Medication Outcome Prediction in Major Depressive Disorder through Custom CNN

Departement of infomration science, University of North Texas, Texas, USA

Shyam Sundar Domakonda
Department of Information Science
University of North Texas
Denton, USA
shyamsundardomakonda@my.unt.edu

Tejesh Bathula
Department of Information Science
University of North Texas
Denton, USA
tejeshbathula@my.unt.edu

Nahid Fathima Syed
Department of Information Science
University of North Texas
Denton, USA
nahidfathimasyed@my.unt.edu

Mani Venkata Sai Pavan Ramisetty
Department of Information Science
University of North Texas
Denton, USA
venkatasaipavanramisetty@my.unt.edu

Sasi Kiran Katamneni
Department of Information Science
University of North Texas
Denton, USA
sasikirankatamneni@my.unt.edu

***Abstract*—Major Depressive Disorder (MDD) is a mental health condition which is often treated with Selective Serotonin Reuptake Inhibitors (SSRIs). In this study, we propose a model using Custom Convolutional Neural Networks (CNNs) to predict medication outcomes in MDD patients. By analyzing EEG data from patients we aim to classify individuals into responders and non-responders. Custom-built Convolutional Neural Networks (CNNs) are utilized to evaluate EEG data along with a number of time-frequency techniques, such as Wavelet Synchrosqueezing, Continuous Wavelet Transform and Discrete Wavelet Transform. Four Convolutional layers make up on our CNN model, followed by batch normalization, a Flatten layer and a Dropout layer. The model also uses an Adam optimizer of learning rate 0.0001 and a K-fold cross-validation with K=5. Results show that Wavelet Synchrosqueezing Transform obtained a top accuracy of 98.89%, Discrete Wavelet Transform coming in second with an accuracy of 92.88%, and Continuous Wavelet Transform with an accuracy of 87.74%.**

***Index Terms*—CNNs, Wavelet Syncrosqueezing, MDD, EEG, CWT, DWT**

I. Introduction

Major Depressive Disorder is a widespread mental illness which is still affecting millions of people around the world. Predicting medication outcomes in diagnosed patients is a challenging task. Traditionally, subjective assessments are conducted and medication is prescribed to the patients based on the results. Collaboration between Machine Learning and Neuroscience has opened up many possibilities for better predictions. Studying Electroencephalography (EEG) signals is one such promising method. These signals provide important information about the brain's electrical activity changes which helps in identifying mental health issues.

This research focuses on using Convolutional Neural Networks (CNNs) along with time-frequency signal processing techniques to predict Selective Serotonin Reuptake Inhibitors (SSRIs) medication outcomes in Major Depressive Disorder (MDD) patients. We particularly focus on evaluating three time frequency techniques—Wavelet Synchrosqueezing (WSST), Continuous Wavelet Transform (CWT), and Discrete Wavelet Transform (DWT)—for analyzing the EEG signals. By leveraging these methods, we can pinpoint important features in EEG data and capture the temporal patterns associated with symptoms of Major Depressive Disorder (MDD).

Our research expands on studies conducted previously, including the recent study [1] where the authors proposed a CNN-based model for MDD medication prediction outcome using EEG signals. They obtained accuracies of 98.89%, 92.88%, and 87.74% using WSST, DWT and CWT, respectively. This study aims to improve the CNN models' prediction capabilities through improved feature extraction and model parameter optimization. We propose that by combining advanced signal processing techniques with deep learning architectures, we can improve the accuracy and relevance of models used to predict medication outcomes in Major Depressive Disorder (MDD). The critical need for personalized medication in treatment of Major Depressive Disorder (MDD) is acknowledged in this research. Each patient has a unique set of biological, social and psychological factors which influence their response to medication. By combining Machine learning with Neuroscience, we aim to develop a personalized predictive model.

