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## Time frequency images as predictors for depressed patients' respondent status to SSRI antidepressant

Wael Korani \*\* , Shyam Sundar Domakonda \*\*

Department of information science, University of North Texas, TX, USA

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#### ABSTRACT

Depression is a mental disorder that might cause self-harm and suicidal thoughts if the level of depression reaches the refractory or recurrent depressive disorder stage. Depression can be categorized into four different levels that are defined based on a psychometric called Beck Depression Inventory (BDI): minimal, mild, moderate, and severe. Depression level is important to narrow down the selection of depression therapy. There are several ways to treat depression and among them medications, Electroconvulsive therapy (ECT), repetitive Transcranial Magnetic Stimulation (rTMS), a combination of medication and rTMS. In the minimal depression level, an antidepressant medication is the best option such as, tricyclic antidepressants (TCAs), monoamineoxidase inhibitor (MAOI), and Selective serotonin reuptake inhibitors (SSRIs). This study introduces a deep learning (DL) architecture trained on time frequency images derived from EEG signals to predict the patient's respondent status to SSRI antidepressant. We introduce an efficient framework that integrate image technique with stat-of-the-art DL models. Various time-frequency methods, including wavelet synchrosqueezed transform (WSST), Continuous wavelet transform (CWT), and Discrete wavelet transform (DWT), are explored to convert EEG signals into time-frequency images. Among these methods, WSST demonstrates superior performance in extracting relevant information encoded within EEG signals, outperforming CWT and DWT. Time-frequency images generated using WSST contribute to the achievement of an accuracy level of 98.89% when fed into a proposed lightweight custom CNN architecture. The results show that WSST is powerful in capturing crucial signal features in detecting the outcome of depression therapy. Our proposed architecture is simple and computationally efficient, despite its simple design, outperforms more complex architectures such as, EfficientNetV2L, ResNet152V2, Xception, DenseNet201, and MobileNetV2. The proposed framework outperforms other models in accuracy, precision, recall, and specificity metrics utilizing 5-fold cross-validation strategy. These metrics demonstrate the robustness of our proposed model in predicting SSRI patients' responses. Our results show that DL might be used to enhance the clinical decision-making, leading to more tailored treatments and improved quality of life for depression patients through personalized medicine.

#### 1. Introduction

Major Depressive Disorder (MDD), commonly referred to as depression, is a severe and debilitating mental health condition. It affects individuals of all ages, genders, and backgrounds, and is recognized as a leading cause of disability worldwide. The exact cause of MDD remains elusive, as it is likely influenced by a complex interplay of genetic, biological, environmental, and psychological factors. Neurobiological abnormalities, including alterations in neurotransmitter levels (such as serotonin, dopamine, and norepinephrine), dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, and structural changes in brain regions implicated in mood regulation (such as the prefrontal cortex and hippocampus), are thought to contribute to the development

and maintenance of depression. Symptoms of MDD encompass a wide range of emotional, cognitive, behavioral, and physical manifestations, which might include persistent feelings of sadness, emptiness, or hopelessness, loss of interest or pleasure in previously enjoyed activities (anhedonia), changes in appetite or weight, disruptions in sleep patterns (insomnia or hypersomnia), fatigue or loss of energy, difficulty concentrating or making decisions, feelings of worthlessness or guilt, and recurrent thoughts of death or suicide. The severity and duration of these symptoms vary among individuals, with some experiencing mild and transient episodes, while others endure chronic and incapacitating depression. The effects of MDD extend far beyond individual suffering, impacting various domains of functioning and quality of life. In

E-mail addresses: wael.korani@unt.edu (W. Korani), shyamsundardomakonda@my.unt.edu (S.S. Domakonda).

<sup>\*</sup> Corresponding author.

addition, to impairments in social, occupational, and academic performance, depression is associated with increased healthcare utilization, elevated risk of comorbid medical conditions (such as cardiovascular disease, diabetes, and chronic pain), and heightened mortality rates, primarily due to suicide. Moreover, depression exerts a profound toll on interpersonal relationships, contributing to marital discord, family conflict, and social isolation.

Despite the considerable burden imposed by MDD, effective treatments are available, offering hope for recovery and symptom remission. The primary modalities for managing depression include pharmacotherapy, psychotherapy, and, in some cases, a combination of both. Antidepressant medications, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs), are commonly prescribed to alleviate depressive symptoms by restoring neurotransmitter balance in the brain. Psychotherapeutic interventions, such as cognitive-behavioral therapy (CBT), interpersonal therapy (IPT), and mindfulness-based approaches, aim to address maladaptive thought patterns, interpersonal difficulties, and behavioral patterns contributing to depression. Additionally, lifestyle modifications (such as regular exercise, healthy diet, adequate sleep, and stress management) and complementary treatments (such as acupuncture, yoga, and meditation) may complement conventional therapies and enhance overall well-being.

Machine learning (ML) and deep learning (DL) techniques have been emerged as promising tools in the field of mental health, including the treatment of Major Depressive Disorder (MDD). These computational approaches leverage the power of algorithms and data analysis to enhance diagnostic accuracy, predict treatment outcomes, and personalize interventions for individuals with depression. ML algorithms is utilized to analyze large datasets of clinical, neuroimaging, and genetic information to identify patterns and biomarkers associated with MDD diagnosis and severity. By integrating diverse sources of data, ML models can be used to assist clinicians in making more informed decisions regarding treatment selection and monitoring. DL, a subset of ML that employs artificial neural networks with multiple layers, offers even greater complexity and flexibility in analyzing complex datasets. DL algorithms excel at extracting intricate features from neuroimaging data, such as functional magnetic resonance imaging (fMRI) and EEG, to elucidate neurobiological correlates of depression and treatment response. These computational techniques hold promise for advancing precision psychiatry by facilitating the development of personalized treatment algorithms tailored to the unique neurobiological signatures of individual patients. Moreover, ML and DL algorithms can facilitate the identification of novel therapeutic targets and the development of innovative interventions for MDD. As the field continues to evolve, ML and DL are poised to play an increasingly prominent role in revolutionizing the diagnosis, prognosis, and treatment of MDD, ultimately improving outcomes and quality of life for individuals affected by this debilitating disorder.

In this study, our primary objective is to predict the patients' respondent status (responders (R) and non-responders (NR)) to SSRI) in treating Major Depressive Disorder (MDD), and enhancing the classification accuracy. To achieve this, we explore three different time-frequency analysis methods: Wavelet Synchrosqueezing Transform (WSST), Continuous Wavelet Transform (CWT), and Discrete Wavelet Transform (DWT). Each channel of the EEG signal is segmented into 30-s intervals, and these segments are converted into images using the three different time-frequency methods, resulting in three distinct datasets. These datasets are then used to train our proposed custom Convolutional Neural Network (CNN), which demonstrates superior performance compared to other methods. Our CNN exhibited computational efficiency and a lightweight architecture, outperforming various machine learning (ML), transfer learning (TL), and hybrid models in terms of classification performance metrics. This research sheds light on the potential of utilizing EEG signals and CNNs to predict SSRI treatment response in MDD patients, offering a promising avenue for improving personalized treatment strategies in psychiatric care.

