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THESIS TITLE

GAME THEORY AND MACHINE LEARNING APPROACH FOR TREATMENT OF SOME NEUROLOGICAL BRAIN DISORDERS

MASTER'S THESIS

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ISTANBUL 2024

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ABSTRACT

Game Theory and Machine Learning Approach for Treatment of Some Neurological Brain Disorders

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Master's Program in Artificial Intelligence
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Diagnosis of depression is the most important part of the treatment process in patients with neurological disorders. These patients use medications that directly affect the brain and depression is one of the most common side effects in these medications. In addition, these patients frequently undergo an electroencephalogram (EEG) test. Therefore, the identification of biomarkers related to depression in EEG can improve the treatment approach in these patients. For this purpose, EEG features of 232 patients including depressed and non-depressed patients were used. Then, Feature EXtraction (FEX) was applied to find significant features and improve the efficiency of dimensionality reduction techniques. After dimensionality reduction using Principal component analysis (PCA) and t-Distributed Stochastic Neighbor Embedding (t-SNE), the model was trained by a convolutional neural network (CNN) which leads to accuracy of 98% and confidence level of more than 60%. Eventually, a SHapley Additive exPlanations (SHAP) illustrates the most effective features on which the model diagnoses depression. Furthermore, a game-theoretic aspect indicates how the performance of the model can be improved if we train the model only on depression biomarkers.

Key Words: Game Theory, Machine Learning, Neurological Disorders, Depression Diagnosis, SHAP Explanation

ÖZ

TEZ
Oyun Teorisi ve Makine Öğrenimi Yaklaşımı ile Bazı Nörolojik Beyin Bozukluklarının Tedavisi

Parisa, Khaleghi
Yapay Zeka Yüksek Lisans Programı
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Nörolojik bozukluğu olan hastalarda depresyon tanısı tedavi sürecinin en önemli parçasıdır. Bu hastalar beyni doğrudan etkileyen ilaçlar kullanıyor ve depresyon bu ilaçların en sık görülen yan etkilerinden biri. Ayrıca bu hastalara sıklıkla electroencephalogram (EEG) testi yapılır. Bu nedenle EEG'de depresyonla ilişkili biyobelirteçlerin belirlenmesi bu hastalarda tedavi yaklaşımını geliştirebilir. Bu amaçla depresif ve depresif olmayan 232 hastanın EEG özellikleri kullanıldı. Daha sonra önemli özellikleri bulmak ve boyut azaltma tekniklerinin verimliliğini artırmak için özellik çıkarımı uygulandı. Principal component analysis (PCA) ve t-Distributed Stochastic Neighbor Embedding (t-SNE) kullanılarak boyut azaltımının ardından model, %98 doğruluk ve %60'ın üzerinde güven düzeyine yol açan bir convolutional neural network (CNN) tarafından eğitildi. Sonunda, bir SHapley Additive exPlanations (SHAP), modelin depresyonu teşhis ettiği en etkili özellikleri gösterir. Ayrıca oyun teorik yönü, modeli yalnızca depresyon biyobelirteçleri üzerinde eğitirsek modelin performansının nasıl artırılabileceğini gösterir.

Anahtar Kelimeler: Oyun Teorisi, Makine Öğrenimi, Nörolojik Bozukluklar, Depresyon Tanısı, SHAP Açıklama

I am sincerely grateful to my dear Arham, who has always been my companion and supporter.
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از آرین عزیزم که در این مسیر به من یاری رساند، بسیار قدردانی می‌کنم.
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LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
AED	Anti-Epileptic Drug
EEG	Electroencephalogram
PCA	Principal Component Analysis
t-SNE	t-Distributed Stochastic Neighbor Embedding
WHO	World Health Organization
ML	Machine Learning
DL	Deep Learning
AI	Artificial Intelligence
PSD	Power Spectral Density
DWT	Discrete Wavelet Transform
STFT	Short-Time Fourier Transform
FEX	Feature EXtraction
SHAP	SHapley Additive exPlanations

Chapter 1

Introduction

Controlling the side effects of medications in treating neurological disorders can affect the entire treatment process. These medications directly affect the brain and can cause negative side effects, especially depression. Therefore, real-time depression diagnosis can improve treatment efficiency as depression can lead to mood swings, hopelessness, and even non-cooperation of the patient to continue the treatment. Hence, this project aims to identify depression biomarkers using Machine Learning (ML) and Deep Learning (DL) techniques such as Feature EXtraction (FEX), Principal Component Analysis (PCA), t-Distributed Stochastic Neighbour Embedding (t-SNE), and Convolutional Neural Network (CNN). In the following, a SHapley Additive exPlanations (SHAP) as an explainable Artificial Intelligence (AI) technique illustrates the most influential features and game theory indicates the most important features to improve the performance of the model.

EEG is one of the most reliable tools used in the medical field that helps in monitoring brain activity in case of neurological disorders specifically disorders associated with seizures (Zhao et al., 2023). It measures the electrical activities of the brain over a period of time and gives deep insights into neuronal function (Zhao et al., 2023) (see Figure 1). This capability of EEG makes it invaluable not only in diagnosing and monitoring neurological disorders but also for psychiatric conditions. Therefore, when a patient undergoes an EEG, both psychiatric and neurological aspects can be monitored and abnormal biomarkers can be diagnosed. In terms of diagnosing depression, if there is any depression-related biomarker, the medical specialist can enhance or change the treatment approach in order to improve the patient's well-being and avoid any inadequate treatment.

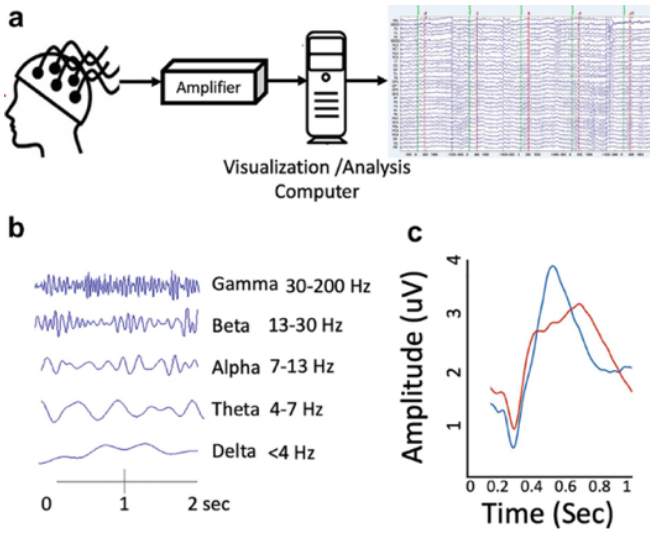

Figure 1. EEG Recording and Frequency Bands (Poudel & Jones, 2022).

Depression as a common global concern, is a mood disorder that causes persistent sadness, lack of interest in activities, and even physical symptoms. Depression affects approximately 264 million people in the world (World Health Organization, 2023) (Figure 2). This is noticeable in the field of neurological disorders because depression is a common side effect of medications used by patients with neurological disorders, and if the patients already have depression, it can directly affect the treatment approach. The interaction between depression and neurological disorders creates a cyclical relationship as it strengthens the symptoms in both depression and neurological conditions (Bølling-Ladegaard et al., 2023).

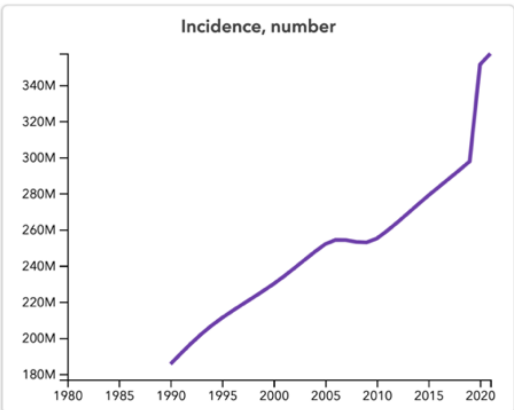

Figure 2. Global Incidence of Depression (1980-2021) (World Health Organization, 2023)

For most of the patients with neurological disorders, using medication is a lifelong approach. Normally, these patients have to change their medications after a while due to drug resistance which makes them more vulnerable to depression. For instance, Patients with epilepsy use Anti-epileptic drugs (AEDs) such as valproate, carbamazepine, lamotrigine, and phenytoin. These AEDs are associated with various side effects (Ogunjimi et al., 2024; Orozco-Hernández et al., 2023) (Table 1)., and depression is the most impactful one among them as it can lead the patient to treatment refusal or lack of willingness to continue with taking medication (Kumar et al., 2020). So, diagnosing depression in this situation can prevent any poor control of the primary neurological condition.

Table 1

Nine most frequent ADRs for each AED (Silvennoinen et al., 2019).

