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Utilizing Machine Learning to Understand Adolescent Psychiatric Development

Keywords: Multimodal Imaging, Mental Health Data Science, Graph Fusion

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Problem Description

Introduction

Background

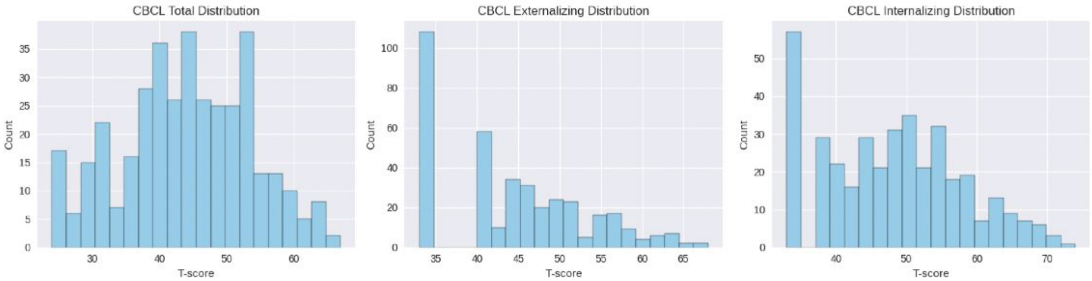
- Adolescence is a period of rapid neurodevelopment when psychiatric symptoms often emerge.
- Resting-state fMRI functional connectivity (FC), sMRI structural connectivity (SC), and T1 morphometric features capture complementary aspects of brain organization.
- Cognitive testing provides a higher level look into brain organization

Child Behavior Checklist Scores

- Total Problems - A global index of behavioral and emotional dysregulation.
- Externalizing Problems - Measures outwardly directed dysregulation (Rule Breaking/Fighting)
- Internalizng Problems - Reflects inwardly directed distress (Depression/Anxiety)

Problem Statement

- Design a machine learning system capable of learning relationships between brain imaging features and cognitive scores
- Provide interpretable attributions to specfic brain regions tied to behavioral targets.



Study Population (Dataset)

Dataset

Human Connectome Project – Development (HCP-D)

- Multimodal MRI data (resting-state fMRI, diffusion MRI, and T1-weighted structural scans) were obtained from the HCP–Development cohort, which captures brain development from childhood through young adulthood.
- Functional connectivity (FC), structural connectivity (SC), and morphometric features were preprocessed using the standardized HCP minimal preprocessing pipelines.
- Target behavior scores were derived from the **Child Behavior Checklist (CBCL)** scores, serving as continuous regression targets for subject-level prediction.

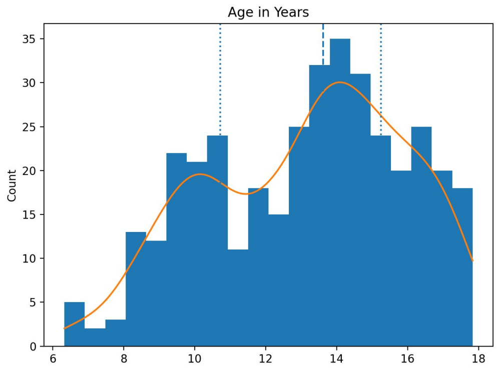
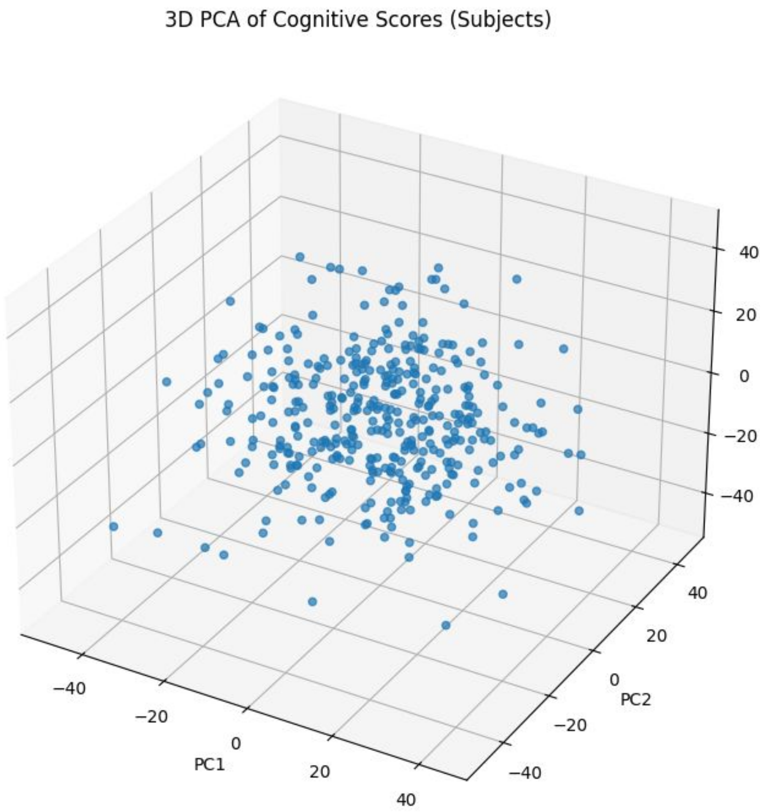


