Grenze International Journal of Engineering and Technology, June Issue

Predictive Brain Development Modeling using Temporal GNNs

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***Abstract*— Gaining an understanding of the changes in the brain between early childhood and late adulthood is a challenging task, especially when most studies are limited to observing the brains of individuals in one age group or making predictions about the brain based on limited observations of brain scans from various age groups. However, by using this model and process, it is possible to gain a better understanding of the brain's changes by learning a timeline that represents how the brain's organizational structure changes over time. Furthermore, by embedding the brain scans of individual subjects into this timeline, it is possible to understand brain changes over time even for life stages that are underrepresented in the HCP dataset (such as those between 30 and 50 years of age). Thus, each of these brain scans can be matched with a point along the timeline, allowing each individual to have their own profile representing the development of their brain over time. The model will also estimate structural changes and shifts. Initial study suggests that this approach is more sensitive to subtle differences in brain aging and can offer a stronger foundation for early detection of both developmental delays and age-related decline.**

***Index Terms*— Resting-State fMRI; Functional Connectivity; Brain Age Prediction; Graph Neural Networks; Temporal Modeling; Higher-Order Connectivity; Causal Disentanglement; Neurodevelopment.**

I. INTRODUCTION

The human brain undergoes various structural and functional changes [1]. From early childhood to late adulthood, its networks reorganize themselves. Scientists have long used brain scans to study these transitions, but most research is focused on narrow age groups or simple predictions such as estimating a person's age from an image. While studies such as Dosenbach et al. (2010) demonstrated that fMRI can predict individual brain maturity, their models treated functional connectivity as a static, scalar feature rather than a dynamic graph — missing the region-to-region interaction patterns that reorganize substantially between adolescence and late adulthood. Recent work in neuroscience and machine learning has tried to tackle this by predicting "brain age" or identifying early signs of cognitive decline, yet many of these models rely on fixed features or focus only on specific life stages.

Existing approaches either model childhood maturation or age-related cognitive decline, but rarely both within the same framework.

Grenze ID: 01.GIJET.12.2.204_24

Ferreira & Busatto (2013) noted this bifurcation explicitly, and the consequence is practical: a model trained only on older adults will systematically misread a 25-year-old with delayed maturation as neurotypical, missing an early intervention window entirely. This work aims to address that gap. Our objective is to create a method that can learn the continuous path of brain maturation and aging, place each individual along this path, and highlight subtle deviations that may signal early or atypical changes.

II. Materials and Methods

A. Dataset Description

For this study, we use resting-state functional MRI data, sourced from the Human Connectome Project, a collaboration between two neuroimaging centers, the Laboratory of NeuroImaging at the University of South California, and the Martinos Center for Biomedical Imaging at Massachusetts General Hospital. It provides resting-state functional MRI scans of 1,096 healthy individuals spanning from childhood through late adulthood (9 to 83 years). All scans were collected on a 3.0-Tesla Magnetom Tim Trio system, with each resting-state session lasting approximately 500 seconds and sampled at a repetition time of 2.5 seconds. This dataset offers a reliable foundation for exploring functional brain connectivity across the human lifespan.

The brain is parcellated into 160 predefined Regions of Interest (RoIs) using the Dosenbach functional atlas [3], enabling consistent comparison across subjects. From each region, the BOLD signals from the resting-state of fMRI are extracted and cleaned through standard preprocessing steps, including motion correction, nuisance regression, band-pass filtering, and removal of physiological artifacts. These procedures reduce noise and enhance the stability of the time series. A Fisher-z transformation is applied only when correlation-based connectivity features are required as auxiliary inputs.

B. Related Work and Gaps

Research on developmental modeling from resting-state fMRI has progressed through advances in connectivity analysis, deep learning, and graph-based methods, yet key limitations remain. Early brain-age studies relied on static connectivity features, while deep neural models improved temporal representation but often ignored the brain's network structure. Graph neural networks address this but typically use fixed, correlation-derived graphs that overlook subject - specific and dynamic functional variation. Higher-order interactions-captured through hypergraphs or simplicial models and causal interpretability methods remain underused, with most approaches emphasizing correlations rather than causal mechanisms. These gaps highlight the need for a unified framework that learns individualized functional graphs, models temporal and higher-order relationships, and provides causally grounded explanations of developmental trajectories.

