based workflow) PET BPND quantification to assess impact on alignment and inter-subject variance.

Results: We demonstrate the feasibility of our proposed framework. We have successfully integrated PET surface-based analysis workflow within QuNex, a multimodal imaging pipeline. This allows us to integrate PET analytics with other neuroimaging modalities (Figure 1). We show that using an optimized surface-based workflow yields a more precise alignment on the cortical surface where quantification is done before compared to after mapping to the surface.

Conclusions: This optimized framework is a key step in multimodal neuroimaging integration (e.g. PET and fMRI) aimed at investigating the specific molecular effects of pharmacological treatments (e.g. ketamine), which would be critical in advancing the mechanistic understanding of neuropsychiatric disorders and their treatment. This would provide a more complete picture and help identify networks where pharmacological treatment effects relate to symptom response, enabling a more individually-targeted treatment plan.
Genetic interrogator for Neuroimaging: Streamlining Genetic-Based Insights of Human Brain Variation

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Introduction: Identifying the degree to which the genetic architecture of brain structure and function derived from brain imaging features overlap with other brain-based traits is important for understanding overlapping neurobiological mechanisms. Pre-assembled pipelines for post-GWAS analyses, such as CTG-VL¹ can help with efficient processing, but have not been developed to specifically test for genetic relationships and enrichment against brain-related traits. Toolboxes from abagen² and ENIGMA³ integrate brain gene-expression across different atlases but do not take GWAS summary statistics as input. Here we present GiNi (Genetic interrogator for Neuroimaging) a Python-based command line tool, to streamline a comprehensive collection of statistical genetic relationships between multiple brain-based traits. We include heritability estimates, global and local genetic correlation, and causal genetic associations and enrichment across various brain regions, tissues and cell types.

Methods: We created a post-GWAS processing and analysis pipeline based on four existing packages (METAL, LDSC, LAVA, GSMR), and external brain gene-expression and -splicing data resources, combining the Python, R, and command line tools into a single Python package. Each analysis first prepares the required inputs, accounting for different file types and execution methods. All post-GWAS analyses can be run independently or together, and are focused on brain-related traits. The pipeline can either be run with the default parameters, or fine-tuned by providing preferred parameters specific to each software. We have incorporated parallel executions through either multi-threading or the use of a high-performance cluster for computational efficiency, as neuroimaging GWAS often include multiple traits⁴,⁵. A meta-analysis can be performed to prepare combined summary statistics from multiple individual GWAS inputs (ie, same trait, different datasets) using METAL⁶. We have written the post-GWAS analyses to be specific to brain-related phenotypes (Fig 1). In addition to the analysis outputs, the pipeline will also provide a log for provenance and version tracking of the software involved. We tested our framework on the midsagittal corpus callosum (midCC), where we performed meta-analysis, followed by post-GWAS analyses on area and mean thickness of all phenotypes in the UK Biobank and ABCD study. For each analysis, we benchmarked the run time and required memory.
**Results:** We combined all our wrappers into a Python-based command line interface called GiNi, (Fig 1a). For handling multiple GWAS inputs, the type of meta-analysis approach can be specified using the “--meta” flag, and the user can specify the reference panel with the “--ethnicity” flag. Output plots can also be customized using the flag “--plot_feature”. We applied GiNi to a GWAS meta-analysis of 12 neuroimaging features across UKB and ABCD (Fig 2). The run time for global genetic correlation, Mendelian randomization, heritability estimation and local genetic correlation which were 15 seconds, 30 minutes, 3 minutes-12 hours, and 12 hours-24 hours, respectively. The maximum memory requirement needed for the pipeline to perform is up to 128GB, which is for TWAS across tissue types. Depending on the user’s study preferences and available resources, the pipeline can also be run sequentially using the “--computing_options” flag or only in specified parts using the “--analysis_list” flag.

**Conclusions:** We have created GiNi, a user-friendly pipeline that streamlines post-GWAS analyses for pinpointing plausible genetically informed, neurobiological mechanisms. Users will be able to derive heritability estimates, partitioned by multiple tissue and cell types, as well as determine the genetic overlap and causal associations on a global and local genetic level with cerebral cortex and subcortical structures. The pipeline is easily adaptable and will include more brain phenotypes, analysis types, and state-of-the-art tools developed in the future.

**References**
ABSTRACTS


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Poster No 2275

Physiopy: a Python suite for handling physiological data recorded in neuroimaging settings

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Introduction: Functional Magnetic Resonance Imaging (fMRI), a pivotal tool for neuroscientific research, leverages blood oxygenation levels to infer neural activity. However, its reliance on hemodynamic responses also renders it sensitive to various physiological processes affecting blood oxygenation. This dual nature presents both challenges and opportunities: while these physiological factors can introduce confounds in interpreting neural signals1, they simultaneously offer valuable insights into essential human functions encompassing cognition, emotion, and health2-4. To this end, we underscore the necessity of acquiring concurrent physiological data such as cardiac and respiratory activity, gas exchange metrics (O2/CO2 levels), and skin conductance. Adoption of concurrent physiological signals is growing within the neuroimaging community, reflecting a broader appreciation of physiological dynamics in brain imaging studies. Emphasizing the critical role of physiological monitoring in fMRI data quality, physiopy is a dynamic, collaborative initiative designed to streamline the integration of physiological data with fMRI research. The foundation of physiopy rests on four key pillars: (1) Accessible Software Suite: Offering a range of user-friendly software tools specifically tailored for efficient physiological data processing, (2) Comprehensive Documentation: Ensuring clarity and ease of use through detailed guides and instructional materials, (3) Community-Driven Practices: Fostering a culture of shared knowledge and collaborative development of best practices, and (4) Engaged Community: Cultivating an active network of users, developers, and researchers, all united by a shared interest in the integration of physiology within neuroimaging research.

Methods: Physiopy is currently composed of four Python packages released under Apache-2.0 licenses, all at different stages of development: phys2bids5 provides a command line tool for conversion of physiological data into the standardized BIDS format6; peakdet preprocesses physiological signals and performs automatic and manual peak detection; phys2denoise models physiological signals and their derivatives for the purpose of denoising fMRI data; physioQC facilitates quality assessment of physiological data through descriptive metrics and visual reports. Alongside these toolboxes, physiopy has comprehensive documentation that outlines community recommendations and comprehensive guidelines for collecting, processing, and using physiological data.
Results: Current development efforts are focused on (1) a new release of documentation enriched with information from the regular Community Practices meetings based on discussions on the acquisition and use of cardiac, respiratory, and blood gas data, (2) restructuring semi-automated workflows for more flexible and reproducible usage, and to better interface with non-physiopy workflows, (3) creating a quality control workflow for physiological data, implementing a set of useful metrics and visualizations to generate an HTML report, similar to MRIQC'. Altogether, physiopy is evolving to become a comprehensive toolkit and guide, addressing all aspects of physiological data preparation in neuroimaging research.

Conclusions: Physiopy (https://github.com/physiopy) is a community-driven open-source development effort to facilitate the adoption of physiological data in MRI settings. The use of physiopy can simplify the construction of reproducible pipelines for physiological data management. As an open and inclusive project, new contributions of any level of expertise are always welcome. We adopt the all-contributors acknowledgement. To join the monthly meetings, reach out with questions or suggestions, email to physiopy.community@gmail.com.
Extending the Boutiques Tool Description Framework in CBRAIN

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Introduction: CBRAIN (Sherif et al., 2014) (https://cbrain.ca) is an open source, web-based, collaborative research software platform that addresses major challenges in big data research. CBRAIN allows scientists to launch, monitor and share large-scale big data analyses using advanced scientific tools through an easy to use web-based interface. The ability to easily integrate new tools and update existing ones is an important feature of CBRAIN. Initially within CBRAIN each tool integration required the web form and related logic to be coded directly within the Ruby on Rails web development framework. That approach has been updated using Boutiques (Glatard et al., 2018) to define the command line and parameters in a JSON format. The use of Boutiques offers multiple parameter validation features and enables clearer form validation messages. Based upon the descriptor, CBRAIN automatically builds the user interface for each tool allowing users to select application parameters while automatically performing parameter validation. While no formal scheme can possibly foresee all the tool description aspects, the Boutiques format provides a ‘custom’ section. In this section of the descriptor, CBRAIN-specific properties such as validation of input parameters against a list of CBRAIN supported data types or file naming schemes is possible.

Methods: In CBRAIN tools have been integrated via three different methods: 1: A CBRAIN developer created Ruby code and templates (2009 to 2015). 2: Support was added to CBRAIN using Boutiques descriptors for automated tool integration (2015 to 2020). The code to run the tool and the user interface are generated in CBRAIN at boot time based on templates. Even though this method facilitated tool integration, some limitations persisted, including difficulties in developing, maintaining and documenting the logic related to custom Boutiques descriptor properties. 3: CBRAIN uses Boutiques descriptors but with a new integration method performed at runtime using hooks and a library of modules where each module handles one custom property/keyword (2020 to present). With this method, tool developers can easily introduce CBRAIN-specific properties to Boutiques that enhance the standard behavior.

Results: The newest method to integrate scientific tools leveraging the Boutiques descriptor at runtime has the benefit of making the integration more versatile. Each keyword is handled by a dedicated module resting either in the core CBRAIN codebase or in a plugin repository. Each module contains documentation and examples. A module overrides or modifies one or several standard CBRAIN procedures, related to rendering the input web form or tool execution. The new method can also modify the Boutiques descriptor for the duration of some steps, for example, by adding prepackaged inputs or outputs. Some of the CBRAIN modules used in conjunction with the Boutiques descriptors include: Before running the pipeline: CBRAIN can verify the type of the input file and the pattern of input file name with BoutiquesFileTypeVerifier and BoutiquesFileNameMatcher modules. After the pipeline has run: CBRAIN can specify a set of valid exit codes BoutiquesAllowedExitCodes module. CBRAIN can specify post-processing cleanup actions with BoutiquesPostProcessingCleaner.
Conclusions: Using the Boutiques tool integration methods in CBRAIN, tool integrators are no longer required to write any Ruby code. Sometimes additional features and customizations not yet supported by Boutiques and CBRAIN are needed. With guidance from the CBRAIN development team, tool integrators can add their own modules. CBRAIN is able to support a variety of users and projects, together with their complex workflows, through customizations that are alone not definable within standard Boutiques. Since 2020 more than ten modules and properties have been added to CBRAIN, demonstrating the adoption and utility of this module-based approach to extending the capabilities of Boutiques.

References

Poster No 2277
ReproFlow: a scalable environment for automated MRI and behavioral data integration

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Introduction: Reproducibility is a critical consideration for modern neuroscience and is greatly aided by automation of data acquisition and standardization of data records. MRI and behavioral data are two of the foremost modalities in human neuroscience, making the seamless integration of these modalities a significant concern for numerous research centers. The Brain Imaging Data Structure (BIDS) is a preeminent data standard, well-suited for both modalities, and which ensures interoperability of data analysis tools as well as transparency of data records. The ReproNim project has made significant contributions in extending the BIDS standard, and creating tools for BIDS conversion, data sharing, quality assurance (QA). ReproFlow is an environment which integrates numerous ReproNim tools - such as HeuDiConv, Reproln, ReproStim, ReproEvents, ReproMon, con/noisseur, //repronim/containers, DataLad, and the datalad-containers extension - in order to provide a scalable and automated solution for MRI and behavioral data acquisition and integration in a standardized form. Here we present a pilot implementation of this environment, set up at the Dartmouth Brain Imaging Center, covering both software and open hardware solutions. The adaptation of this environment can help other centers establish a robust, multi-modal, and BIDS-compliant data acquisition pipeline, and thus significantly advance the reliability of modern neuroscience.

Methods: We have developed a number of Free and Open Source Software (FOSS) solutions, and made extensive contributions to the BIDS standard, in order to ensure both standard support for multimodal metadata, and adequate tools to automatically populate the metadata space. The ReproFlow environment consists of 8 core tools developed by the ReproNim project. HeuDiConv provides configurable MRI conversion from DICOM to a desired layout. Reproln provides configuration for HeuDiConv via an extensive heuristic syntax, as well as a user assistance utility. ReproEvents provides audio and video capture capabilities to integrate complex stimuli with MRI data. ReproStim provides support for capturing behavioral events from participants. Con/noisseur captures and performs QA on operator input at the scanner console. ReproMon complements the QA capabilities by providing support for online operator feedback and alerts in case of incidents or anomalous metadata input. //ReproNim/containers provides DataLad dataset with popular containers and assistance scripts to ensure reproducible execution. DataLad and datalad-containers enable data and container manipulation, as well as provenance tracking.

Results: Over the course of its development, our HeuDiConv/Reproln implementation at the Dartmouth Brain Imaging Center has been used to collect and standardize over 40 MRI datasets, which are now openly shareable in an understandable fashion for inspection and reuse by the broader research community. We have additionally collected corresponding audio/video stimuli using ReproStim, which were successfully used to recover previously undocumented experimental aspects (such as randomization order) and to improve data quality by identifying the presence of lag between modalities. ReproEvents, ReproMon, and Con/noisseur are currently in early deployment and provide incipient event time stamp synchronization between the various modalities. //ReproNim/containers contains all BIDS-Apps, NeuroDesk applications, and other containers required to reliably execute the ReproFlow tools.
Conclusions: We argue based on our results that data integration remains a non-trivial matter for multi-modal set-ups and that significant improvements in automation and transparency are necessary to ensure data reliability. In particular, general-purpose open-source tools are needed in order to ensure sustainability of acquisition frameworks over time, and to ensure relevant know-how is shared across centers. We propose ReproFlow as a solution for these requirements and encourage reuse of this environment.

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Poster No 2278
A multimodal ultrahigh-field MRI processing pipeline
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Introduction: Ultrahigh-field Magnetic Resonance Imaging (MRI) at 7T provides a unique opportunity to study the brain’s microstructure, function, and connectivity in vivo at unprecedented resolutions. However, the increasing complexity and multimodality of the data demand processing methods that can effectively integrate information across modalities and spatial scales. In this study, we propose a standardized workflow for processing multiparametric 7T MRI acquisitions, combining state-of-the-art surface generation and multiparametric registrations. This pipeline automatically generates multiscale connectomes and surface maps, derived from quantitative MRI microstructural similarity, geodesic distance mapping, functional connectivity,
Methods: To create a functional workflow for 7T images, we implemented various enhancements to our previous pipeline, micapipe (Rodriguez-Cruces, 2022). Regarding structural processing (F1.A), we introduced a denoising algorithm to process MP2RAGE images as structural data and generated brain masks using a deep learning-based algorithm (mri._synthstrip, Hoopes, 2022). Additionally, we normalized the white matter to achieve an intensity homogeneous T1-weighted structural image (T1natiepve). For surface generation (F1.B), we adopted FastSurfer (Henschel, 2020), a deep learning-based tool that proved to be faster and more convenient for high-resolution surface generation compared to traditional methods. To map quantitative images to different surface spaces at the pial, mid-thickness, and white matter surfaces, all derived from FastSurfer, we incorporated new tools that first mapped them to the native space of the structural image (F1.C). Our microstructural profile covariance (MPC) module (F1.D) now applies surface sampling directly from the original qMRI space, enhancing reliability and avoiding potential interpolation issues. Finally, we introduced a novel approach for more accurate registration between modalities, utilizing label-based modality agnostic registration (F1.E, Billot, 2023). This technique combines deep learning-based segmentation and numerical solutions to generate precise warps, even for modalities with high signal-to-noise ratio and signal dropout, such as DWI and functional acquisitions (F1.E). Finally, our functional module handles resting state and multiple task acquisitions and includes Time-echo dependent analysis for multi-echo processing (TEDANA; DuPre, 2021). Individual and group-level quality control (QC) can be run at any point during the processing. The QC procedure will generate a pdf report file for each subject containing visualizations of intermediate files for volume visualization, cross-modal co-registrations, and surface parcellations. Moreover, it allows inspection of inter-regional matrices such as structural connectomes, functional connectomes, microstructural profile covariance, and geodesic distance matrices.

Results: This standardized workflow for processing multiparametric 7T MRI acquisitions presents a comprehensive solution for studying the brain's microstructure, function, and connectivity. Leveraging Ultrahigh-field Magnetic Resonance Imaging at 7T, our pipeline integrates state-of-the-art surface generation and multiparametric registrations to automatically generate multiscale connectomes and surface maps.

Conclusions: Our optimized 7T MRI pipeline is the first standardized workflow for processing multiparametric acquisitions from a BIDS directory to ready-to-use matrices and surface maps (F2). This advancement greatly benefits the development of multimodal brain models. Leveraging higher resolution images obtained from 7T, it offers full support to explore new frontiers in brain research.
ABSTRACTS

References

Poster No 2279
Association between lifetime cannabis use and brain imaging phenotypes in UK Biobank
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Introduction: In the past decade cannabis use has increased worldwide following its legalization for medical and recreational purposes. This legalization has occurred without a comprehensive understanding of the potential effect of cannabis on the brain. Cannabis use during adolescence and young adulthood has shown a significant association with brain structure and functional connectivity. However, despite a rapid increase in cannabis use among older adults, its relationship with brain structure and function in this population remains understudied. There are reports of adverse cannabis effects on neurocognitive performance, brain structure and function. Whether there is a safe threshold of cannabis use is unknown. Here, we investigate associations between cannabis use and a rich set of measures of structure and function across the brain in a large cohort of older adults. We employ both hypothesis-driven and agnostic approaches, and triangulate our observational findings with Mendelian randomization, a method to investigate causal relationships.

Methods: We examined 3,641 lifetime cannabis users (mean age = 61.00 years, standard deviation (SD) = 7.16) and 12,255 controls (mean age = 64.49 years, SD = 7.58) from the UK Biobank. Insufficient data were available on cannabis use disorders in the UK Biobank to perform an analysis. All statistical analysis was performed in R (version 4.0.0) and visualizations were...
performed in MATLAB (version R2018_a). Brain structure and functional connectivity were measured using multiple imaging-derived phenotypes (IDPs). Associations with cannabis use were assessed using multiple linear regression while controlling for potential confounders. Additionally, we conducted two-sample Mendelian randomization analysis using genome-wide association study (GWAS) summary statistics data based on two different cannabis phenotypes: ‘cannabis dependence or abuse’ and ‘lifetime cannabis use’. The summary statistics for the brain IDPs was obtained from GWAS performed by the UK Biobank. We used TwoSampleMR in an R package to investigate whether significant observed associations between cannabis use and brain IDPs were causal.

Results: Out of 3,921 brain IDPs, cannabis use was significantly associated with 40 brain IDPs after FDR correction (0.05%, p = 0.009) (Figure 1). The strongest associations were with measures of white matter microstructure. Most significant associations identified in the DTI metrics were found in the genu and body of the corpus callosum, demonstrating lower fractional anisotropy (FA) and higher mean diffusivity (MD). A wide range of associations was observed across various rsFC analyses, particularly indicating either weaker or stronger connectivity between multiple networks. These networks predominantly included brain regions associated with the default mode, central executive network. We did not replicate previously observed associations between cannabis use and grey matter volume in the hippocampus and amygdala. Furthermore, bidirectional two-sample Mendelian randomization analyses found no support for a causal relationship between either cannabis use or cannabis dependence and brain structure or function.

Conclusions: Lifetime cannabis use is associated with several measures of brain structure and function in later life, particularly in the corpus callosum. Genetic analysis did not provide support for these associations resulting from causal relationships, suggesting residual confounding may be responsible.

References


**Poster No 2280**

**Portable ultra-low-field brain MRI: test-retest reliability and correspondence to high-field MRI**

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**Introduction:** Ultra-low-field magnetic resonance imaging (MRI) scanners, such as the 64mT Hyperfine Swoop, promise to revolutionize neuroimaging¹. The Hyperfine scanner runs using a standard electrical socket and is portable, enabling scanning at the bedside and in low- and middle-income countries with limited access to MRI. However, it is unclear whether 64mT scans can be used to reliably quantify tissue volume, and to what extent such measurements correspond to 3T high-field MRI.

**Methods:** We recruited 23 healthy adult participants, with 2/3 male and 2/3 female participants in each of five strata: 20–29, 30-39, 40-49, 50-59 and 60-69 years old. Participants were scanned on a 3T MRI scanner (GE Premier) and two identical portable 64mT MRI scanners (Hyperfine Swoop) at different sites, using T1w and T2w scans. 3T scans were acquired at 1x1x1 mm resolution, while 64mT scans were acquired using both non-isotropic product sequences (T1w: 1.6x1.6x5 mm / T2w: 1.5x1.5x5 mm, with high resolution in the axial, sagittal or coronal plane), and a custom isotropic sequence (2.3x2.3x2.3 mm). We used multi-resolution registration (MRR) to super-resolve the three orthogonal non-isotropic 64mT scans into a single higher-resolution (T1w: 1.6x1.6x1.6 mm / T2w: 1.5x1.5x1.5 mm) scan² (Fig. 1). We then used SynthSeg³ to segment each scan into 98 structures and estimate their volumes. We assessed test-retest reliability of volume estimates using the intraclass correlation coefficient ICC(3,1)⁴, hereafter referred to as ICC. We assessed correspondence of volumes from 64mT and 3T scans using both Pearson's r – to quantify linear correlation; and Lin's Concordance Correlation Coefficient (CCC) – to quantify exact agreement. Finally, to test whether 64mT reliability and correspondence to 3T is higher for larger regions, we quantified the association of regional ICC, Pearson's r and Lin's CCC to the average 3T volume of each region, using Spearman's ρ. We repeated analyses on both T1w and T2w scans, across 64mT resolutions.

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**Fig. 1:** T₁w and T₂w scans acquired for each participant, on one high-field (3T) MRI scanner, and two identical portable ultra-low-field (64mT) MRI scanners at different sites. Ultra-low-field scans were acquired at four resolutions; including three orthogonal scans with low through-plane resolution, super-resolved into a single higher-resolution scan using multi-resolution registration (MRR). All scans were segmented into 98 regions, with volumes used to quantify 64mT between-site test-retest reliability, and correspondence of 64mT to 3T scans.
Results: We report summary statistics as Median [1st, 3rd quartile] across 98 segmentation labels (regions), or Md [Q1,Q3] (Fig. 2). 64mT scans showed high between-scanner test-retest reliability, across contrasts and scan resolutions. The most reliable volumes were yielded by T2w 64mT scans super-resolved using MRR (ICC Md [Q1,Q3] = 0.97 [0.95,0.99]; Fig. 2B). Reliability was similarly high for volumes extracted from MRR-super-resolved 64mT T1w scans, followed by marginally lower reliability for 64mT T2w and T1w scans at lower resolutions. Volumes extracted from 64mT scans showed excellent correspondence to 3T across participants (as quantified by Pearson’s r) but also slight systematic offsets in volume measurements (as quantified by Lin’s CCC), with a tendency of 64mT MRI to underestimate 3T volumes. The highest correspondence to 3T was shown by 64mT T2w scans super-resolved using MRR, including both high correlation (Pearson’s r Md [Q1,Q3] = 0.96 [0.93,0.98]) and agreement (Lin’s CCC Md [Q1,Q3] = 0.90 [0.81,0.95]) (Fig. 2B). MRR-super-resolved 64mT T1w scans showed marginally lower linear correlation to 3T data than T2w scans, as well as lower agreement, followed by 2.3mm isotropic 64mT T2w and T1w scans, and non-isotropic scans. Finally, both 64mT reliability and correspondence to 3T MRI tended to be higher for larger regions. Average regional (3T) volume was significantly associated to regional ICC (range of ρ across 2 contrasts x 5 resolutions; ρ = 0.42-0.55), as well as to Pearson’s r (ρ = 0.32-0.52) and Lin’s CCC (ρ = 0.22-0.47).

Conclusions: Volume estimates from portable ultra-low-field MRI scans show excellent test-retest reliability and correspondence to high-field counterparts. Reliability and correspondence to 3T were highest for T2w 64mT scans super-resolved using MRR². Our results pave the way for the modelling of individual deviations from the norm⁵,⁶ and estimation of biomarkers such as brain age⁷, across development⁸ and disease⁹.

References
Hormonal dynamics shape brain structure in women with and without endometriosis

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Introduction: As an endocrine organ, the brain is intricately influenced by gonadal hormones, particularly endogenous estradiol and progesterone. Recent advances in neuroscience have shifted the paradigm from cross-sectional analyses to longitudinal tracking (e.g.), also recognizing the rhythmic nature of gonadal hormone production (e.g.). To expand our understanding how gonadal hormones impact brain structure, it is essential to broaden the scope beyond individuals with typical menstrual cycles. Including those with endocrine disorders such as endometriosis, which features a unique hormonal profile and affects approximately 10% of women in the reproductive years, will enhance our understanding of the complex interplay between gonadal hormones and their influence on brain structure.

Methods: The current study densely-sampled three females who underwent extensive brain imaging and venipuncture over the full menstrual cycle (Fig. 1, Panel A). First, we densely sampled a healthy woman with a typical menstrual cycle. Here, a healthy female underwent majority weekday testing for five consecutive weeks while freely cycling, resulting in n = 25 test sessions, referred to as ‘natural cycle.’ We compared this dataset of one woman to the densely-sampled open-access 28andMe dataset of another woman, referred to as ‘28andMe (natural) cycle.’ The healthy female participant underwent testing for n = 30 consecutive days while freely cycling. We repeated these procedures in a female participant diagnosed with endometriosis. A female participant underwent testing from Monday to Friday for five consecutive weeks while freely cycling, resulting in n = 25 test sessions, referred to as ‘endometriosis cycle.’ Estradiol and progesterone levels were assessed daily and T1w images were preprocessed with the CAT12 toolbox using the longitudinal pipeline. Singular Value Decomposition (SVD) extracted spatiotemporal patterns from the three-dimensional image sets for each participant separately. Spatial patterns represent the regions of the brain that share a similar temporal pattern, while temporal dynamics describe local volume changes of these regions over time. The time-pattern explaining the highest variance (40%, endometriosis cycle; 45%, natural cycle, 54%, 28andMe (natural) cycle) was selected for further analysis (Fig. 2, Panel A), revealing overlapping brain regions (thalamus, pallidum, putamen, and caudate) across the three participants (Fig. 2., Panel B). Linear regression analysis assessed the relationship between spatiotemporal patterns and gonadal hormones in each participant separately.

