MRI functional *connectivity-based predictive models* of brain organization and cognitive state for healthy and clinical populations.

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Overview

Why to study the brain

How to study the brain

Brain Connectivity and Activity

Connectome Fingerprinting

- Benchmarks of Connectome Fingerprinting
- Cerebellar predictions using Connectome Fingerprinting
- Connectome Fingerprinting for presurgical planning

Connectome Based Predictive modelling of Alzheimer's disease

- Network Analysis
- Connectivity based Predictive Modeling

Why to study the brain?

Al and Neuroscience

- Brain-inspired models like neural networks CNNs, LLMs based on brain organization
- Brain \Rightarrow AI, and AI \Rightarrow brain tools





Brain-Computer Interfaces

• From controlling cursors to enabling speech in paralyzed patients.





Lab to Clinic

• Neurotech aids diagnosis, therapy, and rehabilitation.



What is Neuroscience?

- Study of the nervous system: brain, spinal cord, peripheral nerves.
- Interdisciplinary: biology, psychology, computer science, philosophy



Subfields of Neuroscience

- Molecular
- Cellular
- Systems
- Cognitive
- Computational
- Clinical
- Neuroengineering



Brain Anatomy Overview

- Major parts: Cortex, Cerebellum, Brainstem, Spinal cord.
- Central vs Peripheral Nervous System.



Lobes of the Brain

- Frontal
- Parietal
- Occipital
- Temporal



BIOLOGICAL PERCHOLOGY, Fearth Edition, Figure 1.11 (Part 2) @ 2004 Stream Ave

Neurons and Synapses

- Neurons communicate via electrical impulses and chemical synapses.
- Basic unit of brain function.





Action Potential





Neurotransmitters





Brain Networks

- Somatosensory Networks
- Motor Network
- Salience Network
- Attention Network
- Cognitive Control Network
- Default Mode Network
- Brain as a dynamic system.





How to study the brain?

Experimental Methods

Brain lesions EEG/MEG fMRI/fNIRS Electrophysiology Psychophysics TMS/tDCS/tACS Behavioral data Molecular/Cellular (In vivo/In vitro)



Invasive Electrophysiology



Trends in Cognitive Sciences

EEG/MEG





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Brain Structure Predicts Brain Function

Passingham's Conjecture (2002): Each cortical brain region has a unique pattern of connectivity.



If we can establish these patterns AND measure the connectivity of a particular bit of brain tissue, we can predict the functional brain region identity of the tissue.

Connectome

Connectome is defined as the set of connections between different parts of the nervous system.

Connectomes can be at the *microscale* level like the connectivity between neurons or could be *macroscale* which is connectivity between different regions of brain.

At the macroscale level, structural connectivity is the identification of white matter pathways between different regions using techniques like Diffusion Tensor Imaging (DTI) or Diffusion Weighted Imaging (DWI).



Functional Connectome

Functional connectome is computed as the correlation of the activity of two brain regions.



Connectome Fingerprinting: A computational modeling approach for non-invasively predicting individualized functional brain organization from the individual's connectome

Fornito & Bullmore, 2015

Connectome Fingerprinting: What we know so far?

Structural connectivity predicts face selectivity in FFA (Saygin et. al. 2012), and cortical selectivity for different visual categories across the cortex (Osher et. al. 2015)

Individual differences can be predicted(Tavor et. al. 2016)

Resting state functional connectivity can predict sensory modality-selective regions in the frontal cortex(Tobyne et. al. 2018) and dorsal attention network(Osher et. al. 2019)

Murty et. al. 2020 demonstrated the FFA connectivity fingerprints are similar across congenitally blind and sighted subjects and models trained on one group can predict activations in others.

Benchmarks of Connectome Fingerprinting

Connectome Fingerprinting Method



- B) Select Parcellation
- D) Extract Connectome & Task Activations



F) Analyse Performance



Dataset

Human Connectome Project Young Adult dataset - 1200 subjects and 7 tasks but we used 169 subjects and focussed on the Working Memory task

Parietal and Frontal Search spaces

Resting state data - 4 runs of 15 minutes each





Working Memory Social Relational Emotion Motor Language Gambling

Predictions

Actual



3

Benchmarks of Connectome Fingerprinting

- 1. Quality Of Data: How are predictions affected by
 - a. Task performance
 - b. Amount of Resting State data
 - c. Motion during resting state and task runs
- 2. How do different learning methods perform?
- 3. What if we use naturalistic stimuli data for predictions?
- 4. How does it perform across datasets?
- 5. How is the test-retest robustness of the CF model?

