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Research Article

Major depressive disorder diagnosis from electroencephalogram data and potential treatment with dimethyltryptamine

Sushmit Jahan [a,*]

[a]*Varendra University, Faculty of Engineering and Technology, Department of Computer Science and Engineering, Rajshahi 6204, Bangladesh*

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ABSTRACT

In recent times, there has been increasing interest in utilizing EEG-based techniques for studying Major Depressive Disorder as a dynamic method. Although it is frequently used for identifying depression, the method is still difficult to interpret. The conventional treatment of MDD involves medications such as Selective Serotonin Reuptake Inhibitors, which often have adverse effects. On the other hand, the use of dimethyltryptamine to stimulate brain activity in regions where MDD patients show lower activity has demonstrated promising results. This study analyzed resting-state EEG signals from MDD patients, DMT users, and healthy controls to evaluate and validated a computer-aided approach. The brain activity of DMT users was recorded and compared with MDD individuals and healthy controls. Using Welch's method, the power of several frequency bands was analyzed from the EEG dataset for comparison and diagnosis. The extracted EEG data underwent noise removal and feature extraction. The features from all controls were concatenated to form a data matrix. Furthermore, the data matrix was standardized using the Z-score standardization method. The classifier model logistic regression was employed to train and test the extracted features. The results of the investigations have demonstrated the most important features, such as signal power of the EEG data from the frontal, temporal, parietal, and occipital brain areas, to be significant.

1. Introduction

An important form of mood disorder called depression results in a constant feeling of sadness and loss of interest. Additionally known as a major depressive disorder or clinical depression, it affects your feelings, thoughts, and behavior and can cause several emotional and physical issues. A WHO study from 2021 states that an estimated 3.8% of the population was affected by depression, with 5.0% of adults and 5.7% of persons over 60 years old. Around 280 million individuals worldwide suffer from depression [1]. Major depressive disorder is also associated with other mental illnesses such as anxiety disorder and multiple personality disorder. To diagnose depression from other mental illnesses psychiatrists often use a traditional technique called the beck depression inventory-II or BDI-2 [2]. This technique is often misdiagnosed in some patients with other mental illnesses. The BDI-2 technique's correctness depends on the experience of the psychiatrist. Therefore, it is necessary to diagnose MDD patients with other mental illnesses to treat them properly. The most common medicine used to treat depression is Selective Serotonin Reuptake Inhibitors and Serotonin-Norepinephrine Reuptake Inhibitors. These drugs often cause severe side effects. Dimethyltryptamine or DMT is a psychedelic that can cause hallucinations. Unlike SSRIs, it is observed that DMT can activate brains in certain regions that differ from person to person. Also, it can improve the connectivity of neurons [5]. Recently, Computer-Aided techniques have been used to diagnose MDD patients properly. Various methods of gathering data from the brain, such as mining functional magnetic resonance imaging (fMRI) data using Machine Learning (ML) techniques, have produced promising results [3]. Also, data acquisition called the electroencephalogram or EEG signal can be used to diagnose depression without failure to identify between different mental illnesses. Electroencephalogram or EEG signals are collected from healthy controls and patients diagnosed with MDD by BDI-2 to further analysis to produce a model which can differ between MDD and healthy controls. Welch's

* Corresponding author. Tel.: *+88 017 927 741 95.*
E-mail addresses: sushmitrose@gmail.com (S.Jahan)
ORCID: *0000-0002-5850-3642* (S.Jahan)
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method and Hanning window are used to extract features from EEG signals to train and test the model. The EEG dataset in this study was obtained from a previous study in which participants were selected anonymously through an electronic form. Researchers screened the participants and allowed them to choose a location for themselves, to create a more natural setting. Participants in the study were administered micro-doses of DMT via nasal inhalation. The study was approved by the Committee for Research Ethics at the 'Jose Maria Ramos Mejia' General Hospital and adhered to the Helsinki Declaration [11, 14].

2. Materials and Method

2.1 Study Participants: MDD and Healthy Controls

The dataset used in this analysis was obtained from a prior study [10]. Two groups of volunteers participated, including 33 MDD patients and 30 healthy individuals, recruited from Hospital Universiti Sains Malaysia (HUSM) in Malaysia. Patients were also administered the Statistical Manual testing for depression (DSM-IV), while healthy participants underwent screening for potential mental or physical illnesses and were determined to be disease-free.