AED	Patients with ADR (%)	Weight change	Lethargy	Tremor	Cognitive impairment	Behavioural disorder	Depression	Gastrointestinal ADRs	Adverse cutaneous	Speech disorder
VPA	93 (37.5)	58 (20.8)	19 (6.8)	30 (10.8)	12 (4.3)	6 (2.2)	2 (0.7)	3 (1.1)	0 (0.0)	1 (0.4)
LTG	25 (16.3)	2 (1.2)	4 (2.5)	4 (2.5)	3 (1.9)	0 (0.0)	2 (1.2)	2 (1.2)	4 (2.5)	0 (0.0)
LEV	30 (24.6)	0 (0.0)	11 (8.9)	1 (0.8)	3 (2.4)	16 (12.9)	4 (3.2)	0 (0.0)	0 (0.0)	1 (0.8)
CBZ	9 (14.5)	0 (0.0)	1 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (6.2)	4 (6.2)	0 (0.0)
TPM	25 (45.5)	4 (6.7)	5 (8.3)	2 (3.3)	10 (16.7)	3 (5.0)	3 (5.0)	0 (0.0)	0 (0.0)	3 (5.0)

In the case of patients with neurological diseases, depression diagnosis without solid and reliable tools could be complicated for several reasons. Firstly, diagnosing depression heavily relies on clinical evaluation and self-reported symptoms. Thus, it can be subjective and inconsistent, plus the specialist may not be able to adequately understand the nuances of depression. Second reason is, side effects of medications in patients with neurological decease includes similar side effects with depression like Behavioural disorder. Therefore, the neurologist or even psychiatrist may not be able to decide certainly whether the patient has depression or not. On the top of all these reasons, since depression diagnosis needs the patients notice the symptoms by themselves, the self-report may not happen by the patient by itself unless a specialist notices them. Some patients do not consider some symptoms as signs of serious depression, some avoids to talk about that due to cultural or social reasons, and others avoid reporting symptoms because they suffer from persistent sadness and lack of motivation, which are symptoms of depression. Based on all these reasons, conventional depression diagnosis approaches are not reliable and sufficient.

To sum up, patients with neurological deceases are more susceptible to depression as it is common as a side effect in the most of the medications they use. Besides, depression is a noticeable psychological disorder in the world and it can directly affect the results of the treatment in patients with neurological disorders. Plus, the clinical diagnosis and self-reported symptoms are not adequate in depression diagnosis in these patients. Therefore, a game theory and ML approach can provide a practical depression diagnosis using EEG features to be used in clinical environments.

1.1 Statement of the Problem

After reviewing the reason behind the insufficiency of subjective methods in diagnosing depression, it is obvious that they have limitations when applied to patients with neurological disorders, leading to underdiagnosis or misdiagnosis (Santos et al., 2021). In addition, self-reporting accuracy can be complicated due to patients' cognitive impairments. Hence, benefiting a practical and real-time depression diagnosis method using EEG features, ML and game theory is crucial (Figure 3).

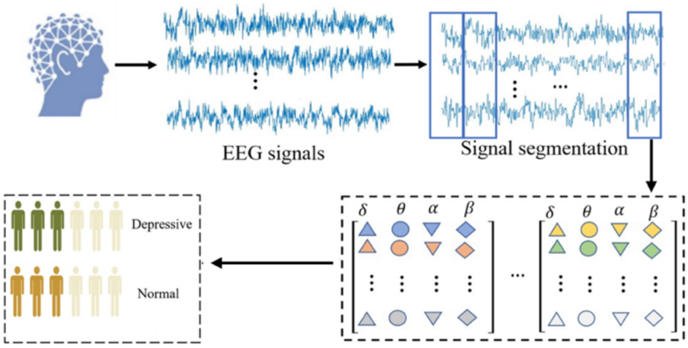

Figure 3. The process of EEG signal classification and identification of depressive patterns through frequency domain characteristics (Yang et al, 2023).

In spite of subjective assessments, EEG features provide a non-invasive, real-time, and objective approach for depression diagnosis which have the potential of being practical in complex neurological profiles. Through these features the biomarkers associated with depression can be identified through abnormalities in brain wave patterns (Dev et al., 2022) and if depression is diagnosed, parallel treatments can be considered to control depression.

In this process, it is important to simplify the resources needed by reducing their amount without losing vital information, because there are many features in an EEG recording. This simplification includes two parts. First by FEX and then by the dimensionality reduction techniques such as PCA and t-SNE in which PCA reduces the dimensions and t-SNE visualizes them (Anuragi et al, 2024). This integration can increase the accuracy of identifying depression-related biomarkers in EEG features (Hao et al., 2024), making it more reliable than traditional and subjective ones. Eventually, using the simplified data for training the machine can improve the accuracy, and game theory provides some theoretical tips to improve the model efficiency.

1.2 Purpose Of The Study

diagnostic accuracy and timely diagnosis of depression in patients with neurological disorders through the use of EEG technology. The primary goals of this research are as follows:

1. To Develop a Diagnostic Model based on EEG Features: The main objective is to develop a robust model that diagnose depression in patients with neurological disorders utilizing EEG features. In this regard, it is also important that research has shown PCA is effective in identifying patterns in EEG data for distinguishing patients with epilepsy who have depression or anxiety disorders (Zhang et al, 2022). Furthermore, t-SNE has been also used to analyse mental illness patterns through EEG data, which demonstrates its capability to identify depressive states (Bhat & S R R, 2024). Therefore, this study focuses on identifying and analysing specific EEG patterns using PCA and t-SNE plus deep learning and game theory to reach this goal.
2. To Validate EEG Biomarkers Related to Depression: Another objective is to test and validate the identified EEG features correlating with depression. In the following, the model can reliably differentiate between individuals with and without depression (Pinotsis et al., 2022). Thus, if the chosen biomarkers are reliable, the EEG's utility as a diagnostic tool in clinical settings can be substantiated.
3. To Integrate EEG Data and Features with the Clinical Practice: Finally, the most significant part is to provide a practical tool for real world situation that can be easily adopted by healthcare professionals with a user-friendly format. Although implementing an EEG-based depression diagnostics needs development of guideline or protocols (Lang et al., 2023), this project hopes to be a step forward to having this technology in a clinical environment

It is expected for this project to provide several significant outcomes related to the fields of neurology and psychiatry, including:

1. Validation of EEG Features: This study aims to predict the validity of certain EEG features that are reliable indicators in diagnosing depression. According to the recent studies, EEG biomarkers are effective and reliable in diagnosing major depressive disorder (Khan et al., 2022). Besides, SHAP explanation can provide the most considerable features among them which might be vary from the features that a specialist considers in diagnosing depression.

2. Development of Predictive Models: The final model in this project can be a window for further developments and optimizations in the future, and other studies have been conducted with the same goal as distinguishing between depressed and non-depressed states in patients with neurological disorders (Khosla et al., 2022). Therefore, each related study can add a new feature to this project in order to make it more accurate, reliable and practical.
3. Enhancement of Clinical Diagnostics: There are patients who have difficulty expressing their mental health status due to neurological disorders (Chu, 2022). Thus, depression diagnosis needs to be objective and EEG features give a reliable chance to revolutionize the clinical diagnostics from subjective to objective.
4. Improved Patient Outcomes: This is a continuation of the previous ones. The successful integration of EEG-based diagnostics, supported ML and DL techniques, is expected to enhance treatment outcomes, leading to have a personalized treatment plan to address both neurological and psychiatric conditions in patients, more effectively.

Based on the mentioned items, the aim is to develop a diagnostic model to validate the depression-related biomarkers in EEG features that is capable of being used is clinical environments. This project could be a step forward for further developments leading to a clear treatment plan that may be personalized for each patient with neurological disorder.

1.3 Research Questions

When it comes to innovating a new solution in different research fields, it always has been questions to find the missing parts of it. In this thesis which is demonstrates the usage of EEG features in diagnosing depression in neurological conditions, there are several key research questions to be addressed, such as:

- In case of patients with neurological disorders, which EEG features can be reliably associated with depressive states?

- How effective is the model in distinguishing between depressive and non-depressive states comparing to traditional methods?
- Is a predictive EEG-based model capable of being developed to accurately diagnose depression in this patient population?
- What are the clinical implications of using this model as a tool into clinical practice for the treatment and management of depression in these patients?

The purpose of these questions is to bridge the gap between clinical practices and effective depression management to offer a significant contribution for both academic research and clinical methodologies.

1.4 Significance of the Study

The significance of this research goes beyond a thesis. This potential lies in changing clinical practices and improving diagnostic protocols for depression in patients with neurological disorders. A study has shown that validating EEG as a tool for developing a depression diagnosis model, could lead to a more objective, accurate, and rapid diagnostic tool in field of depression for this patient population (Avots et al., 2022), compare to current approaches like self-reported symptoms and behavioural assessments which are more subjective and might be different in each individual and duration of time. A diagnostic model facilitates clinicians to make more informed decisions in clinical settings based on real-time and reliable EEG features (Niso et al., 2023), leading to more personalized treatment plans, improving the management of depression is neurological conditions, and improve patients' satisfaction about the treatment approach.