Over all, the paper introduces the following contributions:

- Propose a novel CNN architecture to effectively classify MDD medication outcome into Responders (R) and Non-Responders (NR)
- We introduce a novel method, wavelet synchrosqueezed transform (WSST), to generate time-frequency images and demonstrate its effectiveness in predicting the outcome of SSRI depression therapy.
- Generate and compare different time–frequency images: WSST, CWT, and DWT to determine which time–frequency representation is the best in prediction the outcome of SSRI depression therapy.
- Reduce the usage of the computational resources by avoiding the usage of preprocessing techniques, segmentation, more hidden layers, augmentation transformation.
- Reconstruct several pre-trained architectures and fine-tuning the number of fully connected layers and learning rate and show the effect of adding batch normalization layer and global average pooling to avoid over-fitting.
- Evaluate the performance of the proposed architectures in an unbiased way using CV in terms of accuracy, precision, recall, f1-score, sensitivity and finding the best model to predict the outcome of depression therapy.
- Compare the performance of our proposed architecture with that of other pretrained architectures.

#### 2. Literature review

In [1], Zhdanov et al. addressed the challenge of predicting treatment outcomes for depression using EEG data from the CAN-BIND-1 study, with a support vector machine classifier. Using baseline EEG recordings from 122 patients, the model achieved 79.2% accuracy, which improved to 82.4% by incorporating EEG data after two weeks of treatment. These results, obtained 10-fold CV. In [2], Jaworska et al. aimed to predict antidepressant response in MDD patients using EEG data and machine learning models. The study, involving 51 patients in a 12-week pharmacotherapy trial, achieved 88% accuracy with a Random Forest classifier by analyzing EEG power and clinical data. Results were validated using 10-fold CV, demonstrating the potential of EEGbased ML methods for predicting treatment response. In [3], Rajpurkar et al. conducted a study to predict acute improvement in individual depressive symptoms using a ML approach with gradient-boosted decision trees (GBDT). The study analyzed data from the International Study to Predict Optimized Treatment in Depression (iSPOT-D), which involved 518 adult outpatients with MDD. The primary objective was to predict symptom improvement using pretreatment symptom scores and EEG measures. Using 5-fold CV, the ML model achieved the highest C-index score of 0.963.

In [4], Mahato et al. aimed to classify depression patients and healthy individuals using EEG signals by analyzing both linear and nonlinear features. The study utilized the Mumtaz dataset, which included 34 MDD patients and 30 healthy controls, achieving a maximum classification accuracy of 93.33% with a combination of alpha power and relative wavelet energy using multi-layered perceptron neural network (MLPNN) and radial basis function network (RBFN) classifiers. The study employed 10-fold CV for evaluation.

In [5], Shovon et al. developed a CNN-based framework to classify Motor Imagery EEG signals, enhancing accuracy in Brain–Computer Interface (BCI) systems by transforming EEG time series into 2D images using STFT. Their method, tested on the BCI Competition IV dataset 2b and dataset III from BCI Competition II, achieved an average accuracy of 89.19% on dataset 2b and 97.7% for subject 7 on dataset III, highlighting its potential for improved classification in BCI applications. In [6], Dang et al. introduced a frequency-dependent multilayer brain network integrated with deep CNN to detect major depressive disorder (MDD) using physiological signals. Their approach achieved a state-of-the-art accuracy of 97.27% on a publicly available MDD dataset,

validated through 10-fold CV. In [7], Acharva et al. presented a novel computer model utilizing CNN for EEG-based screening of depression. The research involved EEGs obtained from 15 normal and 15 depressed patients. The model achieved accuracies of 93.5% and 96.0% using EEG signals from the left and right hemisphere, respectively. Employed 10-fold CV for evaluation. In [8], Sandheep et al. conducted an extensive analysis using a computer-aided machine learning approach, specifically CNN, to classify depression using EEG signals. The Mumtaz dataset was utilized included 30 normal and 30 depressed individuals. The deep CNN model achieved a classification accuracy of 99.31% using EEG signals from the right hemisphere and 96.30% from the left hemisphere after 10-fold CV. In [9], Wu et al. developed the sparse EEG latent space regression (SELSER) model to predict response to antidepressants based on resting-state EEG data. This study analyzed data from 309 participants in the largest imaging-coupled, placebocontrolled antidepressant study. The model achieved a relative mean square error (RMSE) of 5.68 using 10-fold CV. In [10], Li et al. proposed a computer-aided detection (CAD) system for recognizing mild depression using a CNN. They adapted the ConvNet architecture through transfer learning. The system achieved an accuracy of 85.62% in distinguishing mild depression from normal controls using 24-fold CV. In [11], Duan et al. proposed a method to identify major depressive disorder (MDD) by fusing interhemispheric asymmetry and cross-correlation from EEG signals. Using data from Beijing Anding Hospital, they analyzed theta, alpha and beta frequency bands from 16 MDD patients and 16 healthy controls to extract structural and connectivity features, which were then combined for classification. Their CNN model achieved an accuracy of 94.13%. In [12], Kang et al. introduced a novel deep-asymmetry methodology that converts EEG asymmetry features into matrix images for input into a CNN, focusing on EEG asymmetry as a key depression biomarker. Common methods like STFT, wavelet, and coherence, their approach achieved a classification accuracy of 98.85% in the alpha band. The results were validated using 5-fold CV. In [13], Seal et al. introduced DeprNet, a CNN, for classifying EEG data of depressed and normal subjects based on Patient Health Questionnaire 9 scores. DeprNet achieved an accuracy of 99.37% with recordwise split data, while subjectwise split data resulted in an accuracy of 91.4% using 10-fold CV. In [14], Loh et al. introduced a deep learning model based on CNN and spectrogram images derived from STFT of EEG signals for detecting MDD. Utilizing a dataset comprising 34 MDD patients and 30 healthy subjects, the model attained a classification accuracy of 99.58% through 10-fold CV. In [15], Imran et al. the study addresses the challenge of accurately identifying gastrointestinal abnormalities in endoscopic images, which is difficult due to the variability in manual evaluations by gastroenterologists. By utilizing a deep convolutional neural network (DCNN) with multiple routes and resolutions, the model achieved a Matthews correlation coefficient of 0.9743 on the Kvasir dataset, demonstrating significant potential for improving diagnostic accuracy.