II. Problem Statement

This research aims to tackle the challenge of predicting medication outcomes in Major Depressive Disorder (MDD) patients and distinguishing them as responders and non-responders. The primary objective is to evaluate the efficacy of various Time-Frequency methods like the Wavelet

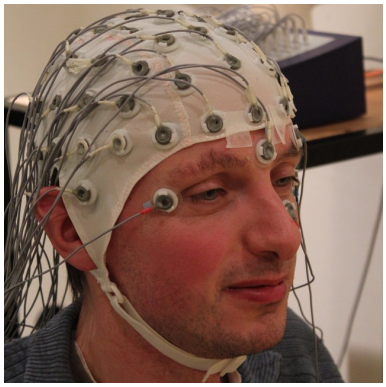


Fig. 1. Patient with EEG cap

Synchrosqueezing Transform, in generating Time-Frequency representations from EEG signals. A key goal is to develop a customized Convolutional Neural Network (CNN) model which is computationally efficient and compare it to conventional Transfer Learning and Hybrid Models. Additionally, comparisons will be made with CNN models utilizing alternative Time-Frequency methods such as the Discrete Wavelet Transform (DWT) and Continuous Wavelet Transform (CWT).

III. Literature Review

In the paper by **Mumtaz et al.** [2], the authors proposed a machine learning (ML) model leveraging pretreatment EEG data to predict outcomes for Selective Serotonin Reuptake Inhibitors (SSRIs). Experimental data was gathered from 34 Major Depressive Disorder (MDD) patients and 30 healthy controls. MDD patients were categorized into responders (R) and non-responders (NR). Time-frequency decomposition of EEG signals was extracted using three distinct techniques: Wavelet Transform (WT), Short-Time Fourier Transform (STFT), and Empirical Mode Decomposition (EMD). An integration of features, comprising WT analysis, EMD, and STFT, were employed to develop a Logistic Regression Classifier which exhibited an accuracy of 91.6%. The study's conclusions provided some intriguing new information about the EEG traits of MDD patients. In particular, Mumtaz et al. found that MDD patients had different EEG features from healthy controls in terms of spectral power, connection, and coherence patterns. Furthermore, Mumtaz et al. found that patients with MDD have changed patterns of functional connectivity between many brain regions, especially the limbic system, default mode network, and prefrontal cortex. These results highlight how crucial it is to investigate network-level dynamics in order to comprehend the pathophysiology of MDD and create focused therapies. All things considered, Mumtaz et al.'s study established the foundation for further research in this area and offered insightful information about the EEG indicators of MDD.

The research by **Sadat Shahabi Mohsen , Shalbaf Ahmad , Maghsoudi Arash** [3] created a deep Transfer Learning (TL) method for separating MDD patients into two groups: those who respond (R/NR) to SSRI antidepressants and those who do not. EEG readings from 19 people with MDD were collected. Utilizing the CWT, multiple time frequency images are created from each EEG channel. DenseNet121 has the best performance with accuracy, sensitivity, and specificity scores of 95.74%, 95.56%, and 95.64%, respectively. More accurate results were achieved by putting these basic models together into an ensemble. The ensemble model got 96.55% accuracy, 96.01% sensitivity, and 96.95% precision, according to the results.

The research conducted by **M. S. Shahabi and A. Shalbaf** [1], aimed to enhance the prediction of treatment outcomes for patients with Major Depressive Disorder (MDD) who are prescribed Selective Serotonin Reuptake Inhibitors (SSRIs). A hybrid model was developed by integrating transfer learning from deep Convolutional Neural Networks (CNNs) with bidirectional Long Short-Term Memory (BLSTM) cells and attention mechanisms. Raw Electroencephalography (EEG) data from 30 MDD patients was utilized, with the EEG signals transformed into third-order and fourth-order tensors to optimize data organization for model training. Various models based on architectures such as VGG16, Xception, and DenseNet121 were constructed. The VGG16-LSTM-Attention model demonstrating the highest performance, achieving an accuracy of 98.21%. Furthermore, an ensemble model was devised, attaining an accuracy of 98.84%.

IV. Methodology

In this section, we delve into the proposed methodologies encompassing data collection, data preprocessing, and CNN architectures. The blueprint of our research endeavor is illustrated in Fig. 2.