For this patient population, especially those undergoing complex medical conditions and treatments, the benefits of an improved diagnostic process are many. This pressure can also be associated with side effects of medications which cause a complicated physical and mental situation. Moreover, all these pressures may stem from depression which can target both physical and mental well-being in patients with brain neurological conditions. If this depression is not treated in time, it may become more severe over time. Therefore, Accurate and timely diagnosis of depression is very important, because it can lead to earlier and more targeted interventions, prevent the deterioration of mental health, and thus manage the complexity of the patient's underlying neurological *conditions (*Alejos et al., 2023*)*.

Moreover, the nature of EEG is non-invasive which makes it patient-friendly and can be easily administered. Thus, it is less stress and discomfort than other diagnostic methods. Therefore, the result of this thesis can lead to increasing the accuracy and speed of diagnosis of depression and significantly improve the quality of life of patients, their overall health outcomes and their ability to maintain a normal daily routine.

1.5 Limitations

In this project, an attempt has been made to improve the treatment process in patients by diagnosing depression. However, there are limitations that should be considered when interpreting the findings. First, only using EEG data to diagnose depression may not capture all the detailed psychological aspects of depression, because EEG data only measures the electrical activity of the brain and may ignore other biological or environmental factors influencing this disorder. Second, the sample size and diversity in the data used may limit the findings. Therefore, to confirm the application of EEG-based diagnostic model, studies including larger and more diverse population groups are necessary. In addition, EEG technology itself has limitations, including sensitivity to external noise and the need for specialized equipment and experts, which may pose challenges for widespread clinical adoption.

1.6 Definitions

Throughout this thesis, various key terms have been used, and to clarify them, the following definitions are provided:

- EEG: A non-invasive method to monitor the electrical activity of the brain in neurological patients, using electrodes that are placed along the scalp.

- Depression: A common and serious mental disorder that negatively affects how a person feels, thinks, and acts, and is characterized by persistent sadness and lack of interest.
- Neurological Disorders: A variety of medical conditions that affect the nervous system, including the brain, such as epilepsy and Parkinson's.
- Biomarkers: Biological criteria that show the biological traces of diseases and are often used in clinical studies to link the presence or risk of diseases with physiological indicators.
- PCA: A statistical technique to reduce the dimensionality of data while preserving their diversity as much as possible. Transforms the data into a new coordinate system with the highest variance.
- t-SNE: A ML algorithm used for dimensionality reduction and visualization of high-dimensional datasets in a low-dimensional space.
- CNN: A DL network architecture that learns directly from data and is useful for finding patterns in data for categorization and classification.
- SHAP: A way to explain the contribution of features in a ML/DL model decision-making.
- Game Theory: A mathematical tool for analysing situations which provides an objective and interdependent decision-making.

In conclusion, this thesis is structured to explore the use of EEG as a diagnostic tool for depression in patients with neurological disorders. Chapter 1 introduces the foundational background, significance, and research objectives. Chapter 2 reviews existing research on EEG and depression diagnosis, identifying current gaps. Chapter 3 details the research design, data collection, and analysis methods. Chapter 4 presents the core findings from the EEG data analysis, highlighting specific biomarkers of depression. Chapter 5 provides detailed statistical and computational analysis to support the findings. Chapter 6 discusses the results, their clinical implications, and assesses the validity of EEG as a diagnostic tool. Finally, Chapter 7 summarizes key findings, revisits research aims, discusses study limitations, and suggests future research directions.

Chapter 2

Literature Review

Patients with neurological disorders have to use medications for the long term. Since these medications directly affect the brain, their side effects will negatively impact the brain. Depression is one of the common side effects that can also be triggered by mental stress during the treatment approach. Therefore, early diagnosis of depression can ease the treatment process and prevent similar drug side effects and drug resistance. In this project, several materials and techniques were used in two aspects technical and theoretical. The technical part includes analyzing EEG data using ML and DL techniques such as PCA, t-SNE, CNN, and SHAP. The theoretical part consists of using a game model to show how interaction between brain regions can improve EEG efficiency. This review will cover understanding the concept of terms and technologies that were used in the project along with the current gaps.

2.1 Depression and Neurological Disorders

2.1.1 Overview of depression. Depression is a mental health condition that progresses and leaves a person withdrawn and isolated, resulting in persistent sadness, loss of interest in activities, and a wide range of additional cognitive and physical symptoms (den Brave et al., 2023). This disorder is very persuasive that affects millions of people in the world and it is associated with some symptoms such as fatigue, changes in appetite, sleep disorder, feelings of guilt or worthlessness, and difficult concentration. Thus, WHO identifies depression as a major reason for disability which has negative impact on both individuals and healthcare systems, making it considerable in patients with any physical condition.

2.1.2 Depression and neurological disorders. This patient population with neurological conditions are particularly vulnerable to depression due to the treatment pressure, physical condition, social or cultural image, and most importantly medications and their side effects. For instance, patients with epileptic seizures have to use AEDs to control them and using these medications for long-term can have adverse side effects (Chu et al., 2023). This is noticeable as depression is the most concerning ADR that can aggravate the physical condition and have a negative effect on the process and outcome of the treatment (Chu et al., 2023). Also, the frequency of seizures can considerably be varied with different emotional states (see Figure 4).

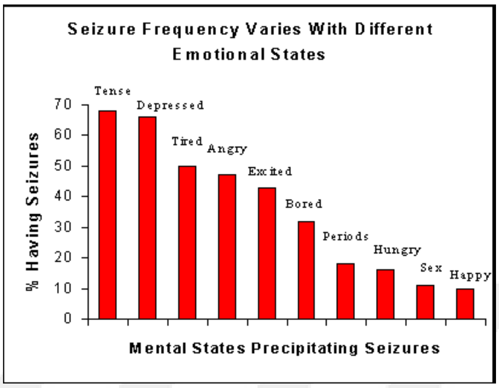

Figure 4. Seizure frequency varies with emotional states, and how different mental states trigger seizures in epilepsy (Canadian Epilepsy Alliance, 2024).

2.1.3 Bidirectional relationship. There is a bidirectional relationship between depression and neurological disorders (Lv et al., 2023). Depression can aggravate the symptoms of neurological diseases, while this exacerbation of the condition in patients leads to stress and disability, which can contribute to the onset or worsening of depression. (Munger Clary, 2023). This cycle that called bidirectional relationship complicates the clinical management of both conditions and highlights the need for effective diagnostic and therapeutic strategies alongside neurotherapeutic strategies.

2.1.4 EEG in neurological diagnosis. Normally patients with neurological conditions are being monitored by EEG time to time. Typically, effective management of their condition involves a combination of medication and lifestyle adjustments alongside the regular monitoring of brain activity through EEG tests, specifically in patients with epilepsy (Alvi et al, 2022). EEG captures real-time data on brain wave patterns which can be a reliable tool to help clinicians to adjust treatment plans based on patient conditions. EEG is non-invasive tool that uses electrodes placed on the scalp to record electrical activity of the brain and measure voltage fluctuations stem from ionic current flows within the neurons. It has high temporal resolution and ability to capture dynamic changes in brain that makes it perfect in clinical and research settings (Praveena et al., 2020).

Table 2

Common Neurological Disorders Diagnosed with EEG (Matoth et al., 2002)

Neurological Disorder	Brief Description	EEG Application
Epilepsy	A chronic disorder diagnosed by recurrent, unprovoked seizures.	To show epileptiform discharges, spike-and-wave patterns, and focal slowing.
Sleep Disorders	Affects sleep patterns, including insomnia, sleep apnoea, and narcolepsy.	To show disruptions in sleep, such as decreased REM sleep and abnormal sleep spindles.
Encephalopathies	Affects brain function, often due to metabolic, infectious, or toxic causes.	To show diffuse slowing, triphasic waves, and periodic lateralized epileptiform discharges (PLEDs).

EEG is particularly reliable in diagnosing and monitoring neurological disorders such as epilepsy, sleep disorders, and encephalopathies (Table 2). EEG in epilepsy detects abnormal brain wave patterns associated with seizures and helps in the diagnosis and classifying seizure types. Plus, the continuous usage of EEG allows clinicians to observe the frequency, duration, and distribution of seizures to have an effective management and treatment planning (Tatum et al., 2022).

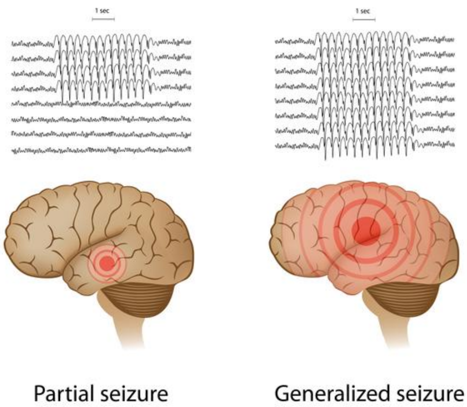

Figure 5. EEG waveform in partial and generalized seizures (Colucci 2019).