Table 1: Cohort after filtering (subjects with brain imaging, CBCL, and cognitive testing)

Characteristic	Count	%
Total subjects	376	
Sex		
Female	209	55.6
Male	167	44.4
Race		
White	255	67.8
Black or African American	27	7.2
More than one race	72	19.1
Asian	16	4.3
Other/Unknown	5	1.3
American Indian/Alaska Native	1	0.3

Cognitive Similarity Visualized



Preprocessing

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- We followed the HCP minimal preprocessing pipelines for sMRI, DTI and fMRI (Glasser et al., 2013).
- For sMRI, the structural imagesare corrected for gradient nonlinearity distortions, as well as intensity homogeneity correction. Following this, the images were registered and resampled to align with an averaged reference brain in the standard space.
- For fMRI, our preprocessing steps included iterative smoothing, frame censoring, motion correction, and motion parameter regressio according to frame-wise displacement thresholds.
- DTI preprocessing is implemented in MRtrix utilizing denoising, distortion, and motion corrections, co-registration, tissue extraction, and streamline analysis to assist in the calculation of structural connectivity metrics within the same regions of interest (ROIs)

Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, Xu J, Jbabdi S, Webster M, Polimeni JR, Van Essen DC, Jenkinson M; WU-Minn HCP Consortium. The minimal preprocessing pipelines for the Human Connectome Project. Neuroimage. 2013 Oct 15;80:105-24. doi: 10.1016/j.neuroimage.2013.04.127. Epub 2013 May 11. PMID: 23668970; PMCID: PMC3720813.

Comparisons:

Models Used

- Lasso Reg.
- Support Vector Regression
- KMeans
- K-Nearest Neighbors
- Graph Neural Network (GNN) with Graph Encoders, Cross Attention, and Pairwise Diffusion
- GNN with Graph Encoders, Cross Attention, and Spectral Hypergraph Fusion

Model Overview: Key Concepts

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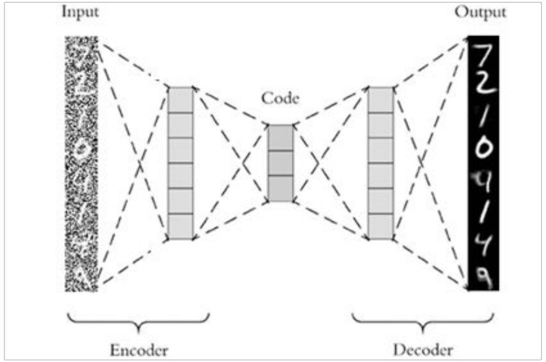
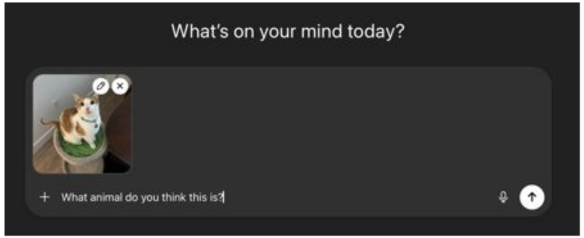
Graph Encoder

A graph encoder is a computational component that transforms a complex graph structure into a lower-dimensional embedding