2.2 Data Acquisition: MDD and Healthy Controls

The EEG data were collected using a 19-channel EEG cap with a linked-ear (LE) reference. The 19 electrodes on the EEG cap are located in the occipital (O1, O2), frontal (Fp1, Fp2, F3, F4, F7, F8, Fpz), temporal (T3, T4, T5, T6), parietal (P3, P4, P7, P8), and central (C3, C4) areas [Figure 1]. The cap was set up with a 50 Hz notch filter, a 0.5 Hz to 70 Hz filter, and a sampling rate of 256 samples per second.

2.3 Study Participants: Participants with Micro-dosing of DMT

The dataset of DMT users was collected from a study set called "Neural and subjective effects of inhaled DMT in natural settings" [11]. In the study, 35 participants from the different groups were given micro-dosing inhales of DMT.

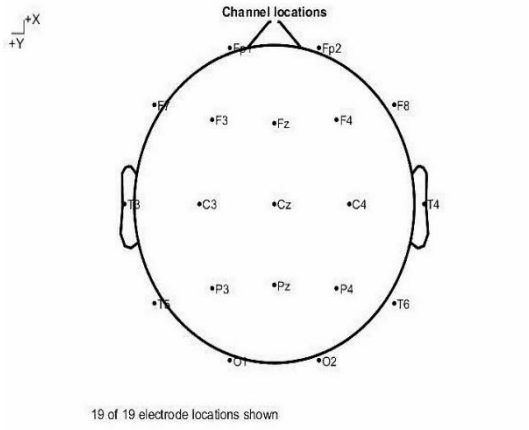


Figure 1. 19 channel EEG cap locations

2.4 Data Acquisition: Participants with Micro-dosing of DMT

With 24 channel EEG cap (Fp1, Fp2, Fz, F7, F8, FC1, FC2, Cz, C3, C4, T7, T8, CPz, CP1, CP2, CP5, CP6, TP9, TP10, Pz, P3, P4, O1, and O2) EEG data were recorded. The data were recorded with a sampling rate of 500 Hz, with 24-bit resolution and, 0–250 Hz pass-band in the resting state of the participants. The data was acquired with eyes closed and eyes opened state. Following the administration of DMT, EEG recordings were initiated at the time of subject exhalation and continued until the subject indicated a return to baseline, which lasted for an average of 6 ± 1.4 minutes [14].

2.5 EEG Data Pre-processing

In this work, composite signals produced by causes other than neuronal activity were mixed in with the recorded EEG data, accounting for them as noise. For instance, various noises such as eye blinks, movements, and muscular activations may distort the EEG data (e.g., the heartbeats). Unfortunately, the EEG data that has been distorted by these artifacts might not accurately depict the underlying brain activity. For this reason, cleaning the EEG data was a necessary pre-processing step before moving on to data analysis. In this study, different source techniques were used in the EEGLAB program to remove these noises. All channels were manually inspected for noise and removed using the EEGLAB program. Independent component analysis (ICA) is used as a technique for noise reduction. We can filter independent components using ICA. The noisy signal components can be identified from the ICA maps [Figure 2].