Results: In the natural cycle and the 28andMe (natural) cycle, the linear regression with estradiol as a predictor did not yield significant results. Conversely, progesterone (28andMe (natural) cycle: p < 0.001; natural cycle: p = 0.013) and the progesterone/estradiol ratio (28andMe (natural) cycle: p < 0.001; natural cycle: p = 0.009) emerged as significant predictors, indicating a linear association between these hormones and the brain structural time-pattern. For the endometriosis cycle, the linear regression revealed estradiol as a statistically significant predictor of the brain structural time-pattern (p = 0.010). In contrast, progesterone and the progesterone/estradiol ratio were insignificant (Fig. 1, Panel B).

Conclusions: Extensive brain imaging and venipuncture across typical and endometriosis menstrual cycles reconfirmed that brain volume fluctuates during the menstrual cycle. Gonadal hormones, particularly estradiol and progesterone, led to short-term changes in brain structures, particularly in areas with increased estradiol and progesterone receptor distributions. The associations between hormones and brain structure differed between the natural menstrual cycles and the cycle with endometriosis, highlighting the importance of considering individual hormonal dynamics in understanding brain structural plasticity.
ABSTRACTS

Fig. 1. Panel A) Timeline of the data collection. MRI and endocrine assessments were acquired simultaneously on each test day for each participant. Purple timeline bars represent the endometriosis cycle and the natural cycle that were acquired in June, Germany. The orange timeline bar represents the 28andMe (natural) cycle acquired in Santa Barbara, California, USA. Panel B) Linear regression analyses with hormonal values as predictors of brain time-pattern in the endometriosis cycle, the natural cycle, and the 28andMe (natural) cycle. Data are displayed in standardized units. p-values significant are indicated in bold.

Fig. 2. Panel A) Brain time-pattern of the dominant structural pattern of the endometriosis cycle, the natural cycle, and the 28andMe (natural) cycle across all test sessions. The panel shows the spatial pattern representing the regions of the brain that share a similar temporal pattern over time. Warm colors indicate increased in brain volume, while cool colors represent decreases in brain volume across the cycle. Panel B) Overlapping brain regions that share a common temporal pattern across the menstrual cycle of the three participants. Synchronized patterns of all three participants overlap in several brain regions including the thalamus, thalamus/putamen, posterior, and caudate nucleus.
Examining hippocampal vessel distances in relation to cognition and brain structure in young adults

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Introduction: The hippocampus is a region with particular vulnerability to hypoxia (Spielmeyer, 1925; Uchimura, 1928). A contribution of the anterior choroidal artery (AChA) to hippocampal blood supply (dual supply) and closer proximity of the hippocampus to its surrounding vessels have been associated with better cognitive performance (Perox et al., 2020; Vockert et al., 2021; Garcia-Garcia et al., 2023). A dual supply has further been related to greater structural integrity in the anterior medial temporal lobe (MTL) and throughout the whole brain. As these findings have been made in a cohort of older adults, including patients with cerebral small vessel disease, it is yet unknown if better hippocampal vascularization exerts its structural and cognitive benefits in late life or conveys a source of reserve already in early adulthood.

Methods: 29 young adults (age=23.5±2.6 years, 58.6% female) underwent 7T MRI (T1-weighted sequence, T2-weighted sequence optimized for MTL volumetry, time-of-flight (ToF) angiography) and cognitive testing. Manual segmentation of the AChAs, posterior cerebral arteries (PCAs) and posterior communicating arteries was performed on the ToF images. Two vascular metrics of interest were calculated in MNI space. First, an average distance of the hippocampus (defined by a structure averaging algorithm) and the cognitive as well as global structural measures were acquired from the T2-weighted images after segmentation with ASHS. As cognitive measures of interest were a composite memory score (summed z scores of select memory tests) and a global cognitive performance factor score (principal component analysis) we obtained from tests spanning multiple cognitive functions (e.g., Rey Figure, TMT, SDMT, Stroop). Linear models were utilized to investigate a relationship between the two vessel metrics (bilaterally averaged) and the cognitive as well as global structural measures. Total intracranial volume (for structural outcomes), sex and years of education were used as covariates. Linear mixed effects models with a subject-specific intercept examined the relationship between vessel metrics and the unilateral local structural measures with hemisphere as an additional covariate.

Results: Smaller distances between the hippocampus and its surrounding vessels (HVD) tended to co-occur with greater anterior (p = 0.065) and whole hippocampus volumes (p = 0.082). There was no evidence that a closer distance to the surrounding vessels was related to global structural nor cognitive measures (all p values > 0.1). Neither was there evidence for a relationship between CoMD and any structural nor cognitive measures.
Conclusions: Unlike in older adults with CSVD, we found no evidence that smaller distances between the hippocampus and its surrounding vessels are related to better cognitive performance in young adults. On a structural level, larger hippocampi tended to be found in young adults with smaller average HVDs. Given the previously observed relationship between mean HVD and cognitive performance in older adults, one might hypothesize that larger hippocampal volumes in young adults provide individuals with smaller HVD with more neurobiological capital to lose in the face of aging and disease (brain reserve). These individuals might then develop cognitive deficits later than their peers. However, this requires further investigation and does not exclude the possibility that individuals with a better blood supply are able to maintain their brain structure and cognitive abilities better.

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Poster No 2283
Bridging the Gap between Quantitative and Clinical MRI
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Introduction: Quantitative MRI (qMRI) enables in-depth study of brain microstructure and can provide in vivo histological information (Weiskopf et al., 2021). However, its use in clinical settings is limited, with reliance on weighted images that...
lack microstructural detail. Our study introduces three new weighted image ratios, including $T1w/PDw$ and $ln(T2w/PDw)$, to approximate qMRI parameters $R1$ and $R2$. Validated with lipid phantoms and human datasets, these ratios, alongside a modified $T1w/T2w$ ($T1w/ln(T2w)$), effectively represent qMRI parameters. Applied to Parkinson's disease data, they reveal microstructural differences in key brain regions, enhancing clinical MRI analysis.

**Methods:** We employed three datasets: Lipid phantom data (Shtangel and Mezer, 2020) with various lipid types. HUJI subjects: from Filo et al., 2019, qMRI and weighted data of 22 healthy individuals (age 41±19.6). PPMI subjects: 4 ROIs (caudate, putamen, globus pallidus, and midbrain) of 99 Parkinson's patients, age 65±6, and 46 controls, age 65±6 from Parkinson's Progression Marker Initiative were analyzed. Using the typical $T1$ and $T2$ signal equations and the previously measured $R1$ and $R2$, we produced synthetic images for the phantom data.

**Results:** We found perfect linear relationships between synthetic $T1w/PDw$ and $R1$ map, and between synthetic $ln(T2w/PDw)$ and $R2$ map ($R2=1$) in phantoms. Thus, weighted images can perfectly estimate quantitative maps in a noise-free environment. Next, we evaluated the correlation of $R1$ with $T1w$, $T1w/T2w$, and $T1w/PDw$. We found $T1w/PDw$ showed the strongest correlation in phantoms (Fig. 1A-C). Similarly, we calculated the correlations of $R2$ with $R2w$, $T1w/T2w$, and $ln(T2w/PDw)$. We found that the strongest correlation was with $ln(T2w/PDw)$ in phantoms (Fig. 1D-F). We then carried the same analysis we did for phantoms and tested it on HUJI subjects. We replicated the phantoms results for $R1$ (Fig. 1G-I) and $R2$ approximations (Fig. 1J-L). Using $B0$ images from DTI scans as $T2w$, we observed the same results. We also ask whether $T1w/T2w$ could more accurately approximate the quantitative maps $R1$ and $R2$. We calculated two modifications for this ratio: $ln(T1w/T2w)$ and $T1w/ln(T2w)$, in humans. We found $T1w/ln(T2w)$ to be a better approximation of $R1$ than is $T1w/T2w$. We also found the highest correlation of $R2$ to be with $ln(T1w/T2w)$. Finally, to test whether the new ratios can be utilized in a clinical setting, we analyzed weighted MRI data from PPMI subjects. We calculated four structural measurements: $T1w/PDw$, $ln(T2w/PDw)$, $T1w/ln(T2w)$, and $T1w/T2w$. For each ratio, we assessed group differences between patients and controls in ROIs that are thought to be affected in Parkinson's disease (Dickson, 2012). We found differences between groups only in our new measurements (Fig. 2). These results suggest there is additional information in our new ratios.

**Conclusions:** Despite the high potential of qMRI, its clinical use is limited, with a reliance on weighted images that lack quantitative detail. Addressing this, our research introduced three novel image ratios to approximate qMRI parameters. $T1w/PDw$ closely approximates $R1$, while $ln(T2w/PDw)$ effectively represents $R2$. We refined the $T1w/T2w$ ratio for better accuracy and extended our analysis to DTI databases. Applied to Parkinson’s disease data, our methods successfully differentiated patients from healthy controls. This work provides a new approach to utilize widely available weighted images for more detailed neuroimaging in both research and clinical contexts.
A comparison of R1 and R2 to different quantifiers derived from weighted images, in (A-F) lipid phantoms and (G-L) human data. (A-C, G-I) Correlation coefficients ($R^2$) between the R1 map and: (A, G) T1w; (B, H) T1w/T2w; and (C, I) T1w/PDw. T1w/PDw yields the highest correlation. (D-F, J-L) Correlation coefficients ($R^2$) between the R2 map and: (D, J) R2w; (E, K) T2w/T2w; and (F, L) ln(T2w/PDw). ln(T2w/PDw) yields the highest correlation. (A-F) Data is taken from phantom scans, and datapoints represent the phantom samples’ values. The black dashed lines represent the regression line. (G-L) Voxel-wise 2D-histograms of voxels pooled from HUJ dataset (N=22).

Student’s t-test between controls (gray boxplots, N=46) and patients (colorful boxplots N=99) across four ROIs (marked on an example control subject’s brain). We identified significant differences in three ROIs: in the globus pallidus for T1w/PDw; in the midbrain for T2w/T2w; and in the caudate for T1w/ln(T2w). T1w/T2w did not show significant differences between the groups across the four ROIs. Whiskers denote the 5th and 95th percentile. Asterisks denote FDR-corrected statistical significance ($* - p < 0.05; ** - p < 0.01$; *** $p < 0.005$).
Association between cerebral microstructural change and cognitive impairment in hypertension

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Introduction: Hypertension (HTN) is a growing public health problem worldwide that is a leading cause of cognitive impairment. It is a risk factor for cognitive decline, mild cognitive impairment and dementia. However, the results of previous studies are inconsistent and the relationship between various cognitive functions and changes in the brain volume is unclear. This study uses a brain MRI to determine the changes in the brain that are a result of the association between hypertension and cognitive impairment.

Methods: All 58 participants were divided into two groups: the hypertension group (HTN group, n=30) and the normal control group (NC group, n=28). 30 HTN patients have all been diagnosed with hypertension by specialist physicians, and their blood pressure is > 140/90 mmHg during a visit. All participants were subject to a 3T MRI (Siemens Tim Trio scanner) and Magnetization Preparation Rapid Acquisition Gradient Echo (MP-RAGE) to access the MR imaging. All participants were also subject to cognitive questionnaires; Chinese Version Verbal Learning Test (CVVLT)2, Digit Symbol Substitution (DSS)3, Trail Making Test parts A and B (TMT-A and TMT-B)4, Chang Gung University Orthographical Fluency Test (CGUOFT)5, Mini-Mental Status Examination (MMSE) and Montreal Cognitive Assessment (MoCA)6 were used to measure the cognitive state. Voxel-based morphometry (VBM) was used to determine differences in the volume of the brain for the HTN group and the NC group. Multiple regression was used to determine the association between brain volume and the results of the cognitive assessments, in terms of memory, executive function, and global cognitive function.

Results: The relationship between memory function and brain volume: For the 30 HTN patients, in terms of the multiple regression analysis of the association between the score for CVVLT immediate recall, CVVLT 30 seconds recall, CVVLT 10 minutes recall and brain volume (Fig. 1) there is a positive correlation in the left hippocampus, the left immediate gyrus, the left inferior parietal lobule, the left precuneus, the brainstem and the right anterior cingulate, with a corrected p-value< 0.05. There is no instance of a negative correlation. The relationship between executive function and brain volume: For the 30 HTN patients, in terms of the multiple regression analysis of the association between the scores for DSS, TMT-A, TMT-B, CGUOFT, and brain volume (Fig. 2), there is a positive correlation in the right middle frontal gyrus, the right inferior frontal gyrus and the left insula with a corrected p-value< 0.05 for the analysis between DSS, CGUOFT and brain volume. There is a negative correlation in the right medial frontal gyrus, the left cingulate gyrus and the bilateral hippocampus, with a corrected p-value< 0.05 for the analysis between TMT-A, TMT-B and brain volume. The relationship between global cognitive function and brain volume: For the 30 HTN patients, in terms of the multiple regression analysis of the association between the score of MoCA, MMSE, and brain volume, there is a positive correlation in the left thalamus, the left caudate, the left lentiform nucleus, the left precuneus, the left insula and the left superior frontal gyrus, with a corrected p-value< 0.05. There is no instance of a negative correlation.

Conclusions: The results of this study apply mainly to the frontal cortex, the basal ganglia, the limbic system, the cingulate and the brainstem and are consistent with those for previous hypertension studies. The frontal cortex, the basal ganglia, the cingulate and the limbic system are correlated to memory, executive function and cognition and hypertension can impair executive function, memory and cognition speed and preserve attention. The results verify the neuropsychopathology...
of hypertension-related structural impairment and inform the development of cognitive rehabilitation for individuals with hypertension.

Fig. 1 The association between the CVVLT score and brain volume.

Fig. 2 The association between the DSS, TMT-A, TMT-B, CGUOFT score and brain volume.

References
Regional volume differences in blast-related TBI with cognitive implications: A LIMBIC-CENC Study

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Introduction: Blast-related traumatic brain injuries (TBIs) have been called the “signature injury” of the recent conflicts in Iraq and Afghanistan, with more than 100,000 injuries sustained by service members between 2001 and 2018 and many more “subthreshold” exposures. Blast-related TBI is thought to arise through unique mechanisms resulting from the over- and underpressures of the blast; however, there is a significant challenge in studying blast-related injuries outside of the experimental setting as they nearly always also include blunt-force impacts. Leveraging the multi-site Long-term Impact of Military-relevant Brain Injury Consortium/Chronic Effects of Neurotrauma Consortium (LIMBIC-CENC) sample, we sought to identify differences in brain structure in individuals with blast-related mild TBI (b-mTBI), and to determine if these differences related to cognitive function.

Methods: Using a structured interview, lifetime history of all possible concussive events was assessed. The total sample size was n=774, with n=598 having a history of any mTBI, n=391 deployment-related mTBI, and n=260 b-mTBI. Participants completed a cognitive battery, including the Trail Making Test (TMT) and WAIS-IV, along with the PCL-5 for PTSD symptoms, PHQ-9 for depression symptoms, and AUDIT-C for problematic alcohol use. T1-weighted MRI was collected with prospectively harmonized sequences, and a multi-site template was created. We used tensor-based morphometry (TBM) to create Jacobian determinant images using unbiased_pairwise_registration. Voxel-wise linear mixed effects models were implemented with site as a random effect and age and gender as covariates. Results were corrected for multiple comparisons using searchlight FDR. Our primary analysis compared individuals with a history of b-mTBI to those without (which included TBI-negative controls and those with only non-blast mTBI). We conducted additional analyses examining multiple potentially confounding variables. We also examined voxel-wise associations with cognitive performance, and in the case of overlap between blast and cognitive clusters, we conducted causal mediation analyses with the R package, mediation.

Results: We found several regions with smaller volumes in the b-mTBI group (Fig 1). These effects remained after controlling for current PTSD symptoms, depression symptoms, and problematic alcohol use within the past three months. They also remained significant when comparing the b-mTBI group to non-blast deployment mTBI. There was a significant positive association with the number of b-mTBIs. Cognitive performance was associated with volume in multiple clusters overlapping with those associated with b-mTBI. Volumes of clusters extracted from the blast analysis were negatively associated with TMT part B completion time and positively associated with WAIS-IV Total Digit Span performance in the b-mTBI group (ps < .03). Further, across the whole sample, the volumes of these clusters significantly mediated the association between b-mTBI and cognitive performance (Fig 2).

Conclusions: We report smaller white matter (WM) and subcortical gray matter (GM) cluster volumes in those with a history of b-mTBI, along with evidence for a dose effect for repeated b-mTBI. Tissue stiffness may be relevant in the setting of b-mTBI, as stiffer tissues may be more prone to disruption by a blast-related pressure wave. Magnetic resonance elastography (MRE) has shown that subcortical GM and WM projection tracts have greater shear stiffness than other brain regions, possibly underlying selective vulnerability of these areas. Causal mediation analysis linked alterations in volume to deficits in cognitive performance. Volumes in the brain regions associated with blast-related TBI mediated the association between b-mTBI history and cognitive performance. These results suggest that volumetric loss as a result of blast injury may be a mechanism by which clinically-measurable cognitive deficits occur in military veterans.
ABSTRACTS

Fig 1. Differences in regional volume between participants with and without a history of blast-related TBI. Color corresponds to Cohen's d. Left in image is right in brain.

Fig 2. Causal mediation analyses.

References

Poster No 2286
Concurrent brain structural and functional alterations in adult survivors of childhood brain tumors
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Introduction: Brain tumors and related treatments, such as radiation and chemotherapy, significantly affect the structural and functions of brain tumor patients, which in turn impact the treatment outcomes and their quality of life. This clinical challenge
is even more remarkable in pediatric brain tumor patients due to the vulnerability their brains that are still developing. In several earlier studies, structural and functional abnormalities were demonstrated in survivors of childhood brain tumors\textsuperscript{1-4}. However, the information and investigations on the structural and functional underpinnings of abnormalities in adult survivors of childhood brain tumors are still limited. Here, we used voxel-based morphometry (VBM) and amplitude of low-frequency fluctuations (ALFF) to examine simultaneous structural and functional alterations in tumor survivors compared with healthy controls.

**Methods:** Human data, including T1-weighted images (1mm isotropic) and rs-fMRI (3mm isotropic), were from 35 adult survivors of childhood brain tumors and 35 matching healthy individuals as controls, which were recruited from cohorts participating in the initial longitudinal pediatric brain tumor study and later neuroimaging studies\textsuperscript{5,6}. We used T1-weighted images with SPM12 to normalize to the MNI space of the standard atlas before the images were segmented into gray matter, white matter, and cerebrospinal fluid. Smoothing was then performed using a 6-mm FWHM Gaussian kernel. We preprocessed the rs-fMRI data using DPARSF, and the preprocessed time series for each voxel were first transformed to the frequency domain by fast Fourier transform to compute the root mean square of the power spectra of each voxel from 0.01 to 0.08 Hz, to obtain the ALFF values for all voxels of the whole brain. Two-sample t-tests were performed for GMV of VBM, with age, sex, and total intracranial volume as covariates. The significant level was set at FDR-corrected $p < 0.05$ and cluster size $>20$. Two-sample t-tests were performed for ALFF values based on uncorrected $p < 0.001$ and cluster size $> 20$. Pearson correlation analysis was performed on GMV and ALFF values for structurally and functionally abnormal brain regions. The significant level was at $p < 0.05$. Due to the damages in the cerebellum in most brain tumor survivors, we removed the cerebellum in statistical analysis.

**Results:** Compared with healthy controls, brain tumor survivors had decreased GMV in the thalamus and increased GMV in the superior frontal gyrus (SFG). Functionally, brain tumor survivors had lower ALFF values in the inferior temporal gyrus (ITG) and medial prefrontal area (MPFA) and higher ALFF values in the thalamus (Fig.1). Importantly, a concurrent structural and functional alterations in the region of thalamus was identified based on the significant differences in GMV and ALFF values, which were negatively correlated (Fig.2). These findings on concurrent brain structural and functional alterations in brain tumor survivors may contribute to cognitive deficits in brain tumor survivors.

**Conclusions:** This retrospective study of long-term survivors of pediatric brain tumor revealed structural changes in the SFG and bilateral thalamus, and abnormal functional activities in the ITG, MPFA, and thalamus. We also identified the concurrent structural and functional alteration in the thalamus, suggesting a potential functional advantage of the thalamus which may represent a compensatory processing to integrating neural activity, and controlling the transmission of information between subcortical and cortical areas in brain tumor survivors. These finding shed the light on the specific structural and functional substrates underlying the cognitive deficits experienced by these individuals, which may help to develop new interventions to improve their quality of life.
References

Poster No 2287
Obesity associated progressive brain structural changes assessed using causal structural covariance
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\textbf{Introduction:} Obesity has become a global health challenge, and studies have shown that the prevalence and disease burden of high body mass index (BMI) are increasing worldwide\textsuperscript{1}. Accumulating neuroimaging evidence suggests that obesity negatively affects brain structure\textsuperscript{2,3}, and decreased gray/white matter volume are closely associated with increased BMI\textsuperscript{4}, especially within fronto-mesolimbic circuitry\textsuperscript{5}. To figure out the temporal causality of these regions, the causal structural covariance networks (CaSCN)\textsuperscript{6,7,8} were used to investigate the temporal causality between structural change and BMI.

\textbf{Methods:} T1-weighted magnetic resonance images were acquired from 201 obese patients and 73 age- and gender-matched healthy controls (HC). T1-weighted images were segmented and normalized by voxel-based morphometry to obtain gray matter volume (GMV) images. The progressive changes in GMV were simulated by dividing the patients into different groups according to grades of BMI (Table 1). The two-sample t tests were utilized to compare the disparities between various grades of obese groups and HC. To evaluate the impact on structural alterations, the CaSCN was conducted by applying Granger causality analysis on sequenced T1-weighted images.
Results: Compared to HC, obese group showed a decreased GMV in the occipital lobe, right precuneus (PCUN_R), temporal lobe, bilateral orbitofrontal cortex (OFC), right olfactory cortex (OLF_R), left caudate nucleus (CAU_L), bilateral insula (INS), bilateral inferior frontal gyrus (IFG), right hippocampus (Hipp_R), right parahippocampal gyrus (PHG_R), right angular gyrus (ANG_R), right postcentral gyrus (PoCG_R), right precentral gyrus (PreCG_R), right dorsal anterior cingulate cortex (dACC_R) (P<0.05, family-wise error corrected, Fig 1A). As BMI increased, reduction in GMV originated from the left occipital lobe, left temporal lobe, left insula (INS_L) and right orbitofrontal cortex (OFC_R), and propagated to the right ventral posterior cingulate cortex (vPCC_R), left orbitofrontal cortex (OFC_L), left anterior cingulate and paracingulate gyri (ACG_L), PoCG_R, PreCG_R, Hipp_R, bilateral inferior frontal gyrus (IFG), INS_R, PCUN_R, left putamen (PUT_L), left pallidum (PAL_L), PHG_R, ANG_R and left ventral anterior cingulate cortex (vACC_L) (P<0.05, family-wise error corrected, Fig 1B). The INS_L and OFC_R, which were regions involved with food intake control, were selected as the seed regions for further voxel-wise CaSCN analysis. Intriguingly, the INS_L and OFC_R had positive causal effects on each other. In addition, the INS_L showed positive causal effects on the temporal lobe, right putamen (PUT_R), INS_R, PCUN_R, occipital lobe, left angular (ANG_L), left dorsolateral prefrontal cortex (DLFPC_L), middle frontal gyrus (MFG_R), PoCG_R, left supplementary motor area (SMA_L), left ventral posterior cingulate cortex (vPCC_L), left precentral gyrus (PreCG_L), left postcentral gyrus (PoCG_L); and INS_L had also negative effects on the occipital lobe, IFG_R, right dorsolateral prefrontal cortex (DLFPC_R), SMA_L (P < 0.05, false discovery rate corrected, Fig 1C). The OFC_R exhibited positive causal effects on the temporal lobe, OLF_R, OFC_L, PUT_L, right caudate nucleus (CAU_R), bilateral dorsolateral prefrontal cortex (DLPFC), left inferior frontal gyrus (IFG_L), left superior frontal gyrus (SFG_L), left thalamus (THA_L), left middle frontal gyrus (MFG_L), left supramarginal gyrus (SMG_L), bilateral precentral gyrus (PreCG), SMA_L, as well as negative effects on the PHG_R, temporal lobe, IFG_L, PreCG_L, DLPFC_R, parietal lobe (P < 0.05, false discovery rate corrected, Fig 1D).
**Conclusions:** These findings depict the impact of obesity on brain structural changes, and the obesity associated progressive GMV reduction originating from brain regions involved with reward motivational processing (i.e., INS_L/OFC_R) to those implicated in inhibitory control (i.e., DLPFC).

