

## INTRODUCTION

- **Key Idea:** Guiding diffusion process at each node by a downstream transformer via diffusion-kernel and multi-head attention.
- **Problem:** Limitations in interpreting the brain networks in a scenario with multiple imaging biomarkers.
  - Convolutional approaches ineffectively aggregate information from distant nodes, while attention-based methods exhibit deficiencies in capturing node-centric information, particularly in retaining critical properties from pivotal nodes.
  - These shortcomings reveal challenges for identifying disease-specific variation from diverse features from different modalities.
- **Contribution:**
  - Proposing a novel framework to aggregate both short- and long- range properties for better prediction of graph labels.
  - Demonstrating superior performance on graph classification in comparisons to the state-of-the-art methods.
  - Showing interpretability on the brain networks in a scenario with multiple imaging biomarkers.

## PRELIMINARY: GRAPH KERNEL CONVOLUTION

- An undirected graph  $G = \{V, E\}$  with  $N$  nodes comprises a node set  $V$  and an edge set  $E$ . A symmetric adjacency matrix  $A$  and a diagonal degree matrix  $D$  can be computed from  $E$ . A graph Laplacian is defined as  $L = D - A$ . It has a complete set of orthonormal eigenvectors  $U = [u_1 | u_2 | \dots | u_N]$  and corresponding real and non-negative eigenvalues  $0 = \lambda_1 \leq \dots \leq \lambda_N$ , so does the normalized Laplacian  $\hat{L} = D^{-1/2} L D^{-1/2}$ .

- From Spectral Graph Theory, the choice of a kernel function determines specific graph characteristics. A heat-kernel between nodes  $p$  and  $q$  is spanned by  $U$  as

$$h_s(p, q) = \sum_{i=1}^N e^{-s\lambda_i} u_i(p) u_i(q) \quad (1)$$

where  $u_i$  is the  $i$ -th eigenvector. The kernel  $e^{-s\lambda_i}$  captures smooth transition between nodes within the scale  $s$  as a low-pass filter. Graph Fourier transform, i.e.,  $\hat{x} = U^T x$ , defines the graph convolution  $*$  of a signal  $x(p)$  with a filter  $h_s$  as

$$h_s * x(p) = \sum_{i=1}^N e^{-s\lambda_i} \hat{x}(i) u_i(p) \quad (2)$$

whose band-width is controlled by the scale  $s$ .