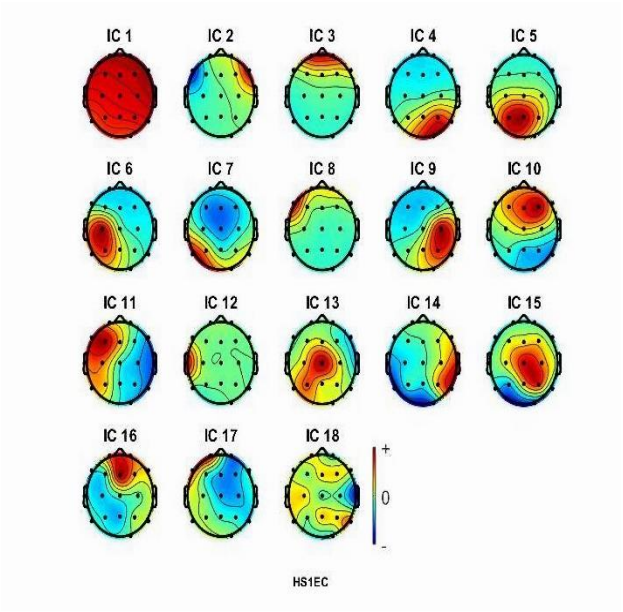


Figure 2. Analyzing noise component by applying ICA

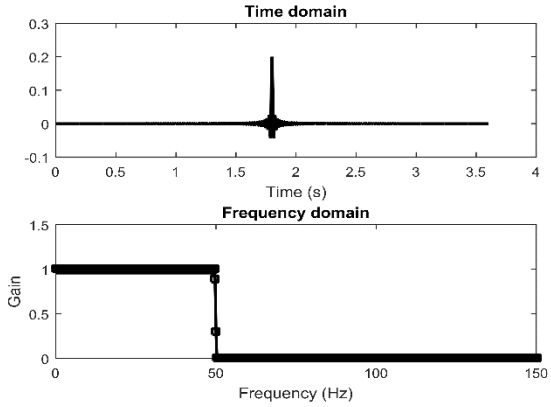


Figure 3. Lowpass filter kernel design

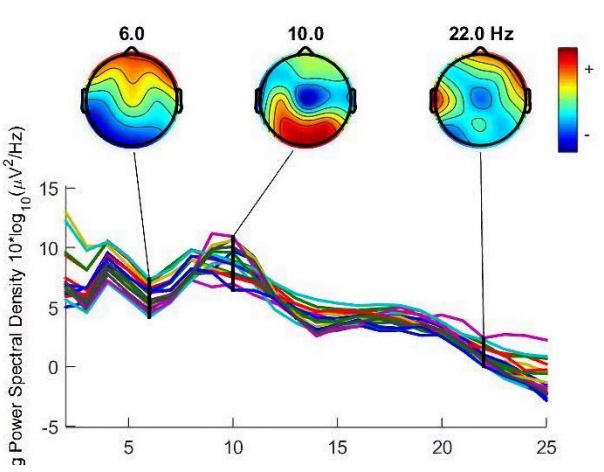


Figure 4. EEG power spectral density

After those eye movements, blinks and muscle movement was removed (estimated 4 ± 2.4 components removed) we reconstruct the improved independent components to get the original signals in their pure form. Also, a lowpass filter Kernel has been designed with a cutoff frequency of 50 Hz [Figure 3]. All the pre-processed EEG data requires to filter through this kernel before processing.