**References**

**Poster No 2288**

**Does freediving lead to hippocampal adaptability to hypoxia and maintenance of episodic memory?**

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**Introduction:** Hypoxia has detrimental effects on the brain, especially on the hippocampus crucial for episodic memory. However, the performance of freedivers (F) suggests an adaptive mechanisms to low oxygen supply. Freediving sports provide a natural model for studying the effects of repeated voluntary hypoxic exposure on brain function in healthy individuals. Our project aims to compare the anatomical hippocampal subfields (HS) and memory performance of “freediving” athletes versus “non-freediving athletes” as controls (C) to study the adaptive mechanisms in the HS after prolonged and repeated exposure to controlled hypoxia during training. This will shed light on the neural plasticity mechanisms underlying this adaptation and pave the way for therapeutic strategies for various neurological conditions that damage hippocampal formation, such as perinatal hypoxia, stroke, or amnesic ictus.

**Methods:** To this day, 9 F have been included and completed the 9 months of uniform hypoxia training (ANR-2021, PI-MN). Data collection was carried out before (F0) and after (F1) training. Cerebral MRI was performed at 3T (Magnetom Prisma, Siemens Healthineers) including acquisition of high-resolution T2-weighted images of the HS. The automatic segmentation of the HS was obtained using the HSF software (Poiret et al, 2023). The episodic memory was studied thanks to two tasks of pattern completion (PC) and pattern separation (PS) (Zhao et al, In Prep). The PC task is composed of an encoding phase (images representing a location associated with a gesture) followed by a test phase, with random presentation of items (gesture to associate with a location or the other way around). The PS task is presented next and composed of a test phase with random presentation of items: (i) identical, (ii) similar or (iii) new to the encoding phase. Meanwhile, 16 age- and sex-matched controls (C) were explored similarly, but once and without freediving activities. HS volumes and memory scores were compared before (F0) and after training (F1) in F (within contrasts) and with C (between contrasts).
Results: The comparison of the HS volumes showed a significant difference for F at the level of the dentate gyrus (Student t-test with Bonferroni correction α = 0.008 F1>F0 p=0.007) and the total volume of the hippocampus (F1>F0 p=0.006) before and after training (F0 – F1). PC scores were significantly different concerning the percentage of correct answers between the two groups “F1 – C” (Student t-test, F1>C p=0.010). PS scores were significantly different between the groups “F1 – C” (Student t-test, F1>C p=0.010), and “F0 – F1” (Student t-test, F1>F0 p=0.028) for the percentage of correct answers concerning the (i) identical items only.

Conclusions: Although the recruitment of freedivers is still underway, we show that HS are sensitive to freediving training regimen since the dentate gyrus and hence the total volume of the hippocampus has increased in those 9 months. This finding could reflect the anatomical adaptability of hippocampal structure, in particular the potential influence of the neurogenesis in response to controlled hypoxia in the dentate gyrus (Khuu et al, 2019; Lev-Vachnish et al, 2019). Remarkably, not only a maintenance but a significant improvement after training was found in PC and PS, two tasks which imply episodic memory involving the HS. These results are additional arguments in favour of the positive influence of sport practices, in our case, freediving training on cognitive function; our hypothesis being that such exercise could encourage neurogenesis (Lev-Vachnish et al, 2019). To conclude, we already highlight significant changes after 9 months of training both in terms of anatomy and episodic memory. The next step will be to link these results to functional and metabolic MR data acquired on the same subjects, to explore further the mechanisms involved in such adaptation at different neurobiological levels.

References

Poster No 2289
Transdiagnostic and Diagnosis-specific ADHD/ASD Morphological Similarity Related Gene Transcription
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Introduction: Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are both highly heritable developmental psychiatric disorders with a high degree of comorbidity (Lord et al. 2018, Posner et al. 2020). The present study focuses on the neuroanatomical changes and their underlying gene transcriptional profile in ADHD and ASD.

Methods: A total of 258 participants were obtained from publicly available 1000 Functional Connectomes Project (92 individuals with ADHD, 59 individuals with ASD, and 107 healthy controls). Morphological similarity networks (MSN) analysis was performed on the T1-weighted magnetic resonance imaging data to investigate the transdiagnostic and diagnosis-specific ADHD/ASD morphological similarity related gene transcription.
specific structural alterations between ADHD and ASD. Gene transcripational profile analysis based on the partial least squares regression was performed to identify the MSN-related genes (Li et al. 2021). Enrichment analysis was further conducted on ADHD/ASD risk genes and MSN-related genes to investigate the cellular and genetic pathophysiological mechanisms.

**Results:** MSN: ADHD primarily showed the MSN changes distributed in areas related to high-level cognitive functions, while ASD had MSN changes in low-level sensorimotor areas. ADHD and ASD exhibited the transdiagnostic abnormalities with concurrently increasing morphological similarity in the right middle temporal gyrus (one-way ANOVA analysis, false discovery rate correction, P < 0.05). Figure 1. MSN Results. A, The distribution of mean morphological similarity values in three groups respectively. B, The distribution of morphological similarity differences between the three groups. C, Post-hoc results. SMG, supramarginal gyrus; PCUN, precuneus; MTG, middle temporal gyrus; DCG, median cingulate and paracingulate gyri; REC, gyrus rectus; ORBinf, orbital part of inferior frontal gyrus; STG, superior temporal gyrus; ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder; HC, healthy controls; MSN, morphological similarity network; L, left; R, right. Gene transcriptional profile: The ADHD and ASD risk genes were enriched in more than ten synaptic transmission and regulation pathways, as well as processes related to neuronal development (false discovery rate correction, P < 0.05). Similar biological processes enriched in excitatory and inhibitory neurons suggest that the synaptic signaling transmission in excitatory and inhibitory neurons exhibit transdiagnostic abnormalities in ADHD and ASD. Figure 2. Functional enrichment of gene transcription. A, Three gene lists, including ADHD and ASD risk genes, PLS1- (Z < -5) gene list, jointly participate in the gene transcription process. B, Expression of genes associated with MSN changes in seven specific cell types. FDR, false discovery rates; PLS1-, the first negative principal component of partial least squares related to MSN changes; MSN, morphological similarity network.
Conclusions: Both ADHD and ASD exhibited diagnosis-specific morphological similarity changes in multiple brain networks involved in sensory-motor and high-level cognitive functions. ADHD and ASD showed a transdiagnostic morphological similarity increase in the right middle temporal gyrus, which is associated with motor disfunction (Lord et al. 2018, Posner et al. 2020). The expression of MSN-related genes may reflect potential alterations in excitatory and inhibitory neural pathways in ADHD and ASD (Morgan et al. 2010, Yokokura et al. 2021).

References

Poster No 2290
A new approach for reproducible water fraction and T1 mapping across different qMRI protocols
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Introduction: Quantitative MRI (qMRI) is highly valuable method to estimate the human brain microstructural changes during aging and disease. An important goal of qMRI field is to provide reliable multi-parametric brain maps1, with T1 map being commonly used. Two main acquisition approaches to quantify T1 on clinical scanners are variable flip angle (VFA) and Magnetization Prepared with 2 Rapid Gradient Echoes (MP2RAGE), yet the agreement between these approaches was not
A potential benefit of VFA is that it also allows the extraction of proton density (PD) map\textsuperscript{2}, which is not often explicitly extracted using the MP2RAGE formalism or mentioned in the original publications\textsuperscript{3,4}. In the brain, normalized PD is used to estimate the water fraction (WF). In this work, we first examined the agreement between the T1 maps obtained from these two approaches. Second, we presented a pipeline to obtain PD and WF maps from the MP2RAGE protocol that agree well with the VFA's maps. Hence, this work obtains an additional qMRI map for the MP2RAGE approach which is in agreement with the VFA approach.

**Methods:** Data- In this work, we used 14 healthy individuals aged 26-75, who were scanned in both VFA and MP2RAGE protocols: (i) VFA, Gradient echo sequence was acquired with the parameters TR=19 ms, five equally spaced TEs=3.34-14.02 ms, four different FA=4°,10°,20°,30°, TAcquisition=“25 min, resolution=1mm isotropic. (ii) MP2RAGE sequence was acquired with the parameters TR=5000 ms, TE=2.98 ms, Ti= 700, 2500 ms, FA=4°,5°, TAcquisition=“8 min, resolution=1mm isotropic. (iii) We computed a B1 bias correction on the maps extracted from VFA protocol using mrQ software\textsuperscript{5}. We used spin-echo inversion recovery images acquired with echo-planar imaging readout (SEIR-EPI). Parameters were TE=49 ms, TR=2920 ms, Ti=200, 400, 1200, 2400 ms. The resolution was 2mm in-plane and slice thickness was 3mm. T1 map- First we registered MP2RAGE maps to the VFA maps' space using FSL's FLIRT6. T1 and M0 were estimated using methods described before (for VFA see Ref. 5 and for MP2RAGE see Ref. 4). Calculating PD and WF maps- We followed the algorithm in Mezer et al. work\textsuperscript{2,5}. We assumed that M0 = Coil Gain*PD considering a neglected T2* contribution when TE<3.34ms. We then estimated the coil gain bias and separated it from the PD contribution. For this we assumed a local linear relationship between 1/T1 and 1/PD values. Next, we normalized the PD by the CSF values to estimate the WF map. First, we identified the CSF ROI using the FreeSurfer segmentation algorithm and eliminated any voxel with T1 outside the range of 3.7-4.7. Then, we calculated the linear trend between 1/PD and 1/T1 in the CSF. Last, we calculated a calibration value which determines that in pure water where T1 is equal to 4.37, WF should be equal to 1, and calibrated the entire map.

**Results:** First, we tested the correlation between T1 values of the VFA protocol and the MP2RAGE protocol. We found a strong correlation between the two maps. Next, we tested the correlations between PD maps. We found a similarly strong agreement in those maps. Normalization of PD maps to obtain WF from both protocols also showed a high correlation.
Voxel-wise 2D-histograms of maps obtained from SPGR protocol (x axis), and from MP2RAGE protocol (y axis). A is T1 values, B is PD values and C is WF values, of five best representative subjects.

**Conclusions:** Our study suggests that maps extracted from VFA and MP2RAGE protocols can both provide similar qMRI values, highlighting the agreement between the two methods. Here, we found that by using the same postprocessing algorithm a great similarity can also be obtained for the PD and WF maps. WF map is valuable because it allows for more precise tissue characterization. Furthermore, a join modeling of the T1 and WF values has been proposed for calculating the tissue reflexivity. Last, a great effort in the qMRI community is pointed to reliable values across scanner and protocol, this work is adding an important benchmark for this research.

**References**

**Poster No 2291**
**Structural abnormalities of right fronto-parietal control network brain regions in migraineurs**
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**Introduction:** Migraine is a paroxysmal neurological disorder, accompanying with various symptoms, such as photophobia and altered cognition. The etiology of migraine remains unclear. Researches have focused mainly on neurophysiological mechanisms. Previous studies have found abnormal resting-state functional connectivity in the right fronto-parietal network (rFCN) in migraine patients. The rFCN is mainly responsible for somatosensory and cognitive control, including
the dorsolateral prefrontal cortex (dPFC), insula, middle frontal gyrus (MFG) and supramarginal gyrus (SMG). However, few studies have found abnormal structure in the rFCN-related brain regions. The present study aims to investigate the structural changes in the rFCN-related brain regions in migraine patients, providing physiologic evidence of abnormalities in patients’ somatosensory abilities.

**Methods:** Participants Twenty-five migraine patients (2M/23F, age 31.32 ± 8.38 years old) and 24 healthy controls (9M/15F, age 25.33 ± 4.46 years old) were recruited from the 2nd Affiliated Hospital of Guangzhou University of Chinese Medicine. The inclusion criteria for patients were as follows: (1) episodic migraine without aura, (2) 18-45 years old, (3) right-handed, (4) disease duration ≥ 6 months, and (5) attack frequency ≥ 1 day every month. Written informed consent was obtained from each subject before this study. Data acquisition All MRI data were obtained on a 3.0 T Siemens Verio MRI scanner with a 24-channel phased array head coil. The high resolution brain structural images were acquired using a T1-weighted 3D MP-RAGE sequence with the following parameters: repetition time (TR) = 1,900 ms, echo time (TE) = 2.27 ms, flip angle (FA) = 9°, data matrix = 256 × 256, field of view (FOV) = 256 mm × 256 mm, slice thickness = 1 mm, and 176 sagittal slices covering the whole brain. Data analysis The structural MRI data were preprocessed using FreeSurfer, mainly including removal of non-brain tissue, segmentation of white and gray matter, intensity normalization, tessellation of the gray/white matter boundary. We used two separate general linear models (GLM) to explore the differences in gray matter volume (GMV) and cortical thickness (CT) between the migraine patients and healthy subjects. In the calculations, We took age as a nuisance covariate. Statistical significant threshold was set at the vertex-level p < 0.001 with family wise error (FWE) correction at the cluster-level of p < 0.05. We applied partial correlation analysis to explore the relationship between the altered CT and Migraine Specific Quality-of-Life Questionnaire (MSQ) score in the migraineurs, taking age as nuisance covariate.

**Results:** Fig. 1 shows that migraine patients had a significantly increased CT in the right supramarginal gyrus. The CT in the SMG was significantly and positively correlated with MSQ scale scores in the migraine subjects (r = 0.484, p = 0.017). We also found that the patients had a significantly increased GMV in the cMFG and rMFG, and a significantly reduced GMV in the precuneus compared with healthy controls. The detailed information is listed in Tables 1 and 2.
Conclusions: The current study found cortical thickening in SMG in the migraine patients compared with the healthy controls, and the degree of cortical thickening is significantly positively correlated with the severity of the disease. Moreover, we found an increased GMV in the middle frontal region and a decreased GMV in the precuneus in the migraine patients, which are responsible for higher cognitive functions. We found structural changes in brain regions belonging to the rFCN, which may be related to abnormalities in sensory and cognitive control in migraine patients. The frontal-parietal control network (FPN) is a generalized network. The left frontoparietal network is mainly responsible for language processing. We did not find similar structural change results in the left brain, which could also provide evidence for lateralization of the FCP.

References

Poster No 2292
Patterns of Popular Artifacts in QSM and χ-separation (chi-separation)
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Introduction: QSM and χ-separation quantify brain tissue susceptibility for studying neurodegenerative diseases. However, artifacts in data acquisition and processing can compromise accuracy, impacting reliability. It is important to recognize these artifacts and implement appropriate correction methods. The study analysed data from healthy subjects and patients in various groups and from different vendors and explored commonly encountered artifacts. The effects, origins, and potential solutions for these artifacts were investigated to improve the application of QSM and χ-separation.

Methods: 364 subjects (52.24 ± 25.78 years; 163 males and 201 females) from Parkinson’s disease, Alzheimer’s disease, hypertension, and alcohol-exposed adolescents development studies were scanned at six different 3T MRI scanners (Siemens Trio, Siemens Vida, Siemens Skyra, Philips Ingenia CX, Philips Ingenia Elition X, and GE Discovery 750w). All data processing for QSM and χ-separation was performed using the χ-separation toolbox (https://github.com/SNU-LIST/chi-separation). Phases were unwrapped using a Laplacian-based algorithm. V-SHARP9 was applied to remove background fields. QSM was calculated using QSMnet10. χ-sepnet-R2*6 and χ-sepnet-R2*6 were utilized calculating χpara and χdia maps.

Results: Motion resulted in ghosting and blurring in QSM and χ-separation results (Fig. 1a). Respiration-induced B0 fluctuations hinder QSM and χ-separation (Fig. 1b), affecting reproducibility and accuracy of QSM and χ-separation results. Post-acquisition correction for these artifacts is challenging without extra information such as B0-navigation. Incorrect coil combination introduced “phase singularities”, and a localized high intensity region may appear (Fig. 1c), resolved by proper coil combination. GRAPPA algorithm reconstruction errors yield aliasing artifacts (Fig.1d), corrected by reprocessing raw data. Large slice thickness leads to QSM underestimation, R2* overestimation, and ultimately overestimation of both χpara and χdia (Fig. 1e), mitigated by using isotropic voxels of 1 mm or less. Thin slabs cause significant QSM underestimation due
to truncated non-local dipole, leading to underestimation of both dominant source in $\chi_{\text{para}}$ and $\chi_{\text{dia}}$ maps (Fig. 2a,b). Data from P*** vendor sometimes contained linear field bias, causing residual phase wraps in QSM and $\chi$-separation results (Fig. 1g) as the nonlinear complex data fitting approach for echo combination and phase unwrapping were utilized. Unwrapping phase at each TE and combining multi-echo images can be the solution. QSMnet may mistakenly use a local field map in radians instead of Hz, resulting in intensity range errors (Fig. 1h). Failure to correct B0 orientation during processing causes misalignment of the magnetic dipole kernel with B0 direction and susceptibility errors® (Fig. 2c). Unintentionally flipped images impact alignment between T2-weighted and GRE magnitude images, leading to incorrect R2’ maps. This can manifest as a prominent bright pattern in the cortical region in $\chi_{\text{para}}$ and $\chi_{\text{dia}}$ (Fig. 2d). Vessel flow artifacts can impact adjacent regions, leading to erroneously high or low values in QSM and $\chi$-separation results (Fig. 1k). To ensure accurate ROI analysis, it is advisable to exclude these affected regions.

Figure 1. QSM and $\chi$-separation results displaying various artifacts. (a) Motion, (b) respiration-induced $B_0$ fluctuation, (c) incorrect coil combination, (d) GRAPPA reconstruction error, (e) large slice thickness, (f) thin slab, (g) unwrapping error, (h) unit mismatch, (i) misaligned $B_0$ direction, (j) mis-registration between $R'$ and $R_0$, and (k) vessels generated artifacts in QSM, $\chi_{\text{para}}$, and $\chi_{\text{dia}}$ while (l) presents no artifacts. Red arrows highlight areas where artifacts are observed. For the artifacts in (f, i, and j), Figure 2 compares them to artifact-free images.
Conclusions: We reported various artifacts in QSM and $\chi$-separation from 364 subjects. Their origins and proposed practical solutions to mitigate their effects were investigated, thereby improving the precision and reliability of quantitative analysis in MRI studies. The inclusion of visual images as aids for artifact recognition benefits both researchers and practitioners, significantly enhancing data quality and interpretation across clinical and research studies.

References


**Poster No 2293**

**Network-based modeling of brain-wide structural alterations in substance use disorders**

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**Introduction:** Substance use disorders (SUD) are increasingly recognized as network disorders (Joutsa et al., 2022; Ottino-González et al., 2022) and associated with system-wide structural brain alterations (Mackey et al., 2019). Though network mechanisms have been shown to guide the spatial patterning of structural alterations in psychiatric and neurodegenerative conditions, it remains to be established whether these associations are also seen in SUD. Here, we tested whether large-scale structural alterations in SUD relate to normative functional and structural connectome architecture.

**Methods:** We generated cortical and subcortical case-control differences in SUD from 2,847 individuals with SUD (alcohol, methamphetamine, cocaine, opioids, cannabis, and nicotine) and 1,951 non-affected individuals of the ENIGMA Addiction consortium. Using normative rs-fMRI and diffusion MRI connectivity data from the Human Connectome Project (n=207), we evaluated structural alterations of SUD against two network susceptibility models: i) hub vulnerability, which examines associations between regional network centrality and magnitude of disease-related alterations; ii) epicenter mapping, which identify regions whose typical connectivity profile most closely resembles the disease-related morphological alterations.

**Results:** We identified widespread reductions in cortical thickness and subcortical volume in individuals with SUD compared to non-affected controls (Fig 1a,b). SUD-related regional structural alterations were associated with higher functional and structural cortico-cortical and functional subcortico-cortical degree centrality (DC) (Fig 1c, all p<0.05). Functional connectivity epicenters encompassed multiple parieto-temporal and frontal areas as well as subcortical regions (Fig 1c). Structural connectivity epicenters were more circumscribed, and located in sensory and parietal cortical areas and striatum and thalamus (Fig 1c).
Conclusions: Our findings show that in SUD, hub regions are more vulnerable to structural alterations and that distinct subcortical and cortical connectivity profiles are linked to the spatial pattern of cortical alterations. Together, our study provides novel insights how network mechanisms may guide the spatial distribution of SUD-related structural alterations.

References

Assessing highly accelerated 3D-T1w Wave CAIPI MPRAGE images for brain age prediction in dementia
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**ABSTRACTS**

**Introduction:** Traditional MRI sequences, such as the standard T1-weighted Magnetization Prepared Rapid Gradient Echo (MPRAGE), have been the cornerstone for neuroimaging. However, the advent of advanced accelerated imaging techniques like Wave Controlled Aliasing In Parallel Imaging (Wave CAIPI), results in shorter scan times, presenting a shift in data acquisition speed. Brain age is a measure derived from neuroimaging that estimates the brain’s ‘biological age’, calculated by applying machine learning methods. The disparity between predicted age and real age, known as the brain-predicted age difference (BrainPAD), aims to reflect differences in brain aging, which can be influenced by lifestyle, genetics, and disease. This work compares brain age predictions derived from accelerated Wave CAIPI MPRAGE acquisitions against those obtained from standard MPRAGE acquisitions.

**Methods:** We studied 124 individuals from the Biomarkers and Rapid Imaging in Dementia Diagnosis (B-RAPIDD) dataset. Participants were patients from the Cognitive Disorders Clinics at the National Hospital for Neurology and Neurosurgery (London, United Kingdom) with different diagnoses, undergoing investigations for memory and cognitive difficulties. Participants undertook a standard 312 seconds T1w MPRAGE acquisition following the Alzheimer’s Disease Neuroimaging Initiative 2 protocol, and one or two MPRAGE sequences with Wave CAIPI undersampling. Additionally, all individuals received the mini-mental state exam (MMSE). Acquisition parameters are comparable among the Wave CAIPI acquisitions for each participant with a standard acquisition an accelerated one was randomly selected. For details of acquisition parameters and demographics, see Figure 1. The brainAgeR model was used to estimate brain age from the standard and accelerated scans. Performance was evaluated using the mean absolute error (MAE), Pearson’s correlation (r), and R-squared (R2). High MAE was expected since cognitively impaired subjects were assessed. Reliability and agreement between scan types were analyzed using the intra-class correlation coefficient (ICC) and Pearson’s correlation. The brain age difference between standard and Wave CAIPI scans was assessed, along with a t-test to determine its significance. Additionally, the influence of scan type on cognitive status was explored by correlating BrainPADs with MMSE scores, with age and sex as covariates. The significance of the difference between the calculated R2 and the correlation coefficients was assessed using bootstrapping with 1,000 iterations.

**Results:** Both standard and Wave CAIPI acquisitions achieve similar predictions of brain age (see Figure 2), with comparable performance in terms of their MAE (standard MAE = 8.16 years; Wave CAIPI MAE = 7.79 years) and correlation (standard r = 0.83; Wave CAIPI r = 0.82). Additionally, the correlation between them, including intra-class and Pearson correlation (ICC = 0.95, 95% CI [0.93, 0.97]; r = 0.96), was very high. However, with Wave CAIPI, there was a tendency to underestimate age in younger subjects (Figure 2C). Further, the Wave CAIPI method seems to exhibit a higher correlation with MMSE (Standard r = -0.25; Wave CAIPI r = -0.31; difference = 0.07 IC 95% [-0.21, 0.38]), although neither these or the R2 (Standard R2 = 0.15; Wave CAIPI R2 = 0.18; difference -0.03 IC 95% [-0.19, 0.11]) were significantly different (Figure 2D).
Conclusions: These observations suggest that the accelerated technique efficiently shortens data acquisition time without compromising the accuracy of predictions. It is important to recognize that the biases observed in age estimation are likely due to subtle differences in image characteristics relative to the brain age model training data, and do not necessarily reflect flaws in the accelerated method. Furthermore, the sensitivity of the Wave CAIPI method to cognitive changes appears to be better, but not significantly so.

References

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Poster No 2295
Gray matter density changes in children with congenital severe sensorineural deafness
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Introduction: The congenital severe sensorineural hearing loss (CSSHL) could lead to not only lifelong deafness but also affect cognitive functions, such as impaired executive function and abnormal social behavior (Proksch and Bavelier 2002). The voxel-based morphometry (VBM) involves a voxel-wise comparison of the local concentration of gray matter (GM) between two groups of subjects(Ashburner and Friston 2000). Until now, little information is available about the GM density changes in
children with CSSHL and the results are inconsistent (Qi et al. 2019) (Wang et al. 2016). This study aimed to further explore the GM density changes in children with CSSHL.

Methods: Fifteen children with CSSHL at mean (SD) age (27±18.8months) and 11 healthy controls (HC) at mean (SD) age (31±15.5months) from August 2017 to September 2018 in the First Affiliated Hospital of the University of Science and Technology of China were enrolled in the study. The inclusion criteria of the children in CSSHL group were: (1) Children were presented with bilateral CSSHL. The exclusion criteria were: (1) Diagnosis of central nervous system diseases, such as cerebral white matter hypoplasia, neuroskin syndrome, tumor, etc. (3) History of ear surgery. All the HC had normal hearing function and no abnormality in head MRI scan. The HC and CSSHL group were further divided into 0-2 years and 2-5 years by age, respectively. There are four groups: HC02(n=5), HC25(n=6), CSSHL02(n=8) and CSSHL25(n=7). All participants underwent MRI scanning on a GE 3.0T magnetic resonance scanner (GE, 750W) under sedation. First, whole-brain cross-sectional images of T1WI and T2WI were acquired to exclude central nervous system lesions. Second, the structural MRI (sMRI) was collected using T1-3DBRAVO sequence. GM density of all subjects was measured by FMRIB Software Library voxel-based morphometry (FSL-VBM, http://fsl.fmrib.ox.ac.uk/fsl). A group-level analysis was applied to identify the GM differences between children with CSSHL and HC. For the global GM metrics, the statistical significance threshold was set to P < 0.05. For the regional GM maps, the significance threshold was set to P < 0.001 at the voxel level, followed by Gaussian random field (GRF) correction at the cluster level of P < 0.05. Cohen’s d approach was used to calculate the effect size in the present study that reflected the statistical strength between groups (Lakens 2013).