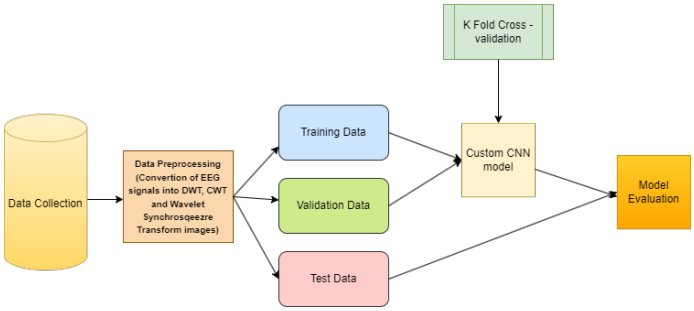


Fig. 2. Research Design

A. Data Collection

The data we used for our research was recorded by Mumtaz et al. [11] They collected EEG signals of 30 Major Depressive Disorder (MDD) patients, whose symptoms ranged from moderate to severe. The EEG signals were recorded in a resting state where these individuals were asked to relax with their eyes closed or eyes open. Then, the EEG signals data was processed and evaluated to look for anomalies or trend patterns that would point towards MDD. For data collection, rigorous standards were upheld to ensure the accuracy and reliability of the EEG signals obtained. The recordings were

conducted at a sampling frequency of 256Hz, utilizing 19-channel electrodes(shown in Fig 1) strategically positioned on the scalp according to the international 10-20 electrode positioning system(shown in Fig 2). This configuration allows for comprehensive coverage of brain activity across various regions. To maintain consistency and minimize artifacts, the linked-ear reference method was employed during signal acquisition.

To enhance signal clarity, band-pass filtering was applied to isolate frequencies within the range of 0.5Hz to 70Hz, to effectively eliminate extraneous noise while preserving relevant signal data. Additionally, a notch filter was implemented at 50Hz to remove any interference from power line noise commonly encountered in the recording environment. This meticulous approach to signal preprocessing ensures that the data captured accurately reflects the underlying neural dynamics associated with Major Depressive Disorder (MDD), laying a robust foundation for subsequent analysis and interpretation. Furthermore, strict adherence to standardized procedures and quality control measures was maintained throughout the data collection process to uphold the integrity and validity of the acquired EEG data.

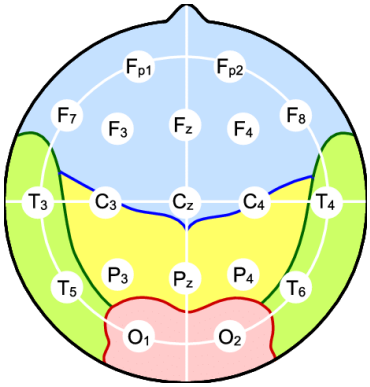


Fig. 3. International 10-20 electrode positioning

Through innovative methods in deep learning architectures and EEG signal processing, our technique improves the prediction of drug outcomes in Major Depressive Disorder (MDD). This builds on previous research. The main phases of our methodology, such as data pretreatment, feature extraction, model architecture, and evaluation, are described in this section.

B. Data Processing

In this section, we elaborate on the steps involved in processing the EEG signals data for our analysis. The dataset is divided into two main sets: a training and validation set comprising 80% of the data and a separate testing set the remaining 20%. This division ensures a balanced distribution of samples across different subsets, helping the model predict better. To further enhance the reliability of our evaluations and mitigate any potential biases, we employ a 5-fold cross-validation strategy. This approach involves dividing the dataset into five equally sized folds, using four folds for training and validation and the remaining fold for testing iteratively. By repeating this process five times with different fold combinations, we ensure a comprehensive assessment of our models' performance.

One crucial step in preprocessing the data involves normalizing the pixel values of the time-frequency images. Normalization is performed to rescale the pixel values within the range of [0, 1], ensuring consistency and aiding in model convergence during training. Additionally, to meet the input requirements of our model architecture, the time-frequency images are resized to a specified input size of (224, 224). This resizing step ensures uniformity in the dimensions of the input data across all samples, facilitating seamless integration into our model architecture.