In [16], Zhang et al. proposed three deep transfer CNNs for automatic cross-subject seizure detection using EEG data from the CHB-MIT dataset. The authors utilized short-time Fourier transform to generate time–frequency spectrum images as input data. The models achieved average accuracies of 98.26% with VGG19, 97.75% with VGG16 and 96.17% with ResNet50 respectively. In [17], Uyulan et al. developed an EEG-based diagnosis model for MDD using deep CNN, specifically ResNet-50, MobileNet, and Inception-v3 architectures. They analyzed EEG recordings from 46 MDD patients and 46 healthy controls across four main frequency bands (Delta, Theta, Alpha, Beta) from 19 electrodes. MobileNet achieved accuracies of 89.33% and 92.66%, using 5-fold CV. In [18], Imran et al. utilized transfer learning and proposed convolutional neural network to detect synovial fluid in magnetic resonance images, achieving an accuracy of 86.77%.

In [19], Shalbaf et al. proposed an automatic methodology for diagnosing schizophrenia (SZ) using EEG signals converted into images via continuous wavelet transform (CWT). Four pre-trained CNNs like

AlexNet, ResNet-18, VGG-19, and Inception-v3 were employed, and their deep features were fed into an SVM classifier. ResNet-18-SVM achieved an accuracy of 98.60%. Results were obtained with 10-fold CV.

In [20], Saeedi et al. a deep learning framework for automatically discriminating MDD patients from healthy controls using EEG signals is proposed. Effective brain connectivity analysis is conducted using Generalized Partial Directed Coherence (GPDC) and Direct Directed Transfer Function (dDTF) methods. Images of EEG signals are constructed based on a novel combination of sixteen connectivity methods across eight frequency bands. The 1DCNN-LSTM model achieves the highest accuracy of 99.24%. In [21], Sharma et al. proposed a fully automated Depression Detection System based on EEG signals, named DepHNN (Depression Hybrid Neural Network). The model utilizes a combination of CNN for temporal learning and LSTM architectures for sequence learning. EEG signals from 21 drug-free, symptomatic depressed, and 24 normal patients are used for training and testing. The model achieves an accuracy of 99.10%. In [22], Pancholi et al. proposed three novel deep learning models for motion trajectory prediction (MTP) from EEG signals. These models, including multilayer perceptron (MLP), CNN-LSTM, and wavelet packet decomposition (WPD) for CNN-LSTM, utilize brain source localization (BSL) for motor intention decoding. Performance is evaluated on the reach, grasp, and lift (GAL) dataset using Pearson correlation coefficient (PCC) and trajectory analysis, achieving a maximum correlation of up to 0.67. Results obtained through k-fold CV. In [23], Sun et al. developed a method to enhance schizophrenia classification accuracy using EEG signals by transforming time-domain and frequency-domain features into RGB images. Their hybrid deep neural networks (combining CNNs and LSTM) achieved an average accuracy of 99.22% with fuzzy entropy as a feature, validated through 10-fold CV. In [24], Wilaiprasitporn et al. presented a study aimed at improving affective EEG-based person identification (PI) using DL. The method involved a combination of CNNs and Recurrent Neural Networks (RNNs) to handle spatial and temporal information from EEG signals, respectively. The study evaluates LSTM and Gated Recurrent Unit (GRU) networks. The proposed approach was tested on the DEAP dataset, achieving up to 100% mean Correct Recognition Rate (CRR) using 32 electrodes and 99.17% CRR with only five electrodes from the frontal region. The results were obtained using 10-fold CV. In [25], Ay et al. proposed a fully automated depression diagnosis system using EEG signals, employing a deep hybrid model that combines CNN and LSTM architectures. The CNN layers capture temporal properties, while the LSTM layers manage sequence learning. Their model achieved classification accuracies of 99.12% for the right hemisphere and 97.66% for the left hemisphere, using 10-fold CV. In [26], Thoduparambil et al. developed a deep model combining CNN and LSTM for depression detection using EEG signals. The CNN learns local characteristics while the LSTM captures signal sequences, with feature maps processed by the LSTM and classified through fully connected layers. Their model achieved accuracies of 99.07% for right hemisphere and 98.84% for left hemisphere EEG signals using random splitting.

In [27], Mumtaz et al. proposed a ML method for predicting the outcome of SSRIs treatment in MDD patients using EEG data to classify R and NR. They used three different time–frequency decomposition methods, including wavelet transform (WT), short-time Fourier transform (STFT), and empirical mode decomposition (EMD), to extract time–frequency features from EEG signals and logistic regression (LR) for classification. The LR model achieved an accuracy of 87.5%, using 10-fold cross-validation (CV). In [28], Shahabi et al. developed a deep Transfer Learning (TL) strategy for predicting the response to SSRIs antidepressants in MDD patients using EEG data. The proposed ensemble TL strategy based on WT images obtained from EEG signal. They utilized pre-trained CNN models. DenseNet121, achieved an accuracy of 95.74% with 10-fold CV. An ensemble of these models further improved the accuracy to 96.55%. In [29], Shahabi et al. developed a hybrid model combining TL of pre-trained CNNs with bidirectional

long short-term memory (BLSTM) cells and attention mechanism to classify R and NR to SSRIs antidepressants using EEG signal images. The VGG16-LSTM-Attention model achieved the highest accuracy of 98.21% with 10-fold cross-validation. An ensemble model of TL-LSTM-Attention models further improved the accuracy to 98.84%. In [30], Mirjebreili et al. developed a novel method for classifying R and NR to SSRIs antidepressants in MDD patients using EEG signals. They employed deep learning and brain effective connectivity analysis to extract features from the EEG data. A hybrid CNN with BLSTM cells based on TL was fine-tuned. The EfficiencyNet-B0 model achieved the highest accuracy of 98.33% with 5-fold CV. In [31], Degirmenci et al. showed that WSST effectively analyzes nonstationary biomedical signals by providing high-resolution TFR with reduced noise. The results showed that WSST enhances classification accuracy, especially with ML and DL algorithms, making it valuable in biomedical analysis. In [32], Degirmenci et al. study conducted to enhance motor imagery (MI) classification using EEG data to support patients with motor disabilities. Leveraging WSST for time-frequency distribution and Non-Negative Matrix Factorization (NMF) for feature extraction, the approach achieves over 95% accuracy, a kappa above 0.90, and an F1 score of 0.99 with classifiers like KNN and RF, though the use of cross-validation is not detailed.

