Graph-Attention-Based Integration of Brain Structure and Function for Trait Anxiety Prediction: Preliminary Results

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Abstract

Trait anxiety is a stable personality trait linked to increased vulnerability for internalizing disorders. Although altered intrinsic activity in individuals with trait anxiety has been reported in resting-state fMRI studies, its relationship to structural connectivity, which is axonal pathways of large-scale brain dynamics, remains underexplored. Leveraging the LEMON dataset (N = 132), we trained a graph-attention network integrating temporally structured functional signals at rest with subject-specific structural constraints. Our model outperformed a traditional structure–function coupling baseline, achieving statistically significant prediction (*r = 0.194, p = 0.026*). Attention based interpretation highlighted importance of frontal–parietal and occipital pathways, suggesting that the attentional and sensory networks may contribute to trait anxiety.

Keywords: Trait Anxiety; Graph Attention Network, Structure-Function, Brain Network

Introduction

Trait anxiety, a stable predisposition to experience heightened anxiety across contexts, is associated with attention and perceptual biases (Gidron, 2020). These biases may manifest in large-scale neural dynamics, and resting-state fMRI (rsfMRI) studies have reported altered activities in individuals with high trait anxiety, particularly in default mode, salience, and frontoparietal networks (Xu et al., 2019). However, the structural substrates of these alterations, involving white matter— the axonal architecture of large-scale brain dynamics— remain underexplored. Prior work has identified structural alterations in individuals with trait anxiety (Saviola et al., 2020; Yang et al., 2020), yet few have examined how structure and function jointly contribute to anxiety-related neural patterns.

To link structural and functional profiles of the brain, structure-function (SC-FC) coupling is commonly used, typically based on region-wise correlations between the connectivity profiles (Gu et al., 2021). Nonetheless, due to fundamental differences in modalities (axons vs. BOLD signals), direct alignment is inherently limited (Honey et al., 2009). Moreover, static coupling metrics fail to capture rsfMRI's temporal dynamics. Meanwhile, individual-level prediction of trait anxiety remains challenging (Boeke et al., 2020), underscoring the need for integrative model that account for both structural constraints and functional dynamics.

Here, we propose a graph attention network (GAT) that encodes structural connectivity and temporally enriched rsfMRI signals. This approach enables individualized trait anxiety prediction while revealing interpretable patterns of *structure-function* associations.

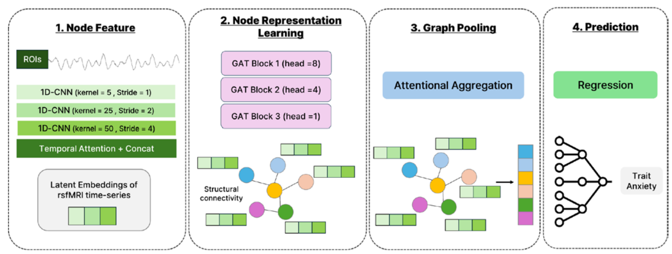

Figure 1. Graph Attention Network Analysis Flow.

Methods

Participants We used the Max Planck Institute's LEMON dataset (Babayan et al., 2019), including rsfMRI, diffusion MRI, and behavioral data. 132 young adults (95 males, age 20–30) with complete neuroimaging and State-Trait Anxiety Inventory scores (Marteau & Bekker, 1992) were included. Structural connectivity was defined as streamline counts; functional data were resting-state BOLD time series. Brain regions were parcellated using a 183-region atlas provided with the dataset (Jimenez-Marin et al., 2024), generated via voxel-wise clustering of rs-fMRI signals within macro-anatomical regions (Diez et al., 2015). This approach aims to capture modular correspondences between structural and functional networks often missed by anatomical templates (Craddock et al., 2012; Diez et al., 2015).

Graph Attention Network

We implemented a GAT model (Veličković et al., 2017) to predict individual trait anxiety scores based on temporal rsfMRI embeddings (node features) and subject-specific structural connectivity (graph edges) (Figure 1).