C. Converting EEG signals data to Time-frequency images

EEG signals, characterized by their temporal dynamics, provide valuable insights into brain activity. However, analyzing raw EEG signals directly can be challenging due to their complex and high-dimensional nature. To address this challenge, we adopt a spectrogram-based approach to transform the EEG signals into time-frequency representations. In Fig. 4, we present an EEG signal.

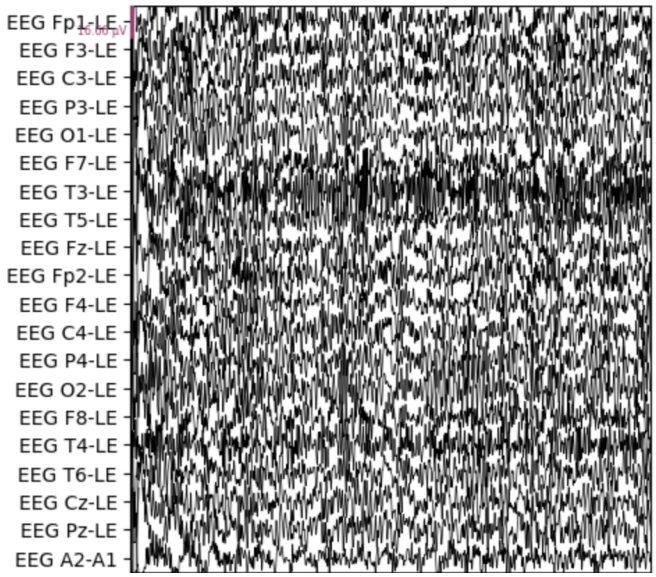
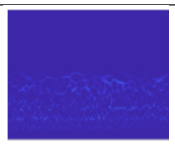
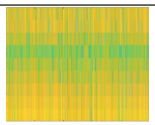
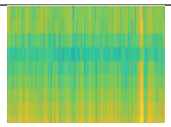
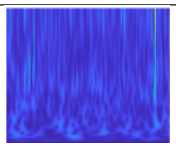
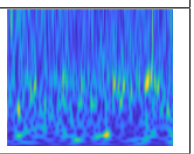


Fig. 4. EEG Signal of MDD patient

The spectrogram representation offers a comprehensive view of the signal's frequency content over time, enabling the extraction of meaningful features for analysis. By applying a sliding window Fourier transform to the EEG signals, we obtain spectrograms that depict the signal's frequency spectrum at different time intervals.

These spectrograms serve as the foundation for our time-frequency images. Each spectrogram is converted into a grayscale image, with the intensity of each pixel representing the magnitude of the corresponding frequency component. This transformation effectively encapsulates the temporal

TABLE I
TIME FREQUENCY IMAGES

Time Frequency Method	Responders	Non-Responders
WSST		
DWT		
CWT		

and frequency information of the EEG signals into a two-dimensional image format, facilitating further analysis using image-based techniques.

Through this process, we transform raw EEG signals into a format suitable for input into our deep learning models, enabling effective analysis and interpretation of brain activity patterns.

To guarantee the quality and suitability of the EEG data acquired from the chosen database for our research, we first preprocess it. To prepare the data for future processing, this entails eliminating artifacts, and noise, and standardizing the format. To capture relevant temporal dynamics associated with the symptomatology of MDD, we also segment the EEG data into appropriate time intervals.

The preprocessed EEG signals are then transformed into useful representations using three different time-frequency techniques: Wavelet Synchrosqueezing Transform (WSST), Continuous Wavelet Transform (CWT), and Discrete Wavelet Transform (DWT). Each method has a distinct benefit for capturing various time-frequency components of the signal. DWT gives a multi-resolution analysis of signal components, CWT delivers a high-resolution time-frequency representation, and WSST improves the accuracy of frequency localization.