Despite significant advancements in EEG-based classification tasks, limited research has been conducted on the Mumtaz dataset, particularly in the context of treatment response classification into Responders (R) and Non-Responders (NR). Previous studies have predominantly focused on using conventional ML, transfer TL, and hybrid models for depression classification problem depressed/non-depressed. Additionally, minimal exploration has been undertaken to transform EEG signals into advanced time-frequency representations for improved analysis to predict the outcome of depression therapy. To address these gaps, our research introduces an innovative approach where EEG signals from the Mumtaz dataset are converted into time-frequency representations using CWT, DWT, and WSST to predict the outcome of SSRI. Unlike prior studies, our primary focus is on WSST time-frequency images due to their ability to provide higher resolution and richer feature representations compared to CWT and DWT. Further, we propose a simple yet efficient CNN architecture tailored to analyze these time-frequency images for classification tasks. This approach is both computationally efficient and highly effective, as it avoids the complexity of hybrid models while maintaining superior classification performance. Through comprehensive evaluations, we demonstrate that.

#### 3. Materials and methods

Our experiments are conducted on a MacBook M1 that has 8-core CPU, comprising 4 performance cores and 4 efficiency cores, an 8-core GPU, and a 16-core Neural Engine. The system's computational power enabled the efficient training and evaluation of our models. An illustration of our proposed research is shown in Fig. 1.

#### 3.1. Dataset

In this study, we examine the pretreatment resting-state EEG signals of 30 individuals diagnosed with MDD, which were recorded while the participants had their eyes closed (EC) [27]. The experimental protocol received approval from the human ethics committee at the Hospital University Sains Malaysia in Kelantan, Malaysia. Diagnosis of MDD was conducted in accordance with the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Among the participants, 12 individuals exhibited a positive response to antidepressant treatment, defined as a reduction of at least 50 percent in Beck Depression Inventory (BDI) scores post-treatment compared to pretreatment scores. The EEG data were captured over a 5-min duration using 19-channel electrodes placed according to the international 10–20 electrode positioning system, with a linked-ear reference. Fig. 2(b)

**Table 1**Summary of MDD patients clinical characteristics.

Information	Responder	Non-Responder	Total
Age [years]	40.7 (±13.0)	41.1 (±12.5)	40.3 (±12.9)
Gender (male/female)	8/8	9/9	17/17
Pre-treatment BDI-II	18.4 (±7.4)	22.8 (±12.5)	20.6 (±8.6)
Post-treatment BDI-II	9.1 (±6.3)	$22.1 (\pm 3.3)$	15.6 (±4.5)

shows the location of the EEG channels on the scalp in the 10–20 international system. To minimize interference, power line noise was eliminated using a Notch filter at 50 Hz, and the signals were band-pass filtered within the frequency range of 0.5 to 70 Hz. The sampling rate utilized was 256 Hz. Each patient's EEG signal was analyzed within a specified time frame. Table 1 shows a summary of MDD patients clinical characteristics. A sample of 20 channels of EEG signals in Mumtaz database for the R and NR groups is shown in Fig. 3.

#### 3.2. Time-frequency methods

CNN models are employed for EEG classification by converting EEG signals to image space using three distinct time–frequency analysis methods. These methods process the signal into time–frequency images, serving as inputs to the CNN. CNN models trained effectively and demonstrated improved learning capabilities with the incorporation of time–frequency images, resulting in enhanced performance in EEG classification tasks. We employ three time–frequency analysis techniques, including Wavelet Synchrosqueezing Transform (WSST), Continuous Wavelet Transform (CWT), and Discrete Wavelet Transform (DWT).

#### Wavelet synchrosqueezing transform (WSST)

The Wavelet Synchrosqueezing Transform (WSST) is an advanced time-frequency analysis method designed to accurately characterize signals composed of multiple oscillating components. Unlike traditional wavelet transforms, WSST mitigates the issue of time-frequency spreading, ensuring sharper signal analysis. It achieves this by reassigning signal energy in the frequency domain while preserving time resolution. This innovative technique is particularly beneficial for analyzing complex signals such as speech waveforms, machine vibrations, and physiological data. The algorithm involves choosing an appropriate analytic wavelet, computing the CWT, and extracting instantaneous frequencies from the CWT output using a phase transform. By reassigning energy in frequency over regions of constant phase, WST sharpens the time-frequency representation of the signal. Crucially, WSST requires signal components to be intrinsic mode type (IMT) functions, meeting specific separation criteria in the time-frequency plane for accurate analysis. The Wavelet Synchrosqueezing Transform (WSST) is an advancement of the CWT that enhances the time-frequency localization of signal components. It addresses the issue of the CWT's inherent trade-off between time and frequency localization by reintroducing better time localization while preserving the CWT's frequency resolution. The WSST achieves this by applying a reassignment technique, known as synchrosqueezing, to the CWT coefficients. This reassignment process redistributes the energy of the wavelet coefficients to better align with the signal's instantaneous frequency, resulting in sharper time-frequency representations. The WSST has demonstrated superiority over traditional time-frequency methods in capturing fine-scale features and has been particularly useful in analyzing complex signals with rapidly changing frequency content, such as biomedical signals and seismic data.

#### Continuous wavelet transform (CWT)

The CWT is a versatile method used in signal processing to analyze signals in both time and frequency domains simultaneously. The CWT is a powerful tool for analyzing non-stationary signals in the time-frequency domain. Unlike traditional Fourier analysis, which provides

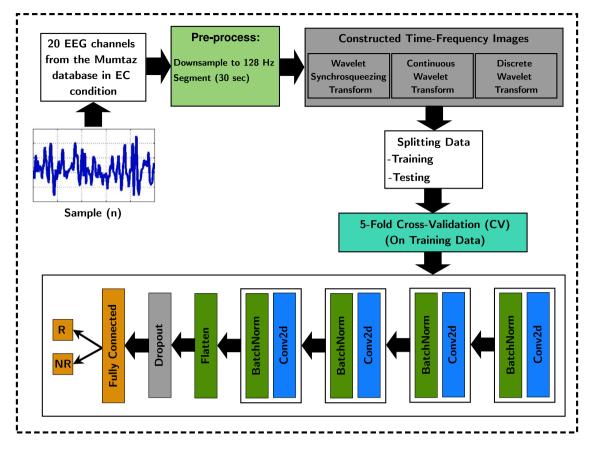


Fig. 1. Research workflow.