Node Feature Encoding For each region, the first and last 10% of time points were removed to reduce edge noise. Three parallel 1D convolutional neural networks (kernel sizes: 5, 25, 50) extracted temporal patterns across multiple timescales, consistent with hierarchical temporal organization in resting-state brain activity (Vidaurre et al., 2017). Outputs were softmax weighted and concatenated as node features.

Architecture and Training The model consisted of three GAT layers (heads: 8, 4, 1) with residual connections, layer normalization, LeakyReLU, and dropout (0.1). Node features were pooled using Attentional Aggregation and fed into a two-layer MLP for prediction. Training used the AdamW optimizer, MSE loss, and a warmup cosine decay scheduler. Hyperparameters were selected based on mean R^2 across inner validation sets. Models were trained for up to 300 epochs (batch size 16) with early stopping. All experiments used nested 3-fold cross-validation, repeated five times with different random seeds. Train, validation, and test sets were identical across models and mutually exclusive to ensure fair comparison. No data augmentation was applied.

Baseline Comparison We compared our approach to a conventional SC-FC coupling model using Spearman correlations between regional connectivity profiles as features, followed by support vector regression with identical cross-validation procedures.

Results & Conclusion

Compared to the traditional structure-function coupling approach, our GAT-based model demonstrated superior predictive performance. While the baseline model yielded low and statistically non-significant results (r = 0.066, p = 0.452, R^2 = –0.053, MAE = 0.814) with high variability across repeated settings (mean R^2 = –0.172 ± 0.157), the GAT model achieved a statistically significant prediction of individual trait anxiety scores (r = 0.194, p = 0.026, R^2 = 0.016, MAE = 0.77) when aggregated across five repeated nested 3-fold CVs. Nonetheless, the overall effect size remained modest, with the average R^2 across test folds (–0.004 ± 0.017), likely reflecting the subtle and distributed neural correlates of trait anxiety. A 5,000-iteration permutation test further confirmed that the observed association was not attributable to chance (r = –0.057, p = 0.515).

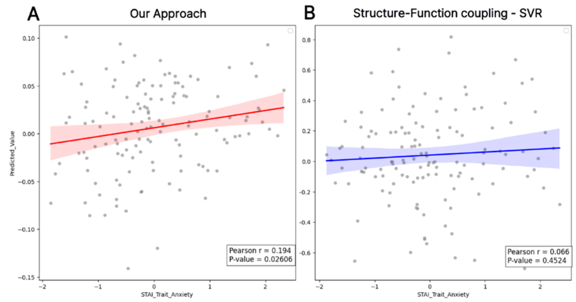

Figure 2. Predicted and actual trait anxiety correlation

Edge-level attention scores revealed the most predictive connections. After z-scoring and thresholding (z > 2), attention maps highlighted prominent attention to frontal–parietal, occipital–temporal, and intra-occipital pathways (Figure 3; Table 1), aligning with prior work implicating attention and sensory networks in trait anxiety (Sylvester et al., 2012; Yin et al., 2016).

These results indicate that GAT-based integration of structural and functional features provides a measurable advantage over traditional SC–FC coupling, yet also highlight the limitations of relying solely on neuroimaging for modeling individual trait anxiety. Incorporating other relevant physiological or behavioral factors may be necessary to improve our understanding of the individual variability underlying trait anxiety.

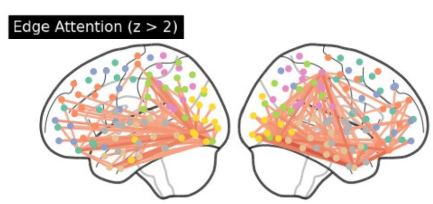

Figure 3. Attention maps of edges (z>2)

Table 1: Top 3 Lobe-Lobe attention scores

Lobe - Lobe	Mean Attention scores	Standard deviation
Frontal-Parietal	2.62	0.801
Occipital-Temporal	2.602	0.486
Occipital- Occipital	2.57	0.47

References

Babayan, A., Erbey, M., Kumral, D., Reinelt, J. D., Reiter, A. M., Röbbig, J., Schaare, H. L., Uhlig, M., Anwander, A., & Bazin, P.-L. (2019). A mind-brain-body dataset of MRI, EEG, cognition, emotion, and peripheral physiology in young and old adults. *Scientific data*, *6*(1), 1-21.

