MULTICROSS ViT: Multimodal Vision Transformer for Schizophrenia Prediction using Structural MRI and Functional Network Connectivity Data

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ABSTRACT

Vision Transformer (ViT) is a pioneering deep learning framework that can address real-world computer vision issues, such as image classification and object recognition. Importantly, ViTs are proven to outperform traditional deep learning models, such as convolutional neural networks (CNNs). Relatively recently, a number of ViT mutations have been transplanted into the field of medical imaging, thereby resolving a variety of critical classification and segmentation challenges, especially in terms of brain imaging data. In this work, we provide a novel multimodal deep learning pipeline, MultiCrossViT, which is capable of analyzing both structural MRI (sMRI) and static functional network connectivity (sFNC) data for the prediction of schizophrenia disease. On a dataset with minimal training subjects, our novel model can achieve an AUC of 0.832. Finally, we visualize multiple brain regions and covariance patterns most relevant to schizophrenia based on the resulting ViT attention maps by extracting features from transformer encoders.

Keywords Deep learning · brain disease · structural MRI

1 Introduction

Vision transformer[Dosovitskiy et al. 2020], also called ViT, is a novel deep learning architecture with attention techniques that was extended from the natural language processing area[Vaswani et al. 2017] to the computer vision field. Several mutations[Zhou et al. 2021, Chen et al. 2021, Hassani et al. 2021] of ViT have been provided for multiple real-life computer vision tasks, which outperformed traditional deep learning models such as CNNs. In addition, ViTs can capture long-term dependencies within the input image, such as the non-local correlation of objects in the image, which CNNs frequently ignore[He et al. 2022].

In this study, we present a multimodal vision transformer that we train to effectively predict and diagnose schizophrenia using multimodality data. Schizophrenia[McCutcheon et al. 2020] is a severe mental condition characterized by an aberrant perception of reality. It may result in hallucinations, delusions, and profoundly chaotic thought and behavior that hamper daily functioning. Due to its nature, schizophrenia may be efficiently identified using fMRI data[Gur and Gur 2010], but it has been difficult to classify using solely sMRI data. Nevertheless, fMRI data is rarely trained using a deep learning model due to the computational cost. To address this issue, we chose a multi-modal combination of 3D sMRI data and 2D sFNC matrices obtained from fMRI[Lewis et al. 2020], which may simultaneously disclose structural aspects of schizophrenia and preserve the information provided by fMRI data.

Recently, effectively trained multimodal vision transformers that deal with 3D medical datasets are uncommon. Specifically,[Singla et al. 2022] developed a 3D-ViT model for gender prediction tasks using structural MRI data, where they obtained over 0.9 AUC on the ABCD dataset, which cannot outperform our earlier work[Bi et al. 2022] using a basic 3D CNN model. [Dai et al. 2022] employed a CNN-Transformer hybrid model to classify brain images
Figure 1: MultiCrossViT’s pipeline: It is typically composed of two modules. The first is the multimodal input and processing module, which uses patch embedding and transformer encoders to process data; the second is the cross-attention module, which can reasonably concatenate outputs from both sides and modalities.

from multiple datasets. It performed particularly well on Alzheimer’s disease-related datasets. Meanwhile, for the purpose of predicting schizophrenia disease based on sMRI data, Oh et al. [2020] purposed a 3D CNN model on five different public datasets, which has received an AUC score of approximately 0.71. fMRI data were utilized to create a modified 3D VGG model for the schizophrenia disease classification challenge by Zheng et al. [2021]. This model attained an accuracy of 84.3%. Nevertheless, these studies contain a number of shortcomings, the most notable of which are a high level of model complexity and a reduced detection rate.

Our paper has several contributions:

- We developed a novel deep learning pipeline, MultiCrossViT, which is a multimodal vision transformer based on a cross-attention mechanism that can be trained utilizing input data from multi-modalities.
- Our model has significantly enhanced the performance of schizophrenia prediction tasks using sMRI and sFNC data instead of fMRI data.
- By taking features from transformer encoders in MultiCrossViT, we can make interesting saliency maps of brain structures that may show brain regions linked to schizophrenia.