D. Model Architecture

Our research work utilizes an EEG-based proprietary Convolutional Neural Network (CNN) architecture which is designed to predict medication outcomes in Major Depressive Disorder (MDD). This section describes the main elements and design decisions of our model, emphasizing how flexible and successful it is in obtaining essential data from EEG data.

a) Layers of Convolution: The four convolutional layers that make up the CNN architecture are the main feature extractors. Convolutional layers are capable of detecting spatial patterns and hierarchical representations by applying learnable filters to the input data. A rectified linear unit (ReLU) activation function is placed after each convolutional layer to add non-linearity and boost the expressive capacity of the model.

b) Batch Normalization: Following every convolutional layer, batch normalization is done to speed up and stabilize the training process. To minimize internal covariate shifts and enhance the model's convergence, batch normalization normalizes the activations of each layer across mini-batches. Through the training phase, this technique makes sure the network stays strong and effective.

c) Dropout Layer: The model incorporates a Dropout layer with a 0.25 dropout rate after the final convolutional layer to prevent overfitting and enhance its generalization abilities. A portion of neurons are randomly deactivated during training by dropout, which compels the network to acquire more resilient and varied representations. The model's capacity to generalize to new data and perform better overall are both improved by regularizing Dropout.

d) Flatten Layer: The multidimensional feature maps are converted into a one-dimensional vector by inserting a flattened layer after the convolutional layers. By ensuring that the data is compatible with the categorization job, this stage gets ready the data for input into the next fully connected layers. The learned representations are preserved while the spatial dimensions of the feature maps are effectively collapsed by the Flatten layer.

e) Fully Connected Layers: Two completely linked layers are added to the architecture to process the retrieved features and carry out classification after the feature maps have been flattened. These layers are made up of tightly coupled neurons that produce prediction scores for each class after learning intricate correlations between features. The last fully connected layer facilitates drug outcome classes by generating probability distributions over them using a SoftMax activation function.

f) Optimization and Training: A stochastic gradient descent (SGD) variation called the Adam optimizer is used to train the model with a learning rate of 0.0001. Adam streamlines and stabilizes optimization by dynamically adjusting the learning rate in response to the gradient magnitudes of individual parameters. The categorical cross-entropy loss function is tuned during training to reduce the difference between expected and observed drug results.

g) Cross-validation with K-folds: Utilizing a K-fold cross-validation approach with K=5, we ensure the resilience and applicability of our model. The dataset is divided into five folds of equal size, with one fold being used as a validation set and the other five folds being used for training. We carry out this procedure five times, using exactly one fold as the validation set each time. We can decrease the likelihood of overfitting to the training data and get a more accurate evaluation of the model's predicted performance by averaging the performance measures over the five folds.

h) Model Assessment: Lastly, accuracy is the main metric we use to assess the performance of our model. We examine the precision attained by every time-frequency technique (WSST, CWT, DWT) in forecasting medication results

for patients with MDD. We assess the model's performance using appropriate measurements including precision, F1-score, recall, and accuracy. Following a thorough investigation and comparison, we identify the optimum time-frequency technique for predicting MDD medication outcomes and give recommendations for future research. We use the most advanced deep learning architectures in conjunction with advanced signal processing techniques to enhance medication outcome prediction in Major Depressive Disorder patients. We aim to increase prediction model accuracy and reliability by exploiting the special characteristics of EEG data and implementing the required architectural modifications to the model.

TABLE II
COMPARING RESULTS

Study	Methods	Results
Mumtaz et al, 2017	Machine Learning	ACC = 91.6%
Mohsen Sadat Shahabi et al, 2021	Ensemble of CNN and TL models	ACC = 96.55%
Ahmad Shalbaf et al, 2022	Ensemble of TL and LSTM Attention	ACC = 98.21%
Behrouz Nobakhsh et al, 2022	Machine Learning	ACC = 89.6%
Reza Kazemi et al, 2023	Ensemble of TL and BLSTM Attention	ACC = 98.86%
Our proposed model	CNN	ACC = 98.89%

The table II above provides a comparison between our work and previous research efforts. Our proposed model outperforms other TL and hybrid models.

The figure. 5 illustrates the training and validation loss, as well as the accuracy of our model using the WSST dataset.