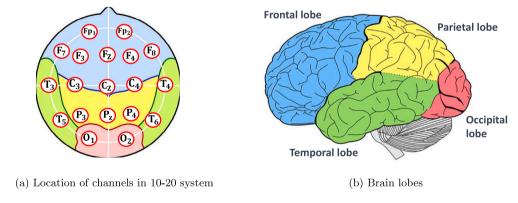


Fig. 2. Illustration of channel locations in the 10-20 EEG system and their corresponding brain lobes.

fixed-frequency resolution, the CWT offers a flexible approach by allowing the scale and position of the analyzing window (or wavelet) to vary continuously. This adaptability enables the detection of transient events and changes in frequency content over time, making it invaluable in applications such as audio and speech processing, vibration analysis, and biomedical signal analysis. By convolving the signal with a family of wavelets characterized by different scales and positions, the CWT generates a time–frequency representation that highlights localized features with high precision. Furthermore, the CWT is capable of capturing both low and high-frequency components of a signal, making it suitable for analyzing complex signals with diverse frequency content. Its effectiveness in identifying subtle changes and patterns in signals has led to its widespread use in diverse fields including image processing, pattern recognition, and environmental monitoring. The CWT's ability to provide detailed insights into signal dynamics while

preserving temporal and spectral information makes it an indispensable tool for researchers and engineers alike.

#### Discrete wavelet transform (DWT)

The Discrete Wavelet Transform (DWT) is a time–frequency analysis method that decomposes a signal into different frequency bands with varying resolutions. Unlike the CWT, which operates over continuous scales, the DWT operates at discrete scales. It achieves this by recursively decomposing the signal using low-pass and high-pass filters, resulting in a multi-resolution representation. This decomposition facilitates the analysis of transient features and abrupt changes in signals. While the DWT sacrifices some time localization at higher frequencies for computational efficiency, it offers a computationally efficient way to capture essential signal characteristics and has found wide application in signal denoising, compression, and feature extraction.

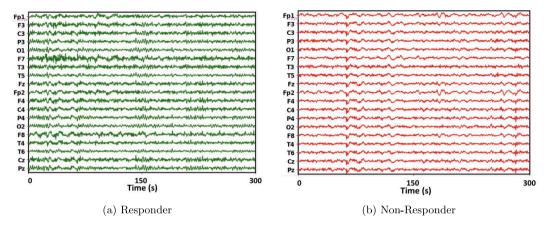


Fig. 3. Sample of responder and Non-responder EEG signal.

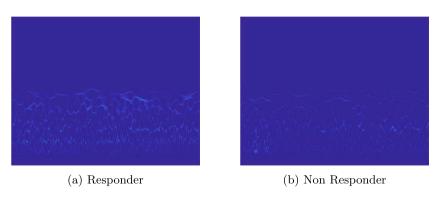


Fig. 4. Sample WSST time frequency images of responder and Non responder.

We generated three datasets using these three frequency analysis methods and trained and tested them on our proposed CNN model.

#### 3.3. EEG signal preprocessing

During preprocessing, the signals underwent filtering. First, a bandpass filter is applied, allowing only frequencies between 0.5 and 70 Hz. Additionally, a 50 Hz notch filter is used to remove power line noise. Following this, the signals are downsampled to 128 Hz, which helps decrease the amount of computational resources required. We implement these steps consistently across all three time–frequency methods to produce time–frequency images.

To preprocess EEG signals into WSST time–frequency images, each channel is segmented into 30-s intervals, which are transformed using the Morlet wavelet as the mother wavelet. This approach enhances time–frequency resolution, allowing for detailed analysis and the extraction of complex signal features. The discrete segmentation ensures localized analysis, while WSST captures essential information within the signal's time–frequency domain. The WSST images are generated at a sampling frequency of 128 Hz, covering a frequency range of 0.5 Hz to 70 Hz, with a 50 Hz notch filter applied to suppress power line noise. By constructing a dataset from these WSST images, our research aims to provide comprehensive insights into neural activity and identify potential biomarkers for neurological conditions. Sample WSST time–frequency images of R and NR are illustrated in Fig. 4.

To convert EEG signals to CWT time–frequency representations, preprocessing steps are implemented. Each EEG channel is divided into 30-s segments to facilitate analysis. The Continuous Wavelet Transform (CWT) is then applied using the Morlet wavelet, which extracts time–frequency information by convolving the signal at various scales and positions. The CWT is configured with a downsampled sampling frequency of 128 Hz and a frequency range of 0.5 Hz to 70 Hz, with a

50 Hz notch filter applied to suppress power line noise. This conversion allows for the analysis of signal characteristics across different frequencies over time, providing valuable insights into the dynamic nature of brain activity. A dataset is constructed from these CWT images, with sample representations of R and NR shown in Fig. 5.

To convert EEG signals into Discrete Wavelet Transform (DWT) time–frequency representations, the signals are first divided into 30-s segments. DWT is then applied to each segment using the 'db4' wavelet at a decomposition level of 5. This decomposition extracts frequency components at various scales, represented as time–frequency images. Converting EEG signals to DWT frequency representations facilitates the analysis of signal characteristics across different frequency bands, capturing both high and low-frequency components. The process operates with a downsampled sampling frequency of 128 Hz, employing a band-pass filter from 0.5 to 70 Hz and a 50 Hz notch filter to suppress power line noise. A dataset is constructed from these DWT images, with sample representations of R and NR shown in Fig. 6.

We preprocess the MDD dataset consisting of responders and nonresponder classes of EEG signals into time-frequency analysis images using three different methods: WSST, CWT, and DWT. By utilizing these methods, we generate three distinct datasets, each representing the time-frequency characteristics of the EEG signals using WSST, CWT, and DWT. Subsequently, we train and evaluate these datasets using our proposed CNN model. This approach allows us to leverage the unique advantages of WSST, CWT, and DWT for capturing different aspects of the EEG signals' time-frequency features, leading to a comprehensive analysis of the MDD dataset and the development of an effective classification model. Then, we reduce the size of the images to  $(224 \times 224)$  in order to optimize the usage of the computational resources, which helps the CNN to perform well in short time. The images are then shuffled before splitting to avoid any bias. The shuffled dataset is divided into 80% (training and validation) and 20% testing. In addition, the 5fold CV strategy is implemented to avoid bias and to ensure a robust

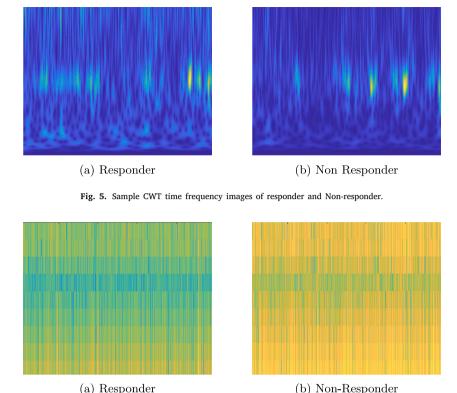


Fig. 6. Sample DWT time frequency images of responder and Non-responder.

assessment of our proposed models. Our framework evaluation utilizes with the testing set, which accounted for 20% of the original dataset. Collectively, these subsets: training, validation, and testing form a meticulously designed hierarchy for training, refining, and evaluating our classification models. The size of these subsets emphasizes the structure and rigorous nature of our approach to robustly validate our model's efficacy and real-world applicability. Then, we apply data preprocessing techniques to optimize image quality for model training and evaluation. The pixel values are standardized in range [0, 1]. This foundational step ensured consistent data representation and enhanced model convergence during subsequent training and testing phases.