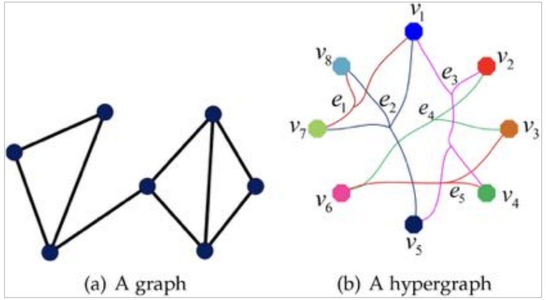
Cross Modal Attention

Way of quantifying how two different modalities influence each other

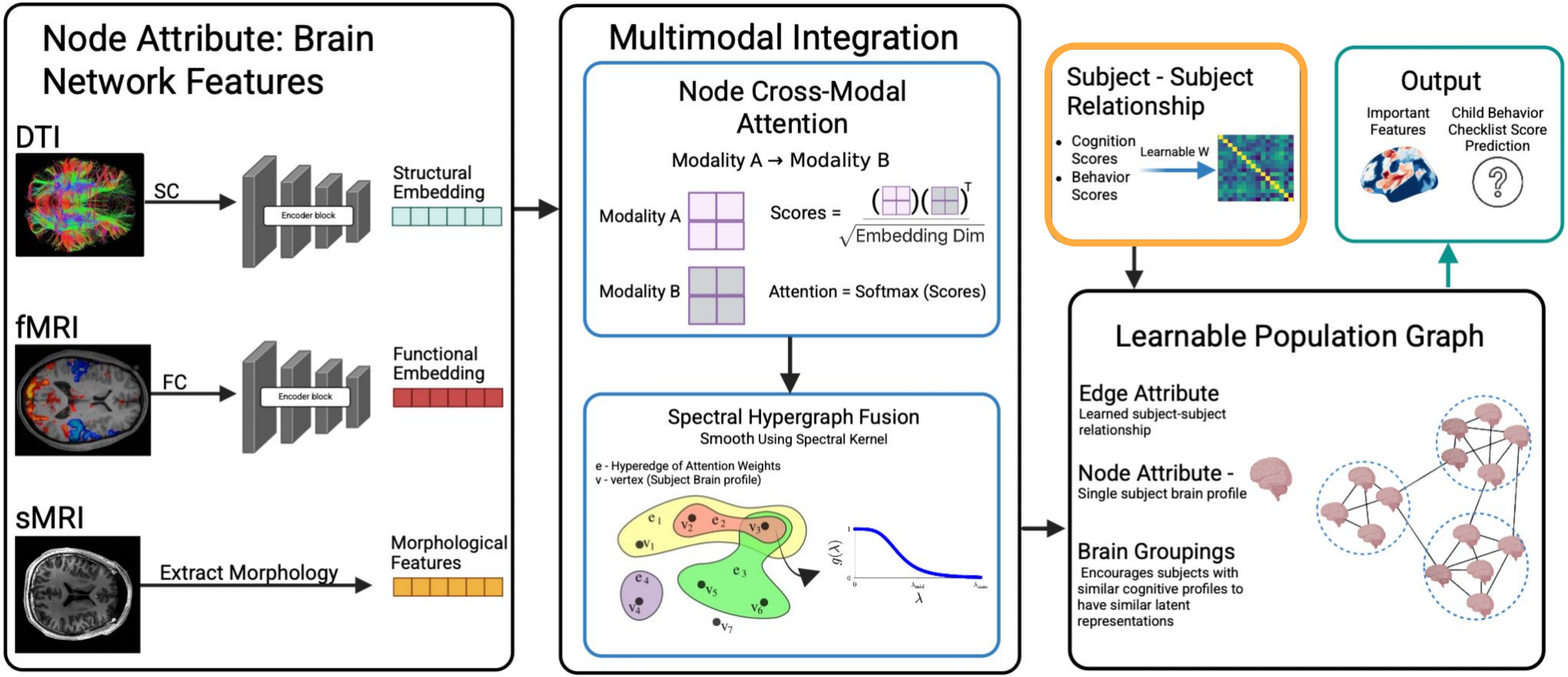


Hypergraph

A hypergraph is a generalization of a standard graph where hyperedges can connect any number of vertices (or nodes), rather than the two vertices of a traditional graph's edges. This allows for the direct modeling of multi-way relationships. (Ie brain networks



Model Overview



Cohort Cognitive Diffusion

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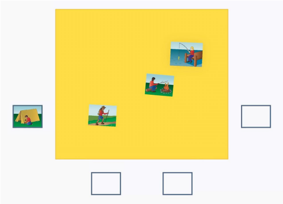
1. Diffuse Cognitive Information across the the hypergraph, influencing subjects with similar cognitive testing scores to have similar latent representations
2. The diffusion effectively aligns neural embeddings (learned from spectral hypergraph fusion) with the behavioral features defined by cognitive testing, producing representations that co-vary with both neural and cognitive organization

EX:

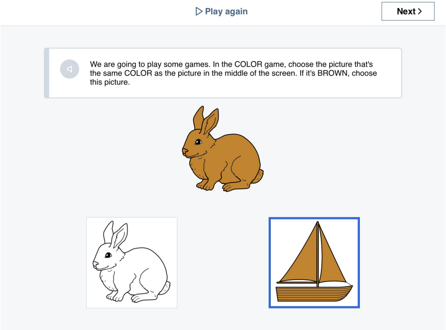
>>>><>>>>	>>>>>>>>>
Incongruent	**Congruent**

