A Transformer-Based Approach to Diagnose Amyotrophic Lateral Sclerosis via Electroencephalogram Analysis

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***Abstract*—Neurodegenerative disorders are the leading cause of physical disability worldwide. In particular, amyotrophic lateral sclerosis (ALS) is one such condition that significantly impacts the quality of life for millions by impairing nerve cell function in the central nervous system. Despite extensive research, ALS remains difficult to diagnose in its early stages and the exact cause is largely unknown, with contemporary methods taking up to 15 months for a definitive diagnosis. Electroencephalogram (EEG) analysis, a non-invasive method for recording brain electrical activity, has shown promise in identifying subtle neural changes associated with neurodegenerative disorders. Transformers, known for their ability to capture complex data dependencies, offer a novel framework for analyzing EEG signals with high temporal resolution. This study introduces a Transformer-based approach to diagnose ALS by leveraging the EEG and eye-tracking dataset of ALS patients (EEGET-ALS), comprising a total of 1,989 recordings. The model achieved exceptional accuracies of 98.49% in training and 99.33% in both validation and testing. Furthermore, with an area under the curve (AUC) of 0.9963, precision of 100.0%, and recall of 96.36% in testing, the model demonstrates promise in enhancing the accuracy and timeliness of ALS diagnosis with a low rate of false positives and false negatives. Overall, this approach represents a significant advancement in the field of neurodegenerative disease diagnosis, potentially improving patient outcomes and quality of life through a two-minute recording.**

***Keywords*—Transformer, ALS, EEG, machine learning**

I. Introduction

Amyotrophic lateral sclerosis, also known as ALS or Lou Gehrig's disease, is a progressive neurodegenerative disorder that impairs the function of nerve cells in the spinal cord and brain. According to the CDC [1], this gradual deterioration and death of motor neurons leads to significant muscle weakness, atrophy, and, ultimately, complete loss of voluntary movement. As the disease progresses, individuals may experience severe disability, requiring assistance with daily activities and relying on ventilatory support.

Despite significant research efforts, the exact cause of ALS remains largely unknown and difficult to identify in the early stages. In fact, the ALS Association [2] quantifies that only 5% to 10% of all cases are linked to family history. On the other hand, over 90% of individuals diagnosed with ALS have no genetic mutation linked to the condition. Not only are the causes of ALS elusive, but also diagnosing the disorder is lengthy and complicated. A study by Pagnoni et al. [3], consisting of 304 individuals with ALS, found that each patient saw an average of three physicians before their condition was confirmed. Additionally, the researchers accentuate that total diagnostic time ranged from 8 to 15 months, prolonging the period of uncertainty and leading to potential delay in treatment.

The challenges in diagnosing ALS are compounded by the limitations of current diagnostic practices. According to the National Institute of Neurological Disorders and Stroke [4], there is no single measure or test that can definitely diagnose ALS. Furthermore, in the status quo, medical diagnosis of the condition often involves a subjective evaluation of the patient done at the discretion of a physician, according to another article from the ALS Association [5]. Contemporary measures that primarily rely on a patient's health history to diagnose the disorder are ineffective. University of Michigan Health [6] also emphasizes that diagnosing ALS can be particularly challenging because many neurologic diseases cause similar symptoms, necessitating a battery of tests to exclude other conditions. Hence, there is an inherent need for an accurate tool to enable early detection and intervention of ALS.

In recent years, advancements in machine learning and artificial intelligence have opened new opportunities for improving diagnostic accuracy and efficiency. According to a 2021 study by Dukic et al. [7], EEG analysis, a non-invasive method for recording electrical activity in the brain, has shown promise in capturing subtle neural changes associated with ALS. However, the integration of machine learning techniques into EEG analysis for ALS remains underexplored.