Task Performance

Comparing the prediction accuracy using the CF model vs task performance (behavioral) for the parietal LH search space in the WM task.



Amount of Resting State Data Required

RS Data needed for subjects with low and high motion



Motion in Task

Comparing mean tstat activation in parietal LH search space (tstat), CF prediction accuracy (r), task performance (%age), averaged relative movement in rest and task runs (mm)



Movement Rest Runs

Learning methods

We are solving $Y_{Vx1} = X_{VxP} \beta_{Px1}$ which can be done in the following ways:

- Ordinary Least Squares (OLS)
- Regularized ridge regression $Y_{Vx1} = X_{VxP} \beta_{Px1} + \epsilon$ where the regularization parameter penalizes overfitting
- Principal component analysis reduces the X matrix $Y_{Vx1} = X_{VxT} \beta_{Tx1}$
- Deep Neural Network (DNN): Dense architectures with 8 variants including regularized and unregularized versions


DNN model performance

DNN model performance for 32 test subjects compared with Ridge based approach. The model was trained on 128 subjects and tested on 32 subjects for DNN. For Ridge there was no difference in prediction accuracy with subjects greater than 50.



Type of Model

- Ordinary Least Squares (OLS) performs poorly overall
- Ridge Regression results peak after around 10 subjects
- Principal Component Analysis (PCA) followed by either Ridge or OLS performs around the same as Ridge regression
- Deep Neural Network (DNN) performs similar to Ridge

Test Retest Analysis

Test retest analysis looks how well we can get similar results on different days.

HCP Test Retest with 42 subjects having the whole protocol repeated twice with an average gap of around 5 months.

Only 39 subjects have full data on all the 7 tasks.

CF prediction accuracy across tasks and sessions



Cross Scanner Predictions

We acquired in-lab dataset performing the same HCP WM task with 18 minutes of resting state data and four runs.

We train the model on one task and predict on the other.

$$Y_{Vx1}^{1} = X_{VxP}^{1} \beta_{Px1}^{1}$$
$$Y_{Vx1}^{2} = X_{VxP}^{2} \beta_{Px1}^{2}$$

$$X^{1}_{VxP}\beta^{2}_{Px1} = y^{21}_{Vx1}$$

Transfer Learning Analysis for 2bk contrast



Summary

We demonstrated the effects of motion in task, resting state and task performance of the CF model prediction accuracy, the amount of resting state data required for optimal model building, the number of subjects required for different types of models.

We analysed if movie data can be used if resting state data is not available or harder to collect.

We tested the efficacy of the CF model in test retest dataset.

We observed good cross scanner predictability of the CF models

Cerebellar Connectome Fingerprinting

Cerebellar Connnectome Fingerprinting

Cerebellum is originally thought to be related to motor function but recent studies have shown that it is involved in working memory, attention and other higher cognitive tasks (e.g. Stoodley and Schmahmann, 2009; Brissenden et. al., 2016; Brissenden and Somers, 2018)

A lot of the research focused on Connectivity fingerprinting has focused on the cerebral cortex, but can we extend this approach to the cerebellum?

Dataset

Human Connectome Project, 169 subjects

Working memory, relational processing, social processing, reward processing (gambling), motor movement, language processing tasks

Cerebellar search space

Resting state data - 4 runs of 15 minutes each



Individualized cerebellar connectivity fingerprints



Tripathi & Somers, NeuroImage (2023)

Individualized cerebellar connectivity fingerprints



Tripathi & Somers, NeuroImage (2023)

Individual specificity in predictions



How are the coefficients related with activations?



Summary

CF predictions in the cerebellum are stronger than group average model for cognitive tasks of the HCP except language task.

We see similar individual specificity in predictions in the cerebellum as earlier studies have reported (Tavor et. al. 2016, Tobyne et. al. 2018).

Activations in the cortex are proportional to model coefficients across tasks.

Neuropredict - Motor

CF for presurgical planning

Gliomas constitute the majority of brain tumors operated across the US.

Some neurosurgeons have started using task fMRI to map out brain regions for presurgical planning to minimize tissue damage due to surgery.

Though not all hospitals have the capability and expertise to run task fMRI protocols.

Some patient populations find it difficult to perform tasks in the MRI scanner.

Can we use CF to aid in presurgical planning by mapping motor and language networks across patients?