#### 3.4. Proposed CNN

Our CNN architecture consists of multiple convolutional layers with ReLU activation functions, each followed by batch normalization for regularization. The convolutional layers have number of filters 4, 6, 8, and 12, respectively, with kernel sizes of (3, 3). The default stride (1, 1) and padding (0, 0) are used for these convolutional layers, ensuring no additional pixels are added and the filter moves one pixel at a time across both dimensions of the input. Additionally, there is a dropout layer with a dropout rate of 0.25 to prevent overfitting. The output layer is a dense layer with a sigmoid activation function for binary classification. We utilized the Adam optimizer with a learning rate of 0.0001 and binary cross-entropy loss function for model training. Early stopping with a patience of three is employed as a regularization technique to prevent overfitting. The architecture of our proposed CNN is shown in Fig. 7. Table 2 summarizes the hyperparameter settings in our CNN.

#### 3.5. TL architecture

We Utilize significant TL architectural adjustments. In this architecture, we integrate a Global Average Pooling layer that is known for its

Table 2
Experimental parameters.

Models	Parameters	Classifier setting
Proposed CNN EfficientNetV2L ResNet152V2 Xception	Optimizer Initial learning rate Batch size Loss function	Adam 0.0001 32 Binary cross-entropy
DenseNet201 MobileNetV2	Epochs	10

feature extraction and dimensionality reduction capabilities. This layer plays a pivotal role in preserving essential information while mitigating overfitting risks. In addition, we introduce Batch-Normalization, a crucial technique that stabilizes training by normalizing activation within the network. These aforementioned modifications enhance our model convergence and generalization. The dense output layer of our model has one neuron, used to predict the output as either the R or NR class. Employing the sigmoid activation function ensured that the model generated probability distributions across these classes, facilitating confident and informed classification. Our models are optimized using Adam optimizer with a lowered initial learning rate, specifically 0.0001. For optimal model performance during training, we adjust the learning rate to 0.0001. This fine-tuning effectively reduces the risk of learning divergent patterns from the pre-trained weights and is built on careful experimentation and observation of convergence dynamics. Our training process includes 10 epochs, with data batches comprising 32 samples each. To enhance training efficiency and effectiveness, we incorporate one essential callbacks: Early-Stopping. Early-Stopping diligently monitors validation loss, allowing us to halt training if it plateaued for an extended period to prevent overfitting. We provide a concise summary of the parameters employed in conjunction with the pretrained models in Table 2.

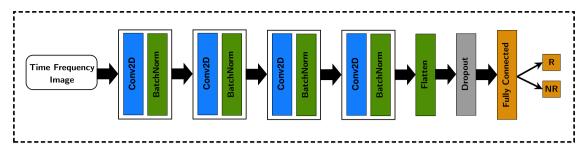
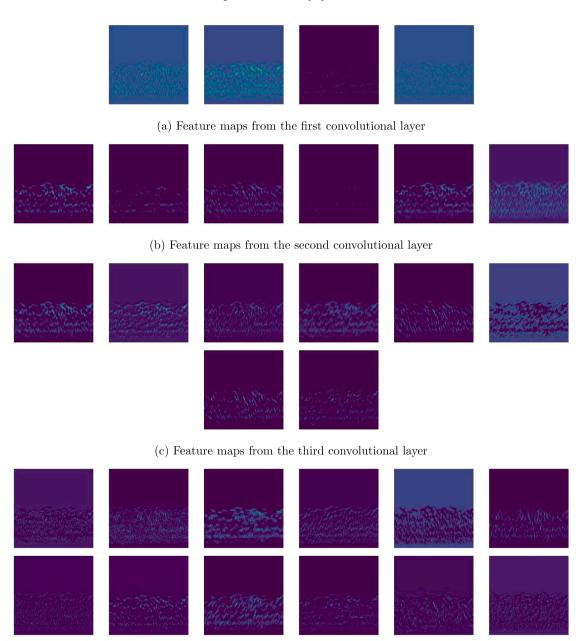


Fig. 7. Architecture of proposed CNN.



 $(\ensuremath{\mathbf{d}})$  Feature maps from the fourth convolutional layer

Fig. 8. Feature maps from the convolutional layers of the CNN. Each row represents feature maps from different convolutional layers, showcasing the filters applied at each layer.

#### 3.6. Feature map analysis of convolutional layers of the proposed CNN

The feature maps in Fig. 8. provide a detailed visualization of the most discriminative features learned by the proposed CNN from WSST

responder image. As the layers deepen, the network captures increasingly complex patterns, starting with basic texture and edge detection in the early layers and advancing to more abstract representations in the deeper layers. This progressive feature extraction demonstrates the

model's ability to effectively capture key time-frequency characteristics critical for accurate analysis and classification.

#### 3.7. Performance evaluation

Various performance metrics can be employed to assess classifier performance; however, classification accuracy remains a fundamental and frequently utilized metric. In our research, we place a primary focus on accuracy as the key evaluation metric for our proposed models. Classification accuracy is defined as the proportion of correctly classified data samples to the total number of data samples evaluated. The accuracy metric underscore the efficacy and reliability of our proposed models within the context of our research.

Our MDD classification centers on an imbalanced dataset, demanding a broader evaluation. To comprehensively assess the proposed models performance, we employ confusion matrix as a vital tool to delve deeper into the intricacies of our responder and non responder classification system. Confusion matrix provides a concise representation, tabulating both accurate and incorrect classifications. we introduce an in-depth analysis of precision, recall, and specificity, all pivotal performance metrics pertinent to our classifier's evaluation. These equations are derived from the confusion matrix, which provides valuable insights into our classifier's effectiveness.

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN} \tag{1}$$

where, True Positives (TP), False Positives (FP), False Negatives (FN) and True Negatives (TN). Precision quantifies the accuracy of positive predictions by calculating the ratio of true positives to the total predicted positives.

$$Precision = \frac{TP}{TP + FP} \tag{2}$$

Recall recognizes as sensitivity, measures the classifier's capacity to identify all relevant positive samples. It is calculated as the ratio of true positives to the total actual positives.

$$Recall = \frac{TP}{TP + FN} \tag{3}$$

Specificity gauges the model's aptitude in recognizing true negatives among the total actual negatives. It is determined as the ratio of true negatives to the sum of true negatives and false positives.

$$Specificity = \frac{TN}{TN + FP} \tag{4}$$

The harmonic mean of precision and recall, which yields the critical statistical measure known as the F-score for each class.

$$F_{score} = \frac{2}{3} \sum_{c=1}^{3} \frac{precision_c \cdot recall_c}{precision_c + recall_c}$$
 (5)

This metric offers a comprehensive assessment of our models performance, considering the nuances of the imbalanced classes.