Moreover, the application of EEG extends beyond the epilepsy. It is used in assessing cognitive function, monitoring brain activity during surgical procedures, and evaluating patients in the intensive care unit. The versatility and efficiency of EEG make it an indispensable tool in neurology, providing insights into brain function and helping to diagnose a wide range of neurological diseases (Pani et al, 2022).

2.1.5 EEG in depression diagnosis. EEG is not only being used in diagnosing and monitoring neurological conditions, but mental and psychological disorders like depression. The integration of EEG in the diagnosis of depression in these patients is less proven, however, considering the impact of depression on the general health and quality of life of these patients, there is an urgent need to investigate the potential of EEG as a diagnostic tool for depression (Bashiri & Mokhtarpour, 2022). This finding is particularly relevant in the context of advanced data analysis techniques such as PCA and t-SNE, which can reveal subtle patterns in EEG data that may indicate depressive states (Bashiri & Mokhtarpour, 2022).

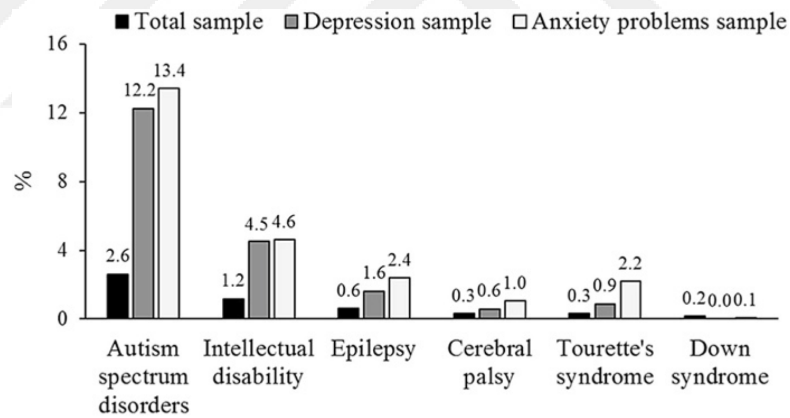

Figure 6. Prevalence of neurologic disorders among children and adolescents with depression and anxiety (Whitney et al., 2019).

Based on Figure 6, the importance of diagnosing depression is obvious as depression can outbreak or even worsen neurological conditions. Therefore, if an advance data analysis technique identifies the depression-related biomarkers through EEG, it can lead to a more targeted treatment plan because it enhances the accuracy and reliability of depression diagnosis (Baghdadi et al., 2021). Thus, in spite of traditional diagnostic methods which are subjective, EEG can offer an objective way to detect abnormal brain wave pattern which may indicate depressive states (Bai et al., 2021).

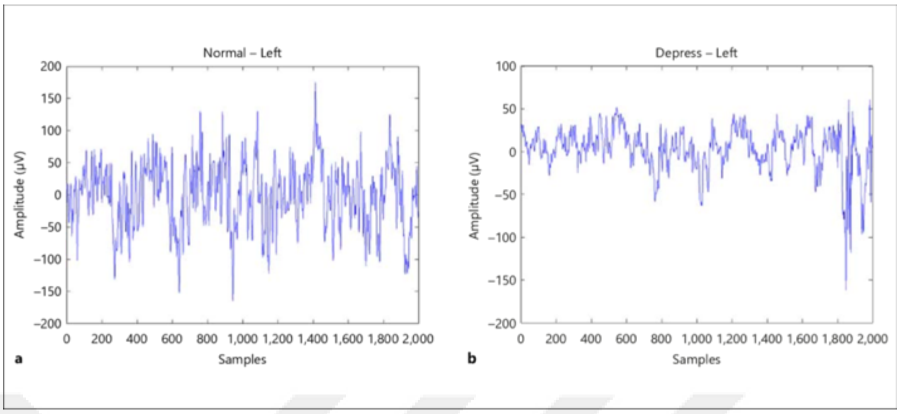

Figure 7. EEG signals from the left-brain hemisphere that shows differences between normal (left) and depressed (right) states (Acharya et al., 2015).

EEG can detect changes in brain wave frequencies such as delta, theta, alpha, beta and gamma waves and there are certain brain wave patterns that are associated with depressive disorders. As proof, increased theta activity and decreased alpha activity, especially in the frontal regions of the brain, have been linked to depression (Sharma et al., 2021; Baghdadi et al., 2021). Hence, these patterns can provide important insights into the underlying neural mechanisms of depression and enable early and accurate diagnosis which makes EEG important for this patient population. So, EEG offers a way to distinguish between neurological and psychiatric symptoms that provides a more comprehensive understanding of the patient's condition compare to traditional methods (Sharma et al., 2021).

In traditional psychiatric methods, only five of features in EEG data are recognized as depression-related biomarkers such as FFT Theta Max Power, Wavelet Detailed Entropy, Mobility, Complexity, and Delta/Alpha Ratio and each of them represent an abnormality in specific region of brain. Figure 8 illustrates that depression usually involves the Frontal region of the brain and in order it proceed to Temporal lobe, Limbic System, Partial lobe, and Occipital lobe.

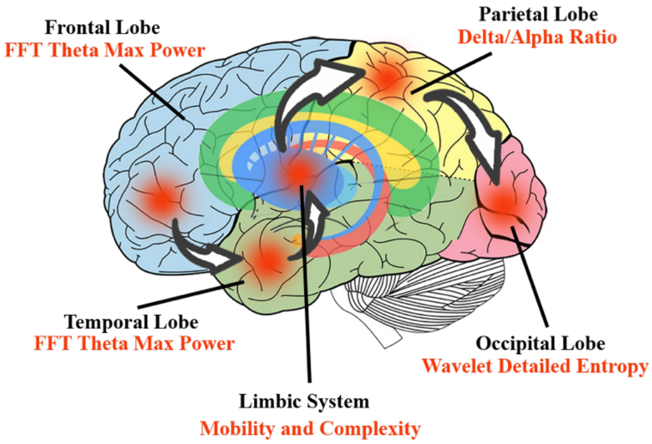

Figure 8. The order of involvement of different brain regions in different stages of depression.

In summary, patients with neurological disorders are more prone to depression and the relationship between depression and neurological deceases is bidirectional. In addition, EEG is a non-intensive tool that can be used for monitoring and diagnosing both neurological disorders and depression, making it considerable to find its potential in order to diagnosis depression is this patient population. Therefore, advanced data analysis ML/DL techniques can help to find the potential of EEG for depression diagnosis.

2.2 Neurological Disorders, Medications and Depression

2.2.1 Side effects associated with medications. As it was mentioned in previous parts, medication treatment is an inseparable part of life in patients with neurological deceases. As an example, patients with epilepsy use AEDs in their daily life to reduce the frequency and intensity of their seizures, while the same medications come with some side effects include both physical and mental one (Bochanova & Gusev, 2024). The severity of these ADRs depends on factors such as dosage, duration of treatment, patient characteristics and the medication by itself, nevertheless, managing these ADRs is a important part of the treatment (Ahmad Mir et al, 2023), minimizing ADRs while maximizing therapeutic benefits.

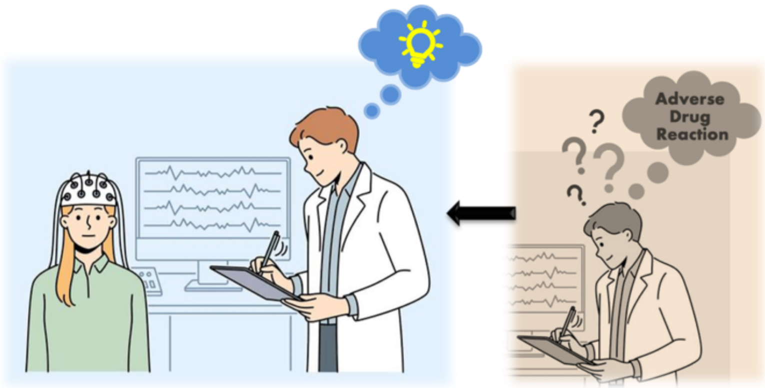

Figure 9. The role of EEG in managing adverse drug reactions (ADRs) and depression in epilepsy patients.