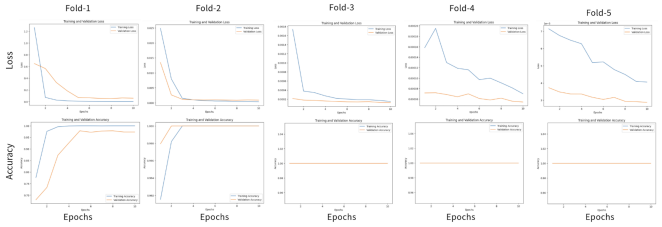


Fig. 5. Training and Validation Loss & Accuracy of our model with WSST Dataset

V. RESULTS

By extending the solid basis established by earlier research and employing the most advanced techniques, our initiative aims to improve the precision of medical outcome prediction in Major Depressive Disorder (MDD). By using particular CNN architectures and time-frequency techniques to assess large amounts of EEG data, we have achieved notable progress in improving the precision and dependability of predictive models for MDD treatment outcomes. Our research's conclusions highlight how crucial it is to use specific signal processing methods and deep learning to extract meaningful information from EEG data. We have shown the value of time-frequency analysis in capturing the temporal dynamics of brain activity related to MDD by utilizing Wavelet Synchrosqueezing Transform (WSST), Continuous Wavelet Transform (CWT), and Discrete Wavelet Transform (DWT). The excellent accuracy of WSST (98.89%), DWT (92.88%), and CWT (87.74%) demonstrate how well these techniques work to distinguish between various medication outcomes and forecast how patients with MDD will respond to treatment.

TABLE III
PERFORMANCE METRICS OF OUR MODELS WITH DIFFERENT TIME FREQUENCY DATASETS

Metrics	WSST		DWT		CWT	
	N	NR	N	NR	N	NR
Precision %	100.0	98.19	91.41	93.83	83.82	90.40
Recall %	97.24	100.0	90.50	94.44	85.50	89.22
Specificity %	100.0	100.0	100.0	100.0	100.0	100.0
Fscore %	98.60	99.09	90.95	94.14	84.65	89.80
AUC	1.00		0.98		0.95	
Accuracy %	98.89		92.88		87.74	

Figure 6 displays the confusion matrix of our CNN model trained on the WSST dataset. It demonstrates the performance of our model in predicting the test images.

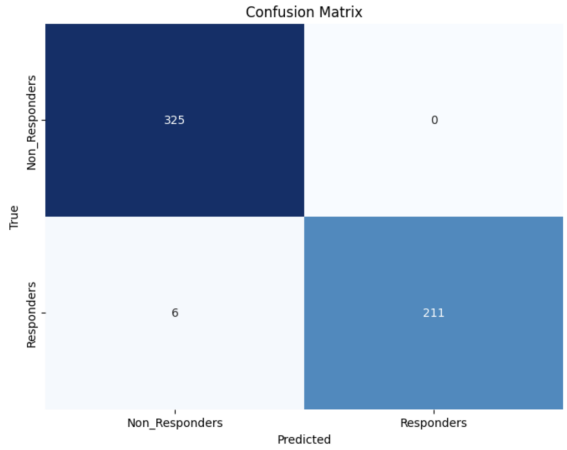


Fig. 6. Confusion Matrix of our model with WSST Dataset

Additionally, our unique CNN architecture—which consists of four convolutional layers, batch normalization, dropout regularization, and fully linked layers—has shown to be flexible and resilient in the face of complicated EEG data. Through the integration of spatial and temporal information collected from EEG data, our model outperforms existing benchmarks and establishes a new benchmark for MDD drug outcome prediction. Employing a k-value of 5 for K-fold cross-validation aids in reducing overfitting and facilitates a comprehensive evaluation of model performance across diverse datasets. This methodology improves the reliability and relevance of our results. By conducting thorough validation and comparison, we've affirmed the efficacy of our technique

while also identifying areas for additional improvement and fine-tuning.

VI. Conclusion

In summary, our research significantly contributes to the fields of personalized medicine and computational psychiatry. By employing modern facilities technologies and techniques, we have expanded our comprehension of the brain processes behind Major Depressive Disorder (MDD), opening the door to more focused and efficient therapeutic approaches. With the long-term objective of enhancing patient outcomes and boosting the standard of living for persons diagnosed with major depressive disorder (MDD) and other related psychological problems, we predict that collaboration and innovation in this multidisciplinary field will continue.

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