In the context of evaluating the performance of machine learning models, the Receiver Operating Characteristic (ROC) curve plays a significant role to evaluate the performance of a proposed model. An ideal ROC curve is one where the Area Under the Curve (AUC) equals unity, which indicates perfect classification. This metric is critical in assessing how effectively a model can distinguish between different classes or categories.

In addition to standard performance metrics, we utilize confusion matrices to evaluate the classification performance of our CNN model. The confusion matrix provides a detailed breakdown of true positives, false positives, true negatives, and false negatives, offering deeper insight into the model's accuracy and error distribution. By analyzing the confusion matrix, we can identify specific areas where the model excels or needs improvement, such as distinguishing between similar classes. This detailed analysis helps in refining the model and improving overall classification performance.

#### 4. Results

We train and evaluate our proposed CNN on MDD preprocessed EEG signal time–frequency analysis datasets generated using three different methods: WSST, CWT, and DWT. We evaluate our processed CNN on various metrics including accuracy, precision, recall, specificity, and F1 score on MDD EEG signal time–frequency analysis datasets. Table 3 show our results.

Our results show that the WSST time–frequency method significantly aids in the extraction of relevant information encoded within EEG signals. Achieved an impressive accuracy of 98.89%, WSST time–frequency images demonstrates its efficacy in capturing crucial features of the signals, highlighting its potential in advancing signal processing methodologies within the medical field. Additionally, the DWT time–frequency images exhibits commendable performance with an accuracy of 92.88%, further underscoring its relevance in medical signal analysis. The CWT time–frequency images follows suit with an accuracy of 87.74%, though slightly less compared to WSST and DWT. WSST is better than CWT and DWT, because it provides good time–frequency localization. The main limitation of the wavelet decomposition technique is to provide both time and frequency resolution at the same time; however, using WSST is capable of resolving this issue and generate images that have more features to better represent the EEG signals.

We conclude that WSST time–frequency images perform significantly better compared to other time–frequency methods such as DWT and CWT. As shown in Table 3, the performance of our CNN with WSST time–frequency images is superior. Therefore, we consider WSST time–frequency images to compare our proposed CNN with pretrained models such as EfficientNetV2L, ResNet152V2, Xception, DenseNet201 and MobileNetV2. Table 4 shows the performance comparison between our proposed CNN and pretrained models.

Table 4 shows that our proposed CNN performs well across all classification metrics compared to pretrained models. The results demonstrate that our CNN is not only computationally efficient but also outperforms pretrained models such as EfficientNetV2L, ResNet152V2, Xception, DenseNet201 and MobileNetV2 in terms of accuracy, precision, recall, and F1-score. This highlights the effectiveness of our custom CNN architecture in analyzing WSST time–frequency images for EEG signal classification. The bar plot showing the accuracy comparison of our proposed CNN and pretrained models is depicted in Fig. 9. Fig. 10 shows the confusion matrix for our proposed CNN and pretrained models, while Fig. 11 displays their ROC curves.

#### 4.1. Comparison with related works

Table 5, presents a comparison of our work with other research studies. From our analysis, it is evident that our CNN model performs exceptionally well across all classification metrics compared to other ML, TL, and hybrid models. Our model consistently outperforms the competing architectures in terms of accuracy, precision, recall, and F1-score. These findings underscore the effectiveness of our proposed CNN architecture in EEG signal classification tasks. Our research extends beyond signal processing, as we introduce a novel CNN architecture designed specifically for EEG signal classification. This CNN architecture proves to be both computationally efficient and highly effective, outperforming other hybrid models in all classification tasks. These findings hold significant promise for the medical field, offering enhanced diagnostic capabilities and improved understanding of neurological conditions.

#### 5. Discussion

In this paper, we investigate EEG classification for responders and non-responders to SSRI antidepressants using a Custom CNN. We explore different time-frequency methods in this study, such as WSST,

**Table 3**Performance measures of our model using three time–frequency methods.

Dataset	Precision %		Recall %	Recall %		Specificity %		F <sub>score</sub> %		Accuracy %
	N	NR	N	NR	N	NR	N	NR		
WSST	100.0	98.19	97.24	100.0	100.0	100.0	98.60	99.09	1.00	98.89
DWT	91.41	93.83	90.50	94.44	100.0	100.0	90.95	94.14	0.98	92.88
CWT	83.82	90.40	85.50	89.22	100.0	100.0	84.65	89.80	0.95	87.74

Table 4
Performance measures of our model with pretrained models.

Model	Precision %		Recall %		Specificity %		F <sub>score</sub> %		AUC	Accuracy %
	N	NR	N	NR	N	NR	N	NR		
EfficientNetV2L	95.89	97.83	96.77	97.23	100.0	100.0	96.33	97.53	1.00	97.04
ResNet152V2	91.10	99.35	99.08	93.54	100.0	100.0	94.92	96.35	1.00	95.75
Xception	74.91	98.07	97.70	78.15	100.0	100.0	84.80	86.99	0.98	85.97
DenseNet201	66.87	98.65	98.62	67.38	100.0	100.0	79.90	80.07	0.97	79.88
MobileNetV2	56.96	83.63	82.95	58.15	100.0	100.0	67.54	68.60	0.83	68.08
Proposed CNN	100.0	98.19	97.24	100.0	100.0	100.0	98.60	99.09	1.00	98.89

Table 5
Related works and comparative analysis on the Mumtaz dataset.

Work	Year	Method	Training data	Cross-validation	Epochs	Accuracy
Mirjebreili [30]	2024	CNN-BiLSTM	80%	With $(k = 5)$	50	98.03%
Shahabi [29]	2022	Ensemble of TL-LSTM-Attention	80%	With $(k = 10)$	50	98.21%
Shahabi [28]	2021	Ensemble of CNN TL	70%	With $(k = 10)$	50	96.55%
Mumtaz [27]	2017	ML	-	With $(k = 10)$	-	87.50%
Proposed	2024	CNN	60%	With $(k = 5)$	10	98.89%

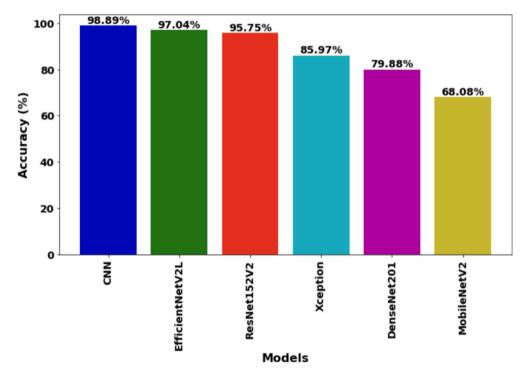


Fig. 9. Accuracy comparison of our proposed CNN and pretrained models.