This paper introduces a Transformer-based approach to diagnose ALS via EEG analysis. Transformers, known for their ability to capture complex dependencies and patterns in data, offer a novel framework for analyzing EEG signals with high temporal resolution and sensitivity [8]. By leveraging

Transformer models, this study aims to enhance the accuracy and timeliness of ALS diagnosis, addressing current gaps in diagnostic practices and providing a robust tool for early detection and intervention.

II. Literature Review

A. Image Classification

Brain magnetic resonance imaging (MRI) is a biomarker that has the potential to effectively diagnose ALS through medical image analysis. Kushol et al. [9] proposed leveraging vision transformer architecture to distinguish between ALS subjects and the control group of healthy individuals in their study, achieving an accuracy of 88.0% and an F1-score of 0.900. Their results suggest a promising approach for expediting ALS diagnosis; however, their level of accuracy represents a modest improvement over existing diagnostic tools. Furthermore, MRI scans primarily focus on structural changes, without capturing the subtle neural changes that occur in early stages of the disease.

B. Audio Transformers

In addition to MRI, speech analysis has emerged as a valuable tool for diagnosing ALS. The advantage of speech classification lies in its non-invasive and accessible nature. Unlike MRI, which requires specialized equipment and often involves logistical challenges, speech analysis can be performed using standard audio recording devices and software. Kurmi et al. [10] developed a machine learning model that assesses voice recordings to distinguish between ALS patients and healthy individuals. The researchers achieved an accuracy of 84.2%, sensitivity of 77.8%, and specificity of 90% using support vector machine (SVM) classification. Thus, voice classification does not offer a notable advantage over neuroimaging in terms of accuracy, but it holds promise in enabling frequent and convenient monitoring of patients.

C. EEG Analysis

EEG analysis has emerged as a valuable non-invasive method for capturing electrical activity in the brain. Recent studies have explored the integration of machine learning techniques with EEG data to improve diagnostic accuracy for various neurodegenerative conditions. Zhao and He [11] developed a deep learning model to identify Alzheimer's disease through EEG analysis. They recorded an accuracy of 92% after training on an SVM model, substantially higher than studies with image and audio classification approaches. In another study, Oh et al. [12] created an automatic detection system for Parkinson's disease that leverages a 13-layer convolutional neural network (CNN) architecture. Their model achieved an accuracy, sensitivity, and specificity of 88.25%, 84.71%, and 91.77%, respectively. Altogether, machine learning analysis on EEG data has attained accurate results for other neurodegenerative disorders with a low rate of false positives and false negatives. In this study, the EEG analysis approach was utilized to distinguish between ALS patients and healthy individuals. Instead of implementing SVM or CNN, however, the model was built on Transformer architecture to attain results with high accuracy and efficiency.

III. Methodology

Source code for the project is located at:

https://github.com/sjain2025/EEG-ALS-Diagnosis

A. Dataset

The model was trained on the EEGET-ALS dataset [13], which contains eye-tracking (ET) and EEG recordings from six ALS patients and 170 healthy individuals. Each participant engaged in nine recording sessions lasting approximately 2 minutes, corresponding to a common human action or demand. Data were recorded once for each healthy individual in a laboratory setting, while data were recorded multiple times for ALS patients at their home. During these sessions, EEG data were captured at a sampling frequency of 128 Hz using the Emotiv EPOC Flex device, which features 32 electrodes configured in a 10-10 system. Fig. 1 illustrates the positioning of the EEG electrodes in this 10-10 standard. The EEG data are stored in European Data Format (EDF). The dataset comprises 1,989 EDF files with EEG data across 32 channels.

B. Data Preprocessing

EEG data were collected at a sampling rate of 128 Hz for approximately two minutes. In order to account for variance in the amount of time between different recordings, all samples were adjusted to 120 seconds—or a length of 15,360 given the 128 Hz sampling rate—using the `numpy.resize` method, which forms a new array with a given length. After converting EDF data into numpy arrays of standard length, each array was assigned a label: 0 for healthy individuals and 1 for ALS patients. In the EEGET-ALS dataset, EDF files located in a folder beginning with 'id' contained data from healthy patients. On the other hand, files located in a folder beginning with 'ALS' contained data from ALS patients. Finally, all 1,989 numpy arrays with EEG data and labels were converted to a `tf.data.Dataset` object using the `from_tensor_slices` method.