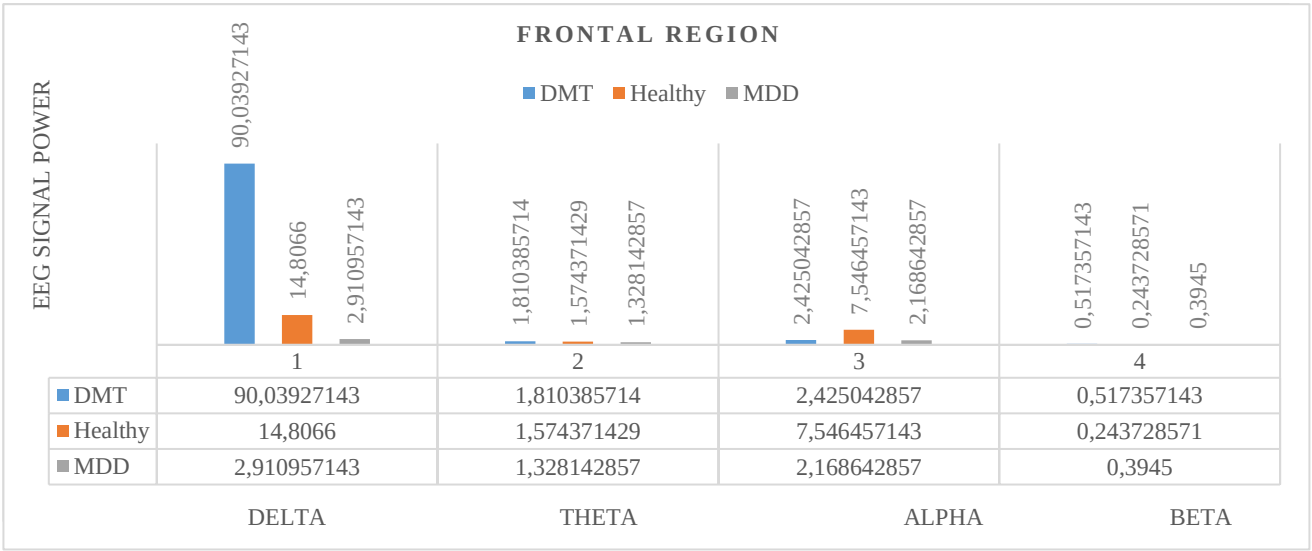
2.6 Feature Extraction

For feature extraction, the artifact-free two minutes epoch of resting-state data was selected from eyes-closed (EC) data per study subject. Therefore, a data matrix was achieved and absolute power was calculated. A dysfunction in various brain regions, particularly the frontal and temporal regions, has been linked to MDD [4][15]. Therefore, absolute power over these regions was calculated for further comparisons with healthy controls. The feature was calculated based on the power spectrum delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), and beta (12-35Hz) [Figure 4].

The EEG signal power's difference between the left and right hemispheres can be observed by computing the average power of each region of the brain also known as interhemispheric asymmetry [6]. For each channel pair, the EEG alpha interhemispheric asymmetry was calculated. The average values of each region were calculated to compute features for classification and look into an overall trend, such as either increasing or decreasing values between the left and right hemispheres of the depressed and healthy controls.

2.7 EEG Spectral Power Calculation

To calculate EEG signal strengths involving the Hanning window, the Welch periodogram method was proposed. Welch's method is widely recognized as a powerful and reliable tool for analyzing EEG data, allowing researchers to estimate the power spectral density of non-stationary signals with remarkable accuracy [13]. The method works by dividing the EEG signal into overlapping segments, applying a window function to each segment to reduce spectral leakage, and then calculating the power spectral density estimate of each segment using the periodogram method.

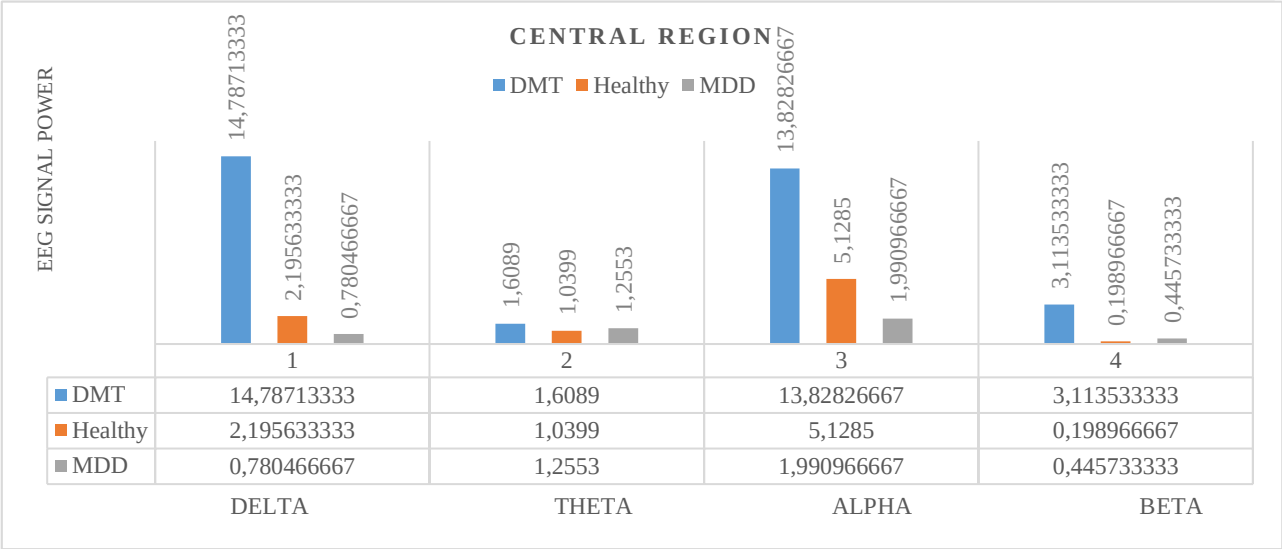


	1	2	3	4
DMT	90,03927143	1,810385714	2,425042857	0,517357143
Healthy	14,8066	1,574371429	7,546457143	0,243728571
MDD	2,910957143	1,328142857	2,168642857	0,3945