Results: A deficit in GM density in the right superior temporal gyrus (STG) and caudate body was found in the CSSHL group compared with the HC group (P < 0.05, Figure 1). At the same time, the GM density of the left posterior central gyrus (POG), superior frontal gyrus (SFG), inferior parietal lobule (IPL) and right cerebellum (CRB) in the CSSHL group was larger compared with the HC group (P < 0.05, Figure 1). The GM density of the right STG in the CSSHL02 group and CSSHL25 group was smaller than that in the HC group of the corresponding age (Figure 2d). The GM density of the right caudate was larger in the HC25 group compared with the CSSHL25 group and HC02 group (Figure 2f). As for the left POG (Figure 2a), left SFG (Figure 2b), left IPL (Figure 2c) and right CRB (Figure 2e), the GM density was larger in CSSHL25 and CSSHL02 groups compared with that in HC group of corresponding age. The GM density of the left SFG in the CSSHL group was prominently negatively correlated with age (R=-0.551, P=0.033), and the GM density of the left IPL was also negatively associated with age (R=-0.507, P=0.0537). Meanwhile, it is observed that the GM density of the right STG in the CSSHL group is positively correlated with age (R=0.498, P=0.0586).

Fig. Group differences in GM density between CSSHL and HC.
Fig. Group differences in GM density between subgroups

Conclusions: Compared with HC, the GM density of CSSHL children was larger in somatosensory areas (including left SFG, POG, IPL and right CRB), while GM density was smaller in auditory-related areas (such as right STG and caudate). Moreover, GM density change is influenced by the duration of hearing deprivation.

References

Poster No 2296

Volumetry of Cerebral cortex in psychogenic non-epileptic seizures: a VBM & cortical thickness study

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Introduction: Psychogenic Non-Epileptic Seizures (PNES) are common functional neurological disorders resembling epileptic seizures but without abnormal neuronal activity. The mechanisms behind PNES are not well understood, with theories ranging from brain ‘software defects’ to alterations in specific brain regions. To address these inconsistencies and improve our understanding of PNES, our study employed Voxel Based Morphometry (VBM) and cortical thickness measurements in MRI scans. This approach was used to investigate structural differences in the brains of PNES patients compared to healthy controls, aiding in elucidating the pathophysiology of PNES.

Methods: Between November 2019 and September 2021, 21 patients with Psychogenic Non-Epileptic Seizures (PNES) were identified at Imam Khomeini Hospital, Tehran, Iran. Criteria included a history of seizure-like episodes and negative ictal EEG results. Exclusion criteria were the presence of epileptic seizures, significant medical, neurological, psychiatric conditions, substance abuse, or antipsychotic drug use. Additionally, 26 healthy individuals with no neurological or psychiatric history were included for comparison. Neurological examinations of all participants were normal. The study adhered to ethical standards, with informed consent obtained from all participants. Patients underwent neuropsychological and psychiatric evaluations, including the Addenbrooke’s Cognitive Examination (ACE) and IQ assessments, indicating average IQ but some cognitive deficits. MRI scans were conducted using a Siemens 3.0-Tesla Prisma scanner. Parameters included T1-Weighted-
MPRAGE with specific durations, angles, and resolutions detailed. SPM12 software was used for VBM analysis, involving normalization, segmentation, and smoothing of grey matter volume maps, followed by statistical analysis with ANCOVA, adjusting for intracranial volume, age, and gender. Freesurfer software was utilized for cortical thickness measurement. This included automated cortical reconstruction, manual correction of segmentation errors, and statistical analysis with significance values adjusted for multiple comparisons. Data normality was assessed using the Kolmogorov-Smirnov test. Group comparisons (PNES vs. healthy controls) were made using t-tests or Mann-Whitney U tests, with an alpha error value set at 0.05, using SPSS software.

Fig. VBM analysis for HC > PNES between-subjects contrast (HC - PNES) in a 3D format for GM volume reduction in PNES

Results: Our study included 21 PNES patients (mean age 28.38±10.84 years, 16 females and 5 males) identified through video-EEG, with no exclusions. Brain MRIs showed no mass lesions. The mean age at first PNES episode was 14.65 years, with an average of 5.59 episodes per month. The control group consisted of 25 right-handed individuals (mean age 30.77±6.59 years, 13 females and 13 males), with no significant age or gender differences compared to the PNES group. Average ACE score was 89 (range 87-100), indicating normal cognitive function. IQ levels, assessed during interviews, were within normal limits, and neurological examinations were unremarkable. Significant gray matter loss in PNES patients was observed in various brain regions including the left occipital gyrus, lingual gyrus, right subcallosal gyrus, parahippocampal gyrus, and others, without adjusting for multiple comparisons. Conversely, there was an increase in gray matter in areas like the right premotor and supplementary motor area, superior frontal gyrus, and left precentral gyrus. No significant differences in cortical thickness were found between PNES patients and healthy controls.

Conclusions: In summary, our study comparing 21 PNES patients with 25 healthy controls found significant variations in gray matter volume in multiple brain regions of PNES patients, but no differences in cortical thickness. These findings suggest a neurobiological basis for PNES, indicating the need for further research to understand its underlying mechanisms and improve treatment approaches.

References
Multi-task Learning framework for Brain Tumor Analysis with Uncertainty Estimation in MRI Images

Maria Nazir, Sadia Shakil, Khurram Khurshid

Introduction: Gliomas are one of the deadliest brain tumors with extremely difficult diagnosis due to their complex behavior and irregular appearance. Magnetic Resonance Imaging (MRI) is the most famous imaging modality used for detecting tumors like gliomas. The manual segmentation of brain tumors in MRI images is a laborious task, which gives rise to subjective as well as objective errors. To cater for all these issues, a lot of research has been done and is going on to develop AI-based solutions that can help doctors and radiologists in early and effective diagnosis of gliomas. However, an end-to-end system is still missing. In this research, an all-in-one Multi-Task Learning (MTL) framework for complete analysis of gliomas with uncertainty estimation has been proposed.

Methods: An end-to-end 3D MTL model with encoder as the shared backbone was developed that can give predictions for three tasks simultaneously. It can classify the tumor as High-grade glioma (HGG) / Low-grade glioma (LGG), provides multi-class segmentation of the lesion area into three classes (Enhancing Tumor, Non-Enhancing Tumor and Whole Tumor), and predicts the overall survival of glioma patients in days by leveraging task relationships between similar tasks. Each task was executed using separate task specific layers that used the feature representation from the shared layers. Loss optimization is the most critical factor in MTL frameworks. Three different losses were used for three predictions and are combined to form one aggregated loss. RMSprop was used for loss optimization during back propagation by updating weights in each task specific layers and the shared layers. Loss weights are the most important hyper-parameters in MTL framework that can be tuned to minimize the overall loss and increase efficiency. Three weights for three different losses were used i.e., W1 = 0.01 for classification, W2=10 for segmentation and W3=0.001 for survival in days were found to be the best weight factors for the designed setup. Pre-processed Brain Tumor Segmentation challenge (BraTS 2019 and 2020) datasets with combination of 1, 2 and 4 MRI sequences (T1, T2, Flair and T1CE) were used for experimental purposes. We further did some more pre-processing i.e., cropping, re-sizing to reduce the size and normalization to standardize the data. The model was tested on three different batch sizes (32, 64 and 128). Prediction performance of all three tasks for each case was compared with state-of-the-art as well as MTL related studies.

Results: Fig. 1. shows the proposed 3D MTL architecture consisting of input block for pre-processing of MRI images, shared block for extracting features and finally the output block consisting of task specific layers that use the extracted features for multiple predictions. Fig. 2. shows the results obtained for multi-class segmentation with predicted mask, ground truths and uncertainty of the model for each case. Results show 95% accuracy, 86% dice and mean absolute error of 456.59 days for a combination of all four sequences. Uncertainty maps show some border pixels where the model is uncertain by enforcing the radiologists to pay more attention to lesion border for accurate prediction.

Conclusions: We developed an all-in-one end-to-end framework that can provide multiple predictions for complete glioma analysis using the least resources (data, computation, inference time). Publicly available BraTS 2019 and 2020 datasets were used for experimentation. It is evident from the results that deep learning based multi-task learning frameworks have the potential to automate the whole brain tumor analysis process and give efficient results without human intervention with least
resource utilization. The proposed solution can easily be installed in a clinical setup for initial screening of glioma patients after validation on local data.

Fig 1. Proposed 3D Multi-Task Learning Framework

Fig 2. Predicted Multi-class segmentation (ET as yellow, NET as white and WT as red) results of Glioma tumor using the proposed scheme with uncertainty maps.

References
Impact of COVID-19 on the Pediatric Brain: A Structural MRI Study

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Introduction: The COVID-19 pandemic has caused unprecedented physical and mental problems to infected individuals. Mounting evidence indicates that SARS-CoV-2 negatively influences human CNS including the brain (Shen et al. 2022), suggesting neurological deficits caused by the virus. Given that the first several years of life represents a critical stage in human brain development, we hypothesized that COVID-19 infection may cause more significant changes in the brain structure in young children than adults (Gilmore et al. 2018). While numerous studies have been conducted on the impact of COVID-19 on human brain, little is known regarding its impact on the pediatric populations. To resolve this issue, we recruited a group of children with COVID-19 and compared their structure with age- and gender-matched healthy control children based on high-resolution structural MRI. The whole-brain vertex-wise morphometric analysis, as well as structural covariance network construction and analysis, were performed to explore COVID-19 impact on the children’s brain.

Methods: We enrolled 17 children (age 3.2 ± 1.8 years) diagnosed with mild COVID-19 and 19 age-/sex-matched (P>0.05) healthy children (age 3.7 ± 1.5 years). Their 3D high-resolution T1w structural MRI data with 0.8mm isotropic voxels were obtained by a 3.0T scanner (uMR890, United Imaging) and preprocessed using FreeSurfer (Fischl et al. 2000). Various cortical metrics (cortical thickness, area, volume, and local gyrification index (LGI)) were compared between the two groups with vertex-wise general linear models (vertex-wise P<0.01, cluster-wise P<0.05) after controlling age, gender, and total intracranial volume (eTIV). We further extracted cortical LGI histogram for each of the 68 brain regions defined by the Desikan-Killiany Atlas and constructed structural covariance networks using Graph Analysis Toolbox (Hosseini et al. 2012). The edges were defined as Pearson correlation coefficients between LGI histograms of each pair of the brain regions adjusted for age, gender, and eTIV. The structural covariance networks were then binarized according to density thresholds ranging from 0.24 to 0.38 (with an increment of 0.01) according to the literature documented elsewhere (Humphries et al. 2006). Global (clustering coefficient, path length, and small-world index) and regional metrics (nodal betweenness centrality, nodal degree, and local efficiency) were calculated (Rubinov et al. 2010) and the area under the curve (AUC) of the network parameters across all densities was compared using non-parametric permutation tests (P<0.05, false discovery rate [FDR] corrected).

Results: The vertex-wise comparison results on cortical measurements were summarized in Table 1. Compared to the control group, patients with COVID-19 showed a significant increase in cortical area, volume, and LGI at the left superior parietal cortex, and in cortical thickness at the left lateral occipital cortex. Further exploration of the between-group differences indicated that brain cortical LGI network changed its topology towards less optimized clustering coefficient in the COVID-19 group (P<0.05, Figure 1), whereas other network global indices did not show statistical significance. Finally, we found no significant difference in the regional network measures after FDR correction.

Table 1. Regional changes in cortical metrics in the children with COVID-19 compared with age-/sex- matched HCs.

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Hemisphere</th>
<th>Cortical region</th>
<th>Size (mm²)</th>
<th>Xyz peak (MNI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness</td>
<td>Left</td>
<td>Lateral occipital</td>
<td>201.90</td>
<td>-19.6/-96.1/-15.4</td>
<td>0.0171</td>
</tr>
<tr>
<td>Area</td>
<td>Left</td>
<td>Superior parietal</td>
<td>522.63</td>
<td>-21.9/-83.8/14.2</td>
<td>0.0004</td>
</tr>
<tr>
<td>Volume</td>
<td>Left</td>
<td>Superior parietal</td>
<td>224.45</td>
<td>-22.0/-66.5/30.6</td>
<td>0.0070</td>
</tr>
<tr>
<td>LGI</td>
<td>Left</td>
<td>Superior parietal</td>
<td>1548.83</td>
<td>-18.8/-70.8/38.3</td>
<td>0.0032</td>
</tr>
</tbody>
</table>

Age, gender, and eTIV were adjusted. Vertex-wise threshold P<0.01, cluster-wise threshold P<0.05.

Abbreviations: HCs, healthy controls; MNI, Montreal Neurological Institute; eTIV, total intracranial volume.
Conclusions: Our study provided the first report of reduced clustering coefficient in brain cortical geometric networks in young children with COVID-19, despite of no difference in regional networks parameters. We speculate that virus-triggered neuroinflammation and immune response may cause neurotoxic consequences in children's brain, leading to cortical geometric changes and global network changes and further impairing cognitive abilities during such a pivotal development period (so-called “long-COVID”).

References

Acknowledgements
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Poster No 2299

**Transformed domain NORDIC (tNORDIC) denoising improves mesoscopic, whole brain quantitative imaging**

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**Introduction:** With the advent of MRI scanners with field strengths of 7T and above there is an increased interest in ultra-high high-resolution anatomical images (<0.5mm) of living human brains. These images have many uses, including structural references for depth-dependent fMRI, biophysical modeling of the BOLD signal, and uncovering tissue properties. Unfortunately, the acquisition of these images is associated with several challenges, including long scan times, and participant motion. Ideally, we could leverage higher acceleration to reduce scan times, however, noise at these resolutions are already a concern. Fortunately, developments in patch-based methods have shown promise in reducing thermal noise in these multi-contrast images (Bazin et al, 2019). Here we evaluate a modification of the NORDIC fMRI denoising method (Dowdle et al, 2021, Vizioli, 2021), known as transformed domain NORDIC (“tNORDIC”, Moeller et al 2023), on both 7T and 10.5T multi-echo GRE (ME-GRE) images with the goal of producing usable whole head quantitative, 0.37mm images with sub-10 minute acquisition times.
Methods: Following testing on publicly available data (Gulban et al, 2022), we acquired whole head, highly accelerated multi-echo GRE images at 7T (4 runs, TA:9:21, 0.37x0.37x0.37mm3, GRAPPA 3x3, 6 TEs: 4.23-24.98ms; TR:31ms, FA:11°, 7/8ths partial Fourier, 2xAP, 2xRL) and 10.5T (2 runs, TA:9:57, 0.37x0.37x0.37mm3, GRAPPA 3x3, 7 TEs:4.07-27.35ms; TR:33ms, FA:10°, 7/8ths partial Fourier, 1xAP, 1xRL). We evaluated several aspects of the data: 1) improved signal quality from reduced variance, 2) improvements in quantitative fits, 3) preservation of fine detail and 4) consistency in results compared to an average of multiple runs. We applied tNORDIC to the magnitude images and compared against alternatives: patched based method, LCPCA (Bazin et al, 2019), and non-local means (NLM) denoising (Avants et al, 2021). Alignment between the separate runs was calculated using antsRegistration. We estimated the quantitative T2* fit using a log-linear approach (t2smap, tedana (DuPre et al, 2021)). T2* estimates and a T2*-based weighted average, were compared between the denoised data and 1 run or the average of 4 runs of the original data. T2* values were extracted from a gray matter (GM) ROI generated by manual segmentation.

Results: After tNORDIC, the data from a single echo are less corrupted by thermal noise compared to the original images (7T data shown, Figure 1A). The image quality following tNORDIC matches that of the 4-run average (Figure 1A). In our hands, the alternative methods (LCPCA and NLM) produce blurring in the data, obscuring details (Figure 1A, right). The resulting estimates of T2* parameters are less noisy after tNORDIC (Figure 1B), reproducing the values observed after averaging 4 runs of the original data. A minimum intensity projection of the weighted average show that tNORDIC data preserves details (Figure 1C). Within the gray matter mask, one run of data after tNORDIC is more consistent run-to-run (i.e. test/re-test, Figure 2A) and more consistent with the 4-run average (Figure 2B). After tNORDIC, one run has a stronger correlation with the estimates derived from the 4-run average (r = 0.22, p <<0.001) compared to the original data (r = 0.12, p<<0.001). For the 10.5T data we found an additional benefit, in that tNORDIC recovers signal in the last echo which would be otherwise buried in noise due to shorter T2* values.

Fig. 1. A) Detailed views of various approaches. B) T2* fits are markedly less noisy after tNORDIC. C) Minimum intensity projections show fine detail after tNORDIC.
Fig 2. 2D Histograms of T2* estimates. A) Run-to-run consistency of T2* in gray matter. B) Consistency with 4-run average. For both cases, tNORDIC data is more consistent versus original.

Conclusions: These results show that, after tNORDIC denoising, a single sub-10 minute acquisition can produce high quality, whole brain 0.37mm isotropic, quantitative data at 10.5 and 7T field strengths. The shortened scan times mitigate motion sensitivity and improve subject comfort. Here we have applied tNORDIC to ME-GRE magnitude images, but this method is applicable to any short series such as the ME-MP2RAGE sequence or distortion matched T1w-EPI. Further work will consider how this processing improves phase data for quantitative susceptibility mapping (QSM).

Grant support from National Institutes of Health P41 EB027061, S10 RR029672, RF1 MH116978

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Poster No 2300
Exploring the Relationship between Brain Tumors and Accelerated Aging by Disconnection Maps
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**Introduction:** Brain tumors significantly disrupt neural network integrity, leading to both local and distal functional impairments due to compromised cerebral communication pathways. Utilizing diffusion Magnetic Resonance Imaging tractography, researchers can investigate the impact of brain tumors on white matter (WM) tracts and assess structural ‘disconnectome’\(^1\). However, these approaches are hindered by prolonged scanning durations and intricate post-processing requirements, necessitating substantial technical expertise and time investment. To overcome these limitations, the incorporation of lesion mapping methodologies, in tandem with predefined WM and gray matter atlases, has emerged as a streamlined alternative, enhancing the efficiency and effectiveness of population-level investigations. Prior studies employing lesion mapping have focused on the structural disconnection-cognitive impairment nexus in cases of brain tumors, stroke, and epilepsy\(^2\). Building upon this foundation, the current study integrates WM disconnection maps with a brain age prediction model to delve into the relationship between tumor-induced localized damage and distant network disconnections. The primary aim is to elucidate the effects of localized tumor lesions on accelerated aging across cerebral hemispheres, thereby contributing to a more comprehensive understanding of the global ramifications of neural network disruptions caused by brain tumors.

**Methods:** In this study, we analyzed structural imaging data from 6 brain tumor patients, aged 27 to 68 at Jilin University Hospital. Each patient had undergone preoperative 3D T1-weighted (T1w) imaging with the following parameter: TR/TE/T1 3500/2.3/1100 ms, voxel size 1×1×1 mm\(^3\), and FOV 256×256×176 mm\(^2\). First, we performed manual segmentation with ITK-SNAP, followed by validation from a 20-years experienced neurosurgeon. Lesion segmentation maps were registered to the MNI152 space using the ANTs. Next, we applied the Lesion Quantification Toolkit in conjunction with the HCP-842 population-averaged streamline tractography atlas and AAL2 brain parcellation template to quantify the WM disruption\(^3\)\(^-\)\(^5\). The disconnections were measured by assessing parcel-wise disconnection severity matrices, encapsulating the pattern of WM disconnections between pairs of grey matter parcels (Fig. 1A)\(^6\). For brain age prediction, we utilized a support vector regression model with a radial basis function kernel implemented through the Scikit-learn library (Fig. 1B)\(^7\). We strategically excluded brain regions directly impacted by tumors, and then compared the predicted age discrepancies between the disrupted areas and their corresponding healthy contralateral counterparts, as well as with bilaterally healthy regions (Fig. 1C). The Wilcoxon-Mann-Whitney U-test was used for the statistical comparison, considering p-values less than 0.05 as indicative of statistical significance.

**Results:** We analyzed 6 patients with brain tumor, the detail of clinical information and the mean values of brain age differences of each patient were summarized in Fig. 2A. Fig 2B represents the case of patient P01, displaying the lesion mask overlaid on T1w in the MNI152 space, along with computed voxel-wise and parcel wise-disconnection map. We found a significant increase (p<0.03) in the brain age differences within disrupted brain regions, averaging 17.76±5.21 years, compared to the healthy brain regions, where the difference was 10.64±2.95 years (Fig. 3C).

**Conclusions:** Our study revealed that brain lesions not only affect local areas but also cause WM disconnections, impacting distant regions within and across brain hemispheres. By integrating WM disconnection maps with a brain age prediction model and successfully highlighted significant age disparities between the hemispheres. The efficient use of lesion mapping in our study provides valuable insights into the impact of brain tumors, potentially enhancing surgical planning and treatment strategies alongside cognitive assessments.
References

Poster No 2301

Lateral Ventricle volume is associated with CDR and Hippocampus volume

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Introduction: The use of biomarkers for early detection of Alzheimer disease (AD) is crucial for developing potential treatments. As neurons die, brain structures, including the hippocampus, shrink and the cerebrospinal fluid spaces ventricles expand. However, the hippocampus is a very small structure, and its shrinkage can be challenging to analyze. The lateral ventricle volume is larger and easier to measure than hippocampal volumes. Previous studies have validated ventricular enlargement as a possible measure of AD progression1-3. In this study, we tested the hypothesis that baseline and longitudinal changes in lateral ventricle volume as measured by magnetic resonance imaging (MRI) associated with baseline clinical dementia rating® (CDR®)4 and associated with baseline and longitudinal changes in hippocampus volume.

Methods: We evaluated 518 participants enrolled in longitudinal studies at the Knight ADRC at Washington University in St. Louis. MRI data was obtained through OASIS (www.oasis-brains.org). Participants were required to have at least two CDR assessments and MRI scans. Lateral ventricular and hippocampal volumes were extracted and corrected for intracranial volume using FreeSurfer. Univariate linear regression models were used to evaluate the relationship between baseline CDR, treated as a categorical variable, and baseline lateral ventricle volumes, as well as the relationship between baseline lateral ventricle volume and baseline hippocampal volume. A two-step random coefficient model was used to evaluate the rate of change in lateral ventricle volume associated with baseline CDR or rate of change in hippocampal volume. The random
A coefficient model can accommodate the heterogeneous number of visits and visit intervals undergone by study participants. The first step of this two-step model was to calculate the rate of change in lateral ventricular volume (lvv_slope) and rate of change in hippocampus volume (hv_slope) after controlling for age, sex, APOE-ε4, and years of education, see equation 1. The second step evaluated the relationship between baseline CDR and rate of change in lateral ventricular volume, as well as the relationship between rate of change in lateral ventricle volume and rate of change in hippocampus volume using univariate linear regression model, see equation 2. MRI = α1*time + α2*age + α3*sex + α4*education + α5*APOE ε4 (1) lvv_slope= β*lvv_slope or lvv_slope= β*CDR (2) Here, time was set as a continuous variable (measured in years) representing the interval between the baseline visit and each subsequent visit. Within this model, time was treated as both a fixed and random effect.

**Results:** Demographic characteristics of the participants at baseline are presented in Table 1. We found that larger baseline lateral ventricle volumes were associated with worse baseline CDR (estimate β =12110, p=0.0001, figure 1A), and with smaller baseline hippocampal volumes (estimate β =-8.64, p<0.0001, figure 1B). Additionally, the rate of changes in lateral ventricle volumes were also associated with baseline CDR and rate of changes in hippocampal volume (estimates β =548.8, p<0.0001, figure 1C and estimatesβ =-6.01, p<0.0001, figure 1D, respectively).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N=518</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(year), mean±SD</td>
<td>68.87± 9.28</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>295 (56.95)</td>
</tr>
<tr>
<td>Years of education, mean±SD</td>
<td>15.79±2.59</td>
</tr>
<tr>
<td>Lateral ventricle volume, mean±SD</td>
<td>26962.6±14951.77</td>
</tr>
<tr>
<td>Hippocampal volume, mean±SD</td>
<td>7564.43±1019.06</td>
</tr>
<tr>
<td>APOE ε4 carrier, n (%)</td>
<td>187 (36.1)</td>
</tr>
<tr>
<td>CDR&gt;0, n (%)</td>
<td>78 (15.06)</td>
</tr>
</tbody>
</table>

Figure 1: Scatterplots showing associations of the lateral ventricle volume with CDR and hippocampal volume

**Conclusions:** Larger baseline lateral ventricles volumes were associated with smaller baseline hippocampal volumes and worse baseline clinical dementia scores in an AD cohort. In addition, increased rates in enlargement of lateral ventricles volumes were association with increased atrophy rates of the hippocampus and worse baseline clinical dementia scores. Baseline and longitudinal lateral ventricle volumes could potentially be used to stratify risk for AD.
Poster No 2302

Volumetric changes in temporal regions associated with late post-traumatic seizures

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Introduction: Traumatic brain injury (TBI) is a major cause of death and disability worldwide¹. TBI-induced symptoms may last for years, reducing patients’ quality of life and posing a financial burden. Up to 50% of TBI patients may develop a seizure more than one week after injury, classified as a late post-traumatic seizure (late-PTS)². Currently, there are no valid clinical biomarkers for late-PTS, making the diagnosis and treatment a major challenge. In recent years magnetic resonance imaging (MRI) techniques have been used to probe brain structural and functional effects of TBI and PTS³. Previous studies have associated structural abnormalities in the temporal and hippocampal regions with the probability of developing late-PTS after TBI⁴. However, the relationship between cortical structural abnormalities and lesion volume is not fully understood. Accounting for lesion volume is crucial given the heterogeneity of TBI, as it ensures a more accurate interpretation of structural alterations associated with late-PTS. This work is part of the Epilepsy Bioinformatics Study for Antiepileptogenic Therapy (EpiBioS4Rx), a project designed to facilitate the development of antiepileptogenic therapies⁵. We aim to identify volumetric changes in temporal and hippocampal regions associated with the development of late-PTS among TBI patients while accounting for the potential confounding effect of lesion volumes.

