# Integrating Slow Neural Oscillations and Physiological Burden for Trait Anxiety Prediction

#### **Anonymous Author(s)**

Affiliation Address email

# **Abstract**

Effective modeling of health outcomes from biomedical time series requires methods that capture both temporal and frequency dynamics. Trait anxiety, a transdiagnostic risk factor, manifests in neural activity and systemic physiology. We present a multimodal graph-attention framework that integrates resting-state fMRI time series with structural connectivity and allostatic-load biomarkers via cross-modal attention. Using 120 participants from the LEMON dataset, the model achieved modest but stable predictive accuracy. Within the brain branch, we systematically compared feature extraction strategies and found that preserving temporal order in slow-4/slow-5 oscillations was essential for prediction, while approaches discarding temporal structure consistently underperformed. Interpretability analyses highlighted limbic-visual circuits and metabolic-immune markers as reproducible contributors. These findings demonstrate that capturing temporal dynamics is critical in health time-series modeling, and show how multimodal graph-attention can provide both predictive value and interpretable digital biomarkers for anxiety vulnerability.

# 1 Introduction

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- Trait anxiety is a stable disposition characterized by heightened anticipatory stress across contexts.

  Neuroimaging has linked it to altered functional connectivity in the default mode and limbic networks

  [1, 2] from resting state fMRI (rsfMRI), and disrupted white-matter pathways [3]. However, existing
  brain-centric approaches rarely account for systemic physiological states that shape neural activity.

  Elevated allostatic load, the cumulative physiological burden from chronic stress adaptation, is
  associated with trait anxiety and may induce inflammation and excitatory/inhibitory neurotransmission
  imbalance [4, 5]. These findings suggest the need for models to integrate brain-body associations
  and to examine neural activity as cellular state changes directly alter regional signals.
- Regional activity metrics such as amplitude of low-frequency fluctuations implicate slow-4/slow-5 oscillations in anxiety disorders [6, 7, 8], yet they capture only amplitude and fail to characterize temporal-frequency dynamics. Prior multimodal efforts have focused on either brain or physiology in isolation, leaving their interaction underexplored.
- We propose a multimodal graph-attention framework that jointly models rs-fMRI time-series features on a structural scaffold and fuses them with allostatic-load biomarkers via cross-modal attention.

  A central contribution is the systematic comparison of feature extraction strategies, showing that preserving temporal order in slow-4/slow-5 oscillations is critical for prediction, whereas frequency-only or order-discarding approaches underperform. This framework also enables us to highlight anxiety-relevant brain connectivity patterns, physiological axes, providing a computational lens on brain-body pathways of anxiety vulnerability.

# 2 Methods

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# 2.1 Dataset and Participants

We used the LEMON dataset [9], with multimodal measures (rs-fMRI, diffusion MRI, blood biomarkers, behavior). From 132 young adults, 120 participants (84 Males, age 20–30) with complete neuroimaging, trait anxiety (STAI[10, 11]), and blood marker data were included. Data were deidentified and relied on the dataset's released preprocessing[12].

# 42 2.2 Neuroimaging and Allostatic Load Data

The rs-fMRI blood oxygen level dependent (BOLD) time series signal (TR=1.4s, timepoints = 522) 43 and diffusion MRI were preprocessed by the standard preprocessing pipelines (motion correction, dis-44 tortion correction, denoising, spatial normalization to MNI152) and parcellated using 183 data-driven 45 regions via voxel-wise clustering of rs-fMRI signals within macro-anatomical regions [12]. Structural 46 connectivity was quantified as streamline counts from diffusion MRI. Allostatic load markers spanned 47 cardiovascular, metabolic, and immune systems (10 biomarkers including, Systolic/Diastolic Blood Pressure, Body Mass Index, Total Cholesterol, Low-Density Lipoprotein Cholesterol, High-Density 49 Lipoprotein Cholesterol, Total Cholesterol to HDL-C Ratio, and Glucose, Creatinine, C-Reactive Protein), following prior anxiety work [13, 14, 15]. Each biomarker was treated as an individual feature without constructing a composite AL marker.

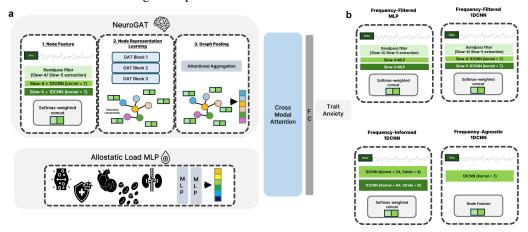


Figure 1: Overview of the model.