CWT, and DWT. WSST, an advanced time–frequency method introduced in our study, significantly aids in the extraction of relevant information encoded within EEG signals. We obtain time–frequency images from EEG signals and generated three datasets using these three frequency methods. By feeding different time–frequency images to our proposed CNN, we achieve a promising accuracy level of 98.89% with WSST time–frequency images. This demonstrates WSST's efficacy in capturing crucial features of the signals, highlighting its potential in advancing signal processing methodologies within the medical field. Therefore, we consider WSST time–frequency images to compare

our proposed CNN with pretrained models such as EfficientNetV2L, ResNet152V2, Xception, DenseNet201 and MobileNetV2. The comparison between our proposed CNN and pretrained models reveals that our CNN performs well across all classification metrics. The results demonstrate that our CNN is not only computationally efficient but also outperforms pretrained models in terms of accuracy, precision, recall, and F1-score. This highlights the effectiveness of our custom CNN architecture in analyzing WSST time–frequency images for EEG signal classification. The primary strength of our proposed method

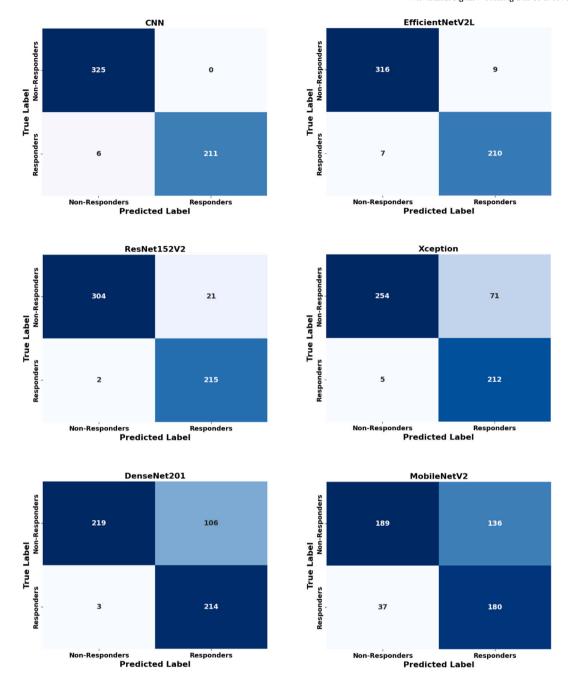


Fig. 10. Confusion matrix of proposed CNN and Pretrained models.

lies in its ability to efficiently capture crucial features from EEG signals using WSST, which outperforms other time-frequency methods such as CWT and DWT in terms of accuracy and feature extraction. Additionally, our custom CNN is computationally efficient while still achieving higher classification metrics (accuracy, precision, recall, and F1-score) compared to more complex pretrained models. This makes it highly suitable for real-time applications in clinical settings. However, a potential limitation is the reliance on WSST for feature extraction, which may not generalize as effectively across other datasets with different signal characteristics. Future work could explore how our method performs with larger and more diverse datasets to further validate its robustness. To integrate our model into a clinical setting, it could be used as a decision-support tool to predict SSRI responsiveness, aiding psychiatrists in tailoring treatment plans for MDD patients. By providing early insights into treatment outcomes, the model could reduce the trial-and-error approach often associated with antidepressant prescriptions. However, challenges in real-world translation include ensuring the model's robustness across diverse patient populations and different EEG acquisition settings. Future research should explore the impact of various EEG recording parameters and longitudinal studies to evaluate the model's ability to track treatment responses over time. Additionally, addressing data privacy and regulatory approval will be essential for clinical adoption.

#### 6. Conclusion

In this paper, we generate images from EEG signals using three different time frequency methods. Then, a fully custom automatic CNN architecture based on our generated images is used to classify depressed patients to responders and non-responders to SSRI antidepressants, utilizing minimal computational resources. The results show that WSST is the best time frequency method to capture more features from EEG

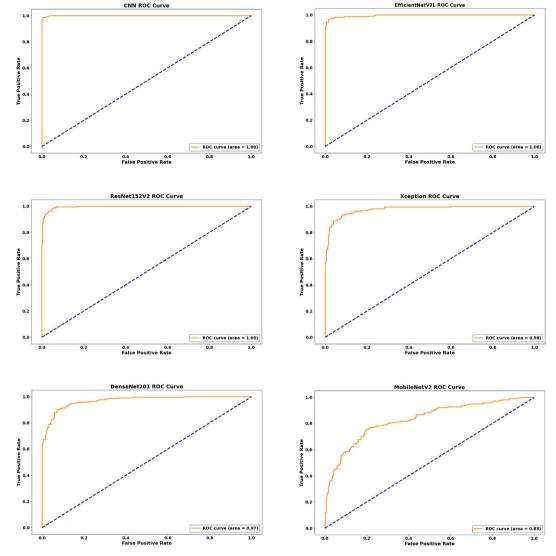


Fig. 11. ROC Curve of proposed CNN and Pretrained models.

signals to detect respondent and non-respondent to antidepressent. The proposed CNN architecture comprises various layers including convolutional layers, batch normalization, dropout layers, and an output layer to extract discriminative features from time-frequency images. The proposed classifier is evaluated using the MDD figshare dataset, recording classification accuracy and other metrics to demonstrate the reliability of the proposed CNN model. Results indicate that our CNN model achieves the highest accuracy level of 98.89% compared to all other previous studies. Our experiments underscore the importance of architectural adjustments, appropriate learning rate selection, and regularization techniques. The use of 5-fold cross-validation emphasizes the robustness and generalization capacity of our model. The introduction of an advanced time-frequency method coupled with our proposed CNN architecture proves to be both computationally efficient and highly effective, surpassing other hybrid models in all classification metrics.

#### CRediT authorship contribution statement

Wael Korani: Writing – review & editing, Project administration. Shyam Sundar Domakonda: Writing – original draft.

#### **Ethics** approval

We did not record the dataset and there is no ethics approval.

#### **Funding**

There is no fund for this project.

#### **Declaration of competing interest**

**Research Support:** This research received no external financial or non-financial support.

**Relationships:** There are no additional relationships to disclose. **Patents and Intellectual Property:** There are no patents to disclose.

Other Activities: There are no additional activities to disclose.

#### Data availability

In 2016, Mumtaz published a MDD Patients and Healthy Controls EEG Data dastaset at figshare [27].

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