Boeke, E. A., Holmes, A. J., & Phelps, E. A. (2020). Toward robust anxiety biomarkers: a machine learning approach in a large-scale sample. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *5*(8), 799-807.

Craddock, R. C., James, G. A., Holtzheimer III, P. E., Hu, X. P., & Mayberg, H. S. (2012). A whole brain fMRI atlas generated via spatially constrained spectral clustering. *Human brain mapping*, *33*(8), 1914-1928.

Diez, I., Bonifazi, P., Escudero, I., Mateos, B., Muñoz, M. A., Stramaglia, S., & Cortes, J. M. (2015). A novel brain partition highlights the modular skeleton shared by structure and function. *Scientific reports*, *5*(1), 10532.

Gidron, Y. (2020). Trait anxiety. In *Encyclopedia of behavioral medicine* (pp. 2255-2256). Springer.

Gu, Z., Jamison, K. W., Sabuncu, M. R., & Kuceyeski, A. (2021). Heritability and interindividual variability of regional structure-function coupling. *Nature Communications*, *12*(1), 4894.

Honey, C. J., Sporns, O., Cammoun, L., Gigandet, X., Thiran, J.-P., Meuli, R., & Hagmann, P. (2009). Predicting human resting-state functional connectivity from structural connectivity. *Proceedings of the National Academy of Sciences*, *106*(6), 2035-2040.

Jimenez-Marin, A., Diez, I., Erramuzpe, A., Stramaglia, S., Bonifazi, P., & Cortes, J. M. (2024). Open datasets and code for multi-scale relations on structure, function and neuro-genetics in the human brain. *Scientific data*, *11*(1), 256.

Marteau, T. M., & Bekker, H. (1992). The development of a six-item short-form of the state scale of the Spielberger State—Trait Anxiety Inventory (STAI). *British journal of clinical Psychology*, *31*(3), 301-306.

Saviola, F., Pappaianni, E., Monti, A., Grecucci, A., Jovicich, J., & De Pisapia, N. (2020). Trait and state anxiety are mapped differently in the human brain. *Scientific reports*, *10*(1), 11112.

Sylvester, C. M., Corbetta, M., Raichle, M., Rodebaugh, T., Schlaggar, B., Sheline, Y., Zorumski, C., & Lenze, E. (2012). Functional network dysfunction in anxiety and anxiety disorders. *Trends in neurosciences*, *35*(9), 527-535.

Veličković, P., Cucurull, G., Casanova, A., Romero, A., Lio, P., & Bengio, Y. (2017). Graph attention networks. *arXiv preprint arXiv:1710.10903*.

Vidaurre, D., Smith, S. M., & Woolrich, M. W. (2017). Brain network dynamics are hierarchically organized in time. *Proceedings of the National Academy of Sciences*, *114*(48), 12827-12832.

Xu, J., Van Dam, N. T., Feng, C., Luo, Y., Ai, H., Gu, R., & Xu, P. (2019). Anxious brain networks: A coordinate-based activation likelihood estimation meta-analysis of resting-state functional connectivity studies in anxiety. *Neuroscience & Biobehavioral Reviews*, *96*, 21-30.

Yang, C., Zhang, Y., Lu, M., Ren, J., & Li, Z. (2020). White matter structural brain connectivity of young healthy individuals with high trait anxiety. *Frontiers in neurology*, *10*, 1421.

Yin, P., Zhang, M., Hou, X., Tan, Y., Fu, Y., & Qiu, J. (2016). The brain structure and spontaneous activity baseline of the behavioral bias in trait anxiety. *Behavioural brain research*, *312*, 355-361.