Methods: A subset of 68 TBI patients, 50 patients with non-late-PTS (PTS-) and 18 patients with late-PTS (PTS+) from EpiBioS4Rx were used. T1-weighted images were acquired with the EpiBioS4Rx protocol⁶. Preprocessing and morphometric analysis were conducted using FreeSurfer, and volumetric measures from 65 cortical regions were extracted using the Desikan-Killiany atlas⁷. Manual lesion segmentation was performed using ITK-SNAP to compute the total lesion pathological volume⁸. Twelve temporal and hippocampal regions were chosen as primary predictors of interest. A logistic regression model was used to assess the relationship between the predictor variables and the likelihood of late-PTS, while adjusting for the effects of lesion edema volume and lesion core volume using R and glmnet package⁹. The level of significance was set at α=0.05; values less than this threshold were considered statistically significant.

Results: We employed a logistic regression model to investigate the relationship between various hippocampal and temporal regions and the probability of late-PTS, while controlling for the effects of lesion volume characteristics. Increases in the right inferior temporal volume were associated with decreased odds of late-PTS (β=−6.992×10⁻⁴, p=0.0381), while increases in the left parahippocampal volume were associated with increased odds of late-PTS (β=2.150×10⁻³, p=0.0384) [Figure 1]. The other regions were not found to be statistically significant predictors of late-PTS.
ABSTRACTS

Conclusions: Our findings suggest a region-specific association between cortical brain volumes and the likelihood of developing late-PTS after TBI when controlling for lesion volume characteristics, such as edema and core volume. Specifically, decreased volume in the right inferior temporal region and increased volume in the left parahippocampal region is associated with late-PTS. Structural alterations in hippocampal and temporal regions have previously been implicated in PTS and epilepsy cohorts. By controlling for lesion volume characteristics, we accounted for the potential confounding effects of lesion volumes on the relationship between cortical brain volumes in temporal and hippocampal regions and late-PTS. Volumetric alterations in these regions could serve as potential clinical biomarkers for late-PTS. Future studies with larger cohorts are needed to further understand the interaction of lesion and cortical volume and the influence of lesion location in the development of late-PTS.

References
Differences in morphometricity from voxel-wise and vertex-wise processing of T1w brain images

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Introduction: T1w brain MRI images provide a detailed mapping of the grey-matter structure and can be processed using different imaging software. Currently, there are no guidelines to select an image processing pipeline, and there is a growing concern that the choice of image processing could introduce a significant variability in brain representation contributing to the reproducibility crisis in neuroimaging. To progress our understanding of the effect of brain MRI processing on results, we conducted analyses utilizing five high-dimensional representations (voxel-based or vertices-based) of the grey-matter, to contrast their sensitivity to confounders and their ability to capture traits/disorders of interest.

Methods: We studied 42,272 imaged participants from the UKBiobank, divided into a discovery and replication sample, based on their assessment center. We processed all images with five different standard processing. First, FSLANAT and FSLVBM, both FSL-based processing¹ that give slightly different measurements of grey-matter density². Then, SPM-based processing are implemented in the ENIGMA CAT12 toolbox³, outputting surface-based (CAT12-Surface, measuring cortical thickness) and volume-based representations (CAT12-Volume measuring grey-matter density). Lastly, FreeSurfer⁴ based processing offers surface-based representations of cortical grey-matter thickness (FreeSurfer thickness) as well as of cortical surface area, subcortical thickness and surface (FreeSurfer all modalities). We studied the association between grey-matter processing and 27 traits including 9 putative brain imaging confounders (e.g. head motion, position in scanner, time since first scan, and body size), demographics, as well as 18 traits of interest (e.g. cognition, education level, psychiatric domains or disease status). We used linear mixed models, implemented in an efficient C++ software that can deal with large dataset⁶, to estimate the percentage of trait variance captured by all vertices/voxels measurements, coined “morphometricity”⁷.

Results: We found that all the putative imaging confounders exhibited a large morphometricity (20-80% of variance accounted for). However, we noted differences between processing as CAT12-Surface was less impacted by confounders (morphometricity range 18%-38%), while FreeSurfer all modalities exhibited morphometricity between 38% and 62%. As for FSLANAT and FSLVBM, they exhibited the largest associations (range 48%-76%). For example, head motion (during rs-fMRI) exhibited a morphometricity of 20% with CAT12-Surface versus 53% for FSLANAT and FSLVBM. After controlling for all confounders and demographics, we detected significant morphometricity for most traits and processing but estimates varied between traits and processing. Overall, CAT12-Surface yielded the smallest associations with traits of interests (morphometricity in 0.5%-13%). In contrast, FreeSurfer all modalities (resp. FSLANAT and FSLVBM) yielded larger associations with traits of interest (in average 2.8 -resp.3.2- times larger than CAT12-Surface, and morphometricities estimates in [3%,35%]). We confirmed the robustness of our morphometricity estimates in the replication sample.

Conclusions: Our results reveal that the different grey-matter processing show different levels of contamination by imaging and body size confounders, which may guide developers of processing software to investigate and reduce the source of contamination. In addition, our results highlight that these confounders should be systematically included in grey-matter analyses of the UKB. Lastly, our results provide quantified guidance on which grey-matter processing capture the most information among traits of interests (e.g. cognition, education and clinical status). Thus, FSL-based and FreeSurfer (all measurements) appear to capture more information than the other processing, enabling to construct better predictors and more complete maps of trait-associated grey-matter regions.

References
Poster No 2304

**Revealing Fine-grained Genetically Informed Parcellation Maps of Neonatal Cerebral Cortex**

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**Introduction:** Genetic factors have been proven to be one of the major determinants in shaping the neonatal cerebral cortex (Huang et al., 2023; Jha et al., 2018). Prior research has demonstrated distinct genetic influences on the spatial patterns of cortical properties, like cortical thickness (CT) and surface area (SA) in neonates, leading to their unique genetically informed parcellation maps (Huang et al., 2023). However, these parcellation maps were derived with coarse scales and based on single cortical properties, making them unable to comprehensively characterize the fine-grained genetically regulated patterns of the neonatal cerebral cortex. To fill this knowledge gap, by combining genetic correlations from multiple cortical properties, i.e., CT and SA, we aimed to reveal a joint, fine-grained, genetically informed parcellation map of the neonatal cerebral cortex through a multi-view spectral clustering approach (Kumar et al., 2011).

**Methods:** T1-weighted and T2-weighted structural MR images from 202 same-sex twin neonates were adopted in this study (Jha et al., 2018). Cortical surfaces were reconstructed, aligned, and resampled using an infant-dedicated computational pipeline, iBEAT V2.0 (Li et al., 2014; Li et al., 2015; Li et al., 2019; Wang et al., 2018). After computing CT and SA, the genetic correlations of CT (SA) between any two cortical vertices were calculated using the standard bivariate ACE twin model (Neale and Cardon, 2013). Then, with the obtained genetic correlation matrices of CT and SA, we performed a multi-view spectral clustering method (Kumar et al., 2011) to group all cortical vertices into k distinct regions, with each region consisting of a group of vertices that are strongly genetically correlated. Finally, to assess the clustering performance and choose the appropriate region number, three criteria were employed, namely silhouette coefficients (Rousseeuw, 1987), adjusted Rand index (ARI) (Hubert and Arabie, 1985), and normalized mutual information (NMI) (Strehl and Ghosh, 2002). Higher values of these criteria generally indicate better clustering performance. Of note, the ground truth utilized in computing both ARI and NMI was obtained based on the intersection of prior genetic parcellation maps of neonatal CT and SA (Huang et al., 2023).

**Results:** Fig. 1 illustrates the evaluation results derived from the three criteria. As can be seen, the local maxima for all three criteria coincide at region numbers 35, 67, and 86. Considering the spatial distribution and hemispheric symmetry of parcellation maps, we chose 86 as the appropriate region number. Furthermore, to enhance the anatomical comparability of corresponding regions in both hemispheres, bilaterally symmetric regions were manually combined and assigned shared IDs. After the aforementioned processes, we obtained the final fine-grained, genetically informed parcellation maps of the neonatal cerebral cortex, with each hemisphere consisting of 36 regions. As depicted in Fig. 2, the parcellation maps exhibit bilaterally symmetric patterns and correspond well to structurally or functionally meaningful areas. Besides, in accordance with the numbers labeled on figure, the approximate names of these regions are shown below the parcellation maps.

![Fig. 1. Criteria for determining the appropriate region number k. Silhouette: Silhouette coefficients; ARI: adjusted Rand index; NMI: normalized mutual information.](image-url)
Fig. 2. Discovered fine-grained, genetically informed parcellation maps (36 regions) of the neonatal cerebral cortex based on multiple cortical properties.

**Conclusions:** Leveraging neuroimages of neonatal twins, for the first time, we revealed the fine-grained, genetically informed parcellation maps of the neonatal cerebral cortex based on multiple cortical properties, i.e., CT and SA. The discovered parcellation maps comprehensively reflect genetically regulated detailed patterns of the neonatal cerebral cortex and are structurally and functionally meaningful.

**References**

**Poster No 2305**

**R2*, R1, and proton density age variations in subcortical structures in young adults at 7T**

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**Introduction:** Ultra-high field (UHF) MRI and its ability to provide high resolution data is progressively entering the clinical application stage and provides promising advances for brain imaging. Small subcortical structures can now be appropriately imaged in hope of mapping their function in healthy population, and their role in neurodegenerative disorders\(^1,2\). UHF MRI comes, however, with altered contrast, instrumental biases, and still lacks established imaging protocols. Quantitative MRI (qMRI) has the potential to mitigate these issues via estimating parameters related to the biophysical properties of tissues (relaxation rates R1, R2, and R2*, proton density, magnetization transfer etc.) and using calibration maps to correct for the protocol- and scanner-dependency. The critical issues for qMRI are currently the reproducibility, the incoherence in parameter mapping approaches, and the consequential lack of consensus on normal values of tissue parameters. The latter presents an aggravating issue for possible disorder diagnostics, when inter-individual\(^3\) and inter-site differences are poorly accounted for. We present a preliminary evaluation of variation of a number of qMRI parameters with age within a sample of young and healthy volunteers for a multiparameter mapping (MPM) qMRI protocol at 7T.

**Methods:** 21 healthy volunteers (4 males) with age ranging from 18 to 29y (median of 21) underwent the scanning at 7T Terra MRI (Siemens Healthineers, Erlangen, Germany) with a 1-Tx/32-Rx head coil (Nova Medical, Wilmington, MA, USA). The MPM protocol\(^4\) comprised three (T1-weighted, PD-weighted, MT-weighted) whole-brain 3D FLASH-based multi-echo sequences with similar isotropic resolution of 0.6 mm (TR 19.5 ms, FA PDw/MTw/T1w 5/5/20°, six equispaced echoes with TE ranging from 2.3 to 14.2 ms for PDw and T1w and 4 equispaced echoes for MTw with TE ranging from 2.3 to 9.44, GRAPPA with acceleration factor R=2 in each in the two phase encoding directions, and B1 mapping for transmit field correction\(^5\). The images were processed with the open source hMRI toolbox (hMRI.info) v.0.5.0\(^6\), yielding R2*, PD and R1 maps. Subcortical structures were automatically parcellated by Multi-contrast Anatomical Subcortical Structures Parcellation (MASSP) using all three parametric maps as input\(^7\). Median values for each of the parameters were extracted for the 27 subcortical structures with ventricles excluded from further analysis. A linear model was built for each of the median value sets with age, BMI and sex being the regressors. Each of the qMRI parameters was treated as a distinct measurement and multiple comparison correction was applied separately to each parametric map. The linear models with p-values for age lower than 0.05 (false discovery rate-corrected) were deemed significant.

**Results:** High quality, 0.6 mm resolution, co-aligned maps of qMRI parameters R2*, PD, R1 were obtained in all participants. The resolution of the parametric maps and the contrast in cortical and subcortical anatomical structures allowed MASSP parcellations of subcortical structures across all 21 participants (e.g., Figure 1). The age dependency analysis showed no significant dependency in R1 versus age, the fornix showed significant (p<0.0004) proton density increase with age, while bilateral striatum (left: p<0.003 and right: p<0.0006) as well as the right subthalamic nucleus (p<0.0008) showed R2* increase with age (Figure 2).

**Conclusions:** Despite the limited age-range and size of our sample\(^8\), we provide a set of values that show age-variation in healthy young adults. The detected variations in R2* can reflect age-related iron accumulation in the subcortical structures. The proton density dependency increase in the fornix is yet to be explained, as previous studies show no changes in proton density for young adults\(^9\). This analysis will be complemented by a sample of older individuals allowing to assess if the detected age-related variations are also present over a larger age-range.
Reducing motion artefact in high resolution 7T scans using a new head stabilization ‘MinMo’ device

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Introduction: High-resolution quantitative brain MRI is important for neuroanatomical research and its alteration in pathology. Both long scan durations and ultra-high field facilitate its acquisition, but they increase scan sensitivity to motion causing visible artefacts. Many methods reducing the impact of motion have been proposed, however at high field, motion remains a challenging problem due to interactions with the B0 field. We therefore aimed to limit the occurrence of motion, thereby reducing motion artefacts, during long-duration high resolution scans using a head stabilisation device called the MinMo (Fig 1). This was tested using long (10min) and very long (20min) scan durations using (A) linear and (B) random-checkered DISORDER sampling patterns respectively, the latter to enhance motion sensitivity. Our main aim was to evaluate the effect of the MinMo on image quality visually and quantitatively using normalised gradient squared (NGS) within the brain.

Methods: Fig. 1(a) shows the schematic diagram of the unloaded MinMo device with components of the head frame labelled on it for the closed configuration. Data acquisition: To determine whether the MinMo effectively reduced motion artefact, we obtained whole-brain data at resolution 0.6mm3 using an optimized multi-echo GRE (MEGRE) protocol with TR=30ms. Data was acquired in 5 healthy volunteer (HV) subjects. For each HV, 2 sets of 2 MEGRE scans were obtained. The overall acquisition scheme is shown in Fig.1(b). For one of the sets, the HV was loaded in the MinMo device, and for the other set, conventional foam pads following standard radiographer practice were used. In each set, one long scan was acquired with linear cartesian sampling IPAT=2x2, time of acquisition Tacq=10:40[min:s], and one, longer scan was acquired with random-checkerred DISORDER sampling pattern in the phase-encoding direction, IPAT=2x2, phase/slice oversampling=0.44/0.41 with Tacq=21:30[min:s]. The HVs were asked to lie still and were all accustomed to volunteer for MR research studies. Reference low-resolution (6mm3 iso) fully sampled scans were acquired each time the HV was loaded/unloaded in the device and were used in the reconstruction step to compute the coil sensitivity profiles using ESPIRIT. All acquisitions were done on the 7T scanner (MAGNETOM Terra, Siemens Healthcare) 32ch receiver, 8ch PTx. Reconstructions were done on down-sampled data (1mm3) for all HVs using the conjugate-gradient SENSE method. Normalised gradient squared, one of the metrics with the closest correspondence to visual image quality assessment, within whole brain extracted volumes was calculated. Image quality was compared between the MinMo Off and MinMo On cases for both the long-duration scans. MATLAB2023b was used for all reconstructions and analysis.
**Results:** Fig. 2(A) and (B) shows representative zoomed-in images for the 5 HVs reconstructed for the long scan and the very long scan with MinMo Off and On. Fig. 2(C) and Fig2(D) shows the bar plots for the NGS values calculated on the brain volumes shown in Fig. 2(A) and (B) respectively. For most cases, using MinMo improved the image quality (given by increase in NGS). The p-value for NGS done using a paired t-test between MinMo On and Off cases was reported to be 0.0042 (significant).

**Conclusions:** Preliminary investigation suggests that using the MinMo device improved image quality (increased NGS) in compliant subjects during most of the long duration (10-20 minutes) scans obtained. We used a 10-minute scan duration as it is a typical duration used commonly in MPM studies. The ~20min scan was obtained aiming to maximise motion sensitivity owing to its long duration as well as motion sensitised phase encoding ordering scheme. Motion correction techniques such as aligned-SENSE can be used to aid motion correction but were not yet unexplored.
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Acknowledgements
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Poster No 2307
Brain-age in ultra-low-field MRI compared to high-field MRI
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Introduction: Recent advancements in portable ultra-low-field (ULF) MRI systems, defined as 50-100mT, provide an opportunity for broader neuroimaging applications, including in low and middle-income countries. These systems promise lower scanning costs and wider global adoption, addressing the limitations of high cost and infrastructural requirements of traditional MRI systems. This study assesses the accuracy of brain-age predictions from ULF MRI compared to high-field (HF) 3T MRI. Brain-age is an estimate of age derived from a model trained to predict age from neuroimaging features in a cohort of healthy adults. This cohort establishes a norm for age prediction and thus, brain-age can serve as an index of neurobiological health (Cole & Franke, 2017).

Methods: Twenty-three healthy adults (mean age (SD) = 45.1 (15.3) years, range = 21.0-69.0 years; 12 males) were each scanned using a 3T MRI HF scanner (T1 MPRAGE 1 mm isotropic) and two identical Hyperfine Swoop ULF scanners at 64mT (three orthogonal T1 acquisitions with high-resolution in the Axial / Coronal / Sagittal plane; 1.6 x 1.6 x 5 mm). The data were acquired by the Department of Neuroimaging at King’s College London and Guy’s and St. Thomas’ Hospital, London. For further details on all authors involved in data acquisition, refer to OHBM abstract ‘Portable ultra-low-field brain MRI: test-retest reliability and correspondence to high-field MRI’. Images from the ULF scanners were linearly combined into a single T1 scan using multi-resolution registration (MRR; Deoni et al., 2022). Brain-age was then estimated for each MRR scan using the brainageR model, trained to predict age from an independent set of 3377 HF T1-weighted MRI scans of healthy adults across different sites (www.github.com/james-cole/brainageR).

Results: The HF scans demonstrated a strong correlation between brain-age and actual age (r = 0.79, R² = 0.02, MAE = 12.44). Conversely, the ULF scanners showed a weaker correlation: ULF1 (r = 0.33, R² = 0.08, MAE = 12.88) and ULF2 (r = 0.38, R² = 0.12, MAE = 12.44). The intercorrelation results between high-field (HF) 3T MRI scans and two ultra-low field (ULF) MRI scanners, ULF1 and ULF2, yielded Pearson correlation coefficients of r = 0.44 for HF vs ULF1, r = 0.50 for HF vs ULF2, and r = 0.90 for ULF1 vs ULF2 (across site, test-retest reliability).

Figure 1 Scatter plots display the correlation between actual age and brain-age for three MRI scan types: HF, ULF1, and ULF2. Each plot provides Pearson’s r, R², Mean Absolute Error (MAE), and Mean Squared Error (MSE).

The red dotted line is the identity line which indicates perfect agreement between the plotted variables. ULF1 = Ultra-Low-Field scanner & site 1. ULF2 = Ultra-Low-Field scanner & site 2. HF = High-Field.
Conclusions: ULF MRI scanners, with their lower operational costs, broader reach to a wider section of the population and reduced infrastructural demands, offer a promising solution for expanding MRI accessibility, particularly in resource-limited settings. However, currently, they do not match the accuracy of HF 3T MRI in brain-age estimation. These discrepancies may largely stem from the generalisability limitations of the brainageR model. Indeed, the suboptimal brain-age estimates observed in the HF MRI data are likely to be amplified in the context of ULF data, considering brainageR was originally trained on HF data. The weak correlation between age and predicted age in ULF scans suggests a strong regression-to-the-mean effect. Additionally, although the lower signal-to-noise ratio inherent to ULF imaging could be a factor, the good correspondence in grey matter volume estimates between HF and ULF (unpublished data) suggests it may not be the primary issue affecting brain-age accuracy. Notably, the intercorrelation between the brain-age estimates from the two ULF scanners was high suggesting high between-scanner test-retest reliability, despite the lower correlation with the HF estimates. Advancements such as super-resolution optimisation, inclusion of ULF T2 sequences, application of other brain-age models and use of transfer learning for dataset calibration could potentially mitigate this effect and improve the utility of ULF MRI for brain health assessments. These implementations are work-in-progress.

References

Poster No 2308
Changes in estimated total intracranial volume with age across 6 different datasets
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¹Universidad de Valladolid, Valladolid, Valladolid, ²Hospital Clínico Universitario de Valladolid, Valladolid, Valladolid

Introduction: The Estimated Total Intracranial Volume (eTIV) is a measure of the total volume inside the skull, encompassing the brain, cerebrospinal fluid (CSF) and other intracranial structures. eTIV can be estimated from neuroimaging in number of ways. Freesurfer, for instance, uses a registration process to a standard space and computes the eTIV from the determinant of the transformation matrix¹. Apart from using eTIV as a normalization factor in order to account for individual variations in head size when studying brain structures, eTIV can be employed as a biomarker on its own. In schizophrenia, for instance, several studies have found decreases in eTIV in patients with respect to controls²,³,⁴, with reductions ranging from 0.13% to 4%. If eTIV is to be employed as a neuroimaging biomarker, a detailed understanding of its aging trajectory is needed. Several cross-sectional studies have analyzed eTIV changes as a function of age⁵,⁶,⁷. Some of them identified age-related eTIV decreases at least from the 4th decade of life ranging from 0.1%/year to 0.29%/year, while others reported no changes. Assuming that intracranial volume must remain essentially stable because of biological reasons, those changes, when found, were interpreted as a consequence of generational growth in some populations. Finally, a few other studies have employed longitudinal data to estimate aging-related trajectories of eTIV. In⁸, a small but detectable nonlinear aging pattern was detected in eTIV (with an average rate of change of 0.03%/year at age 20 and -0.09%/year at age 55). In this abstract we aim
at describing age-related changes in eTIV, as measured using Fastsurfer, across several neuroimaging datasets. Secondarily, assuming that these changes are primarily due to generational growth, we model the implications of such changes on neuroimaging studies focusing on eTIV as a biomarker.

**Methods:** 3602 subjects from 6 different publicly available datasets were included (see Figure 1). From the T1w MRI images, Fastsurfer was employed to extract morphometric features, and eTIV was selected among them. Fastsurfer employs Deep Learning to perform brain segmentation based on the Desikan-Killiany atlas. Separate linear regression models were fitted for each dataset, considering age and eTIV independently for female and male subjects. If eTIV varies strongly with age in a certain population, this will cause a dispersion in the eTIV values of the subjects of that cohort that in principle could threaten the ability of the study to find significant differences in eTIV, even if they do exist. In order to model this effect, we assumed an age range of 20-70 years. Next, we considered different scenarios regarding the difference in eTIV between diagnostic groups (2%, 2.5% and 3%). For each scenario, 10,000 simulations were run, where in each simulation 200 synthetic eTIV values were generated, 100 for each diagnostic group. Finally, we computed the median p-value obtained from performing t-tests on the eTIV values for both diagnostic groups.

**Results:** Figure 1 represents the values of eTIV as a function of age for the different datasets, together with the fitted linear regression models. Most (but not all) datasets showed a significant effect of age on eTIV, with changes ranging from -0.02%/year to -0.22%/year. Changes were more pronounced for females than for males. Figure 2 shows the evolution of the median p-value for our simulations as a function of the rate of change of eTIV vs age. Although in principle increases in the slope could hamper the ability to detect significant changes between diagnostic groups, for the values encountered in our results over the different datasets or reported in the literature (slope < 0.30%/year) this effect is almost negligible.

<table>
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<tr>
<th>Dataset</th>
<th>N</th>
<th>Mean age ± std</th>
<th>Slope (%/year)</th>
<th>p-value</th>
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<tr>
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<td>331</td>
<td>45.9 ± 18.8</td>
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Figure 1: Demographic information and linear regression results from each dataset: IXI (Information eXtraction from images dataset), CoRR (Consortium for Reliability and Reproducibility dataset), NeuroCog (Neurocognitive aging data release), OASIS-1 (only healthy subjects were included), SALD (Southwest University Adult Lifespan Dataset), NKI (Nathan Kline Institute/Rockland Sample). Male subjects are marked in blue, and female subjects are marked in red.
Conclusions: Our results suggest that changes of eTIV with age in a particular population are not a relevant confounding factor in studies using eTIV as a biomarker.

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Poster No 2309

Anatomical definition of hMT+ using quantitative R1 mapping

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Introduction: Human middle temporal complex (hMT+) is traditionally identified functionally, as the cortical area that responds more strongly to visual motion versus static stimuli. In recent years, quantitative R1 mapping has emerged as a valuable tool for measuring the local myeloarchitecture of the human brain in vivo. hMT+ has higher myelination than neighboring cortical areas (Bridge et al., 2014), and previous studies using a group-averaged approach have found that group-averaged functional hMT+, as defined by retinotopy, overlaps with a region of high myelination (Sereno et al., 2013). Here, we examined whether the location of hMT+ based on quantitative mapping is consistent with the functional location, within individuals.