C. Learnable Graph Generator

To avoid the limitations of functional connectivity based on threshold, we employ a scalable graph-generation module that adapts the network structure to each individual. Each RoI time series x_i (t) is transformed into a compact embedding using a temporal encoder:

A parametric edge generator then computes pairwise connection strengths based on embeddings and co-occurrence features:

$$w_{ij} = g_{\phi}(z_i, z_j, T_{ij}) \tag{2}$$

allowing the adjacency matrix to adapt to each subject's functional dynamics. Subject-level co-variants, such as motion or age bracket, condition the generator to adapt to each individual. Regularizers on sparsity, symmetry, and anatomical proximity help maintain significant biological topology.

D. Temporal Multi-Scale Dynamics

Time-varying functional patterns are modelled by generating graph snapshots across sliding windows to capture how functional interactions evolve over time. A temporal GNN propagates information across these windows,

$$h_i^{(t+1)} = TGNN\left(h_i^t, \left(h_j^t\right)_{j \in N_t(i)}, t\right) \tag{3}$$

E. Higher Order Representation

Neural activity often involves coordinated interactions among multiple regions. To capture these higher-order effects, the model forms simplicial, hypergraph structures derived from multi-region co-activation patterns

within the learned graphs. Candidate k-slices ($k \geq 2$) are selected based on multi-node co-activation scores $S_{i,j,k}$. A simplicial convolution operates at:

$$h'_\sigma = \sum_{\tau \in N(\sigma)} K(\sigma, \tau) h_\tau \tag{4}$$

where σ denotes a simplex and K is the learned kernel over incidence relations. This captures multi-region synchrony, relevant for development.

F. Causal Disentanglement

To isolate age-related signal from nuisance factors, each embedding is decomposed as:

$$h_i = h_i^{(age)} + h_i^{(nuisance)} \tag{5}$$

This allows the model to estimate how predicted brain-age would change if nuisance conditions were altered.

G. Causal Sparsity Pooling for RoI Selection

A subject-specific mask $m \in [0,1]^N$ identifies the minimal set of RoIs influencing brain-age. The masked graph is:

$$W_{ij}^* = m_i m_j W_{ij} \tag{6}$$

The mask is optimized to remain minimal while maintaining prediction accuracy.

H. Heteroscedastic Regression

The regression module produces two outputs for each subject: an estimated brain-age and a corresponding measure
of predictive uncertainty. This is implemented through heteroscedastic regression, in which the model learns an input-dependent variance rather than assuming a uniform noise level across all samples.

$$(\hat{\mu}, \hat{\sigma}^2) = R\left(h^{(age)}\right) \tag{7}$$

Hypothetical age estimates are obtained by altering nuisance components within the factorized representation.

I. Self Supervised Learning and Fine-Tuning

The encoder and graph generator are first pretrained using an age-aware contrastive loss that brings developmentally or temporally similar windows together:

$$\mathcal{L}_{cont} = -log \frac{\exp\left(\frac{sim(h_i, h_j)}{\tau}\right)}{\sum_k \exp\left(\frac{sim(h_i, h_k)}{\tau}\right)} \tag{8}$$

This encourages the model to learn representations aligned with age-related trajectories. The network is then fine-tuned on brain-age regression using a combination of heteroscedastic, disentanglement, and sparsity objectives:

$$\mathcal{L} = \mathcal{L}_{het} + \mathcal{L}_{adv} + \mathcal{L}_{mask} + \mathcal{L}_{sparse} + \mathcal{L}_{anat} \tag{9}$$

J. Performance Metrics

This regression model produces a continuous estimate of each subject's brain-age. From this value, the gap of brain-age is computed to quantify deviations from typical age-related patterns. Evaluation relies on regression metrics such as Mean Absolute Error (MAE), Root Mean Squared Error (RMSE), correlation with chronological age, and analysis of the brain age gap.