# 2.3 Model Architecture

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We propose a multimodal framework (AlloNeuroGAT) combining brain and physiology (Fig. 1a).

**NeuroGAT**: Three GATv2Conv layers with residual connections, each followed by LayerNorm, LeakyReLU, and dropout (0.2). Node features were represented with features extracted from rs-fMRI time series, and diffusion MRI–derived structural connectivity provides the binary adjacency matrix (Fig.1b). Strategies for node feature extraction are as follows:

- Frequency-Filtered MLP: Per-band MLP on slow-4 (0.027–0.073 Hz) and slow-5 (0.01–0.027 Hz) band-pass filtered signals.
- Frequency-Filtered 1D-CNN: Per-band 1D-CNN (kernel=7) on slow-4 and slow-5 band-pass filtered signals.
- **Frequency-Informed 1D-CNN:** Two 1D-CNNs (kernel=64/24; stride=8/4) on unfiltered signals, which are combined to capture both long and short-range temporal dynamics.
- **Frequency-Agnostic 1D-CNN:** A single 1D-CNN (kernel=7) on unfiltered signals. We used softmax-weighted concatenation to combine the outputs of the per-band models, generating a 64-dimensional node feature vector for each brain region.

Allostatic load markers Projection: A two-layer MLP (Leaky ReLU, dropout=0.2) embeds ten biomarkers into a 64-d representation. Inputs are z-scored within each train/val/test splits.

- 70 Cross-Modal Attention: Brain representation (query) attends to AL representation (key/value) via
- 71 2-head cross-modal attention, producing a fused embedding passed to a linear head for trait anxiety
- 72 prediction.

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#### 2.4 Training and Evaluation

- 74 Models were trained with AdamW and MSE loss with early stopping (patience = 20). The learning
- rate and weight decay were selected via a grid search over learning rate = [0.001, 0.0005, 0.0001,
- 76 0.00005] and weight decay = [0.001, 0.01] based on the validation set performance. Performance
- vas evaluated using nested 3-fold subject-level cross-validation, repeated five times with different
- splits and reported on held-out tests using R<sup>2</sup>, MSE, and Pearson correlation coefficient (Pearson r).

# **9 3 Experimental Results**

Table 1: AlloNeuroGAT Feature Extraction Model Performance

Model	$\mathbf{MSE} \left( \downarrow \right)$	$\mathbf{r}^{2}\left(\uparrow\right)$	Pearson r (†)
AlloNeuroGAT-Freq_filtered_MLP	$1.008 \pm 0.06$	$-0.034 \pm 0.061$	$0.115 \pm 0.056$
AlloNeuroGAT-Freq_agnostic_1DCNN	$0.940 \pm 0.035$	$0.036 \pm 0.036$	$0.206 \pm 0.072$
AlloNeuroGAT-Freq_informed_1DCNN	$0.934 \pm 0.017$	$0.042 \pm 0.017$	$0.236 \pm 0.025$
AlloNeuroGAT-Freq_filtered_1DCNN	$0.924\pm0.028$	$0.052 \pm 0.028$	$0.257 \pm 0.05$

#### 3.1 Performance of Node Feature Extraction Strategies

- 81 We systematically compared four temporal feature extraction strategies to evaluate the importance of
- 82 frequency filtering and temporal dynamics for capturing trait anxiety from rs-fMRI signals (Table
- 1). Performance differences across the strategies were modest but consistent across repeated runs
- 84 (Kruskal–Wallis: r p = 0.048,  $R^2 p = 0.069$ , MSE p = 0.072).
- 85 The frequency-filtered 1D-CNN consistently yielded the best performance (table 1). This model
- 86 explicitly targets slow-4 and slow-5 oscillatory bands, which are neurobiologically relevant to anxiety
- 87 [6] while retaining temporal ordering via convolution. By contrast, the frequency-filtered MLP, which
- discards temporal order, consistently underperformed. (post-hoc Dunn's test, p value of r = 0.053,
- 89  $R^2 = 0.062, MSE = 0.067$ ). These results underscore that temporal dynamics, not just frequency
- 90 content, are essential for predicting trait anxiety.