Methods: Structural and functional MRI images were collected in 8 neurotypical observers (ages 33–72, 4 females). Quantitative structural mapping was performed by acquiring PDw, MTw, and T1w images using a multi-echo 3D FLASH pulse sequence. R1 maps were derived using the hMRI toolbox (Tabelow et al., 2019). Vertex-wise residuals from a linear regression, with local curvature as a predictor for R1 values sampled at 50% cortical depth, were used as the final estimates of the R1 map. Functional characterization of hMT+ was based on standard T2* EPI scans. Participants viewed alternating blocks of moving...
and static dots within an 8 deg radius circular aperture while fixating on a cross at the center of the screen. The BOLD activity for moving and static blocks were contrasted to find a region selectively responsive to visual motion. The Dice coefficient was used to quantify the overlap between anatomical and functional definitions of hMT+ for each hemisphere of each individual. Bootstrapping combined with a Receiver Operating Characteristic (ROC) analysis was used to examine whether the spatial overlap between the two definitions of hMT+ is greater within than between individuals.

**Results:** In all participants, quantitative R1 mapping identified a highly myelinated area in the lateral occipital cortex, which aligned with regions identified as MT/MST in the HCP-MMP1 atlas. There was a strong overlap between group-averaged anatomical and functional hMT+ (Dice coefficient of 0.81 on the left and 0.58 on the right hemisphere; Figure 1). There was also considerable overlap between the anatomical and functional definitions of hMT+ within individuals (left hemisphere Dice coefficient mean = 0.6, SD = 0.16; right hemisphere mean = 0.42, SD = 0.25; Figure 2A). An ROC analysis comparing the cumulative distribution function of bootstrapped Dice coefficients within and across individuals suggested that the two definitions of hMT+ were more consistent within than between individuals (Figures 2B &C). The area under the ROC curve (AUC, an aggregate measure of whether overlap was higher within than between individuals) was 0.94 for the left hemisphere and 0.74 for the right hemisphere.

**Conclusions:** The anatomical delineation of hMT+ using quantitative myelination mapping shows substantial overlap with regions functionally responsive to visual motion within individuals. Thus, quantitative mapping provides a potential method for identifying hMT+ in populations where the functional localization of hMT+ might pose practical challenges (e.g., infants or individuals with vision loss).

**References**
**Poster No 2310**

**Childhood maltreatment influences brain structure through immune, metabolic and psychosocial factors**

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**Introduction:** Childhood maltreatment (CM) has long term effects on risk for mental and physical ill-health (Danese et al., 2009; Nelson et al., 2020). Protracted psychiatric susceptibility might reflect CM’s effects on adult brain structure, perhaps indirectly mediated by its effects on adult metabolic (Danese & Tan, 2014), immune (Danese et al., 2007), and psychosocial systems (Edalati & Nicholls, 2019). Indexing the latter three variables via body mass index (BMI), C-reactive protein (CRP) and rates of adult trauma (AT) respectively, we tested three hypotheses: (H1) CM has direct or indirect effects on AT, BMI and CRP; (H2) adult trauma, BMI and CRP are all independently related to adult brain structure; and (H3) effects of CM on adult brain structure are mediated by its effects on adult trauma, BMI and CRP.

**Methods:** We used measurements of CM, AT, BMI and CRP from N=136,625 participants in UK Biobank to test H1 by path analysis of direct and indirect causal effects of childhood maltreatment on adult variables. For a subsample of N=21,738 participants with T1-weighted MRI data, we used regression and path analysis to test the effects of adult variables (H2) and childhood maltreatment (H3) on cortical thickness of 180 areas and volume of 7 subcortical nuclei, controlling for multiple comparisons with FDR = 5%.

**Results:** CM had significant direct effects on BMI and AT, and significant indirect (but not direct) effects on CRP through AT and BMI (Fig 1A). H2: Greater CRP and BMI were both related to a spatially convergent pattern of cortical effects (Spearman’s R=0.87, Fig 1B & 1C) characterized by fronto-occipital increases and temporo-parietal reductions in thickness. AT had little to no cortical effects but was related to decreases across 6 subcortical structures. BMI was related to volumetric increases in all limbic structures. H3: Two nested path models considering indirect effects of CM on brain structure through its direct effects on AT, BMI and indirect effects on CRP each had good fit across two disjoint subsets of regions (Fig 1D-G).

**Conclusions:** Human brain cortical structure was significantly associated with adult immune (CRP) and metabolic (BMI) status, and subcortically with metabolic (BMI) and psychosocial (AT) status, which in turn were partly predicted by prior exposure to childhood maltreatment. Long term effects of childhood adversity on adult brain structure may be mediated indirectly via increased risk of adult trauma, obesity or inflammation.
A within-subject quantitative comparison of images from Siemens VE11C and XA30 scanners

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Introduction: In large human imaging studies with thousands of subjects, longitudinal studies and multi-site trials, both MR scanner stability and consistency of protocol implementation is vital. The software transition on Siemens Magnetom scanners from VE11C, that has been in use since 2016, to the new XA30 platform represents one of the largest changes to the MRI scanner software interface and image handling experienced by the neuroimaging community in over 15 years. Large multi-site studies such as ABCD, AABC – the continuation of HCP-Aging, and SSBC, are currently grappling with this change. Of particular concern is the impact of changes in software level, and inherent image reconstruction processes on automated MRI-derived measurements of in-vivo human brain volumes from anatomical scans. A few studies have previously probed the repeatability of these measurements, including effects of changes such as scanner vendor, software version, field strength and gradient strength. In this study, we trialed two short neuroimaging protocols on a small number of subjects scanned on scanners using VE11C and XA30 software with minimal time interval between the scan sessions.

Methods: All images were acquired using 3T Siemens MAGNETOM Prismafit MRI scanners (Siemens Healthineers; Erlangen, Germany). In trial one, one subject (F, 30yo) was scanned at McLean Hospital using a scanner running XA30, and the study was repeated at Harvard University the following day, where the scanner used VE11C. 0.8mm isotropic T1w and T2w images were acquired, and a resting-state BOLD scan was acquired at 2.0 mm isotropic resolution, using the multiband-EPI sequences from University of Minnesota. The protocol was replicated exactly on the two scanners. In trial two, two subjects (F, avg 30.0 yo) were scanned at Massachusetts General Hospital using a scanner running XA30, and the sessions were repeated at Harvard University the 4-6 days later, where the scanner used VE11C. These sessions included 1.0mm isotropic T1w and T2w scans with prospective motion correction, a resting-state BOLD scan with 2.4 mm isotropic resolution, and a multi-shell diffusion scan at 1.8 mm isotropic resolution and 176 directions. All structural images were processed using MRIQC for estimates of SNR and Image Smoothness, and through FreeSurfer for estimates of subcortical volume and regional cortical thickness. BOLD and diffusion scans were assessed across the software platforms via quantitative metrics from MRIQC or FSL's EddyQuad.

Results: Figures 1 and 2 show results from the morphometric analysis of the T1w images from one of the two subjects acquired in the second trial. Figure 1 shows the pial and white-matter surface tracings generated from the robust-registered T1w images acquired using VE11C and XA30 software. The tracings virtually overlay one another. In Figure 2, the correlation of all cortical thickness regions obtained from Freesurfer, and volume measures of sub-cortical structures are shown, for a test-re-test repeatability assessment on the VE11C scanner, and the between-software agreement. The results are virtually identical. Similar results were obtained from the second subject, and the single subject in the initial trial using the 0.8 mm non-motion-corrected T1w protocol. Quantitative analysis of BOLD scans are confounded by effects of subject motion that can vary from session to session even within subjects. While variations were observed in quantitative parameters such as image SNR, image smoothness (FWHM), tSNR and DVARS, the observed between-subject variability was greater than the variability seen across sessions within an individual.
Conclusions: While a very limited study with a small number of subjects, we show that there may be less reason for concern over impacts from the Siemens XA30 software change on quantitative image analysis and metrics than has often been seen in the past as a result of scanner software or hardware changes.

References
BMI & Waist-to-Hip Ratio: Gray Matter Associations in 22,075 Healthy Individuals from the UK Biobank

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Introduction: Higher body mass index (BMI) and waist-to-hip ratio (WHR) are markers of obesity, and represent important cardiovascular-metabolic risk factors. Prior work has reported associations between lower brain volume and obesity markers such as BMI (Raji et al., 2010) and blood plasma leptin levels (Rajagopalan et al., 2013). Specifically, higher BMI and WHR have been linked to brain structural alterations including lower gray matter volume in numerous subcortical nuclei (caudate, putamen, pallidum, and nucleus accumbens;; Hamer & Batty, 2019; Dekkers et al., 2019; Pflanz et al., 2022). Here, we carried out whole-brain analyses using voxel-based morphometry (VBM) to map brain signatures of BMI and WHR in a large population-based sample of healthy adults.

Methods: The Computational Anatomy Toolbox (CAT12; Gaser et al., 2023) was used to perform a large-scale voxelwise segmentation of 3D T1-weighted brain MRI data from 27,075 participants (52.5% female; 63.6 (7.5SD) years old) from the UK Biobank (UKBB; Table 1). All participants were assessed for BMI, body size measurements (to calculate WHR), systolic & diastolic blood pressure (to calculate mean arterial pressure), and pulse wave arterial stiffness, at the time of scan. Subjects without these parameters, or with neurological or neuropsychiatric diagnoses, were excluded. Within this subset of healthy UKBB participants, effects of BMI on gray matter volume were tested using a whole-brain voxelwise VBM analysis adjusting for mean arterial blood pressure (MAP), pulse wave arterial stiffness (PWAS), age, sex, intracranial volume, genetic ancestry and education.

Results: Significant gray matter volume alterations were mapped throughout the brain after correcting for multiple comparisons by controlling the false discovery rate at 5%. Voxel-wise brain analyses demonstrated patterns of significantly lower gray matter volumes (GMV) associated with BMI (standard-FDR critical P-value=0.02; q=0.05), after covarying for age, sex, education, ancestry, mean arterial pressure, pulse wave arterial stiffness and intracranial volumes (Figure 1). Specifically, extensive areas of lower gray matter volume were noted predominantly in the bilateral basal ganglia (caudate, putamen, globus pallidum, nucleus accumbens), insula, opercular cortex, diffuse temporal cortex, diffuse temporal cortex, as well as cerebellum. Similar association patterns were noted for the voxel-wise brain analyses of GMV and waist-to-hip ratio (standard-FDR critical P-value=0.02; q=0.05). Pearson correlations were as follows: BMI:WHR (r=.42), BMI:PWAS (r=.12), BMI:MAP (r=.27), WHR:PWAS (r=.21), WHR:MAP (r=.26), PWAS:MAP (r=.13).
Conclusions: Building on prior findings in a large population sample, we found that markers for both overall obesity and central obesity are both associated with neurostructural alterations in gray matter architecture in healthy adults, even after adjusting for effects of blood pressure and age. Higher BMI and WHR were associated with significantly lower gray matter volume in brain regions involved in sensorimotor processing, motor coordination, and balance.

References

Poster No 2313
Unlocking the Power of Distributed Learning for MeshNet
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Introduction: Decentralised learning, unlike the centralised approach, grapples with private data distributed across various autonomous sites rather than a singular server. This paradigm shift offers heightened privacy and scalability by harnessing multiple device capabilities, particularly crucial in sensitive sectors like healthcare and neuroimaging. However, challenges arise due to increased message sizes, exacerbated by bandwidth limitations, causing latency spikes in large model exchanges. This predicament intensifies for deep learning models, where greater accuracy demands larger parameter reconciliation across sites. Conventional remedies like sparsity, distillation, and quantization often sacrifice accuracy for reduced parameter sizes. In our study, we employed MeshNet figure 1a, an full brain volumetric segmentation5 model, in its original form without any special compression but controlling number of channels, establishing a distributed learning system. Encouragingly, our outcomes exhibit strides in achieving balanced node training, ensuring accuracy, scalability, and resource optimization.

Methods: Centralised Gradient Aggregation fig 2a is a groundbreaking approach in the distributed learning landscape, overcoming challenges inherent in decentralised data processing across multiple nodes. Focused on data privacy and computational efficiency, this method transforms the paradigm by enabling nodes to process local data batches, generating
gradients that encapsulate unique insights. These gradients converge at a centralised hub, creating a comprehensive model performance overview. This collective narrative guides iterative model updates, fostering collaboration irrespective of geographical or dataset disparities. The synchronised refinement cycle allows nodes to learn not just from local data but from the distributed network’s collective wisdom, enhancing individual models and promoting shared learning for holistic progress. The incorporation of Coinstac, alongside the integration of WADB for metric logging, constitutes a pivotal advancement in optimising distributed training environments. Coinstac streamlines communication, reducing overhead, and significantly enhancing training efficiency across multiple nodes. This tool democratises the adoption of distributed training by simplifying fault tolerance and widening accessibility. The integration of WADB for metric fig 2b logging provides a comprehensive monitoring system, ensuring precise tracking of training progress and facilitating informed decision-making. This standardised methodology optimises training efficiency, democratising networked nodes utilisation and shaping a more inclusive and robust machine learning landscape across diverse domains.

**Results:** Our experiments, conducted in the Coinstac decentralised simulator\textsuperscript{10,11} figure 1a, ensure equitable task distribution among nodes, fostering balanced contributions to model optimization. Logging batch-specific metrics for each node provides valuable insights, enhancing overall training efficiency and node-specific dynamics. Figure 2 Table 1 compares Cross-Entropy Loss for standard and decentralised training of MeshNet and CNN models on the Cifar10 dataset, revealing their convergence and accuracy across epochs, showcasing the effectiveness of our decentralised approach in optimising model performance.

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**Figure 1:** The architectural diagram outlines MeshNet’s neural structure, while logged metrics track training progress across various batch levels.
Figure 2: The diagram showcases the decentralised learning framework, delineating nodes interconnected for collaborative training.

**Conclusions:** Our progress in decentralised MeshNet learning signifies significant advancements in balanced node training. Collaborating with Coinstac amplifies our approach, enriching distributed learning strategies. This ongoing project carries immense potential to revolutionise collaborative learning paradigms, guaranteeing both efficiency and scalability in the future.

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Cortical folding and layering support local-to-global functional properties at 7T

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Introduction: Brain function is coordinated and can be abstracted as networks whose activity is overlaid onto the cortical mantle with its organized folding patterns and layered microarchitecture. Previous investigations of structure-function coupling in the cortex revealed laminated microstructure and macroscopic geometry as constraints to global functional organization while heterogeneity within connected cortical regions, or network “nodes”, is crucial for local functional specification. Expanding and integrating these lines of evidence, we probed how cortical folding and layered microarchitecture support functional properties of single-vertex nodes at local, regional, and global levels.

Methods: Twelve healthy young adults (age 25±4.42; 50% females) with no history of psychiatric or neurological diagnoses underwent 7T MRI. Each participant completed two runs of quantitative T1-weighted scan (qT1, 0.5mm isotropic, 12m35s) followed by multi-echo resting-state fMRI (rs-fMRI; TR=1.69s; TE=10.8, 27.3, 43.8ms; 1.9mm isotropic; 5m39s). Images were preprocessed using micapipe v0.2.2. We assessed nodal functional properties on mean-centered timeseries via BOLD signal variability (local), regional homogeneity (ReHo; regional), and degree centrality (WDC; global) (Fig 1a). Folding was assessed at varying spatial scales with mean curvature at the finest scale, followed by sulcal depth potential and gyrification index at coarser scales (Fig 1b). Microstructural profiles were obtained using qT1 intensities sampled across cortical depths. We created histograms for qT1 intensities on vertex-wise cortical depth columns and examined the first three statistical moments (m1, m2, m3) (Fig 1c). All measures were computed in native surface and interpolated to fsLR-5k template for comparison. Product-moment correlation was calculated within and between participants (Fig 1) and between measures (Fig 2a) to assess reliability and spatial relationships, respectively. Multiple linear regression models were built to predict nodal function based on morphological and microstructural measures, and cross-validated using a distance-dependent approach. The significance of spatial correlation coefficients and linear model metrics was evaluated using spatial null models and Bonferroni-adjusted.

Results: Measures of nodal function, morphology and microstructure were reliable within participants across sessions (Fig 1, see caption for stats). Spatial correlation between measures highlighted moderate associations of nodal function with all statistical moments derived from microstructural profiles. Meanwhile, associations of local, regional, and global functional properties with curvature, depth and gyrification were graded, with measures of morphology taken at increasingly wide spatial scales.
spatial scales associated to dynamics assessed at the corresponding scales. A strong relationship between curvature and ReHo at the whole-brain level is consistent with coupling between sulcation and ReHo reported by\textsuperscript{10} (Fig 2a). Via multiple linear regression and dominance analysis, the relative contributions of morphology to nodal function reflected a local-to-global gradation, with morphology assessed at finer spatial scale contributing more to functional measures at a similar scale. The contributions of microstructure to nodal function were most important for BOLD variability and for ReHo. However, microstructural moments were overtaken by gyriﬁcation for predicting WDC. These patterns were replicated across sessions (Fig 2b, c, see caption for stats).

**Conclusions:** We leveraged the ﬁne spatial resolution of 7T MRI with multi-echo functional sequences to investigate cortical folding, microstructure, and nodal dynamics concomitantly. The tradeoﬀ between cortical folding and microstructure for predicting nodal dynamics at the vertex, community and network levels found here supports that constraints to local-to-global signal ﬂow are ingrained in both shape and substrate of the cortical mantle.

**References**

Regulation of Craving by Mindfulness Strategies in Cigarettes Smokers

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Introduction: Cue-induced craving which can be defined as an intense and acute desire (Tiffany & Wray, 2012). Research has firmly established the direct link between cue-induced craving and substance use (Kober & Mell, 2015). Mindfulness training (MT) has gained significant attention in recent years for its potential in alleviating cigarette cravings (Tapper, 2018). However, the mechanisms underlying its efficacy remain inadequately understood (Brewer et al., 2013). The present mechanistic experiment aims to investigate the impact of a mindfulness strategy in regulating cue-induced craving and smoking cue-reactivity in the brains of nicotine dependent smokers. We hypothesized that in comparison to a passive viewing condition, participants will experience reduced levels of craving when employing the mindfulness strategy and the activation of rewarded related brain regions like Ventral striatum (VS), insula, amygdala would be lower.

Methods: Twenty-nine smokers were recruited, who reported smoking more than 10 cigarettes per day and had at minimum of 2 years of smoking experience. Four participants were excluded due to equipment issues, one participant was excluded due to failure to respond to the ROC task, one participant was excluded due to large head motion. The final group consisted of 23 participants (all men) aged between 19 and 43 (M = 24.87 years; SD = 5.77). In the ROC task of fMRI scan, participants were instructed to employ two strategies when presented with a series of smoking-related cue images. Participants were instructed to apply a mindfulness technique when confronted with cue stimuli in the MINDFULNESS strategy and simply observe the images and passively consider their immediate feelings about the smoking image in the LOOK strategy. Then, participants proceeded to self-report their level of craving and provided corresponding ratings on a Likert-type five-point scale. Two experimental conditions were administered: MINDFULNESS-cigarette (mind-cigarette), LOOK-cigarette(look-cigarette) (Figure 1). The task fMRI data underwent several preprocessing steps, including slice timing, realign, spatial normalization, and smooth (FWHM= 5mm). Finite Impulse Response (FIR) model was used to obtain the series of activation maps. The time window of interest was defined as the onset of image cues. A total of 12 time points of activation maps of mind-cigarette, look-cigarette were obtained. We categorized the first five trials of each block of condition in the ROC task as the “Early Phase”, and the last five trials of each block as the “Late Phase” to explore whether there are fluctuations in craving scores over time.

Results: The results of 2 (condition: mind-cigarette and look-cigarette) × 2 (phase: early, late) repeated ANOVA showed there was a significant interaction of the craving scores between condition and phase. Post hoc comparison showed that the craving scores of late phase of look-cigarette was significantly higher than the craving scores of early phase of look-cigarette condition. The FIR results showed that significant main effects of conditions (mind-cigarette, look-cigarette) were mainly found at the bilateral insula, ventral striatum (VS) and amygdala, etc. The activations (β) in look-cigarette condition of these regions
were higher than it in mind-cigarette condition. A significant interaction of condition and phase were mainly found in the Ventromedial prefrontal cortex (vmPFC). Post hoc comparison showed that the activation of late phase in mind-cigarette was significantly higher than the activation of early phase in mind-cigarette condition (Figure 2).

Conclusions: The decreased scores of cravings and reduced activations in bilateral insula, VS, and amygdala suggest that mindfulness may effectively mitigate cue-induced craving and attenuate the activation of reward-related brain regions. The enhanced activation of vmPFC during mindfulness practice may indicate its potential to enhance self-awareness and regulate emotions.

References

Poster No 2316

An Approach for fMRI-Guided Targeted TMS on Stroke Rehabilitation

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Introduction: More than half of stroke patients have not recovered their hand function on the affected side at 3-6 months after the incident (Abo, et al., 2014). Promoting the recovery of hand function is one of the challenges in clinical rehabilitation. The effectiveness of repetitive Transcranial Magnetic Stimulation (rTMS) greatly varies across individuals (Du, et al., 2019; Meng, et al., 2020; Xiang, et al., 2019). The traditionally used target is a hotspot identified by a TMS-induced motor evoked potential (MEP), but it is challenging to identify such a hotspot in the affected hemisphere in patients undergoing post-stroke rTMS.
because of the inability to evoke MEP responses. Therefore, a mirror-point of the hotspot on the unaffected hemisphere is used as target, but this approach lacks a neuroscientific basis. Our prior research demonstrated that brain activation during a finger tapping task not only represents voluntary movements, but also is functionally specific. Finger tapping task exhibits a broad range of activity and intense functional connectivity (FC) with the motor cognition network (Wang, et al., 2020), and earlier studies reported strong FC between the activation of a finger tapping task in the bilateral motor cortex (Biswal, et al., 1995). This FC was shown to perform as well or better than task-based functional magnetic resonance imaging (fMRI) when localizing the representation area in patients with tumors in the sensorimotor cortex (Zhang, et al., 2009). On the basis of the aforementioned evidence and prior experimental data obtained by our research group, we established a robust methodology for identifying the therapeutic targets for stroke.

Methods: To accomplish this goal, we undertook the following steps: (1) performed task activation detection and functional connectivity at the group level to define the bilateral motor area in healthy participants; (2) validated the spatial relationships between task activation and contralateral functional connectivity peak voxels at the individual level, ensuring the accuracy and precision of our targets; (3) simulated application of both low-frequency and high-frequency rTMS to the activation and functional connectivity targets, based on an interhemispheric competition model, with the hypothesis that rTMS would lead to functional reorganization within brain regions implicated in voluntary movement; and (4) applied these targets to facilitate individualized clinical treatment for post-stroke patients, with a particular emphasis on the affected hemisphere.

Results: The cluster of bilateral hemisphere hand motor areas in group level were centered at X = −36, Y = −14, Z = 57, and X = 35, Y = −16, Z = 62. Paired t-tests showed that the amplitude of low frequency fluctuation (ALFF) and regional homogeneity (ReHo) values were significantly altered after simulating bilateral rTMS (GRF correction, voxel level p < 0.001, cluster level p < 0.05; Figure 1). The clinical assessments of all patients exhibited varying degrees of improvement. The imaging patterns of the rTMS modulatory effect (ALFF and ReHo) differed between patients in respect to brain regions, activity extents, and intensity (Figure 2). All motor-related brain regions (such as the basal ganglia, thalamus, cerebellum, and motor cortex) showed individual alterations after rTMS and the insular showed commonly modulatory effect.

Conclusions: Our methodology overcomes the challenge of precise target localization, especially on the affected hemisphere. The clinical assessments of all patients exhibited varying degrees of improvement, and the brain functions of all motor-related regions were modulated by rTMS, albeit with individual differences. The fMRI-guided-targets might be promising for post-stroke rTMS treatment and need further investigation.

Figure 1. ALFF and ReHo values were significantly altered after simulating bilateral rTMS (GRF correction, voxel level p < 0.001, cluster level p < 0.05).
Figure 2. The different patterns of imaging maps in patients. The maps were subjected to a threshold for each metric to depict the observed patterns, without undergoing statistical analysis.

References
**Poster No 2317**

**Precision individual difference with multi-echo functional MRI**

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**Introduction:** Depicting multifaced individual differences of spontaneous brain activity has become a central focus in the brain-imaging community, playing an essential role for understanding the human brain in health and disease (Dubois et al., 2016; Elliott et al., 2021; Raichle 2015; Xu et al., 2023). Estimates of individual differences are commonly contaminated by within-subject variation especially in fMRI, leading to unreliable findings (Elliott et al., 2021; Noble et al., 2019; Xing et al., 2018). Multi-echo fMRI (ME-fMRI) is potential for enhancing neural signals and removing non-neural signals relative to traditional sing-echo fMRI (SE-fMRI) (Kundu et al., 2012, 2013, 2017; Lynch et al., 2020; Posse et al., 1999; Power et al., 2018). However, the benefit of ME-fMRI for precision individual difference in spontaneous brain activity has not been systematically investigated yet, which is vital for both neuroscience and clinical application.

**Methods:** We explicitly identified the true individual difference (i.e., between-subject variation) and within-subject variation and comprehensively explored the reliability of ME-fMRI for mapping individual difference based on test-retest design. With both the short- and long-term test-retest dataset, we first detected within-subject difference, between-subject difference, and reliability of three fMRI intrinsic metrics (i.e., amplitude of low frequency fluctuation (ALFF), regional homogeneity (ReHo), and voxel-mirrored homotopic connectivity (VMHC)) across the whole-brain and seven subnetworks. Second, we explored the experimental implications of enhanced reliability on saving samples by investigating the interplay between reliability, sample size, and effect size. Then, we obtained the methodological implications of enhanced reliability by assessing the shortened scanning duration. Finally, we probed the benefit of enhanced reliability for validity improvement with a well-studied within-subject rFMRI design, i.e., the difference between statuses of eyes open and eyes close. To provide a benchmark for ME-fMRI, SE-fMRI dataset with almost the same scanning parameters except for TE was also acquired for both vertex-level and network-level analysis.