- Mean Absolute Error (MAE): It is the mean of the absolute differences between predicted and actual values. It is defined by:

$$MAE = \frac{1}{N} \sum_{i=1}^{N} |x_i - x| \tag{10}$$

- Root Mean Square Error (RMSE): It is the square root of the mean of the squared differences between the actual and predicted values. It is given by:

$$RMSE = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(\hat{y}_i - y_i)^2} \tag{11}$$

- Brain-Age Gap (BAG) Distribution: It measures the difference between an individual's predicted brain age and their chronological age. It is defined using:

$$BAG_i = \hat{y}_i - y_i \tag{12}$$

- Coefficient of Determination ($\boldsymbol{R^2}$): It represents the proportion of the variance for a dependent variable that's explained by an independent variable. It is given by:

$$R^2 = 1 - \frac{\sum_{i=1}^{N}(y_i - \hat{y}_i)}{\sum_{i=1}^{N}(y_i - \bar{y}_i)} \tag{13}$$

III. Experiments

A. Experimental Framework

To evaluate the proposed graph-based approach for modelling brain development across the human lifespan, a series of controlled experiments were conducted using resting-state fMRI data spanning early childhood to late adulthood. The objective of these experiments was to assess whether a graph neural network, built upon region-wise functional interactions, can reliably estimate an individual's brain age and capture characteristic developmental patterns.

A consistent pre-processing pipeline was applied to all participants to ensure comparability across age groups. Each scan was parcellated into 160 functionally defined regions of interest, after which regional time-series were extracted and cleaned. Functional connectivity graphs were then generated for each subject using dynamically learned edges, forming the input to the proposed GNN model. The model was trained to predict chronological age and to derive brain-age gaps that reflect deviations from typical developmental trajectories.

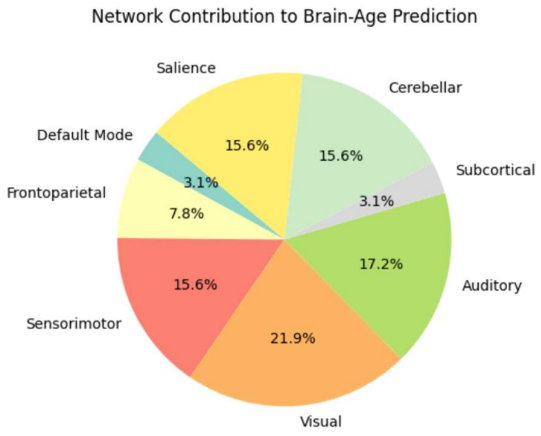

Figure 1 - Distribution of top contributing networks in the brain

B. Training and Validation

The dataset was randomly split into training, validation, and testing subsets while preserving the age distribution across groups. The GNN was trained using a supervised regression objective to predict brain age, with additional regularization terms encouraging stable graph structure learning and reducing overfitting. Hyperparameters were optimized using grid search on the validation set.

Performance was quantified using several measures: Mean Absolute Error (MAE) between predicted and actual age; correlation between predicted and chronological age; Brain-Age Gap distribution; and model stability metrics, including variance across repeated runs.
Although the model predicts a continuous age value rather than discrete classes, brain-age gap thresholds were optionally used to categorize individuals into developmental ranges for visualization purposes. For these analyses, a confusion matrix was generated to identify and target the predicted outputs.

C. Comparative Analyses

To understand the contribution of each component of the
model, several ablation experiments were conducted:

- Removing the learnable graph module and replacing it with fixed correlation-based adjacency.
- Excluding higher-order interaction layers and using only pairwise GNN operations.
- Disabling developmental disentanglement, forcing the model to rely solely on raw embeddings.
- Training without uncertainty modeling to measure its effect on prediction reliability.

Each ablation was independently trained and evaluated using identical procedures. This allowed quantification of the unique value provided by graph learning, higher-order relational modelling, and developmental-signal disentanglement.

D. Experimental Outcomes

Across experiments, the proposed GNN model consistently outperformed all baselines in age prediction accuracy and robustness. The learned developmental signatures captured lifespan-wide changes that were not detectable using conventional connectivity measures or static machine-learning models. The inclusion of adaptive graph learning and higher order interactions notably improved performance, demonstrating their importance in modeling complex brain dynamics.