Figure 5. Frontal regions activity of DMT, Healthy and MDD patients

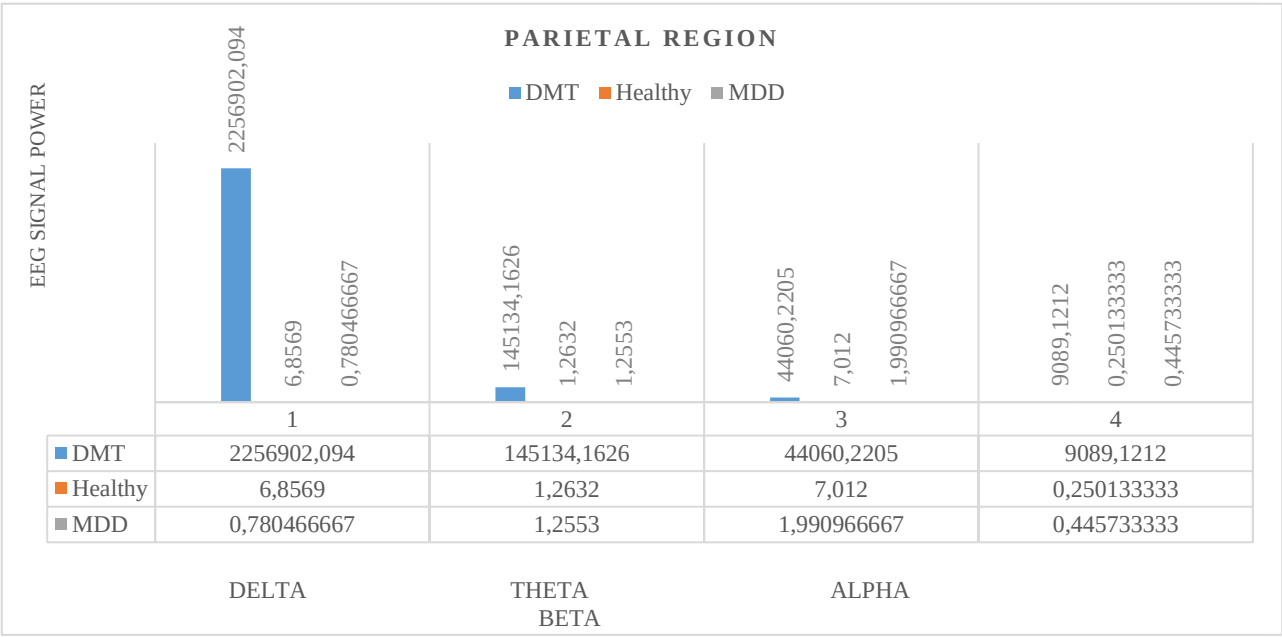
These power spectral density estimates are then averaged together to obtain a smoothed estimate of the EEG signal's power spectrum. One of the advantages of Welch's method over other existing methods is that it provides a more accurate estimate of the EEG signal's power spectrum, particularly in situations where the EEG signal is non-stationary or contains artifacts [16]. This is because the method uses overlapping segments and a window function to reduce the effects of spectral leakage, which can distort the power spectrum estimate. Additionally, the method allows for the detection of changes in the power spectrum over time, which can be useful in analyzing EEG data in response to different stimuli or during different cognitive states.

However, one disadvantage of Welch's method is that it requires a larger amount of data compared to other methods since it involves dividing the signal into overlapping segments. Moreover, Welch's method can be more demanding in terms of computational resources compared to alternative methods, which could restrict its practicality in certain situations. Given the large amount of data in our study, Welch's method was deemed a more appropriate choice for the analysis. The EEG signal was initially split into separate datasets with a 50 overlap before the periodogram algorithm computed the signal power. To determine the power of the EEG signal, the spectrum was also determined for each segment and averaged over all segments. The calculated spectral power was absolute, and the difference's calculated statistical significance was less than 0.01.