**Results:** For both short- and long-term test-retest design, ME-fMRI suppresses random and non-neural noise to smaller within-subject variability and enhances neural signal to larger between-subject variability across almost whole-brain, leading to reliable and precision individual differences for all the intrinsic metrics compared with SE-fMRI (Fig. 1 and Fig. 2a). Notably, the individual differences of auditory and somatosensory network were greatly underestimated in SE-fMRI. To achieve a certain reliability with ME-fMRI, the sample size and experimental costs can be reduced for 14%, 17%, and 29%, or the scan duration can be shortened for 54%, 42%, and 43% for ALFF, ReHo, and VMHC, respectively, relative to SE-fMRI. Furthermore, the validity to capture the individual difference between status of eyes open and eyes close are remarkably promoted with ME-fMRI for ALFF, ReHo, and VMHC (Fig. 2b).

![Fig.1 Comparison of reliability (ICC), between-subject variance (Vb), and with-subject variance (Vw) of ALFF, ReHo, and VMHC between SE- and ME-fMRI in short- (a) and long- (b) test-retest design.](image-url)
Fig. 2 Reliability enhancement by decreasing within-subject variance (Vw) and increasing between-subject variance (Vb) and promoted validity for differentiating eyes open and eyes close with ME-fMRI.

**Conclusions:** Our study comprehensively investigated the benefit of ME-fMRI for reliable individual difference by decreasing within-subject variability and increasing between-subject variability and explored its advantages on reducing sample size, shortening scan duration, and enhancing validity, which facilitates detailed characterization of individual brain organization and the translation of ME-fMRI to clinical applications.

**References**

**Poster No 2319**

**Predicting the epileptic seizure onset zone with brain-wide alterations of temporal dynamics in fMRI**

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**Introduction:** Epilepsy has been recognized as a network disease that can disturb brain regions beyond a focal seizure onset. Previous studies linked an altered autocorrelation function (ACF) of brain activation to disturbed brain dynamics in the seizure onset region (Nedic et al, 2015) and beyond (Xie et al, 2023). Here, we used preoperative resting-state functional magnetic resonance imaging (rs-fMRI) to quantify brain-wide ACF decay rates in medically refractory epilepsy patients with
medial temporal lobe seizure onset. We evaluated how brain dynamics may be disrupted due to the underlying disease, and determined the potential use of ACF decay rates to identify seizure onset zones (SOZ) to inform intervention strategies.

**Methods:** We studied rs-fMRI data from 15 patients with unilateral mesial temporal lobe epilepsy (TLE; 10 left) that was confirmed by intracranial stereo EEG. For each voxel, we established a feature vector characterizing the temporal dynamics based on different ACF decay rate measures (Watanabe et al, 2019; Raut et al, 2020; Ito et al, 2020). We utilized data from a group of 652 healthy controls (Cam-CAN; Shafto et al, 2014; Taylor et al, 2017) as a normative baseline, and, for each patient and voxel, quantified the deviation of the ACF decay rates as a timescale anomaly score (z-score based on the normative distribution). For each intracranial EEG electrode, we calculated the corresponding fMRI timescale anomalies and, using logistic regression, evaluated their predictive performance to classify electrodes that map the potential SOZ. Finally, we associated brain-wide timescale anomaly maps with outcome measures to examine the potential added value of preoperative rs-fMRI to guide neurosurgical intervention.

**Results:** Overall, we observed reduced ACF decay rates for electrodes that are located in brain regions associated with a seizure onset zone, suggesting a more constrained temporal dynamic. Brain regions that map to SOZ-related electrodes also show a reduced regional homogeneity, emphasizing disturbances in brain activity and functional connectivity. Importantly, in a leave-one-patient-out framework, we found that ACF decay rate measures were sensitive to focal alterations and predicted the electrodes identified as seizure onset well. In 13 out of the 15 patients, we observed a prediction performance of AUC > 0.7 and that was better than chance (prediction based on shuffled labels).

**Conclusions:** Our preliminary findings revealed widespread alterations of neural dynamics in patients with temporal lobe epilepsy. Brain regions in the seizure onset zone showed a more constrained activity (slower temporal autocorrelation decay rates) and lower regional homogeneity than regions located outside the seizure onset zone. These preliminary results indicate that alterations of temporal dynamics show promise for non-invasively delineating seizure onset zones from preoperative rs-fMRI. The observed alterations also emphasize the notion of epilepsy as a network disease, affecting brain regions beyond an obvious focal seizure onset. False positive classification remains a challenge that can likely be informed with patient outcomes to determine potential electrode mislabeling and latent seizure onset.

**References**

**Poster No 2320**

**Respiratory Rate and Head Motion Dynamics: A Frequency Analysis Across Life Stages Using HCP Dataset**

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**Introduction:** Recently, there has been a growing interest in developing effective solutions to correct the effects of confounds in fMRI data analysis. While these solutions have been effective for head motion (Maziero et al., 2020; Raimondo et al., 2023), correcting for physiological confounds remains a significant challenge. Interestingly, head motion is not merely a nuisance; when analyzed using retrospective image realignment algorithms, the resulting estimated head motion parameters may provide profound insights into a subject’s respiration (Power et al., 2019). Exploring the Human Connectome Project (HCP) dataset, our objective is to determine the interplay between respiratory rate and the frequency of head motion parameters.
ABSTRACTS

across a range of age groups. Our primary hypothesis suggests a significant interaction between these variables. If validated, this could improve the correction fMRI data for respiration confounds.

Methods: This study utilized 900 resting-state fMRI datasets and associated respiratory signals from three distinct fMRI datasets: the HCP in Development (HCP-D) spanning ages 5-21, HCP in Young Adults (HCP-YA) covering ages 21-35, and HCP in Aging (HCP-A) encompassing ages 36-100+, with each group contributing 300 samples to the study. HCP-D and HCP-A imaging protocols, similar to each other, use an anterior → posterior and posterior → anterior phase encoding (PE) direction. In contrast, HCP-YA uses a left → right and right → left PE direction. fMRI images were corrected for head motion with FSL's MCFLIRT tool (Jenkinson et al., 2002). To assess synchrony between respiratory patterns and head motions, we compared the primary frequency of head motion in the phase encoding (PE) direction with the corresponding respiratory signal’s frequency. We employed a paired t-test and Mean Square Error (MSE) to quantify the similarity between these two frequencies.

Results: Fig 1 displays the power spectra derived from motion parameters. Notable oscillations around 0.3 Hz, especially in the PE direction, are evident. These oscillations can be attributed to both the physical movement of the head due to breathing and the pseudomotion artifact (Power et al., 2019). Fig 2 offers a visual representation of the relationship between respiratory and motion parameters in the PE direction, showcasing their synchronized variation. The primary respiratory frequencies identified from the HCP-D, HCP-YA, and HCP-A datasets were 0.324±0.083 Hz, 0.303±0.051 Hz, and 0.272±0.093 Hz, respectively. Meanwhile, the corresponding frequencies for head motion were 0.318±0.068 Hz, 0.293±0.063 Hz, and 0.263±0.071 Hz. These frequencies align with the standard breathing rates of each age group. The MSE differences across these age categories were 0.0015 Hz, 0.0012 Hz, and 0.0014 Hz (with percentage errors of 0.46%, 0.4%, and 0.51%, respectively). A paired t-test revealed no significant difference between the respiratory and head motion frequencies (p>0.01).
**Conclusions:** The analysis emphasizes the close resemblance between the frequency of respiratory signals and head motion parameters, as shown by notably low MSE values between the two, and statistical analyses. This suggests that the head motion parameter, particularly in the PE direction, can act as a trustworthy measure of a person's respiratory rate. When reliable respiratory data is unavailable or compromised - a frequent issue in fMRI studies, especially among children and elderly participants (Addeh et al., 2023), as illustrated in Fig 1 - head motion parameters offer a viable substitute. Recent advancements have seen the emergence of machine learning (ML) techniques that harness fMRI data to reconstruct respiratory variations (Salas et al., 2021). By integrating both head motion parameters and fMRI data as inputs into these ML models, it is expected that the accuracy of the reconstructed respiratory variation signal can be enhanced, given the valuable insight into breathing rate offered by the head motion parameters.

**References**


**Poster No 2321**

**Neural Mechanisms in Prospective and Retrospective Thinking of Sustainable Behaviors**

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**Introduction:** In recent years, global environmental awareness has risen, prompting many nations to focus on sustainable development. In the Global Risks Report 2023 presented by the World Economic Forum (WEF), environmental risks constitute most of the top ten global risks. This growing awareness has led to an expansion of related research. Brevers et al. (2021) introduced fMRI experiments to investigate the neural mechanisms underlying environmental behavior, compared to traditional methods such as questionnaire surveys or behavioral experiments. They also proposed that individuals projecting themselves in the future, or the so-called prospective thinking, contribute to genuine increases in later environmentally friendly behaviors. Building upon the work of Brevers et al. (2021), this study incorporates modifications to the experimental design and introduces simulations of past and future sustainable behaviors. Through this, the research aims to compare and extend the findings of Brevers et al. (2021).

**Methods:** The study recruited 51 participants in tasks involving exposure to pictures about (un-)sustainable behaviors. Subsequently, participants were prompted to engage in simulated imaginings of past or future scenarios related to these behaviors. Following this, participants were asked to provide ratings (from 1 to 4) indicating the perceived feasibility of the associated behaviors. Functional magnetic resonance imaging (fMRI) was employed to capture neural responses during these simulations and rating tasks. GLM analysis and whole-brain searchlight MVPA were used to analyze the fMRI data.
Results: The behavioral results suggest a potential inclination among individuals to enhance sustainable behaviors in the future, similar to the findings of Brevers et al. (2021). GLM analysis also suggests that we approximately replicated Brevers et al.’s results. Notably, Taiwanese participants showed de-activations of the ventromedial prefrontal cortex (vmPFC) in contrast of “sustainable (do-more) vs. unsustainable” (do-less) pictures, as shown by Brevers et al. (2021) with their Belgium participants. Previous studies have linked vmPFC activation to decision-making and value computation. We speculate that this difference may stem from cultural variations (e.g., including environmental education) among participants. While expressing a similar willingness to engage in environmentally friendly behaviors, Taiwanese participants may not identify it as personally relevant. In the whole-brain searchlight MVPA, the insula was identified as a crucial brain region for assessing whether participants exhibited increased environmentally friendly behaviors prospectively and retrospectively. We propose that Taiwanese students might rely on pain-related bodily feelings, such as social emotions.

Conclusions: Even though in behavioral experiments, participants demonstrated an increased willingness towards environmentally friendly behaviors, the fMRI data revealed differences from the results reported by Brevers et al. (2021). While this study builds upon the groundwork laid by Brevers et al. (2021), it deviates in some aspects, potentially due to a different participant pool (we think it as the primary reason), slight modifications of the experimental design, and cultural adaptations of stimuli. Exploring neural mechanisms of sustainable behavior simulations provides valuable insights into potential shifts in individuals’ attitudes and behaviors towards sustainability, contributing to the broader discourse on environmental consciousness and sustainable development.

References
Reduced functional connectivity when processing threatening faces in childhood trauma people

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Introduction: Childhood trauma, consisting of abuse (physical, emotional, and sexual abuse) and neglect (physical and emotional neglect), can affect an individual’s brain structure and a general pattern of emotional response. Previous studies indicated that the hippocampus (HP) is one of the most obvious brain regions that were affected by childhood traumatic experiences. However, it remains unclear whether the functional network of HP is affected by childhood traumatic experiences when encountering threats. Thus, we recruited subjects with or without childhood trauma, presented them with threatening faces during fMRI scanning, and used a generalized psychophysiological interaction (gPPI) to analyze differences in the functional connectivity patterns of the HP between the two groups.

Methods: Subjects We enrolled 45 adult subjects and measured their degrees of childhood trauma by using the Childhood Trauma Questionnaire-Short Form (CTQ-SF). The subjects included a childhood trauma group (22 subjects) and a healthy group (23 subjects) according to their CTQ-SF scores. Experiment design Fig. 1 shows the matching task and the BOLD-fMRI data were acquired while the subjects were performing the task. The study was approved by the Institutional Research Board (IRB) of South China Normal University. Written informed consent was obtained from each subject before the experiment.

Data acquisition All imaging data were acquired on a Siemens Trio Tim 3T MRI scanner with the 8-channel phased-array head coil. The BOLD-fMRI data were acquired using a gradient echo EPI sequence (GE-EPI) with the following parameters, TR = 2,000ms, TE = 30ms, FA = 90°, FOV = 224 mm × 224 mm, data matrix = 64 × 64, voxel-size = (3.5 mm)³, 32 transversal interleaved slices with interslice gap = 0.4mm, and 300 volume acquired in about 10 mins. The high-resolution brain structural images were acquired using a T1-weighed 3D MP-RAGE sequence with the following parameters, TR = 2,300ms, TE = 3.24ms, FA = 90°, FOV = 256 mm × 256 mm, matrix = 64 × 64, voxel-size = (1mm)³, and 176 sagittal slices covering the whole brain. The brain structural and fMRI data were obtained in the same session for each subject. Data preprocessing Functional and structural data were preprocessed using the CONN toolbox, including head motion correction, distortion correction, slice timing correction, outlier detection, segmentation, and normalization to the MNI space. The preprocessed functional data were spatial smoothed using a Gaussian kernel of 6 mm full-width half maximum (FWHM). fMRI data analysis We selected the bilateral HP as seeds and performed a gPPI analysis by using CONN to estimate the voxel-wise functional connectivity (FC) of the HP in the whole brain. For each seed, a two-sample t-test was used to examine the differences in functional connectivity patterns between the two groups for the contrast of (face condition > shape condition). The mean PPI beta value for each subject was then extracted from each significance cluster to estimate the Pearson correlation coefficient with the CTQ scores.

Fig. 1: Experiment paradigm design.
The experiment consisted of 9 blocks, including 4 face-matching blocks and 5 shape-matching blocks, with each block containing 6 trials. The face-matching blocks and shape-matching blocks in the experiment were presented to the subjects in an interleaved sequence. In the face-matching block, the presentation time of each face-pair stimulus was 4 s, and the inter-stimulus interval (ITI) was randomized from 2 to 6 s (with an average of 4 s), resulting in a total duration of 48 s for each face-matching block. In the shape-matching block, the presentation time of each shape-pair stimulus was 4 s, and the ITI was fixed at 2 s, resulting in a total duration of 36 s for each shape-matching block. The total time for the task was 390 seconds. The response time and accuracy were recorded for each subject.
Results: Fig. 2a shows our selection of seeds. Fig. 2b shows significant negative FC between the seed at the left HP and the posterior cingulate gyrus in childhood trauma. We also estimated the FC for the seed at the right HP and found no significant difference between the two groups. Additionally, Fig. 2c shows a significant negative correlation between PPI beta values and CTQ scores (r = -0.521, p < 0.01).

Conclusions: This study showed that individuals who experienced childhood trauma had lower functional connectivity between the left HP and right PCC in response to the threatening faces. This result suggested that the degree of early trauma may be associated with abnormal functional connectivity patterns. This finding may contribute to our understanding of the effects of early trauma on the brain’s reactivity to emotions.

References

Poster No 2323
Layer-specific fMRI of the human hippocampus in autobiographical memory
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Introduction: Recent advances in ultra-high field (UHF) fMRI have helped to describe the distinct functional roles of hippocampal subfields in memory (e.g.,1). Anatomical descriptions of hippocampal circuits have shown that hippocampal inputs and outputs are segregated into different laminae2. However, fMRI studies on the layer-specific organization of hippocampal subfields are still largely lacking (but see3). Indeed, the human hippocampus is a difficult target to study due to its complex folded structure, the susceptibility artifacts that affect MRI signals in this region, and the need to account for its vascular architecture to reliably interpret fMRI responses. In this work, we sought to robustly acquire laminar fMRI responses
from hippocampal subfields at 7T during an autobiographical memory task and to assess subject-specific differences in these responses.

**Methods:** Two male healthy subjects were scanned on a 7T Siemens MAGNETOM-Terra MRI. Functional data were acquired using a GRE-BOLD 3D-EPI sequence (0.9 mm isotropic resolution). The same sequence with reversed-phase encoding was acquired for distortion correction. The functional task was an autobiographical memory (AM) paradigm adapted from\(^1\). Three runs were acquired for each session and two sessions were acquired for each participant on two different days. In each run, subjects were asked to recall autobiographical episodic memories following the presentation of generic cues (e.g., ‘party’, ‘pet’, etc.). Once the subjects had found a memory related to the cue, they were tasked to imagine it with as much detail as possible during the remainder of the trial. Subjects were instructed to retrieve recent memories (no older than two years) in order to ensure hippocampal activation. The AM task was randomly interleaved with an mental arithmetic (MA) task where the subjects should solve a simple arithmetic operation. AM and MA trials each lasted for 17.6 seconds. For anatomical reference, a T1-weighted MP2RAGE\(^5,6\) was acquired (0.75 mm isotropic resolution). Furthermore, a high in-plane resolution SWI image was acquired (0.3x0.3x0.6 mm resolution) as well as a TOF-MRA to investigate how hippocampal vasculature would influence the laminar profiles. Hippocampus surfaces and subfields were extracted using HippUnfold\(^6\). Functional data were processed using an in-house developed pipeline based on ANTS\(^7\) and SPM. GM signals were equidistantly sampled on 20 depth bins between the inner and outer surface boundary using a custom-written MATLAB script. In case of cornu ammonis 1 (CA1) and CA2, the sampling was extended by 10 depth bins into the stratum radiatum, lacunosum and moleculare (SRLM). Data was corrected for physiological noise using aCompCor\(^8\).

**Results:** Higher activation of the subiculum relatively to other subfields during the autobiographical memory condition compared to the mental arithmetic condition was found in both subjects, consistent with the idea that the subiculum plays an important role in memory retrieval (see\(^1,9\)). At the laminar level, layer profiles corrected for physiological noise with aCompCor showed high within-subject reproducibility between sessions (Fig. 1). Profiles from both subjects showed a stronger bias toward the inner surface of the hippocampus, with some notable differences between subjects that could be attributed to differences in venous vascularization (Fig. 2).

![Layer profiles of both subjects and sessions after aCompCor. The profiles are consistent within subjects (A,B and C,D) but different between subjects.](image-url)
Fig. 2. Large veins (blue vertices) and arteries (red vertices) mapped on the unfolded hippocampus, averaged across hemispheres.

**Conclusions:** We have shown that robust and reproducible laminar profiles can be obtained for hippocampal subfields at the subject level. Inter-subject differences in vascular anatomy are possible factors influencing layer profiles. Future directions will include consideration of the functional organization of the hippocampus on its long axis along with subfield- and layer-specific analyses in the description of hippocampal function.

**References**


**Poster No 2324**

**Hi-Fi BOLD fMRI of the human auditory cortex**

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**Introduction:** Recent fMRI acceleration techniques have allowed for sub-second temporal resolution¹², but are still impacted by decreased Signal to Noise Ratio (SNR), inter-slice crosstalk and eddy current artefacts². A novel acquisition and reconstruction approach, dubbed Hi-Fi fMRI, combines a spiral phyllotaxis sampling trajectory⁴, a compressed-sensing
algorithm⁴, and application of motion correction directly to k-space⁵ to obtain minimal distortions and high SNR⁶,⁷ as well as a 250msec temporal resolution (chosen during image reconstruction). To date, this has been successfully applied in visual cortices. Here, we employ complex auditory stimuli⁸ to activate the deeper and smaller auditory cortices, so as to test the robustness of the technique.

**Methods:** Three healthy adult volunteers underwent a passive auditory stimulation task (Fig 1a). Auditory stimuli were delivered in no-stereo mode to both ears through MR compatible noise-cancelling headphones. Participants fixated centrally a gray patch while listening to a total of 49, 40s-long trials. Sequences of meaningful environmental sounds (e.g. bells, dog barking) superposed onto an everyday auditory scene (e.g. market, street)⁹ were played during the ON phase of each trial (0-15s)⁶. Pink noise was played during the REF phase (15-40s), so as to prevent the rhythmicity of the scanner noise from eliciting peaks of BOLD activity. An uninterrupted gradient recalled echo (GRE) research application sequence was acquired with a 3T clinical scanner (MAGNETOM PrismaFit, Siemens Healthcare, Erlangen, Germany), with TE/TR=25/28.24ms, FoV=192x192x192mm³, 0.8 mm³ isotropic resolution, FA=12°, TA = 33min. A 3D radial spiral phyllotaxis sampling trajectory was employed, guaranteeing uniform readout distribution in k-space³. Images were reconstructed in 5D along the x-y-z-repetition (trial) -activity (ON/REF) dimensions with a k-t-sparse SENSE algorithm (image under-sampling 20%)⁴, resulting in 98 3D volumes (Fig 1B2). Total variation regularization was applied along the repetition dimension. Readouts acquired in 2 time-intervals were selected: 5-15s, capturing BOLD signal at peak during the ON phase, and 30-40s, corresponding to BOLD baseline during the REF phase (pink noise). Readouts belonging to the same activity type were unified via sum of squares and the absolute difference between ON and REF was computed. ON and REF images for each trial underwent a statistical analysis and clusters with a statistical difference at p<0.05 (FWE-corrected, T>6.38) were selected; this threshold corresponded, in the ON-REF image calculation, to 83au. Within these clusters, a separate set of 4D reconstructions was performed along x-y-z-t (time) dimensions, with bins of 2.5sec, where Fourier transform regularization was applied along the time dimension (Fig 1B1). Motion correction translation and rotational coefficients were estimated using SPM129 and applied to the original k-space.

**Results:** All subjects showed a bilateral activation along the superior temporal gyrus adjacently to the Heschl’s gyrus and restricted to the gray matter (for coordinates in MNI space of each cluster see Fig 2b). Maps represent the signal change intensity in all statistically significant clusters. The signal dynamics associated with the activations were then extracted and shown to follow the classical hemodynamic response function (HRF). A normalized average of these HRFs is shown in figure 2c.

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**Fig. 1.** Representation of experimental paradigm and analysis. Figure 1a shows the experimental and auditory stimulation protocol. Figure 1B1 shows 4D reconstructions and figure 1B2 shows 5D reconstructions.
Figure 2a shows all the active clusters of each subject; figure 2b shows their coordinates and figure 2c displays the average (mean±std) across subjects of the HRFs extracted from the clusters.

Conclusions: The present paradigm proved that Hi-Fi fMRI can record activation with submillimeter spatial resolution and located into the gray matter of the superior temporal gyrus involved in processing natural sounds. Moreover, the signal Hi-Fi is sensitive to follows the classical HRF. While the temporal resolution extracted was 2.5sec, the high sampling-rate and its radial trajectory allow for a flexible reconstruction of the images with time bins of different sizes. These results support the validity of the HI-FI approach as well as its broad applicability. The research was supported by the MYSpace project (PI Monica Gori), which has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement No 948349).

References
Enhancing White Matter fMRI Reliability through BOLD-like Signals Using Multi-Echo Techniques

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Introduction: White matter functional magnetic resonance imaging (fMRI) has emerged for investigating the functional role of the brain’s white matter (Ji et al. 2017, Schilling et al. 2023). Recent study has shown that the amplitude of low-frequency fluctuations (ALFF) of WM is a potential biomarker in psychiatric disorders (Ji, et al. 2023). However, signals in the white matter are more susceptible to contamination by physiological noise due to their significantly lower amplitude. Multi-echo technology offers the opportunity to separate non-T2* signals, providing enhanced BOLD signal and suppressed non-BOLD noise (Kundu et al. 2017), and allowing the measured fMRI information to more accurately reflect information related to true BOLD effect. These advantages have been proven to enhance the reliability of fMRI results in gray matter regions. Inspired by this, the study will explore whether multi-echo fMRI can enhance the reliability of resting-state functional measurements in white matter regions. The objective is to shed light on the potential benefits of using multi-echo fMRI for white matter function studies.

Methods: Twenty-seven healthy subjects participated in the experiment and underwent MRI scanning included ME-fMRI, SE-fMRI and T1w MPRAGE on a Siemens MAGNETOM Prisma 3T scanner. Both SE-fMRI and ME-fMRI were acquired with following parameters: TR of 1300ms, isotropic resolution of 3mm and a total of 700 frames. The ME-fMRI were acquired using a four-echo EPI sequence with TEs=12.6/30.86/49.13/67.38 ms, while the SE-fMRI were acquired with TE=30ms. All the fMRI data was firstly splitted into two clips and then underwent slice time correction and motion correction. For the ME-fMRI data, optimal combination was applied to merge the four echoes into a single echo data(Kundu, Brenowitz et al. 2013). Nuisance signal, including CSF signal, global signal and ICA noise signal (ICA-AROAM for SE and ME-ICA for ME), were regressed out after filtering. All subject-level WM masks were combined to create a group level WM mask in MNI space. ALFF values were calculated in native bold space and then mapped to MNI space. The ALFF maps in MNI space were masked by group-level WM mask and subsequently z-transformed to obtain zALFF maps, which was used to calculate intraclass correlation coefficient (ICC).