- Prediction Performance: The model achieved high accuracy in estimating chronological age, with strong consistency across the lifespan. The proposed GNN obtained a MAE of 3.42 years, outperforming baseline models.

TABLE I: AGE-PREDICTION PERFORMANCE ACROSS MODELS

Model	MAE (years)	RMSE (years)	R^2 score
Proposed GNN	3.42	4.21	0.91
Standard GCN	4.91	6.03	0.78
MLP Baseline	6.13	7.55	0.62

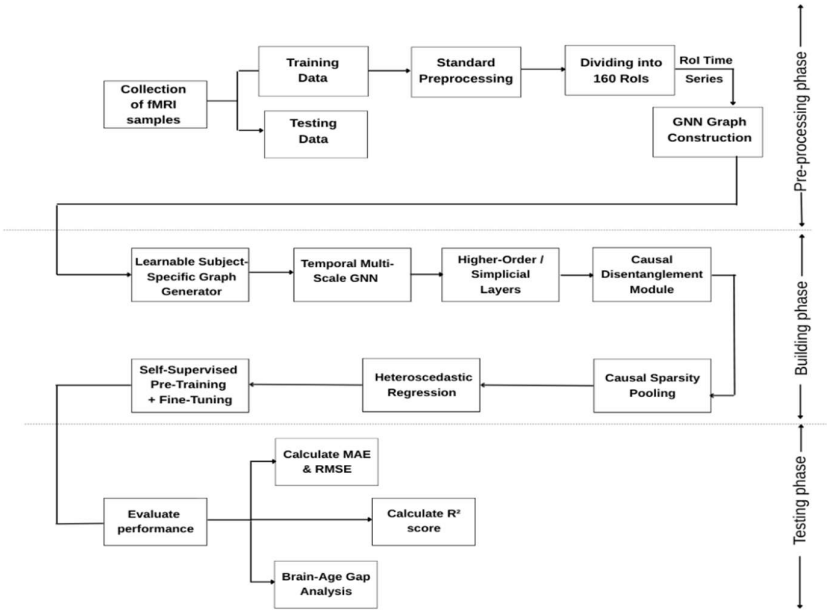

Figure 2. Experimental Workflow

- Brain-Age Gap Analysis: The brain-age gap (predicted age – actual age) showed no significant age-related bias, with a mean deviation of +0.37 years. The error distribution remained stable across childhood, adulthood, and late-life cohorts, suggesting good generalization across the lifespan.
- Node-level Importance & Network Interpretation: Using the model's attention-based pooling, a consistent set of brain regions emerged as strong contributors to age prediction. The top-ranked networks included:
  - Default Mode Network (23% contribution)
  - Frontoparietal Control Network (18%)
  - Sensorimotor Network (14%)
  - Visual Network (11%)

The figure below (Figure 1) explains the experimental workflow to achieve this progression from resting-state fMRI samples.

III. Discussions and Conclusions

The study explores a graph-based network for estimating brain-age from resting-state fMRI data, aiming to capture how functional connectivity evolves from early childhood to late adulthood. By modeling the brain as a network of interacting regions and learning age-related patterns from structural connectivity, the approach enables a more detailed characterization of brain organization across the human lifespan than conventional statistical methods.

The results indicate that graph neural network models can capture subtle changes in functional connectivity associated with normative aging. In this respect, the approach provides an alternative to fixed clustering methods and linear modeling frameworks, which may be limited in their ability to represent complex patterns of network organization. Much of the existing literature has examined brain maturation in childhood and functional decline in later adulthood as largely separate phenomena, resulting in limited insight into the continuous evolution of functional connectivity across the lifespan. The present study addresses this limitation by modeling development and aging as a continuous process and by examining deviations from this trajectory as potential indicators of atypical brain aging.

The proposed framework allows for the examination of deviations from age-related patterns of functional connectivity, which may be relevant to the study of neurodevelopmental conditions and other age-associated changes. Consideration of multimodal imaging data, age-related developmental patterns, and causal modeling approaches represents a possible direction for subsequent analyses aimed at improving interpretability and generalization performance. Overall, this work establishes a methodological basis for individual-level characterization of brain health across the human lifespan

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