2.2.2 Importance of depression as an ADR. Since depression has the bidirectional relationship with neurological disorders, it is not only reducing patient quality of life but also complicates the treatment approach (Minwuyelet et al., 2022). Because, the bidirectional relationship creates a vicious cycle Which in turn can lead to heightened feelings of hopelessness and despair (Mula et al, 2021). On the other hand, some AEDs have a higher risk of inducing depressive symptoms, either through direct drug effects or by exacerbating existing vulnerabilities due to disease conditions (Panholzer et al., 2024). As proof, the balance of neurotransmitters in the brain may be altered, leading to excessive mood disorders. Additionally, other factors can trigger the development or exacerbation of depression, including the nature of the disease and psychosocial stressors associated with living with a neurological disorder (Panholzer et al., 2024). Therefore, the use of advanced and objective analytical methods leads to accurate diagnosis of depression and improvement of treatment results. (Wei et al., 2023).

2.3 ML and DL Techniques in EEG Analysis

ML techniques have revolutionized the analysis of EEG data as they extract and identify the meaningful patterns and features from complex datasets (Rossini et al, 2022). They have mathematical algorithms that learn from data by identifying the hidden structures and relationships that might not be noticeable through traditional methods (Rahman et al., 2022). In case of EEG analysis, ML methods are well known for classifying brain states, detecting anomalies, and predicting clinical outcomes. There are different types of algorithms, some are called supervised that use the labelled data, some are called unsupervised that use the unlabelled data and the others are called semi-supervised that are a combination of the previous two. Among all these ML techniques applied to EEG data analysis, PCA and t-SNE stand out due to their ability to reduce data dimensionality and visualize complex datasets (Alalayah et al., 2023), which can be strengthened by using FEX at first and the training the model with CNN as a DL technique at last. In addition, a SHAP explanation can provide the most effective features that have led to the model's current accuracy and confidence level.

2.5.1 FEX for extracting the features. The use of FEX is critical in EEG data analysis, as it transforms raw EEG signals into meaningful representations that can be useful for models. This section explains the FEX techniques that was used in the EEG signals to prepare data for the diagnostic model:

- Wavelet Features: This process involves using wavelet transforms to decompose a signal into different frequency components, and captures both spatial and frequency information, providing the possibility of extracting features that show the details of the signal at different scales and locations. This process is useful in pattern recognition and signal analysis like EEG data because they provide a detailed and localized representation.
- Power Spectral Density (PSD) Features: PSD analysis represents the power distribution of the EEG signal across different frequency bands, and identifies the dominant frequencies and the energy associated with them. PSD This is especially useful in EEG analysis for characterizing the frequency content of signals. For example, it represents the energy in specific frequency ranges such as delta (0-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-50 Hz), which makes it perfect in finding the significant biomarkers in EEG features.
- Short-Time Fourier Transform (STFT) Features: The STFT provides a time-frequency representation of the EEG signals by applying the Fourier transform to small, overlapping segments of each signal. This approach helps

to identify non-stationary patterns that are characteristic of EEG data by showing how the frequency content of the signal changes over time.

- Statistical Features: This process calculates the various statistical measures from data, including mean, standard deviation, skewness, and kurtosis of the EEG signals which summarizes the distribution, spread, and shape of the data to capture essential characteristics of the EEG patterns.

For instance, Figure 10 illustrates the EEG signal before and after STFT. The top graph represents the raw EEG signal, showing its change over time. The middle graph represents the spectrogram of the EEG signal and its change over time in which the colour intensity indicates the power at different frequencies in Hertz. Eventually, the bottom graph highlights the special features and noise reductio, focusing on certain frequency bands. This visualization is a sample to demonstrate the transformation of raw data into a simplified or more interpretable form using FEX

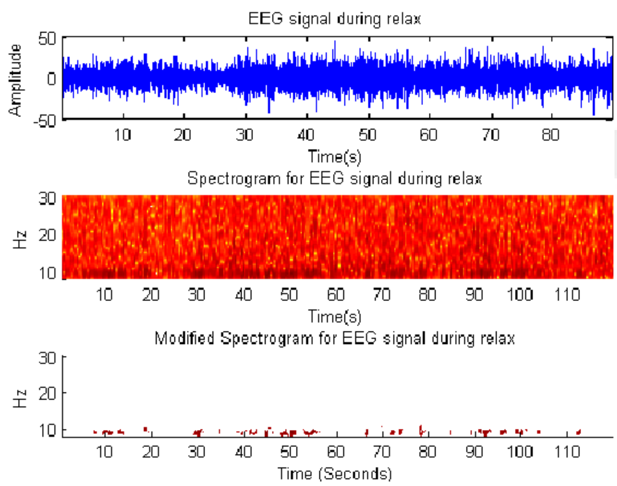

Figure 10. EEG signal before and after STFT (Zabidi et al, 2012).

Since wavelet, PSD, STFT, and statistical features provides a comprehensive representation of EEG data, a combination of them captures both time-varying and frequency-specific characteristics. This approach facilitates effective classification and diagnosis, making it powerful through PCA. Also, this process makes the PCA process easier to compress high-dimensional datasets so that PCA preserves significant information and reduces noise.

2.5.2 PCA and its applications. PCA as a powerful statistical technique is used for dimensionality reduction, data compression, and FEX. It captures the most significant variance in the dataset by transforming the high-dimensional data into a lower-dimensional space by identifying the principal components. Generally, EEG data are complicated as they consist of multiple channels and time points. Therefore, PCA helps to condense the data into a smaller set by preserving the more critical features and facilitates subsequent analysis and interpretation (Boonyakitanont et al., 2020). PCA can improve the performance and efficiency of classification algorithms and it has been applied to identify patterns in different cognitive states, such as attention, relaxation, and stress (Zubair et al., 2021). In addition, PCA has been used to detect seizure-related activity by highlighting the most epileptic features in EEG (Guerrero et al., 2021). So, the significance of PCA is proven in identifying the related biomarkers in both neurological and psychological conditions.

2.5.3 t-SNE and its application. t-SNE in another hand is an advanced ML technique used for data visualization. In term of dimensionality reduction, despite of PCA, which focuses on linear transformations, t-SNE is designed to find non-linear relationships in the data and it is effective for visualizing high-dimensional datasets in a lower-dimensional space (Svantesson et al., 2023). t-SNE models each high-dimensional object as a point in a two or three-dimensional space, and places similar objects close together while maps dissimilar objects further apart.

However, in EEG analysis, t-SNE is used to visualize complex brain activity patterns and makes it easy to identify distinct states or conditions. As proof, researchers have used t-SNE to distinguish various mental states, such as sleep stages, cognitive load levels, and emotional responses (Salim & Tiwari, 2023). Plus, in another research, t-SNE helps to visualize the transition between normal brain activity and seizure events (Yıldız et al., 2022), and it can also reveal clusters of brain activity associated with depressive and non-depressive states (Wang et al., 2021). Thus, these workings indicate the applications of t-SNE in both neurological and psychological disorders.

2.5.4 Combining PCA and t-SNE for EEG analysis. The combination of t-SNE and PCA, can significantly improve the accuracy and interpretability of a diagnostic model using EEG (Rahman et al., 2020), offering a robust approach for both dimensionality reduction and visualization. PCA reduces the dataset's dimensions, while t-SNE preserves local structures by mapping the data into a lower dimensional space. This combination comes with strengths, such as:

- Enhanced Visualization: This dual reduction approach provides the identification of distinct patterns and clusters that may be difficult to discern with traditional methods (Thakur et al, 2021).
- Improved FEX: This combination helps preserve the most relevant biomarkers while reducing noise, leading to more accurate and interpretable results (Thakur et al, 2021).
- Better Classification: This integration has shown the better classification of different brain states, such as depression, seizure activity, and other different cognitive and emotional states, making it capable to develop a reliable diagnostic model (Gajic et al, 2014).
- Complementary Strengths: PCA and t-SNE complement the limitations of one technique with the strengths of another. PCA simplifies data by linear reduction, while t-SNE finds non-linear relationships (Sánchez-Rico et al., 2023).

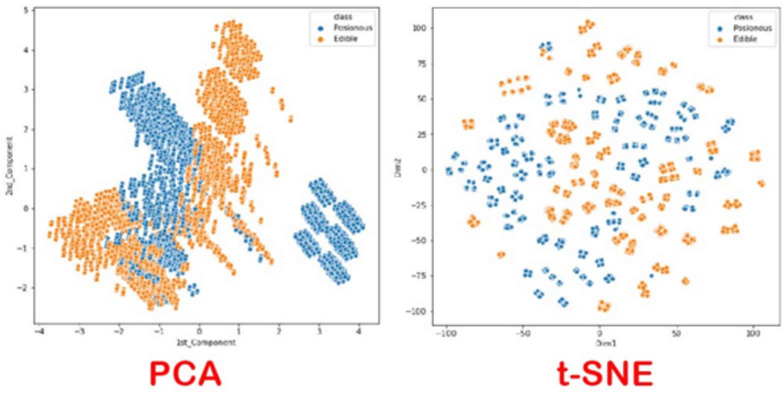

Figure 11. Comparison of PCA output alone and after combining with t-SNE

Despite of these advantages, combining PCA and t-SNE for EEG analysis presents some challenges:

- Computational Complexity: This integration can be computationally intensive, specifically with large EEG datasets. Because, PCA requires high computational resources to process high-dimensional data, and non-linear mapping in t-SNE is complex and time-consuming (Hamid et al, 2020).
- Parameter Tuning: Parameters in both PCA and t-SNE need to be tuned carefully to achieve optimal results which can be challenging (Gajic, 2014). PCA has the number of principal components, while t-SNE's performance depends on perplexity and learning rate.
- Data Preprocessing: EEG data often require significant preprocessing before applying PCA and t-SNE to ensure the quality and consistency of the data, such as artifact removal, filtering, and normalization (Gajic et al, 2014).
- Interpretability: Although this combination improves visualization and classification, can make it challenging to interpret and understand the result and relationships between the features in low-dimensional. So, work with the brain activity requires careful analysis (Sánchez-Rico et al., 2023).