Table 2: Multimodal Model Performance Comparison

Model	MSE (↓)	$\mathbf{r}^2 \left( \uparrow \right)$	Pearson r (†)
NeuroGAT_Only	$0.986 \pm 0.022$	$-0.012 \pm 0.023$	$-0.068 \pm 0.081$
ALMLP_Only	$0.948 \pm 0.051$	$0.028 \pm 0.052$	$0.187 \pm 0.095$
AlloNeuroGAT-Node_coordinate	$0.951 \pm 0.026$	$0.025 \pm 0.026$	$0.198 \pm 0.055$
AlloNeuroGAT-Edge_FC	$0.936 \pm 0.049$	$0.040 \pm 0.050$	$0.204 \pm 0.091$
AlloNeuroGAT-QAL/KV_BrainRep	$0.938 \pm 0.028$	$0.038 \pm 0.029$	$0.218 \pm 0.048$
AlloNeuroGAT (Best)	$0.924 \pm 0.028$	$0.052 \pm 0.028$	$0.257 \pm 0.05$

# 3.2 Ablation Study

To disentangle the contribution of brain and physiology, we compared unimodal baselines (NeuroGAT-

- 93 only, using brain features only; AL-only, using biomarkers only) and several architectural variants
- 94 against the full model. The NeuroGAT-only model failed to generalize, while the AL-only model
- 95 showed modest predictive value (Table 2). The full AlloNeuroGAT significantly outperformed the
- brain-only variant (Mann–Whitney: r p = 0.0008, MSE p = 0.012), confirming that physiological
- 97 markers provide complementary signal, although gains over the AL-only model were not statistically
- 98 reliable.
- 99 Within the brain representation, substituting temporal node features with static ROI coordinates
- marginally degraded performance (Mann–Whitney: rp = 0.095), and replacing the structural graph

with a functional connectivity graph also showed no benefit. Reversing the cross-modal attention roles (Q=allostatic load, K/V=brain) likewise impaired performance. Overall, these findings indicate that both brain and physiological modalities contribute uniquely, and that optimal prediction requires temporal features embedded in a structural scaffold, fused with physiology through brain-driven queries.

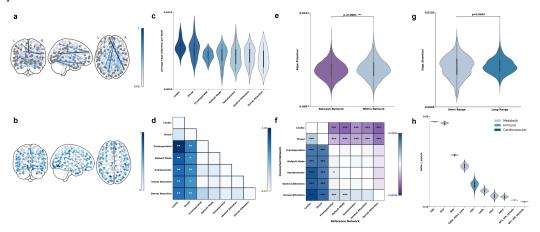


Figure 2: Model Interpretations.

#### 3.3 Model Interpretation

We aggregated attention maps from five runs of the best AlloNeuroGAT to derive edge attention (averaged over layers) and node importance (mean incident–edge attention; Fig. 2a–b). Node importance significantly differed across Yeo networks [16] (Kruskal–Wallis  $H=31.03,\,p<10^{-4}$ ); with Limbic and Visual network consistently ranked above others after FDR-BH correction (Fig. 2c-d). This pattern indicates that affective and sensory systems carried greater predictive weight for trait anxiety.

At the edge level, within-network connections received higher attention than between-network ones (Mann–Whitney U,  $p < 10^{-4}$ ; Fig. 2e). Limbic network showed significantly higher within-network attention than edges to any other network and Visual network also favored within-network edges except for the Limbic–Visual pairing (all  $p(corrected) < 10^{-3}$ ). By contrast, edges projecting from Frontoparietal, Default Mode, or Ventral/Dorsal Attention to Limbic or Visual exceeded those networks' own within-network attention (all  $p(corrected) < 10^{-3}$ ; Fig 2f). Together with node importance, this highlights Limbic and Visual as anxiety-relevant hubs that integrate both local and cross-network signals. Model attention also showed a trend toward favoring long-range over short-range connections (Mann–Whitney U, p = 0.064; Fig. 2g), suggesting distributed pathways are relevant for prediction.

Finally, permutation importance within the allostatic-load branch (1,000 shuffles per marker) highlighted metabolic and immune axes: shuffling creatinine, glucose, body mass index, and C-reactive protein produced the largest drops in performance, underscoring that systemic load in these domains interacts with brain dynamics to shape anxiety vulnerability (Fig. 2h).

# 4 Conclusions

We introduced a multimodal graph-attention framework for modeling health time series that inte-grates rs-fMRI temporal features, structural connectivity, and allostatic-load biomarkers. Experiments showed that preserving temporal dynamics of slow-4/slow-5 oscillations was essential for prediction, while approaches discarding temporal order underperformed. Multimodal fusion with physiology provided modest but consistent gains. Attention-based analyses suggested that limbic-visual con-nectivity and metabolic-immune markers contributed most to model decisions. Although predictive accuracy was modest, the reproducibility of these signals indicates that capturing temporal dynamics can yield stable and interpretable patterns from heterogeneous biomedical time series, positioning brain-body integration as a promising direction for future health research.

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