2 Methods

Our pipeline, MultiCrossViT, consisted of two major components: First, two modalities (sMRI and sFNC) are passed through independently from separate input channels, followed by 3D and 2D patch embedding, and both information is encoded using two distinct transformer encoders. Second, a cross-attention approach is applied after each layer of the transformer encoder to perform data fusion. This strategy attempts to merge the two modalities and capture their joint information, which can be useful for both prediction and visualization. Figure 1 shows an overview of our pipeline.

2.1 Data Inputs

Our model aimed to classify schizophrenia based on sMRI and sFNC data which is calculated using the cross-correlation among fMRI time series derived from independent component analysis (ICA) using a fully automated spatially constrained ICA algorithm using the neuromark_fMRI_1.0 template as spatial prior [Du et al. 2020]. The sMRI data is preprocessed through a voxel-based morphometry pipeline and modulated by Jacobian of the spatial transform to produce voxelwise gray matter volume data. The resulting GMV data is provided as a series of batches.
of 3D gray-scale images $\mathbf{V} = (V_1, V_2, \cdots, V_N)$, $V_i \in \mathbb{R}^{L \times W \times H}$, where $N$ is the batch size, $L$, $W$ and $H$ represent length, width and height of the 3D volume; Secondly, the input of sFNC data is a number of batches of 2D squares, which is $S = (S_1, S_2, \cdots, S_N), S_i \in \mathbb{R}^{L^2}$, where $L$ represents the length of 2D square matrices. For sMRI, we chose a patch size of $P$ to downscale the original 3D sMRI input into $L \times W \times H / P^3$ small 3D patches, which are then vectorized by the linear projection layer. Similarly, we downscale sFNC input data into $L^2 / p$ non-overlapped 2D patches with patch size $p$.

2.2 MultiCrossViT

Our model combines the architectures of a vision transformer and a cross-attention mechanism, both of which are based on multiscale, multimodal input channels that are able to process a variety of different types of input data. Our model’s fundamental concepts include self-attention and cross-attention mechanisms.

Self Attention. Specifically, each transformer encoder contains a multi-head attention layer that projects the input embedding $\mathbf{X} \in \mathbb{R}^{C \times C / h}$ using the self-attention approach into three matrices with same dimension which are Query($\mathbf{Q}$), Key($\mathbf{K}$) and value($\mathbf{V}$), where $C$ and $h$ are the embedding dimension and number of heads. The self-attention method can be represented as:

$$\text{Attention}(\mathbf{Q}, \mathbf{K}, \mathbf{V}) = \text{softmax}(\frac{\mathbf{QK}}{\sqrt{C/h}})\mathbf{V}$$

(1)

We integrated two modalities by utilizing the cross-attention approach.

Cross Attention. In the Cross Attention module [Chen et al. 2021], similarly to attention module, value($\mathbf{V}$) and Key($\mathbf{K}$) are calculated by attention features from the input of sMRI, whereas Query($\mathbf{Q}$) is generated by attention features derived from input of sFNC. In the training process, $\mathbf{Q}, \mathbf{K}, \mathbf{V}$ are calculated by input features and trainable weight matrices $\mathbf{W}_q, \mathbf{W}_k, \mathbf{W}_v$. It can be calculated as:

$$\mathbf{Q} = x_1 \mathbf{W}_q; \mathbf{V} = x_2 \mathbf{W}_v; \mathbf{K} = x_2 \mathbf{W}_k$$

(2)

Where, $x_1$, $x_2$ are features generated by transformer encoders from sFNC and sMRI input channels.

3 Experiments

3.1 Experimental Setup

Datasets. In our experiments, we employ data from a multi-site study of schizophrenia gathered by TRENDs on a 3T MRI scanner (N=2130) using a BOLD fMRI echo planar imaging sequence with TR=2s and TE=30ms. The sMRI data has 3D shape with (121, 145, 121) and the sFNC data is calculated from 53 regions of interest and has 2D shape with (53, 53). In order to fit our model, we resized sMRI and sFNC data by (120, 140, 120) and (54, 54) using Torchio, which is a open-source Python library for efficient loading, preprocessing, augmentation of 3D medical imaging data. Meanwhile, we augmented our data using several strategies such as RandomCrop, RandomAffine, RandomFlip, Add GaussianNoise provided by Torchio. Our experiments are applied using PyTorch deep learning framework and NVIDIA RTX v100 GPUs.