To sum up, combining PCA and t-SNE for EEG analysis offers valuable advantages about visualization, FEX, and classification accuracy. However, its challenges should also be considered in promise an accurate diagnosis, such as complex computation, tuning the parameters, data preprocessing, and interpretability.

2.5.5 CNN as a DL algorithm. CNN is a well-known DL algorithm and considered a powerful tool in the analysis of EEG data, particularly in term of diagnosing neurological and psychiatric disorders. After applying FEX, PCA and t-SNE, the efficiency of employing CNNs can be improved, leading to identify complex temporal and spatial patterns, and eventually detect the subtle biomarkers within EEG signals. Even in recent researches CNNs were successful in recognizing temporal-spatial patterns associated with psychiatric disorders and have helped to classify emotional distress and other mental health disorders (Shah et al., 2023). The use of CNNs is not limited to food psychiatric conditions. As proof, CNNs have shown their potential in seizure detection after integration with FEX algorithms, they have provided improved accuracy in epileptic seizure detection (Pouryosef et al., 2024). In another similar case related to neurology, CNNs were capable of analysing EEG-based biomarkers in early diagnosis of Alzheimer's disease (Modir et al., 2023). These workings prove the application and capability of CNNs in improving diagnostic processes for both field of neurology and psychiatry.

2.5.6 SHAP and explainable AI. Recently, SHAP has become an essential tool in EEG analysis, specifically in interpreting ML models that used for diagnosing neurological disorders. SHAP is a method that displays the ratio of the influence of each feature in the output of the model, which makes the decision-making process of complex models more transparent. Hence, it can be a valuable tool to analyze EEG signals, where the patterns are subtle and complex.

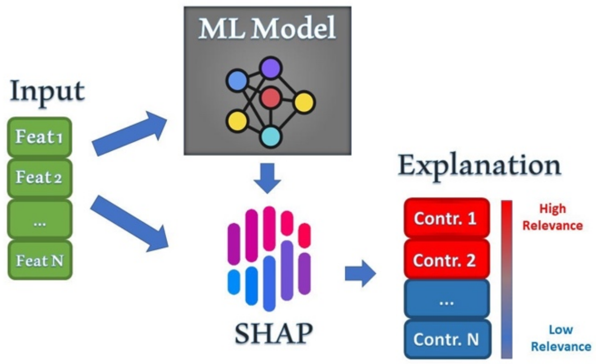

Figure 12. SHAP explanation about the most and least important features

For example, in a research case, SHAP resulted in increased sensitivity of EEG signals in event-related potential analysis, enabling more precise changes to be identified for understanding critical cognitive processes (Sylvester et al., 2024). Moreover, SHAP has been used to investigate the reproducibility of EEG biomarkers in schizophrenia between different ML models and has provided a robust framework for reliable diagnosis (Ellis et al., 2022). In another case related to mental health, SHAP was used to detect depression-related biomarkers to understand the role of anhedonia, or lack of pleasure, which helped to understand depression-related brain patterns by analysing brain images and data (Wang et al., 2024). These applications can prove the power of SHAP to improve the accuracy of EEG-based diagnostics in neurobiological conditions and various mental health disorders.

2.4 Game Theory

Game theory has been widely used to increase the understanding and management of neurological disorders through EEG analysis. This method is usually used to model strategic interactions between different factors and in a structured framework, which can be useful in optimizing treatment strategies and analysing cognitive patterns. For instance, in a study related to managing juvenile myoclonic epilepsy, an equilibrium strategy has been provided in order to reduce the side effects associated with the medications, proving the capability of game theory in decision-making related to clinical settings (Hamidoğlu et al., 2024). In another study, researchers used game theory in the analysis of EEG patterns to classify them and provide insights into the underlying neural mechanisms (Zuckerman et al., 2022). Moreover, the integration of game theory with multimodal neuroimaging has been shown to significantly improve EEG-based analyses (Esposito, Tamburis, & Choi, 2020). Based on all these workings, game theory is capable in addressing complex challenges in neurological research and diagnostics.

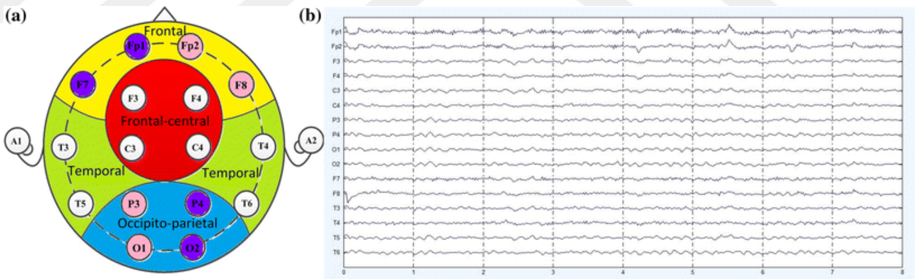

Figure 13. The aspect of game theory that considers brain regions as players in a game (Deng et al, 2017)

For better understanding, Figure 13 shows how EEG captures the brain's strategic interactions. In the left side, there is a map of electrodes placed on the scalp that each of them linked to specific brain regions as players in a game. The right side represents the EEG signals that are generated by these regions to the dynamic "moves" of each brain area per time. These interactions are a proven sample in game theory to understand cooperation and competition between different parts of the brain during cognitive tasks.

2.5 Current Gaps and Future Directions

2.5.1 Identification of gaps in the current literature. Although EEG has made significant progress in diagnosing depression in patients with neurological conditions, there are several gaps remain in this literature. A major gap is that there is still a complete lack of understanding of how specific EEG biomarkers relate to different types of depression and its severity (Fernández-Palleiro et al., 2023). Although various studies have identified general patterns associated with depression, the nuances that distinguish depression in mild, moderate, and severe stages are still unknown. Another gap is that a single method has not been used in different studies, and the diversity in EEG recording methods, data preprocessing, and FEX makes it difficult to compare results and draw definitive conclusions (Gajic et al., 2014), which can be solved by standardizing these methodologies. Additionally, there is a lack of diverse and large-scale datasets that do not cover a wide range of demographic and disease conditions. In most studies, relatively small samples and homogeneous populations have been used, which limits the generalization of the findings (Hasan & Tatum, 2021). Therefore, to utilize this project in clinical practices, these gap should be addressed.

2.5.2 Future research directions in eeg-based depression diagnosis. To address these gaps, future research related to depression diagnosis using EEG analysis should focus on several key areas:

1. Exploration of Subtype-Specific Biomarkers: How EEG biomarkers change across different types and severity of depression should be explored to help identify unique patterns associated with specific depressive states (Zhu et al., 2020).
2. Standardization of Methodologies: Instead of different methods, standard protocols for EEG recording, preprocessing and analysis should be used to improve the comparability and reproducibility of research findings (Pani et al., 2022).
3. Large-Scale, Diverse Datasets: To increase the generalizability of EEG-based diagnostic models, it is better to use a larger and more diverse dataset that includes information from patients from different fields (Zhu et al., 2020).

4. Longitudinal and Real-World Studies: Studies should monitor EEG changes over time using real data and confirm findings in clinical settings to more accurately identify EEG biomarkers associated with depression (Ruijter et al., 2022).
5. Integration with Other Modalities: A more comprehensive understanding of depression can be provided by integrating EEG and other methods, such as neuroimaging, genetics, and clinical assessments, as these multifaceted approaches can increase the accuracy and depth of depression diagnosis (Zhu et al., 2020).
6. Advancements in ML: Due to the continuous progress in ML algorithms and their application, it is possible to investigate complex patterns in EEG data by combining or comparing the potential of new techniques. (Zhu et al., 2020).