Dataset

HCP dataset - 169 healthy subjects with motor and language tasks.

Motor task: finger tapping/toe squeeze/tongue movement.

Language task: story comprehension

Clinical dataset from Brigham and Women's hospital with 15 patients and 15 healthy controls:

4-7 mins of resting state scan.

Language task: sentence completion.

Motor task: hand & foot movement, lip pursing.



Left Hand - Avg (e



Tripathi et al., Human Brain Mapping (2024)

Effect of Task Contrasts



Effect of Parcellation **Schemes**

a)





Role of Search Space



Effect of Task Reliability



Cross Scanner Predictions

a)



Condition

Patient Predictions



Patient Predictions



Patient predictions without ground truth



Summary

For prediction of the motor network, the 'vs-avg' contrast, Schaefer parcellation, motor only search space works betters

We need about 20 subjects and greater than four mins of resting state data for optimal training.

For making predictions, the more the amount of data per subject, the better.

We are able to make good predictions for some patients.

We need better strategies for cross scanner and sequence harmonization.

Patients with higher grade gliomas are harder to predict.

Alzheimer's Disease modeling

Network Analysis and Connectivity based Predictive Modeling

Connectome Based Predictive modelling of Alzheimer's disease (AD)

AD progression starts years before the first symptoms occur.

Can we use CPM method to predict tau/amyloid concentrations across different AD types?

Dataset

Colombia Boston (COLBOS) Cohort study - Autosomal Dominant AD:

32 PSEN1 carriers including 7 MCI subjects

35 PSEN1 non-carriers

Connectome Based Predictive Modelling (CPM)

Connectome Based Predictive Modelling (Finn et. al. 2015, Rosenberg et. al. 2015, Shen et. al. 2017) shows association and predictability of connectome and behavioral measures like attention, fluid intelligence etc.

CF connectome is voxels x parcels whereas CPM connectome is parcels x parcels





Shen et. al. 2017

Amyloid-β FLR 1.40 1.5 1.35 1.4 Predicted Predicted 1.30 • r = 0.53 r = 0.21.25 1.2 1.20 1.1 1.0 1.2 1.4 1.6 1.8 2.0 1.2 1.5 1.6 1.1 1.3 1.4 Actual Actual Positive Network Positive Network

Predicting tau/amyloid in Presenilin1 Carriers

Predicting behavioral scores




Tripathi et al., medRXiv(2024)

Subcortical Contributions



Entorhinal Tau

Summary

Tau/amyloid concentrations and rate of deposition differs across PSEN1 and APOE4 carriers

Global, node and edge level differences between the groups are present across the groups.

CPM able to predict significantly tau concentrations in PSEN1 carriers across entorhinal, precuneus and inferior temporal regions.

CPM able to predict significantly amyloid concentrations in PSEN1 carriers across entorhinal region.

When combined with non carriers, the predictions were non significant for tau/amyloid concentrations and word list recall values.

Models trained on APOE4 carriers and non-carriers were not significant suggesting that COLBOS groups denotes consistent change with the group different from sporadic AD progression.

The model has less false positive rate suggesting possible usability clinically.

Overall Summary

Connectivity based techniques can predict network organization in healthy subjects.

Cerebellar-cerebro connectivity predicts individual specific brain activations.

CF can be used to make predictions in motor and language networks on clinical populations but more work is needed.

Autosomal Dominant AD causes different network disruptions in the brain.

CPM can make strong predictions within ADAD but not in sporadic AD.

What we do?

Integrative Neuroscience & Technology Lab

Our lab operates at the intersection of neuroimaging, neurophysiology, neuroanatomy, data science, and AI to explore the organization of the human brain. We investigate the localization and dynamics of various cognitive functions, how these processes are disrupted in cognitive disorders, and whether predictive models can be developed to better understand and diagnose these conditions.

labs.iitgn.ac.in/int



EEG Foundation Challenge

From Cross Task to Cross Subject EEG Decoding



Figure 1: HBN-EEG Dataset and Data split. A. EEG is recorded using a 128-channel system during active tasks (i.e., with user input) or passive tasks. B. The psychopathology and demographic factors. C. The datasets split into Train, Test and Validation. Details in subsection 1.2 for the proposal.

Acknowledgements





Collaborators at Brigham and Women's Hospital, Charles River Analytics, Mass General Hospital





National Institutes of Health



Thanks a lot for listening

Integrative Neuroscience & Technology: labs.iitgn.ac.in/int