Models. We implemented a series of models, including traditional machine learning models (e.g., SVM, MLP) and deep learning models (e.g., CNN, 3D-CNN), as baselines in our experiments. We separately trained baseline models using sMRI and sFNC data in order to compare the multimodal performance to that of a single modality. In addition, as another baseline, we constructed a bench of multimodal pipelines that combined sMRI and sFNC, including 3DCNN-MLP, 3DCNN-CNN, and 3DVIT-ViT. These pipelines can generate alternative baselines that demonstrate the potential benefits of combining multiple modalities. Finally, we built a novel model called MultiCrossViT, which can realize advanced information mixup between two modalities using cross-attention mechanisms other than simple concatenation at the final point of the pipeline.

Training and Evaluation. All pipelines, including baseline models and MultiCrossViT, were trained utilizing advanced training techniques, such as the AdamW optimization, StepLR scheduler, and Warmup (30 epochs). We choose a training set, a validation set, and a testing set by a factor of 8:1:1. For each model, we employed a 5-fold cross-validation approach to achieve accurate results. In particular, the initial hyperparameters for MultiCrossViT training are the 3e–4
learning rate, the 1e–3 weight decay, and 200 epochs. We evaluated our models using general accuracy, balanced accuracy, AUC, F1 score, and precision. At the same time, we wrote down how many parameters each model had in order to show model complexity.

3.2 Results and Visualization

Our MultiCrossViT model achieved 0.833 AUC which is significantly higher than average 0.766 AUC for one modality baselines and average 0.78 AUC for multimodal baselines. MultiCrossViT, on the other hand, has less training parameters than the other two multimodal architectures. Table 1. shows details of results in each model.

| Models            | Data         | Acc  | AUC  | F1  | #Para |
|-------------------|--------------|------|------|-----|-------|
| 3DCNN             | sMRI         | 0.775| 0.781| 0.792| 1.9M  |
| 3DViTSingla et al [2022] | sMRI         | 0.778| 0.774| 0.784| 4.6M  |
| CrossViTChen et al [2021] | sMRI         | 0.741| 0.743| 0.71 | 4.8M  |
| 2DViT             | sMRI         | 0.742| 0.745| 0.72 | 2.6M  |
| MLP               | sFNC         | 0.78 | 0.78 | 0.775| 0.8M  |
| 3DCNN-CNN         | sFNC+sMRI    | 0.791| 0.784| 0.771| 11.3M |
| 3DViT-ViT         | sFNC+sMRI    | 0.777| 0.776| 0.773| 12.3M |
| Multi-CrossViT    | sFNC+sMRI    | 0.831| 0.833| 0.840| 10.9M |

Table 1: Results of each models including accuracy, AUC, F1 score and number of parameters.

To study brain regions associated with schizophrenia, we analyzed and visualized attention maps from our MultiCrossViT model, which can highlight brain regions in both healthy individuals and SZ patients. We employ the attention rollout approach, which can average/maximize attention maps from each head and provide final attention maps throughout each layer of the transformer encoder. On the basis of the saliency maps, we identify consistent patterns that link the controls and and patients. The Figure 2 shows the details of saliency maps generated by attention output from MultiCrossViT. Primary regions included gray matters in right temporal, thalamus, and visual regions, with patients showing more posterior temporal lobe and thalamus. FNC pairs for patients were more salient for intra-cerebellar connectivity as well as auditory-motor and auditory-visual connectivity. Results highlight the potential for combining multimodal structural and functional neuroimaging data.

Figure 2: Saliency maps of important brain regions from controls and SZ patients (left) and important Functional networks connectivity pairs for patients and controls (right).

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