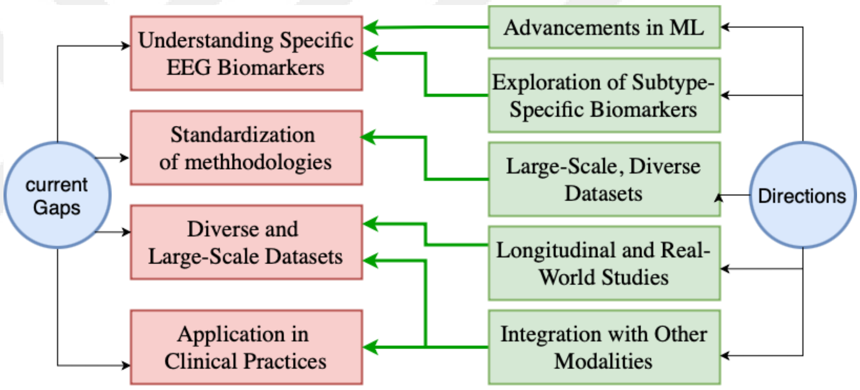

Figure 14. Current research gaps and directions

2.6 Conclusion

This literature review has covered the critical aspects of diagnosing depression using EEG in patients with neurological deceases. It started with ADRs associated with medications, the importance of depression and its bidirectional relationship with neurological disorders. Then, it highlighted the role of EEG in neurology and its application in detecting depression. Next, this literature mentioned about the usage of ML and DL techniques such as FEX, PCA, t-SNE, CNN, and SHAP in EEG analysis to simplify the complex EEG signals, train the model and interparent the model using explainable AI. The review continued with the role of game theory in providing strategies to address complex challenges in field of neurology and mental health. Eventually, this chapter identified major gaps in the current studies and represented future directions to enhance the reliability and applicability of EEG-based depression diagnostics.

Table 3

Comparison of Research Contributions

Authors	Depression Diagnosis	Neurological Disorders	Utilizing EEG	EEG Data Preprocessing	Identified Biomarkers	PCA Technique	t-SNE Technique	Utilizing PCA and t-SNE	CNN	SHAP	Game theory
Yasin et al. (2021)	✓	✗	✓	✗	✓	✗	✗	✗	✓	✗	✗
Hamidoğlu, A., et al. (2024)	✗	✓	✓	✓	✓	✗	✗	✗	✗	✗	✓
Delgado-García et al. (2023)	✓	✓	✓	✗	✓	✗	✗	✗	✗	✓	✗
Deshpande et al. (2022)	✓	✗	✓	✗	✓	✗	✗	✗	✗	✗	✗
Yu et al. (2022)	✗	✓	✓	✗	✗	✓	✓	✓	✓	✗	✗
Xiong et al. (2020)	✗	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗
Wu et al. (2021)	✓	✗	✓	✓	✓	✓	✓	✓	✗	✗	✗
Sadek et al. (2023)	✗	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗
Shah, S. J. H., et al. (2023)	✓	✓	✓	✓	✓	✗	✗	✗	✓	✗	✗
Modir, A., et al. (2023)	✗	✓	✓	✓	✓	✓	✗	✗	✗	✗	✗
Pouryosef, M., et al. (2024)	✗	✓	✓	✓	✓	✗	✗	✗	✗	✗	✗
Sylvester, S., et al. (2024)	✗	✗	✓	✗	✗	✗	✗	✗	✗	✓	✗
Ellis, C. A., et al. (2022)	✗	✓	✓	✓	✓	✗	✗	✗	✗	✓	✗
Wang, W., et al. (2024)	✓	✗	✓	✓	✓	✗	✗	✗	✗	✗	✗
Esposito, C., et al. (2020)	✗	✓	✓	✓	✓	✗	✗	✗	✗	✗	✓
Zuckerman, I., et al. (2022)	✗	✗	✓	✓	✓	✗	✗	✗	✗	✗	✓
Qiao Yuanhua et al. (2020)	✓	✗	✓	✗	✓	✗	✗	✗	✓	✗	✗

Table 3 (cont.d)

Authors	Depression Diagnosis	Neurological Disorders	Utilizing EEG	EEG Data Preprocessing	Identified Biomarkers	PCA Technique	t-SNE Technique	Utilizing PCA and t-SNE	CNN	SHAP	Game theory
Pastor & Vega-Zelaya (2023)	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
Islam, et al. (2023)	✗	✓	✓	✗	✓	✗	✗	✗	✓	✗	✗
Tang et al. (2023)	✗	✓	✓	✗	✓	✗	✗	✗	✗	✓	✗
Parsa et al. (2023)	✓	✓	✓	✗	✓	✗	✗	✗	✓	✗	✗
Dini et al. (2023)	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
Pastor & Vega-Zelaya (2023)	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
Rossetti et al. (2020)	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
Rasheed et al. (2021)	✗	✓	✓	✗	✗	✗	✗	✗	✗	✗	✗
Sun, Li, et al. (2020)	✓	✗	✓	✗	✓	✗	✗	✗	✓	✗	✗
Mahato & Paul (2020)	✓	✗	✓	✗	✓	✗	✗	✗	✗	✗	✗
Watts et al. (2022)	✓	✗	✓	✓	✓	✓	✗	✗	✗	✗	✗
Koller-Schlaud et al. (2020)	✓	✗	✓	✗	✓	✗	✗	✗	✗	✗	✗

Chapter 3

Methodology

This thesis aims to ease treatment approach in patients with neurological disorders. The idea is to target depression diagnosis using EEG signals as this patient population normally undergo EEG test and they are at risk of depression. The overall approach for this purpose is using ML and DL techniques to analyse EEG features for diagnosing depression which includes using FEX, PCA, t-SNE for simplifying the data, train the model with CNN, and eventually interparent the model using SHAP.

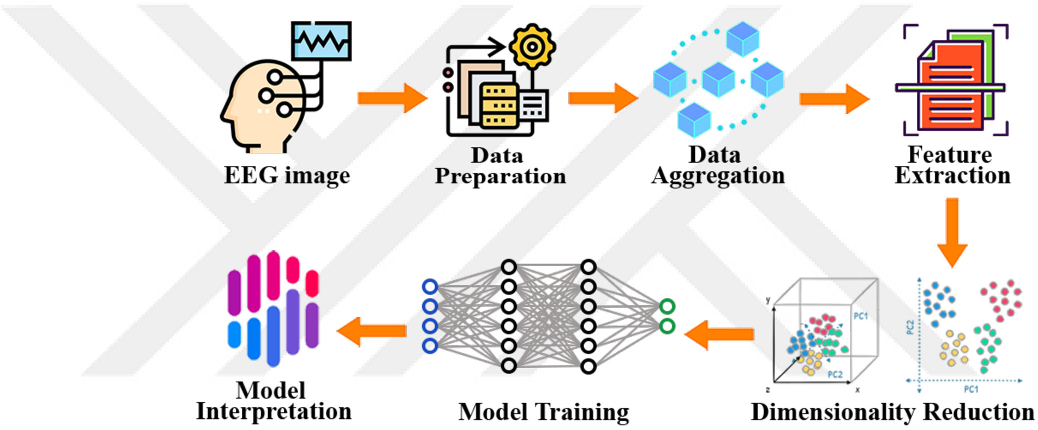

Figure 15. Technical methodology and steps

Eventually, the chapter ends with a game theoretic step in which an equilibrium strategy will analyze the flow of EEG data across the brain regions to comment some tips and enhance the accuracy and confidence level in the depression diagnosis model. This chapter will examine the methods adopted in each phase, the reasons for using each method, as well as the related adjustments and changes in each phase.

3.1 Data Collection and exploration

For this project, the targeted dataset collected from Kaggle which represents the rest EEG features for 232 patients with depression and some of them might have abnormalities in the brain waves. The EEG dataset consists of EEG features which means it provides different characteristics or patterns extracted from the raw EEG signals. Table 4 represents the name of 31 existing features in the datasets that it was recorded in six different rows for six region of brain such as Frontal, Central, Temporal, Parietal, Occipital, and Prefrontal region.

Table 4

List of feature names in EEG dataset

Feature Name	Feature Name	Feature Name
Mobility	Delta/Alpha Ratio	Wavelet Detailed Entropy
Complexity	FFT Theta Max Power	Coefficient of Variation
Min	1st Difference Max	Wavelet Approximate Mean
Max	2nd Difference Max	Wavelet Approximate Std Deviation
STD	1st Difference Mean	Wavelet Detailed Mean
Mean	2nd Difference Mean	Wavelet Detailed Std Deviation
Median	FFT Delta Max Power	Wavelet Approximate Energy
Activity	FFT Alpha Max Power	Var of Vertex-to-Vertex Slope
Kurtosis	FFT Beta Max Power	Wavelet Approximate Entropy
Skewness		Mean of Vertex-to-Vertex Slope
Delta/Theta		Wavelet Detailed Energy

Among all these traits, only five of them are recognized as depression-related biomarkers when it comes to traditional psychiatric methods. These features are FFT Theta Max Power, Wavelet Detailed Entropy, Mobility, Complexity, and Delta/Alpha Ratio. For each feature, there is a normal and abnormal range values that can be used as biomarker for depression diagnosis (Table 5).