## GNN WITH TRANSFORMER-GUIDED ADAPTIVE DIFFUSION (GTAD)

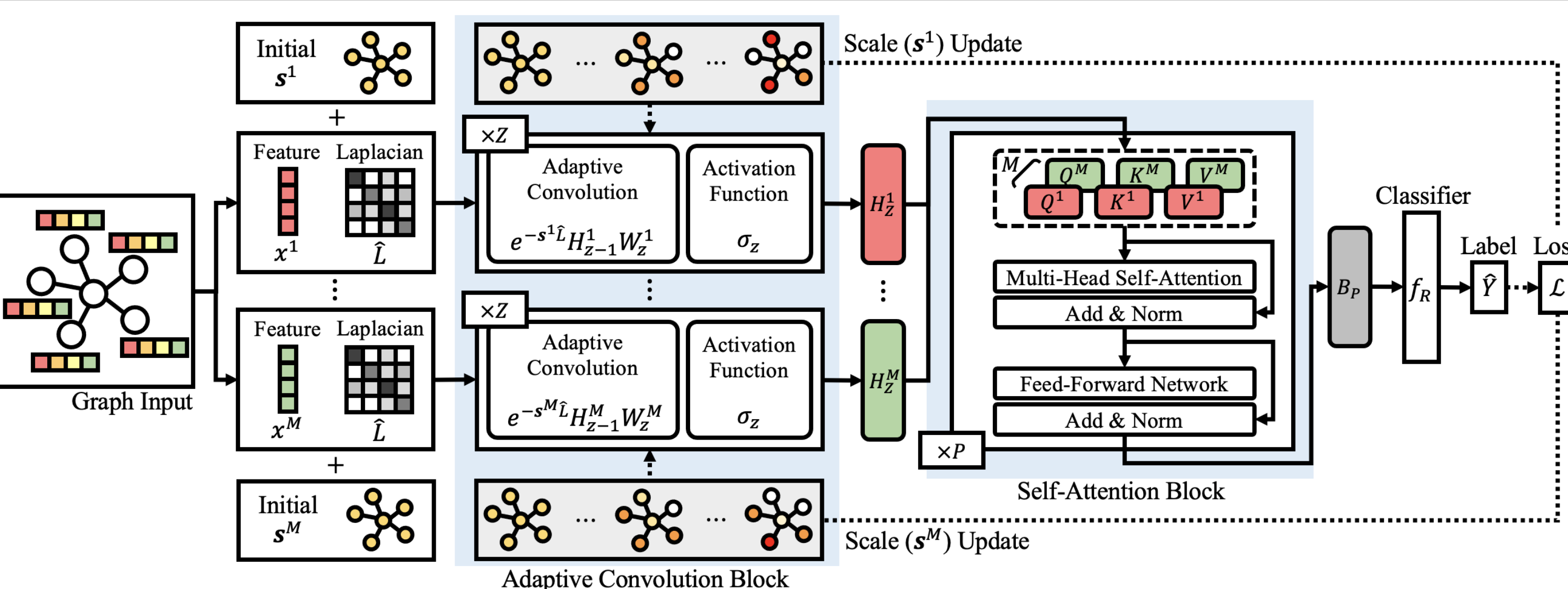


Figure: Illustration of our framework (GTAD). A novel end-to-end framework GTAD that learns node-centric parameters of a diffusion kernel which are governed by a transformer.

- **Modality-wise Adaptive Convolution Block.** Consider  $G$  given as  $\hat{L} \in \mathbb{R}^{N \times N}$ , a set of features (i.e., imaging measures)  $X = \{x^m\}_{m=1}^M$  defined on  $N$  nodes from  $M$  modalities, a set of trainable scales  $\{s^m\}_{m=1}^M$  where  $s^m \in \mathbb{R}^N$  and a graph label  $Y$ . Each encoder consists of multiple graph convolution layers that adaptively aggregate features for each node with a non-linear activation function  $\sigma_z$  as

$$H_z^m = \sigma_z(e^{-s^m \hat{L}} H_{z-1}^m W_z^m). \quad (3)$$

- **Modality-wise Self-Attention Block.** The obtained embeddings  $\{H_z^m\}_{m=1}^M$  are inputted to an attention block to compute node-wise attention scores. Using the self-attention scores, a self-attention value is computed as

$$\phi(Q^m, K^m, V^m) = \sigma\left(\frac{Q^m K^{mT}}{\sqrt{C}}\right) V^m. \quad (4)$$

- **Transformer-Guided Scale Update.** To update a scale  $s_n^m$  at the  $n$ -th node for the  $m$ -th encoder, the objective function is defined by cross-entropy between the true value  $Y_{ij}$  and the prediction  $\hat{Y}_{ij}$ .

$$\mathcal{L} = -\frac{1}{T} \sum_{t=1}^T \sum_{j=1}^J Y_{tj} \ln \hat{Y}_{tj} + \alpha \frac{1}{M} \sum_{m=1}^M \sum_{n=1}^N \mathbb{1}_{s < 0} |s_n^m|. \quad (5)$$

Update of the modality-specific scales is performed as  $s \leftarrow s - \beta \frac{\partial \mathcal{L}}{\partial s}$  via gradient-descent with a learning rate  $\beta$ .

## ALZHEIMER'S DISEASE NEUROIMAGING INITIATIVE (ADNI)

- On the same parcellation, region-wise imaging features such as Standard Uptake Value Ratio (SUVR) of metabolic intensity from FDG-PET,  $\beta$ -Amyloid protein from Amyloid-PET and cortical thickness from MRI were measured.
- Diagnostic labels: Control (CN), Significant Memory Concern (SMC), Early Mild Cognitive Impairment (EMCI)

Table: Demographics of the preclinical ADNI dataset.

Category	CN	SMC	EMCI
# of subjects	333	172	414
Gender (Male / Female)	156 / 177	62 / 110	240 / 174
Age (Mean±Std)	73.0 ± 5.9	71.7 ± 5.2	71.0 ± 7.7

## CLASSIFICATION RESULT

Table: Preclinical AD classification performance (CN/SMC/EMCI) on ADNI data.