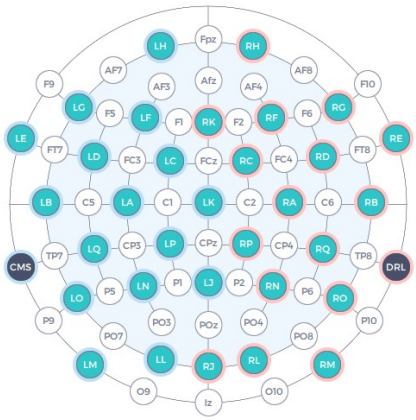

Fig. 1: EEG electrodes position with 10-10 standard [13]

C. Model Architecture

The model constructed for this study is a Transformer-based neural network designed for binary classification. The model architecture is depicted in Fig. 2. It begins with an input layer designed to accept sequences of shape (32, 120 × 128). Next, the model employs three Transformer layers, each featuring multi-head attention with 4 heads and a key dimension of 64. After each multi-head attention operation, the output is normalized using layer normalization with an epsilon of 10^{-6} to ensure numerical stability. These outputs are then passed through dense layers with ReLU activations, increasing in size from 64 to 128 to 256 neurons in successive layers.

Following the Transformer layers, the model flattens the output and includes additional dense layers with ReLU activations, progressively reducing the dimensionality to 64 and then 32 neurons, before applying batch normalization. The final output layer is a dense layer with a sigmoid activation function, as the model is designed for binary classification tasks.

D. Training

A random split of 70% for training data, 15% for validation data, and 15% for testing data was applied to the dataset comprising 1,989 samples using the custom `generate_train_test_val_splits` method. Each subset was then batched with a size of 16 for efficient training and evaluation. A learning rate scheduler, ReduceLROnPlateau, was integrated to reduce the learning rate by a factor of 0.5 if the validation loss did not improve for 3 consecutive epochs, helping to fine-tune the model during training. The model trained using an A100 Google Colaboratory GPU instance, which is known for its high-performance computing capabilities. The training spanned a total of 403.88 seconds over the course of 70 epochs, demonstrating its lightweight capabilities. Compiled with the Adam optimizer at a learning rate of 10^{-4}, the model uses binary cross-entropy as its loss function. Its equation is given as follows:

$$\text{Loss} = -\frac{1}{N}\sum_{i=1}^{N}[y_i \log(\hat{y}_i) + (1 - y_i)\log(1 - \hat{y}_i)] \quad (1)$$

where N is the number of samples, y_i is the true label, and $\hat{y}_i$ is the predicted probability of the positive class. This loss function is particularly suited for binary classification tasks as it measures the performance of a classification model whose output is a probability value between 0 and 1.

IV. Results and Discussion

A. Performance Metrics

The model was evaluated on five performance metrics: accuracy, loss, AUC, precision, and recall.

Accuracy measures the overall correctness of the model by comparing the number of correct predictions to the total number of predictions. It is given by the equation:

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (2)$$

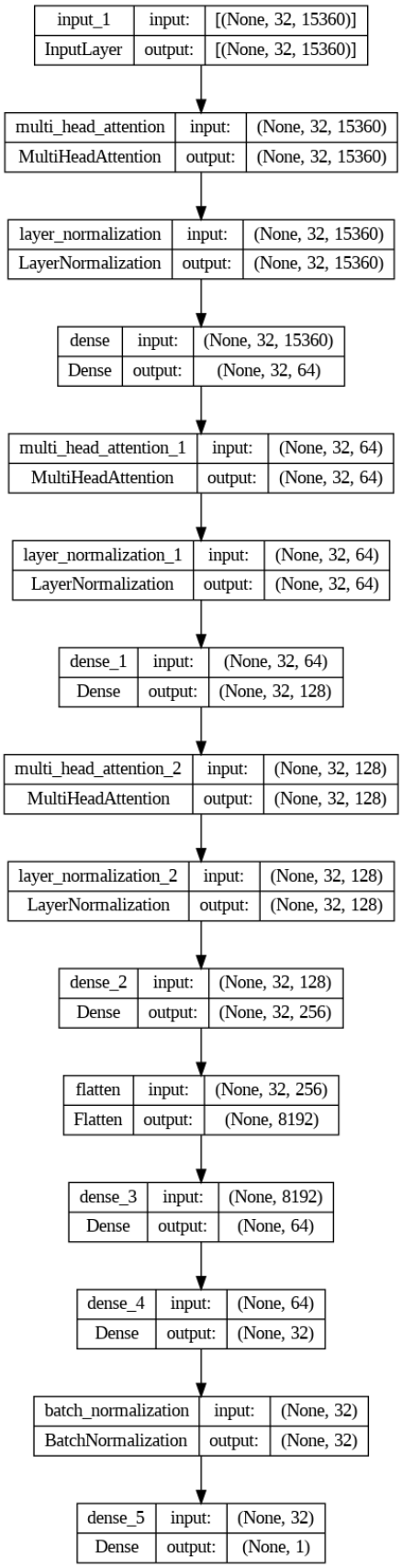

Fig. 2: Summary of Transformer model architecture

where TP is the number of true positives, TN is the number of true negatives, FP is the number of false positives, and FN is the number of false negatives.

AUC measures the ability of the model to discriminate between positive and negative classes. It is defined as the area under the Receiver Operating Characteristic (ROC) curve. The ROC curve plots the true positive rate (TPR) against the false positive rate (FPR):

$$\text{TPR} = \frac{TP}{TP + FN} \tag{3}$$

$$\text{FPR} = \frac{FP}{FP + TN} \tag{4}$$

A high AUC value indicates better model performance, with a value of 1 representing a perfect model and a value of 0.5 representing random guessing. The formula for AUC is:

$$\text{AUC} = \int_0^1 \text{TPR}(\text{FPR})\, d(\text{FPR}) \tag{5}$$

In discrete form, AUC is given by the equation:

$$\text{AUC} = \sum_{i=1}^{n-1} (\text{FPR}_{i+1} - \text{FPR}_i) \cdot \left(\frac{\text{TPR}_{i+1} + \text{TPR}_i}{2} \right) \tag{6}$$

where n is the number of thresholds and FPR_i and TPR_i are the false positive rate and true positive rate at the i-th threshold, respectively.

Precision measures the accuracy of the positive predictions and is given by:

$$\text{Precision} = \frac{TP}{TP + FP} \tag{7}$$

High precision indicates that the model has a low FP rate.

Recall, also known as TPR or sensitivity, measures the model's ability to identify all relevant positive instances. Its equation is given in (3). High recall indicates that the model has a low FN rate. The model's results on these five metrics is shown in Table 1.

B. Performance Metrics

TABLE I: Model Performance Metrics

Metric	Training	Validation	Testing
Accuracy	98.49%	99.33%	99.33%
Loss	0.0954	0.0581	0.0630
AUC	0.9787	0.9974	0.9963
Precision	98.48%	100.0%	100.0%
Recall	95.31%	97.33%	96.36%

With a testing accuracy of 99.33%, AUC of 0.9963, precision of 100.0%, and recall of 96.36%, the model significantly outperforms those created in other studies. Moreover, as portrayed in Fig. 3-6, accuracy, AUC, precision, and recall all improved over the 70 epochs. Hence, the model demonstrates exceptional performance and reliability, making it a highly effective tool for real-world applications. In addition, loss decreased over the training period as shown in Fig. 7, demonstrating the model's capability to learn effectively and generalize well to unseen data.