<- Flanker

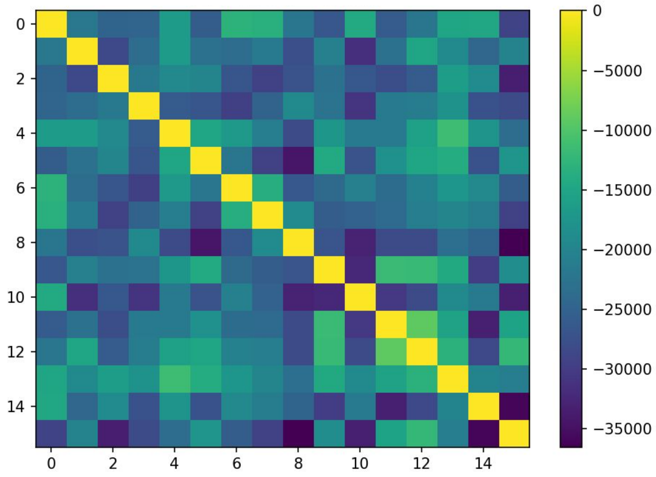


^
| Picture Sequence Memory

Directional Card Change Sort ->



Cognitive Similarity for Batch Size 16 Subjects



Model Comparison

Table 1: Benchmark comparison across models (Validation / Test MSE).

Method	Val MSE	Test MSE
LASSO	146.54	139.51
SVR	83.60	98.36
KNN	86.08	105.77
Kmeans	67.50	97.96
No Hypergraph	75.64	740.40
With Hypergraph	**67.99**	**91.25**

Interpretability for Brain Imaging Types

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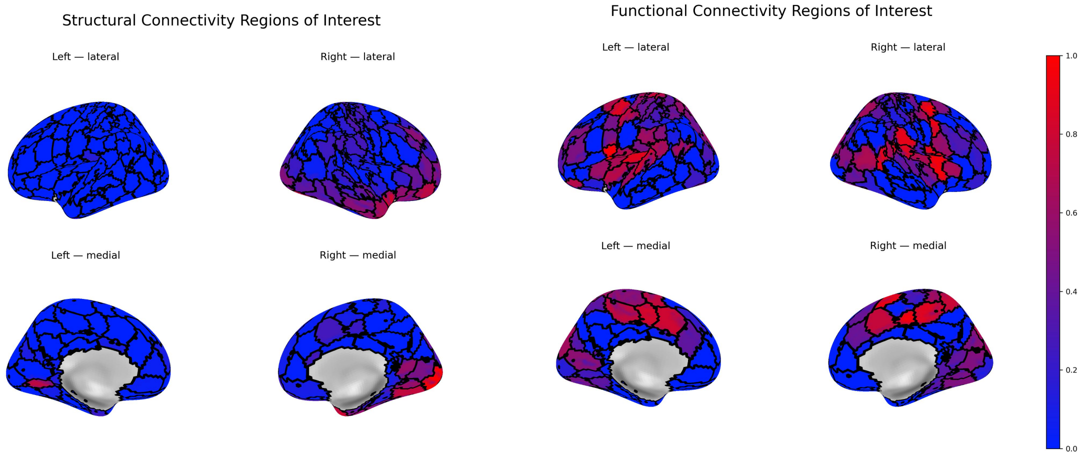
1. **Functional Connectivity (FC):**
   (a) Dominant networks: Salience/Ventral Attention ≫ Somatomotor ≫ Dorsal Attention
   (b) Key hubs: FrOperIns, Medial salience cortex, Pre/Post-central gyrus, Frontal Eye Fields
   (c) Interpretation: Behavioral variance in CBCL is driven by hyper-synchrony of salience and sensorimotor circuits, reflecting arousal, attention dysregulation, and externalizing behaviors
   (d) Laterality: Predominantly right-hemisphere, consistent with heightened emotional and attentional reactivity
2. **Structural Connectivity (SC):**
   (a) Dominant networks: Visual ≫ Salience/Ventral Attention ≫ Limbic ≫ Control ≫ Default
   (b) Key hubs: Occipital (Vis_1–10), Temporal pole & OFC (Limbic), PFCl/PFCv (Control)
   (c) Interpretation: CBCL variance reflects stable anatomical coupling in sensory-emotional pathways—visual-limbic-salience tracts supporting perception–emotion integration
   (d) Laterality: Strong right-hemisphere bias emphasizing emotional–perceptual dominance



Conclusion/Discussion

- This study was conducted on a typical developing population, meaning that the effect of the models can only be so powerful
- More Cross-Site validation would be helpful
- More powerful machine learning models are needed to fully understand complex brain data
- The newly proposed method was able to improve on testing metrics and generate interpretable results aligned with neuroscientific principals