Modalities	Cortical Thickness & $\beta$ -Amyloid			Cortical Thickness & FDG		
Methods	Accuracy	Precision	Recall	Accuracy	Precision	Recall
GCN	0.861±0.04	0.772±0.06	0.780±0.06	0.873±0.02	0.802±0.02	0.813±0.03
GAT	0.896±0.01	0.827±0.03	0.839±0.02	0.882±0.02	0.811±0.03	0.844±0.03
GraphHeat	0.868±0.02	0.777±0.05	0.797±0.04	0.887±0.03	0.821±0.04	0.834±0.03
GDC	0.858±0.02	0.767±0.03	0.786±0.04	0.842±0.01	0.743±0.02	0.765±0.03
ADC	0.906±0.02	0.835±0.03	0.861±0.04	0.896±0.01	0.831±0.01	0.847±0.02
LSAP	0.911±0.01	0.847±0.03	0.872±0.02	0.934±0.02	0.899±0.05	0.904±0.03
NodeFormer	0.916±0.02	0.856±0.04	0.865±0.02	0.944±0.01	0.913±0.03	0.921±0.02
DIFFormer	0.930±0.01	0.877±0.03	0.900±0.02	0.954±0.01	0.923±0.02	0.944±0.01
SGFormer	0.941±0.01	0.894±0.03	0.911±0.02	0.959±0.01	0.931±0.01	0.945±0.01
GTAD (Ours)	<b>0.945±0.02</b>	<b>0.901±0.03</b>	<b>0.919±0.02</b>	<b>0.963±0.01</b>	<b>0.935±0.02</b>	<b>0.948±0.01</b>

Modalities	$\beta$ -Amyloid & FDG			All Imaging Features		
Methods	Accuracy	Precision	Recall	Accuracy	Precision	Recall
GCN	0.880±0.01	0.806±0.02	0.813±0.02	0.888±0.02	0.816±0.02	0.826±0.02
GAT	0.877±0.02	0.815±0.03	0.814±0.04	0.912±0.01	0.858±0.02	0.864±0.02
GraphHeat	0.880±0.02	0.804±0.05	0.824±0.03	0.893±0.02	0.824±0.03	0.839±0.03
GDC	0.866±0.02	0.787±0.03	0.790±0.03	0.867±0.02	0.779±0.03	0.799±0.02
ADC	0.910±0.01	0.865±0.02	0.856±0.02	0.904±0.02	0.855±0.04	0.858±0.02
LSAP	0.922±0.02	0.862±0.05	0.893±0.03	0.912±0.01	0.844±0.04	0.879±0.02
NodeFormer	0.931±0.01	0.887±0.03	0.893±0.03	0.938±0.02	0.900±0.03	0.902±0.03
DIFFormer	0.951±0.01	0.919±0.03	0.933±0.02	0.953±0.01	0.920±0.02	0.936±0.02
SGFormer	0.954±0.01	0.923±0.03	0.936±0.02	0.951±0.01	0.911±0.02	0.933±0.02
GTAD (Ours)	<b>0.962±0.01</b>	<b>0.935±0.02</b>	<b>0.946±0.02</b>	<b>0.963±0.01</b>	<b>0.943±0.01</b>	<b>0.941±0.02</b>

## INTERPRETATION OF THE TRAINED GTAD

- **Discussion on the Scales**

- The trained model yields node-wise optimized scales, where each node corresponds to a specific ROI in the brain.

