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Graph theory based Transformer architecture for migraine biomarker detection on multi-center functional MRI datasets

Overview

Migraine diagnosis relies on clinical criteria. While recent MRI and machine learning studies aim to predict and identify biomarkers of migraine, most are single-center with small sample sizes, limiting generalizability. In this study, we plan to build a vision Transformer model which well adapts to graph-theory based MRI features and raw fMRI data, and to explore potential features which could distinguish migraine from other headaches and healthy controls. We shall validate the findings on the third independent dataset. We have collected resting-state fMRI with around 400 participants (migraine, cluster headache, tension-type headache, and healthy controls) from three study centers. We will apply graph theory approach to construct functional connection matrix and extract relevant features. We will modify the Transformer-based model to adapt to our imaging features as input and locate the biomarkers which can effectively distinguish migraine from other types of headache and healthy individuals. The training will be conducted on two study sites and testing will be conducted on the third one. The average F1 score, accuracy, precision, and recall will be calculated for model evaluation metrics.

Results

We have preprocessed fMRI data from 197 previously collected participants, and extracted the edge-centric metrics and also retained the original fMRI volumes . We have established an end-to-end functional interaction learning approach using original fMRI volumes. The framework models local cues within each voxel with 3D convolutions and captures global correlations among distant regions using specially designed attention mechanisms in a three-branch parallel architecture. An extra exchange unit facilitates information flow and mutual guidance among branches. The model was tested on our dataset ECHO, which consisted of 107 individuals with migraine, 38 individuals with medication-overuse headache, and 52 healthy controls. We then compared our method with recent

representative methods. And we used gradient-based localization to visualize the disease-related biomarkers. Meanwhile, we adopted a 3D convolutional neural network model based on edge-centric metrics. The model comprised nine 3D convolutional layers, with the output 3D volume features pooled before being fed into the classification layer. The model was trained using cross-entropy loss and optimized with the Adam optimizer over 100 epochs. Each training batch contained 64 samples. Next, we plan to fuse these two models and test the edge-centric metrics on the Transformer-based architecture with fMRI data from all the participants.

Under the support of this grant, we have two oral presentations at the IHC2025 in Sao Paulo (1. Headache Classification with Functional Interaction Learning from functional MRI Volumes; 2. Abnormal cerebellar-subcortical-cortical interactions in edge communities of cluster headache: evidence from cross-validated MRI data across three cohorts), and two articles under review (1. Dysregulated Cerebellar-Subcortical-Cortical Interactions in Cluster Headache: An Edge Analysis; 2.Brain Disease Classification with Functional Interaction Learning from Single fMRI Volume).

Summary

This study will advance headache knowledge by identifying robust, multi-cohort validated neuroimaging biomarkers for migraine using graph-theory metrics and a vision Transformer framework. By distinguishing migraine from other headache disorders and healthy controls on multi-center data, it will address the limitations of small, single-center studies and improve the objectivity of migraine diagnosis. The findings will clarify the functional brain networks underlying migraine pathophysiology and provide interpretable, biologically meaningful biomarkers. The validated model and identified brain signatures may support future objective classification, early detection, and targeted treatment evaluation across headache subtypes.

This grant has been critical for establishing my independent research line in neuroimaging and machine learning for headache disorders. It supported data preprocessing, model development, validation, and dissemination via international oral presentations and peer-reviewed publications. The multi-cohort framework and Transformer-based methods built under this award form a solid foundation for future grant applications and collaborative projects. The outputs strengthen my expertise in fMRI analysis, and headache neuroscience, supporting my academic and research career development as an independent investigator in headache and brain imaging research.

The research was presented during the 22nd International Headache Congress, São Paulo, Brazil, September 2025.