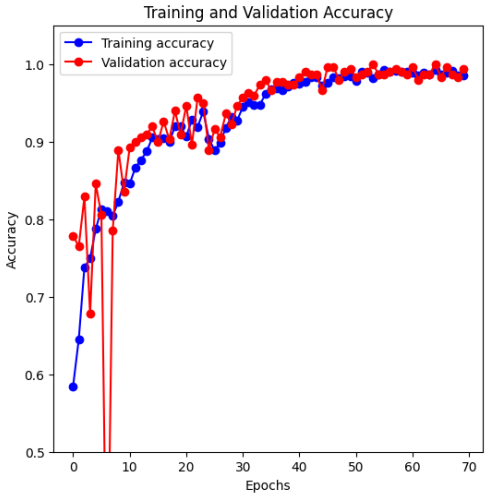

Fig. 3: Training and validation accuracy plot

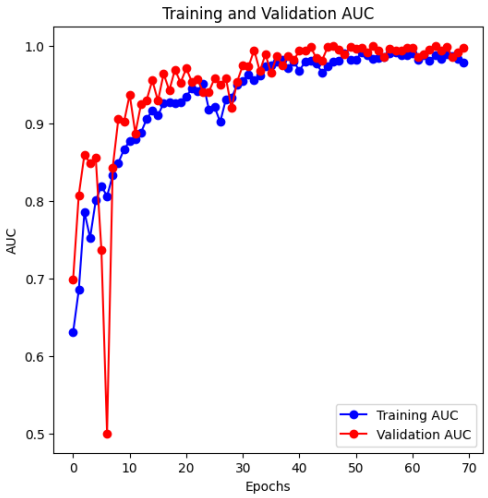

Fig. 4: Training and validation AUC plot

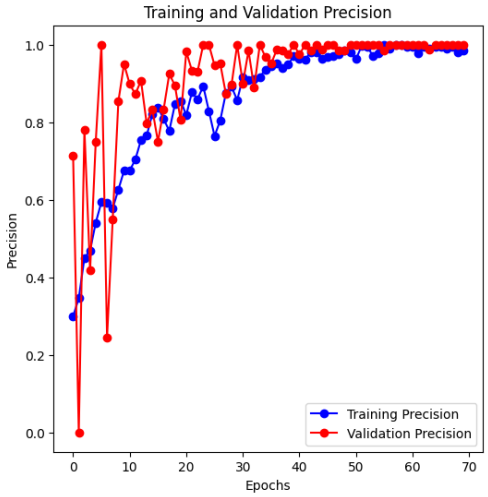

Fig. 5: Training and validation precision plot

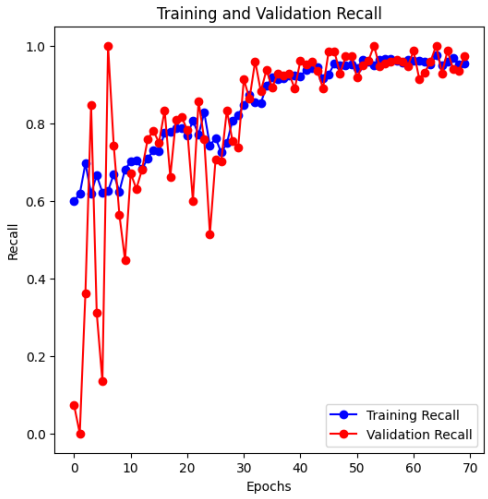

Fig. 6: Training and validation recall plot

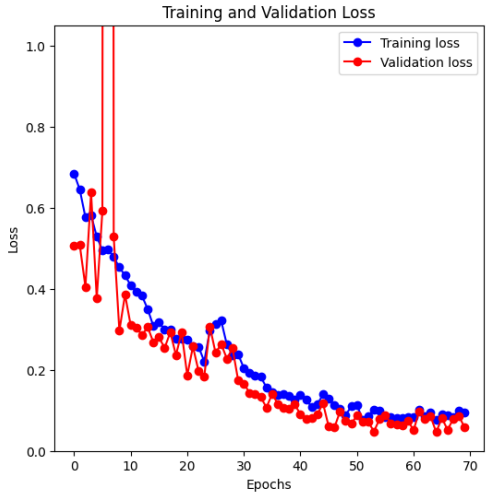

Fig. 7: Training and validation loss plot

C. Comparative Experiments

The model developed in this study offers significant advantages over existing ALS diagnostic tools and methods. The first issue with previous methods is the significant delay in reaching a definitive diagnosis. Campos et al. [14] analyzed the diagnostic pathway for 1,405 ALS patients from four different countries, finding that the median delay was 11 months from first symptom onset. In response to this issue, Babu et al. [15] developed a novel diagnostic tool aimed at expediting ALS diagnosis. Currently, their "thinkALS" tool is the leading solution in the market, reporting less than 4-week wait times for diagnosis. Nonethless, their technology still faces limitations in terms of efficiency; on the other hand, this study's Transformer model substantially enhances diagnostic speed, achieving results in just two minutes.

Another limitation of ALS diagnostic tools is the low performance and effectiveness of existing machine learning methods. For instance, in the study conducted by Tafuri et al. [16], researchers created a machine learning-based classification pipeline to distinguish ALS patients from healthy individuals using MRI scans. Despite offering a promising approach to characterize brain abnormalities via radiomics, the model only achieved 81.1% accuracy with the Support Vector Machine (SVM) algorithm. In another recent study, Alzahrani et al. [17] predicted ALS using a deep learning approach. Their average accuracy ranged between 82% and 87% with an F-score of approximately 86%. Geevasinga et al. [18] had similar results in their study that assessed a novel ALS diagnostic index (ALSDI). The researchers found 83.5% diagnostic accuracy, 84% specificity, and 83.3% sensitivity in testing, suggesting that these models are not effective enough for clinical application in the status quo.