	1	2	3	4
DMT	14,78713333	1,6089	13,82826667	3,113533333
Healthy	2,195633333	1,0399	5,1285	0,198966667
MDD	0,780466667	1,2553	1,990966667	0,445733333

Figure 6. Central regions activity of DMT, Healthy and MDD patients



	1	2	3	4
DMT	2256902,094	145134,1626	44060,2205	9089,1212
Healthy	6,8569	1,2632	7,012	0,250133333
MDD	0,780466667	1,2553	1,990966667	0,445733333

Figure 7. Parietal regions activity of DMT, Healthy and MDD patients

In the literature, MDD has been linked to dysfunction in a variety of brain regions, including the frontal and temporal lobes.

2.8 Classification Model

The reduced set of features used in this study was regarded as independent variables, while the treatment results (MDD cases and controls) were regarded as the dependent variables Eq.(1).

$$E(Y/x) = \frac{e^x}{1+e^x} \quad (1)$$

The maximum likelihood method served as the foundation for the estimate of the coefficients for the *Logistic Regression* classifier. The likelihood value *L(x)* of the LR classifier, where $0 \leq L(x) \leq 1$, was an indication of participants that were either connected with MDD cases or controls. If *L(x)* exceeded the cut-off value of 0.5, the person was classified as having MDD; otherwise, they were placed with healthy participants.

3. Results

3.1 EEG Signal Power Analysis

The tables (Fig 5, Fig 6, Fig 7, Fig 8) shows comparisons between MDD patient, the healthy control group, and DMT users' EEG signal power. The EEG signal power was calculated and averaged over the brain's region to understand specifically the brain's neural activity. According to the results, MDD patients has less delta, theta, and alpha power as compared to healthy patient and DMT users. Moreover, MDD patients have higher beta power in the parietal, central, and temporal regions than healthy controls. As the study suggests, higher beta power in temporal and parietal regions is due to anxiety [12].

Also, less activity in other parts of the brain means less consciousness and failure in different cognitive tasks. Although in healthy participants less beta power is prominent meaning healthy participants were less anxious than the MDD patients. But in the case of participants with DMT micro-dosing, they are much more anxious than healthy participants but less anxious than the MDD patients as the beta power of DMT users suggests. It could be because the participant of DMT micro-dosing gets anxious about inhaling a new chemical compound. But the MDD patient shows high beta power as they were anxious. Nearly 50% of MDD patients are suffered from anxiety. Furthermore, MDD patients show higher theta power than healthy patients in the central region of the brain. The central region of the human brain is controlled by the heart's rhythm, breathing, and blood flow. Therefore, MDD patients have dysfunctions in these conditions. From the results, MDD patients can be detected from controls.

3.2 EEG Signal Power Analysis of DMT Users

The participants with DMT inhalation exhibit higher power in almost all of the brains region. The frontal part of the brain shows higher delta and beta power than healthy controls (Fig 5). As the study suggests, the frontal part is controlled cognition such as skills and math solving. Therefore, it can be said that DMT users have more cognition while taking DMT than others. In DMT study participants, their parietal lobs delta, theta, alpha, and beta power is higher than others. Somatosensory information from the body, such as touch, pain, temperature, and the perception of limb position, is processed by the parietal lobes. The parietal lobes play a role in integrating information from several modalities, just like the temporal lobes do.