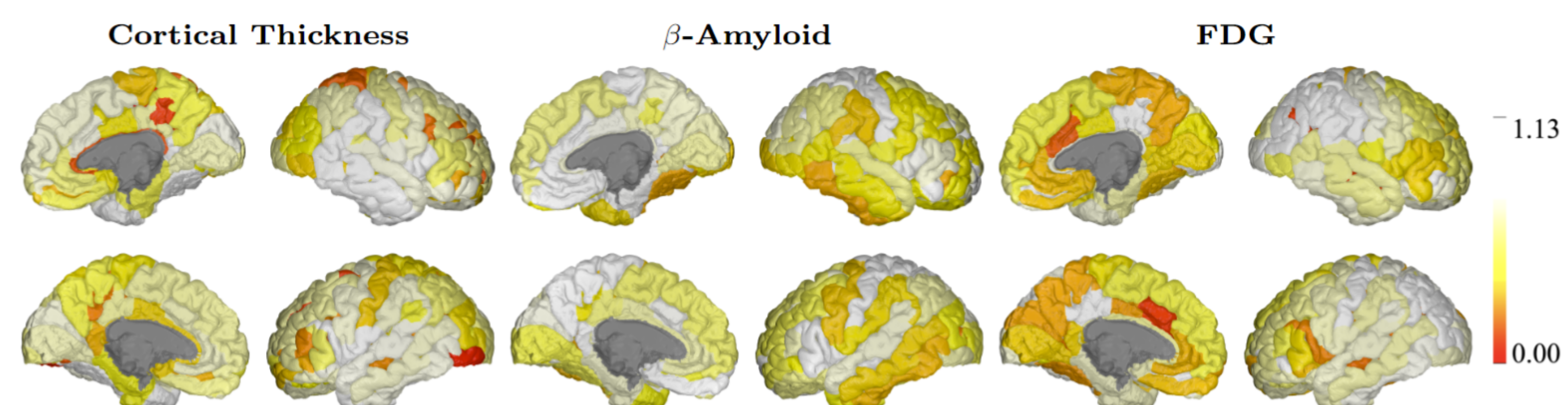


Figure: Visualization of learned scales on the cortical regions of left (top) and right (bottom) hemispheres.

- **Pre-clinical AD via ROI Attention**

- From the attention block, each ROI gains long-range characteristics from other ROIs by modality-wise attention mechanism.
- Most relevant ROIs in Preclinical AD prediction can be detected by total attention scores that represent the intensity of attention at each ROI in the brain.

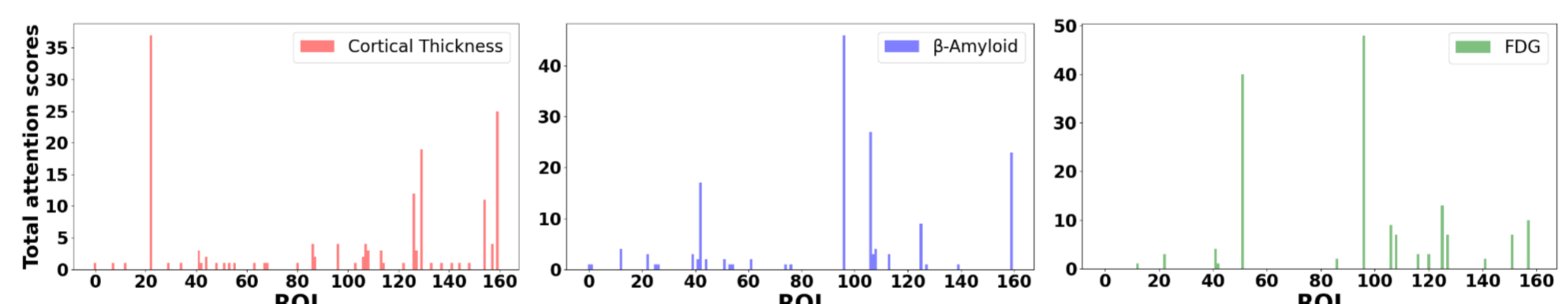


Figure: Distribution of attention scores across all brain regions with cortical thickness (left),  $\beta$ -Amyloid (center) and FDG (right).

- **Ablation Study on the Blocks**

- To explore the effect of each block, ablation study on convolution types and attention types for preclinical AD classification is given.

Table: Performance comparisons of different blocks. For attention block, our multi-modal (MM) attention and existing position-wise attention are compared.

Convolution Block	MM Attention	Accuracy	Precision	Recall
Multi-Layer Perceptron	✗	0.939±0.03	0.893±0.05	0.913±0.04
	✓	0.947±0.02	0.906±0.04	0.933±0.02
Graph Convolution Layer	✗	0.899±0.01	0.835±0.03	0.849±0.03
	✓	0.900±0.01	0.834±0.03	0.852±0.02
Adaptive Convolution Layer (Ours)	✗	0.945±0.03	0.903±0.05	0.922±0.04
	✓	<b>0.963±0.01</b>	<b>0.943±0.01</b>	<b>0.941±0.02</b>