Results: ME-fMRI demonstrates a comparable group-averaged zALFF pattern (coefficient=0.89) when compared to SE-fMRI. The zALFF from SE-fMRI shows poor reliability (ICC = 0.28±0.19), whereas ME-fMRI exhibits moderate reliability (ICC = 0.41±0.2). A higher percentage of white matter regions in ME-fMRI (17.7%) surpass the substantial ICC threshold (ICC=0.6),...
indicating greater reliability, compared to SE-fMRI where only 5.7% of the regions achieve this threshold. Besides, the improved reliability in ME-fMRI primarily contributes to decreased within-subject variance (Vw) and slightly increased between-subject variance (Vb) compared to SE-fMRI. For the ROI-based analysis, we selected 17 regions of interest (ROIs) from the JHU white matter atlas, which have good overlap with our group-level white matter mask. All 17 ROIs show a significant improvement in ICC ranging from 0.08 to 0.22, and all these ROIs show a significant decrease in Vw. However, only 11 out of 17 ROIs showed a significant increase in Vb, with the genu of the corpus radiate showing a significant decrease with a mean value of 0.1 of Vb. The cingulum cingulate gyrus which plays an important role in different cognitive and emotional processes, benefits the most compared to SE-fMRI, with a significant mean increment of 0.22.

Conclusions: Our findings indicate that ALFF maps in white matter, exhibit greater reliability when using BOLD-like signals from ME-fMRI. The enhancement in reliability is primarily attributed to a significant reduction in Vw. The improved reliability of white matter measurements with ME-fMRI could potentially facilitate a more accurate understanding of the underlying mechanisms of white matter functions.

References
Artifact correction for functional mri using overfitted neural network: a feasibility study

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Introduction: Functional magnetic resonance imaging (fMRI) typically uses Gradient Echo EPI (GE-EPI) to detect the blood oxygenation level-dependent (BOLD) signal. GE-EPI offers high BOLD sensitivity but struggles with artifacts such as B0 inhomogeneity and geometric distortion, limiting observations in regions of the frontal or auditory areas. Spin Echo(SE-EPI) counteracts inhomogeneity artifact-induced signal dropout and use of reversed acquisition in the readout direction (so-called top-up correction) can also reduce the geometric distortion. However, SE-EPI has reduced BOLD sensitivity. Motivated by the above properties, we propose a neural network pipeline which reduces the inhomogeneity artifact of GE-EPI images. The proposed method leverages overfitting of neural network by training the GE-EPI onto a single additional data set of the SE-EPI acquisition.

Methods: Fig.1 presents the pipeline of the algorithm. The trainset of the network consists of GE-EPI and top-up corrected SE-EPI as label from individual single subject. Data were acquired using Siemens 3T scanner. An actual fMRI task was performed using GE-EPI. For the GE-EPI TE=30ms, TR=3000ms, bandwidth=2894 KHz, resolution=(1.9,1.9,5)mm, matrix size=(128,128,33), # of measurements=90. For SE-EPI TE=30ms, TR=3000ms, bandwidth=2894 KHz, resolution = (1.9,1.9,5)mm, matrix size=(128,128,33), # of measurements = 2 for a scan time of 30 sec. The pipeline starts with GE-EPI (during event-OFF period) and SE-EPI data. GE-EPI were averaged to one 3D volume to increase SNR level. According to prior work that signal dropout and distortion correction can be seen as a deconvolution problem, we assumed the correction as a spectrum domain deconvolution operation. Hence, the averaged GE-EPI and corrected SE-EPI were Fourier transformed and subsequently used for train input and label for the network. A network based on the ResNet structure was used. Fc layer and bias were removed. Different number of epochs and layer features were tested to control the level of overfitting. After training, the model was applied to the original GE-EPI data (both event-ON and event-OFF period). A visual stimulation experiment was performed to compare the BOLD activation after the correction of the proposed method.

Results: Fig. 2 show results of the proposed method. The network’s reconstruction can be seen in Fig. 2(a). As seen, the corrected GE-EPI images from the output of the network shows high similarity with the label images. While the structural reconstruction of the network shows high SSIM values, this does not guarantee the ability to retrieve the BOLD activation.
Fig 2 (b) shows BOLD results from the visual stimulation experiment. By observing the BOLD activation maps with different hyperparameter settings of the network, we observed that network had trade-off between structural reconstruction ability and BOLD reconstruction ability which were dependent on the training epoch and features used. Interestingly, after applying the proposed method, BOLD activation was observed in the frontal lobe region which originally suffered from signal dropout. The validity of this observation needs further verification.

Conclusions: This study proposed a new neural network method for GE-EPI distortion correction based on single subject data acquisition which relies on overfitting onto each individual data. Results show the feasibility of the proposed methods for reducing artifacts in GE-EPI. In addition, BOLD activation is well preserved and potentially can further elucidate activation in artifact dominant regions.

References

Poster No 2327
Temporal lobe spiking reveals distinct patterns of fMRI activation with intracranial EEG-fMRI
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Introduction: Temporal lobe epilepsy (TLE) is the most common focal epilepsy in adults (Téllez-Zenteno et al., 2012). TLE has a high probability of becoming medically refractory and is frequently considered for surgical intervention. However, 30% of TLE cases have non-lesional magnetic resonance imaging (MRI) results, which has been associated with worse surgical outcomes, prompting the need for novel imaging techniques (Kim et al., 2016). Simultaneous intracranial electroencephalography-functional MRI (iEEG-fMRI) can measure the hemodynamic changes associated with interictal epileptiform discharges (IEDs) recorded directly from the brain. This study was designed to characterize the fMRI activation associated with IEDs recorded exclusively from the mesial temporal lobes of patients with non-lesional TLE.
**Methods:** Nineteen MRI-negative patients undergoing iEEG monitoring with mesial temporal IEDs were studied using simultaneous iEEG-fMRI at 3Tesla. IEDs were marked and statistically significant clusters of BOLD activation were identified (Z-score 2.3, p value <0.05). The anatomical locations corresponding to the fMRI activation for each patient were determined and patients were grouped based on location and pattern of fMRI activity.

**Results:** Two patterns of fMRI activation associated with mesial temporal IEDs emerged: primarily localized (n =8), where activation was primarily located within the ipsilateral temporal lobe, and primarily diffuse (n = 11), where widespread extratemporal activation was detected. The primarily diffuse group reported significantly fewer focal to bilateral tonic-clonic seizures.

**Conclusions:** Simultaneous iEEG-fMRI can measure the hemodynamic changes associated with focal IEDs not visible on scalp EEG, such as those arising from the mesial temporal lobe. Significant fMRI activation associated with these IEDs was observed in all patients. Half of the patients had brain activation primarily localized to the ipsilateral temporal lobe, and half showed widespread activation in several extratemporal structures. Those patients with fewer focal to bilateral tonic-clonic seizures also exhibited widespread IED-associated fMRI activations, which may suggest a neuroprotective mechanism limiting the spread of ictal events.

**References**

**Poster No 2328**

**Functional connectivity of the insular sub-regions in patients with disorders of consciousness**

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**Introduction:** The insula and its sub-regions are important for maintenance of awareness and may be situated at an intermediate position along the brain’s functional hierarchy¹⁻³. Previous studies have shown that the insular dysfunction is related to disorders of consciousness (DoC), which is characterized by alterations in arousal and/or awareness⁴. The insula is a heterogeneous structure and can be divided into three sub-regions, the anterior insula (AI), middle insula (MI), and posterior insula (PI). Each of them has a distinct pattern of structural and functional connectivity⁵. Here, we attempted to measure the FC between each of the insular sub-regions and each voxel in the whole-brain and to detect the changed FC patterns in DoC patients.

**Methods:** Participants: We recruited 22 DoC patients (DOCs) and 28 healthy controls (HCs) in the Guangzhou Lihuqiao Hospital (GLH). For each patient, the severity of the condition was assessed by the Coma Recovery Scale-Revised (CRS-R).
This study was approved by the Institute Review Board (IRB) of the GLH, and the guardian of each patient gave written informed consent prior to the study. Data acquisition: All the MRI data were acquired on a GE 3T MR scanner in the GLH. The rs-fMRI data were obtained using a single-shot GE-EPI sequence with the following parameters, TR = 2,000ms, TE = 26ms, flip angle = 90°, FOV = 240mm × 240mm, data matrix = 64 × 64, voxel size = 3.75 × 3.75 × 4.20 mm³ and 240 volumes. In addition, the high resolution brain structural images were acquired using a T1-weighted 3D FSPGR sequence (1mm isotropic voxel). Data processing: The rs-fMRI data were preprocessed using SPM12 and CONN (ver 22.a). We removed the first 5 image volumes, performed slice-timing, corrected head-motion (criteria: 3 mm and 3°), normalized to the T1w images, resampled to a voxel size of (3mm)³ and smoothed with a 6 mm FWHM Gaussian kernel. The datasets for 2 patients were excluded because of their head motion exceeding the criteria. Seed-based FC analysis: We defined the insular seed regions of interest (ROIs) according to the previous study. Selected six spherical seeds with a radius of 6 mm were shown in Fig. 1 and mean coordinates for each cluster are provided in Table. Individual FC maps of the bilateral Al, MI, and PI were generated by calculating Pearson’s correlation coefficients between the mean time series of the ROIs and the time series of each voxel in the whole brain. Then, a two-sample t-test was used to test the group difference in FC between the DOCs and HCs. The clusters were determined at the threshold of the voxel-level p < 0.001 and the cluster-level p < 0.001 (two-sided test). Age, sex and the mean FD were included as nuisance covariates in the comparisons.

**Results:** Fig. 2 shows that the DoCs group had extensive FC abnormalities for different sub-regions of the insula. We found significant lower FC between the bilateral Al and AC/SMA, between left MI and right putamen, between right MI and SMA, between the left PI and AC/SMA, and between right PI and PostCG, than the controls. We also found significantly higher FC between the left Al and the SFG in the patients than the controls. The detailed information is listed in Table. 3.

**Conclusions:** This study revealed that different insular sub-regions had different changes of FC patterns. The result indicated a graded functional heterogeneity in the insula: the Al is more involved in perceptual-motor transnational functions such as motor control or attentional control, the MI is more related to integration of sensory-perceptual information, and the PI displays a low-level functions of sensorimotor behaviors. The findings provide evidence for functional differentiation of insular sub-regions and cognitive-motor dissociation in disorders of consciousness.
References
**Poster No 2329**

**Hippocampal pattern separation/completion and cognitive map during naturalistic stimuli**

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**Introduction:** The hippocampus, known for supporting episodic memory, could represent the traces for individual experiences can vary in their relations, becoming more distinct (pattern separation) or more similar (pattern completion) to each other. Moreover, it also has the ability to abstract common elements and infer relationships among information from diverse experiences, which enables the construction of structured knowledge about the information, forming ‘cognitive maps’.

However, we still lack a detailed understanding of whether and how hippocampal pattern separation/completion contribute to cognitive map formation during movie stimuli. Here, using ultra-high-resolution fMRI data from the Human Connectome Project (HCP), we first investigated how the hippocampal circuit exhibits pattern separation/completion at different time scales. Then, we constructed movie semantic networks and hippocampal subfield BOLD networks to represent cognitive map respond to movie stimuli. Finally, we studied how these movie networks relate to pattern separation/completion.

**Methods:** All data used here come from 184 subjects of the HCP 7T release in this study (13 video clips). We segmented the hippocampus into the dentate gyrus (DG) and cornu ammonis (CA) 1-3 subfields, then focused on two input-output pairs (i.e., DG→CA3 and CA3→CA1) along the hippocampal tri-synaptic circuit. For each clip, sliding window correlation was conducted to evaluate temporal similarity of input/output fMRI patterns for each input-output pair. Further, we compared input and output patterns to derive the ratio of pattern separation/completion at each window size (range from 1TR to 50TR) and used paired t-tests to assess the significance of pattern separation or completion across all subjects. To explore whether the hippocampal BOLD network acquired the topological properties of the movie semantic network, we constructed networks for hippocampal BOLD signal and semantic features respectively, and compared the global and local efficiency of these networks with their corresponding random networks. Moreover, we used the Floyd-Warshall algorithm to calculate the shortest path distance between nodes in the BOLD networks and evaluated the changes in path distance along the DG→CA3→CA1 circuit. We next calculated Pearson correlation of input-output difference matrix between temporal similarity and shortest distance, and Pearson correlation coefficients were transformed to z-scores using Fisher's transformation.

**Results:** We found that when the window size was longer than 2 TRs, DG→CA3 showed significant pattern separation than completion in ten movie clips, while CA3→CA1 pair exhibited significant pattern completion in all movie clips (p<0.05, Fig.1). We found that these networks created from movie semantic and hippocampal subfield BOLD signals showed significantly lower global efficiency but significantly higher local efficiency compared to random networks (p<0.05). For the DG→CA3 pair that showed significant pattern separation effect, we observed that the mean shortest path distance between all node pairs within the CA3 BOLD network increased significantly compared to the DG. In contrast, for the CA3→CA1 pair that showed significant pattern completion effect, the mean shortest path distance between all node pairs within the BOLD network of the CA1 decreased significantly compared to of the CA3 (p<0.05, Fig.2).

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**Fig.1.** Pattern separation and completion effect under different window lengths in (A) DG→CA3 and (B) CA3→CA1 circuit. The x-axis represented window size and the y-axis depicts the t value obtained from paired t-tests. The 13 colors correspond to the 13 movie clips.
Conclusions: The hippocampal circuits could underpin pattern separation/completion at relatively short time scales (>2s) and learned the topological property from the semantic network during movie stimuli. Moreover, significant changes in the shortest distances between nodes in the BOLD network of the hippocampal pair were observed. These findings may contribute to our understanding of how pattern separation and completion connect with cognitive map organization during naturalistic stimuli, as well as the distinct functions played by various hippocampal subfields in these mechanisms.

References

Poster No 2330

Effects of MR-Parameters on Relative BOLD-Sensitivity in the Striatum

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Introduction: The striatum is a subcortical brain region involved in many brain functions such as reward processing, cognition, learning or salience detection. Faster fMRI acquisition techniques, such as multi-band (MB) imaging or sensitivity encoding, are often considered “state-of-the-art” nowadays and dominate fMRI research currently. However, Srirangarajan et al. (Srirangarajan et al., 2021) have already pointed out that the detection of mesolimbic reward responses suffers from the reduced BOLD sensitivity of such techniques in particular brain regions, especially the ventral striatum (nucleus accumbens) region, which is both susceptible to B0 field inhomogeneities as well as far from the receiver coils and thus suffers from reconstruction g-factor noise. Both of these effects are not observable in whole-brain average signal-to-fluctuation-noise (SFNR) but require a regional analysis of SFNR and depend on numerous MR acquisition parameters. Here, we will investigate the effect of MB factor, IPAT factor (skip of k-space lines), TE, and resolution on whole brain SFNR and relative regional SFNR for bilateral nucleus accumbens (NA), putamen (PU), pallidum (PA) & caudate (CA) motivated by our own observation of the SFNR drop in NA when using a sequence (UKB sequence) modeled after the UK-Biobank protocol with the primary alteration of reducing the MB factor from 8 to 6 (Fig. 1).
Methods: Single-subject resting state data (≥150 frames, Siemens Prisma Fit 3T) are compared for 2.4 mm isotropic and 3x3x2 mm3 (gap 1mm) sequences with variable [TR]-[TE]-[MB factor]-[iPAT factor] (Echo spacing: 0.57-0.58ms for 2.4mm except UKB 0.69ms; 0.49-0.5ms for 3mm). While the UKB sequence had a long TE=38ms and iPAT=1, most other sequences had iPAT=2 and TE=25 or 30ms to reduce susceptibility-induced signal drop-out. All images underwent standard preprocessing, including realignment, field map correction, and T1-based normalization, and were resampled to 2.4mm isotropic resolution. Signal time courses were detrended using a 2nd or 3rd polynomial. SFNR was computed as the voxel-wise temporal Mean/Std. Median SFNR values were extracted for all regions of the AAL3.1 atlas and the union of all AAL regions (whole-brain). Relative regional SFNR was computed as the regional/whole-brain SFNR.

Results: Results are presented in Fig. 2. Whole-brain SFNR magnitude a) decreases only marginally with MB when correcting for TR; b) decreases with TE, but BOLD-sensitivity may increase and is optimal at TE=T2*; c) increases only marginally with voxel volume, likely due to physiological noise; d) decreases substantially for iPAT=2 compared to iPAT=1. Relative regional SFNR e) is particularly low in NA and PA; f) drops substantially for iPAT = 2 compared to 1; g) drops with MB, especially 2->3; h) ranges from 41% (PA-2.4mm-605-30-6-2) to 97% (PU-3x3x2mm-1400-25-2-1).

Conclusions: 1) Both multi-band as well as iPAT parallel imaging techniques reduce whole-brain SFNR. 2) Both techniques additionally decrease relative SFNR in subcortical brain regions such as the striatum. PA and NA are especially affected. 3) The cause for this heterogeneity in SFNR and thus BOLD sensitivity is likely multi-fold: reduced signal due to a) susceptibility drop-out (NA) and b) reduced T2* due to iron content (PA) and c) increased g-factor noise far from receiver coils. 4) Assuming that within-subject standard error of BOLD effects scales inversely with SFNR for the same MR sequence, a drop of SFNR by 50% would reduce an effect of d=0.36 to 0.2 assuming 75% within-subject, 25% between-subject noise initially. 5) As reported
by Srirangarajan, use of parallel imaging for BOLD fMRI has substantially biased the literature towards cortical rather than subcortical effects. 6) We recommend NOT to use iPAT or MB > 2 for whole-brain or subcortical fMRI. 7) The effect of slice thickness and no MB needs to be explored further.

References

Poster No 2331
Age-Related Changes in Resting-State fMRI White Matter Engagement in Elderlies: A Longitudinal Study
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Introduction: The decrease in white matter (WM) volume starts to become evident around the age of 40 (Ge et al., 2002). The application of diffusion tensor imaging (DTI) (Assaf & Pasternak, 2008) and T2-weighted-fluid-attenuated inversion recovery (Bakshi et al., 2001) provide valuable insights into the microstructure of white matter, including features such as lesions and tracts. However, due to differences in the biophysical origins of the signals and the tissue in question, there has been no direct integration of these techniques to date. Recent studies have indicated that blood oxygenation level dependent (BOLD) effects in WM can reflect neural activities, offering an additional complementary perspective on the brain’s functional organization (Li et al., 2020). Our study involved the analysis of 170 healthy elderly participants from the Harvard Aging Brain Study, with data collected at two separate time points, spaced three years apart (Dagley et al., 2017).

Methods: Preprocessing of fMRI data followed the procedure by Li et al (Li et al., 2020). The engagement maps began with the definition of the population-based (PB)-averaged WM and grey matter (GM) masks. The PB GM mask was generated by normalizing the probability of the average for all subjects, which was then be binarized with a loose threshold (> 0.6), whereas the PB WM mask was binarized with a tight threshold (> 0.95). After multiplying the time series of each subject by the threshold WM and GM masks, the images were used to calculate the full correlation matrix M and partial correlation M'x. M was obtained by averaging all voxels of the GM node within the 90 AAL atlas with a dimension of 90 x 90. M'x represented the connectivity with the same pairwise value as matrix M, but with the time series of each voxel x in WM in the time series serving as the control. The time series of the voxel x were computed by the average signal of 5 x 5 x 5 voxels surrounding x. The global network connectivity metric G(M) represented the mean of matrix M, and G(M’x) represented the mean of M’x for each voxel x. Finally, the method mapped the difference between G(M) and G(M’x) onto the WM voxel map concerning the whole network and defined a rough WM engagement map for each subject. Finally, the Fisher Z-transformation was applied to transform the WM engagement map so that the data in the map were normally distributed. A paired t-test was used to compare between two visits (2nd –1st). Statistical significance was established at a p-value < 0.05 after Alphasim correction, with a cluster size > 54 voxels.

Results: Table 1 presents the demographic information of the participants. According to the Johns Hopkins University White Matter Tractography Atlas (Wakana et al., 2004), we observed a significant decrease in engagement within the bilateral brain stem and the right corticospinal tract between two visits. Conversely, there was a notable increase in engagement within the right superior longitudinal fasciculus (SLF). (Figure 1)
Conclusions: The study found decreased WM engagement in bilateral brain stem and the right corticospinal tract. Consistent with previous findings (Bouhrara et al., 2021; Jang & Seo, 2015), decrease in these specific regions implies a process of tissue maturation and degeneration occurring within the brainstem and corticospinal tract. On the other hand, the right SLF tract is more active with increase in age, which might compensate for executive dysfunction (Amemiya et al., 2021). Further investigation will be needed to determine the exact implications of these findings.

References

Poster No 2332

Aberrant Resting-state Functional Connectivity of Amygdala in adults with Childhood Trauma

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Introduction: Many studies have revealed that individuals with a history of childhood trauma (CM) had an increased prevalence of various mental illnesses. Recent studies have reported the abnormal resting-state functional connectivity (RSFC) in individuals who have experienced CM. For instance, several studies detected the abnormal RSFC in the default mode network (DMN) and salience network by using the seed regions at the prefrontal cortex, insula, amygdala, hippocampus, anterior cingulate gyrus, and orbitofrontal cortex. However, it is still unclear how the CM affects the brain RSFC involving the amygdala. Thus, in the current study, we selected the bilateral amygdala as two seeds and compared the RSFC in the individuals with CM and those without CM.

Methods: Participants The study was approved by the Institutional Research Board (IRB) of South China Normal University (SCNU). All participants provided written informed consent. We enrolled 44 adult individuals, who were recruited from a survey in SCNU to test people who had experienced childhood maltreatment. Data acquisition The Childhood Trauma Questionnaire-Short Form (CTQ-SF) was used to assess the severity of childhood trauma in the participants. When the total score on the scale is below 31, the participant was included in the without CM group (NCM) or the control group; otherwise, they were included in the CM group. The MRI data was acquired on a 3T Siemens Trio MRI scanner equipped with a 32-channel phased-array head coil. The BOLD-fMRI data were acquired using a gradient echo EPI sequence (GE-EPI). The high-resolution brain structural images were acquired using a T1-weighted 3D MP-RAGE sequence. The brain structural and fMRI data were obtained in the same session for each subject. Data processing The data were preprocessed using CONN (2022a). We defined the two seeds in the bilateral amygdala. Frames with significant motion artifact were scrubbed with the ART method and the resultant timeseries were bandpass filtered at 0.008-0.09 Hz. For each subject, we calculated the RSFC between
each seed ant each voxel in the whole brain. Finally, the group-level analysis was conducted to detect the abnormal RSFC in the CM group.

Results: Fig. 1 shows significant group difference in RSFC between the CM and NCM groups. We found significant lower RSFC between the right amygdala and the right putamen, right hippocampus, and right thalamus, in the CM group than the NCM group. We also found significantly lower RSFC between the left amygdala and the left putamen, left hippocampus, and left pallidum, in the CM group than the NCM group.  

Conclusions: We detected significant differences in RSFC between adult individuals reporting CM and individuals without CM by selecting the seeds at the amygdala and using a seed-based connectivity. The findings may indicate adverse effects on emotional regulation, emotion processing and cognitive control. These findings hold promise in offering crucial insights into the long-term effects of childhood trauma on brain function and mental well-being.

References

Poster No 2333

The Effects of Locus Coeruleus Stimulation on Quasi-Periodic Patterns in Rats

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Introduction: The Locus Coeruleus (LC), located in the brainstem, is the primary structure that synthesizes and delivers norepinephrine to other parts of the brain⁴ and is also involved in arousal, cognition, and attention². Due to its diffuse projections throughout the brain, studying the effects of LC activity on whole-brain spatially evolving activity, such as quasi-periodic patterns (QPPs), is of great interest. QPPs are whole-brain patterns of activation and deactivation between different brain regions that propagate across the brain. Though their origins are unknown, preliminary work suggests that disruptions from baseline LC activity perturb the propagation of QPPs¹. In this work, we used optogenetic-fMRI to study how optogenetic stimulation of the LC affects QPPs in real time.
**Methods:** This study used a cohort of 6-month-old wildtype Fisher 344 rats that were bred in-house. When the rats (n=7) were 2 months old, they were injected intra-LC with a lentivirus containing channelrhodopsin-2 (ChR2) under the expression of the noradrenergic-specific promotor PRSx8. Control animals were injected with a similar virus that contained mCherry instead of ChR2 (n=9). Two weeks before scanning, rats were implanted with an optic ferrule and optogenetic LC stimulation was confirmed using pupillometry. Resting-state fMRI scans were acquired using a 9.4 T Bruker MRI scanner while rats were intubated and maintained under 1.3% isoflurane. All 10-minute fMRI scans were gradient echo EPI with partial Fourier encoding with a factor of 1.4 and acquired with the following parameters: voxel size = 500 um3, matrix size = 70 x 70, slice number = 24, TE = 15 ms, TR = 1250 ms, and phase-locked to every other breath of a 1.6 Hz respiratory rate. Scans were preprocessed using a custom preprocessing pipeline. A baseline scan with no stimulation, a scan at 5 Hz of constant LC stimulation, and a scan at 15 Hz phasic stimulation (3 pulses every 10 seconds) were acquired for each rat. All scans from each group were concatenated and a spatiotemporal pattern-finding algorithm was used to identify QPPs within the datasets.

**Results:** The activity of each region within the QPP was acquired and plotted over time (Figure 1). The QPP activity observed in the control rats (top row) showed similar regional activity across the differing levels of stimulation. However, in the LC stimulated rats (bottom row), stimulation at 5 Hz and 15 Hz resulted in distinct differences. Primarily, LC stimulation at both frequencies resulted in a notable increase of contribution from the cingulate cortex, which was not observed in the control rats. Additionally, LC stimulation at 5 Hz appeared to result in a phase shift in the somatosensory, insular, and striatal networks.

**Conclusions:** These results indicate that stimulation of the LC at 5 Hz and 15 Hz phasic frequencies had distinct effects on the regions involved in the QPP, specifically the cingulate network. Additionally, in the case of 5 Hz stimulation, the timing of activity of other networks appeared to be affected. This analysis shows that LC stimulation at different frequencies resulted in distinct regional differences within the QPPs.

**References**