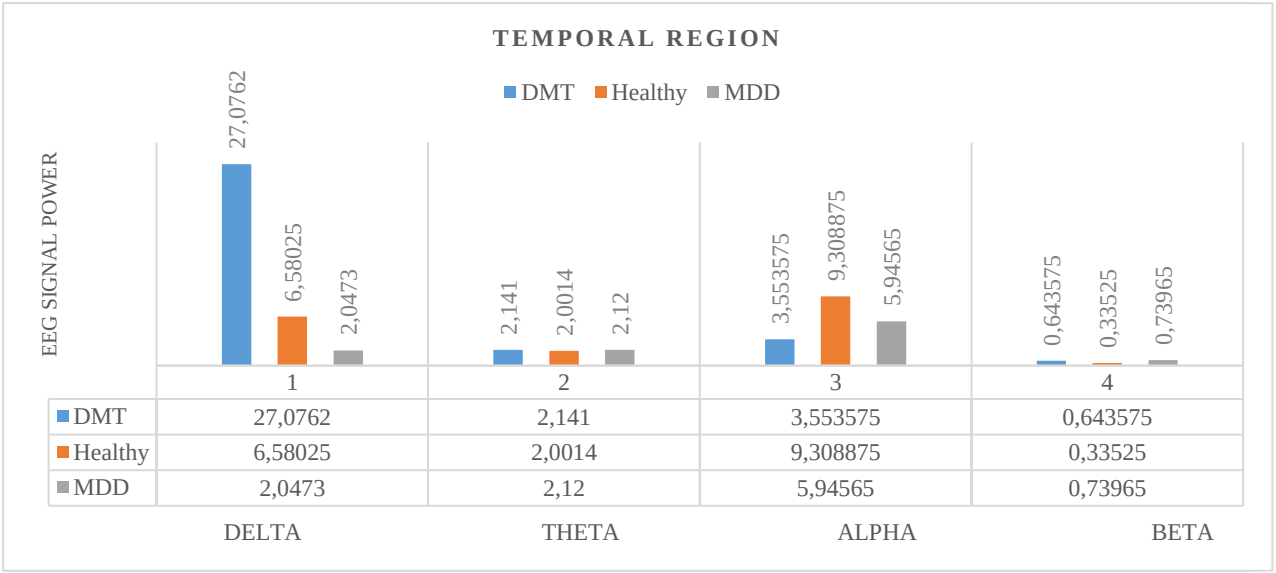


Figure 8. Temporal regions activity of DMT, Healthy and MDD patients

Therefore, the DMT users were more sensitive to touch, temperature, and pain and this sensitivity led to hallucination (Tab 1). Also, the participants have higher delta and theta power than the control in temporal lobes. Higher theta power in the temporal lobes, which are frequently linked to the processing of auditory information and the storing of memory, can also result in hallucinations.

Table 1. DMT user's health observation

Sensitivity	**Touch, temperature, pain**
Brain connectivity	High
Cognitive function	High
Auditory process	High
Heart rate	High

3.3 Classifications

Regarding the LR classifier, the link function showed an association between the EEG features and clinical issues [7]. Given that logistic regression was the chosen classifier, the value was set to Logit. The binomial distribution is predicated on binary classification; this was chosen since the data were expected to come from two classes, namely MDD cases and healthy controls. The LR classifier's mathematical model had a constant term, but the offset value was set to 1.

4. Discussion and Conclusion

Brain-computer interface (BCI) research has advanced significantly in recent years and is currently regarded as one of the most successful uses of neuroscience [8]. There are billions of cells in the brain, half of which are neurons and the other half of which assist and enable the activity of neurons. Through synapses, these neurons are intricately connected. When these synapses interact with other neurons, they generate electricity.

In this research, we detected major depressive disorder patients by comparing them with healthy subjects using their brain signals [9]. There are chemicals in the brain called neurotransmitters such as dopamine, serotonin, and norepinephrine. These chemicals produce electrical activity during different stages in the brain. In any case, chemical imbalance causes different chemical activity therefore brain produces different types of EEG signals during the chemical changes of the brain. In different emotional stages and learning times, the brain produces different EEG signals and it defines the cognitive functions of a person. People with MDD and other psychological problems have a chemical imbalance in their brains, therefore producing different EEG signals rather than a healthy person. Therefore, this study detected MDD patients from healthy controls by comparing their EEG signal power. Also, the use of DMT can improve mental health but with some potential side effects. Dimethyltryptamine can be a great candidate for treating major depressive disorder as it improves brain connectivity. Based on the findings of this study, it is suggested that further research is needed to investigate the potential of using EEG signals as a diagnostic tool for detecting MDD and other psychological disorders. Additionally, more research should be done to explore the effectiveness of DMT as a treatment for MDD and its potential side effects, to provide clinicians with more options for treating this condition. Furthermore, it is important to consider the ethical implications of using DMT as a treatment and to ensure that it is administered in a safe and controlled manner. Finally, continued advancements in BCI and psychedelic drug research can lead to the development of new and innovative treatments for a range of neurological and psychological disorders.

Declaration

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The author(s) also declared that this article is original, was prepared in accordance with international publication and research ethics, and ethical committee permission or any special permission is not required.

Author Contributions

Sushmit Jahan is responsible for all sections of the paper.

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