Furthermore, logistic regression algorithms also lack results with high accuracy. Vu and Le [19] found an AUC score of 87.90% in their study that implemented the least absolute shrinkage and selection operator (LASSO) regression algorithm for ALS diagnosis. The highest performance was recorded by Wang et al. [20], who implemented a longitudinal speech transformer to predict ALS progression and found an AUC of 91.0%. While Transformer-based approaches are the most effective, they are yet to demonstrate accuracies that are high enough for clinical application. Despite the limitations of previous machine learning approaches, the model in this study achieved 99.33% accuracy for both validation and testing. Thus, it is a significant improvement from other solutions on the market.

V. Conclusion

The Transformer-based approach presented in this study offers a significant advancement in the early and accurate diagnosis of ALS through the analysis of EEG signals. By leveraging the EEGET-ALS dataset, the model achieved exceptional performance metrics, including a testing accuracy of 99.33%, an AUC of 0.9963, precision of 100.0%, and recall of 96.36%. These results not only surpass existing diagnostic methods but also highlight the potential of Transformer models in capturing complex dependencies within EEG data. The robustness and high accuracy of this model suggest it could be a valuable tool in clinical settings, potentially reducing the diagnostic time and improving patient outcomes by enabling earlier intervention.

In the future, the research conducted in this study could be expanded upon by incorporating more diverse EEG recordings from a larger and more varied cohort of ALS patients to enhance the generalizability and robustness of the model. Additionally, the Transformer architecture could be refined in future research by exploring different hyperparameter configurations and incorporating additional features such as eye-tracking data to further improve diagnostic accuracy. Moreover, a user-friendly software application that integrates the model could be developed, enabling clinicians to utilize this tool in a practical, real-world setting.

Overall, the model developed in this study heralds a new era in medical diagnostics, with the promise of improved

outcomes and enhanced quality of care for ALS patients through a two-minute recording.

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