Table 5

Depression-related EEG feature and their normal and abnormal range

Feature	Normal Range	Indicative Range for Depression
FFT Theta Max Power	0.0005 - 0.0007	Above 0.0007
Wavelet Detailed Entropy	0.0012 - 0.0015	Below 0.0012
Mobility	0.30 - 0.40	Below 0.30
Complexity	4.0 - 5.0	Below 4.0
Delta/Alpha Ratio	50 - 70	Above 70

3.2 Data preparation

The data preparation includes two phases. Since the current dataset includes the EEG features for individuals with depression and this project requires both depressive and non-depressive groups, firstly, the EEG features for half of the patients was modified with a random abnormal value. This process provided a balanced dataset consists of two group of depression and non-depression. (Table 6)

Table 6

Statistic information about patients in the EEG dataset

	Total Patients	Depressed	Non-depressed
Number	232	116	116
FFT Theta Max Power	-	> 0.0007	0.0005 - 0.0007
Wavelet Detailed Entropy	-	< 0.0012	0.0012 - 0.0015
Mobility	-	< 0.30	0.30 - 0.40
Complexity	-	< 4.0	4.0-5.0
Delta/Alpha	-	> 70	50-70

The second phase is about data aggregation. As it was mentioned in literature review chapter, when it comes to combining PCA and t-SNE, the computation is going to be complex and time-consuming. Moreover, in the EEG data, there are six different records for each patient. For this reason, a strategy of data aggregation was considered. This process has been done based on the information in Table 7, in which the features were categorized into three groups. In first two groups, if the feature expected to be recognized by the model as a biomarker of depression and must be greater than a certain value, a maximum value should be considered, and if it must be less than a specific number, a minimum value should be calculated. Finally, for the rest of features, the mean value should have been taken (Table 7). After this phase the dataset is ready for the next step.

Table 7

List of modifications in the data after data aggregation

Feature	Method	Feature	Method
Mobility	Min	Wavelet Detailed Entropy	Min
Complexity	Min	1st Difference Max	Mean
Delta/Alpha Ratio	Max	2nd Difference Max	Mean
FFT Theta Max Power	Max	1st Difference Mean	Mean
Kurtosis	Mean	2nd Difference Mean	Mean
Min	Mean	Coefficient of Variation	Mean
Max	Mean	Wavelet Approximate Mean	Mean
STD	Mean	Wavelet Approximate Std Deviation	Mean
Skewness	Mean	Wavelet Detailed Mean	Mean
Mean	Mean	Wavelet Approximate Energy	Mean
Median	Mean	Wavelet Detailed Energy	Mean
Activity	Mean	Wavelet Approximate Entropy	Mean
FFT Delta Max Power	Mean	Mean of Vertex-to-Vertex Slope	Mean
FFT Alpha Max Power	Mean	Var of Vertex-to-Vertex Slope	Mean
FFT Beta Max Power	Mean	Wavelet Detailed Std Deviation	Mean

3.3 Data Preprocessing

The original dataset used in this study, which consisted of EEG features, was pre-extracted, structured and specifically designed for depression analysis. Therefore, standard preprocessing techniques such as normalization or handling of missing values were unnecessary and the data were directly ready for analysis and use in subsequent steps.

3.4 FEX as Feature Extraction

Now, the EEG data is ready for applying major techniques which is starts with extracting the most significant features. This is done in order to highlight and transform the data to simplify computational operations when implementing PCA and t-SNE. For this purpose, four FEX techniques in specific order were employed.

The first technique is Wavelet Transform which is tasked to offer a detailed and multi-level view of the brain's activity. It uses the 'db4' wavelet to capture the smooth and detailed structure in EED data, and divides EEG signals into different frequency bands which allow it to analyse the features in multiple scales and reveal highlighted characteristics of the signal like transient spikes or oscillatory patterns. Next, it isolates the more significant features and allows them to stand out by ignoring certain types of noise or irrelevant data. This process helps in understanding the data as it breaks down the data in meaningful components that helps to see details in different aspects of the signal.

Then, the SPD technique was applied that measures how energy is spread across the frequency bands and how the signal's power is different with frequency. In this process a Welch method was used that is an estimating technique for PSD. The Welch divided the signal into overlapping segments, computes a periodogram for each, and then takes average from these periodograms. Applying PSD after wavelet transform and using Welch method, help PSD in quantifying the power within different frequency range such as Delta, Theta, Alpha, Beta, and Gamma (Table 8). This is useful because in EEG data, different frequency bands are associated with different brain activity.

Table 8

Common EEG Frequency Bands and Their Associated States

Frequency Band	Range (Hz)	Associated States
Delta	0-4	Deep sleep and unconscious states
Theta	4-8	Drowsiness, meditation, and early stages of sleep
Alpha	8-13	Relaxed, calm states, often with eyes closed
Beta	13-30	Active thinking, focus, and problem-solving
Gamma	30-50	High-level information processing and cognitive functions

Next, STFT tracked the frequency changes of EEG signals over time. It separates the signal into overlapping segments that called windows, and applies the Fourier

Transform to each. Then, STFT provides the time frequency of the signal, which shows how the various frequency components change over the duration of the signal. Next, it calculates the average magnitude of these frequency components for each time segment that reveals the strength of each frequency across the entire signal.

Table 9

Parameters in STFT

Parameters	Description	Data Value
Data	Input EEG signals to be analysed.	-
fs	Sampling frequency of the signals.	256 Hz
nperseg	Number of samples per segment.	128 samples

Eventually, Statistical Features was extracted from each record to reveal the overall distribution and characteristics of the signal. This process, complies the results into an array that each index represents the statistical summary of a specific EEG record that offers insight into their overall behaviour and distribution.

Table 10

Computed statistical features

Parameter	Description
Mean	The average value of the signal.
Standard Deviation	A measure of the signal's variability or spread.
Skewness	A measure of the asymmetry of the signal’s distribution.
Kurtosis	A measure of the peakedness or flatness of the signal’s distribution.

In summary, employing these four techniques helps to understand the EEG data from different aspect and provides a detailed and multi-dimensional view of signal behaviour and characteristics. In addition, this process helps PCA and t-SNE to reduce high-dimensional data to lower dimensions by preserving the most important features and patterns.

Table 11

Summary of the FEX phase

Technique	Purpose	What it Captures	Output
Wavelet Transform	Decomposes EEG signals into frequency bands	Multi-level view of brain activity	Average values of wavelet coefficients
PSD	Measures energy distribution across frequency bands	Energy in specific frequency ranges (Delta, Theta, Alpha, Beta, Gamma)	Power in each frequency band
STFT	Analyses time-frequency dynamics of EEG signals	Frequency changes over time	Average magnitude of STFT coefficients
Statistical Features	Describes distribution characteristics of EEG data	Central tendency, spread, asymmetry, peakedness	Mean, standard deviation, skewness, kurtosis

3.5 PCA and t-SNE

After FEX, a combination of PCA and t-SNE were employed to manage the high dimensionality of the processed EEG data and to ease the visualization and analysis of patterns and biomarkers related to depression diagnosis.

Table 12

Settings in PCA and t-SNE

Technique	Settings	Application
PCA	21 components	Simplifies the data by keeping only the most important features.
t-SNE	Perplexity: 50, Iterations: 300	Creates a clear visual separation between depressed and non-depressed groups.

3.5.1 PCA. This phase started by applying PCA to reduce the dimensionality of the EEG dataset. In this process, the number of components for PCA was configured as 21 to retain around 95% portion of the variance in the data. This process is needed to simplify the dataset, preserve the most significant EEG feature and biomarkers, and classify the data into depressive and non-depressive states. This dimensionality reduction minimizes the noise and redundancy and maximizes the efficiency of the further analysis.

3.5.1 t-SNE. Afterward, t-SNE was employed for visualization, because the EEG data was in high-dimensional and complex and t-SNE can illustrate them in more understandable way. t-SNE has two key parameters as Perplexity and Iterations.

Perplexity is focuses on local and global relationship in which local relationship is about the relation between data points with their nearest neighbours, and global relationship stands for considering the furthest neighbours and the overall structure of the data. This key parameter normally has a value between 5 to 50. A low perplexity, which is a range between 5 to 30, focuses on local relationships and details. In the contrary, a high perplexity is between 30 to 50 or even higher, and it focuses on global relationships and cluttered visualizations while it might lose some small details. However, a perplexity of 50, is considered as a balanced representation and maintains the relationships among local points while it also preserves the overall structure EEG the EEG data.

Iterations as the other key parameter is a number that decides how long the t-SNE algorithm runs. Tuning this parameter is very important as it effects on finding a stable and meaningful arrangement of data points. A low iteration might lead to incomplete or unstable patterns, while a very high iterations normally decreases the efficiency. In this project a value of 300 for Iterations was considered to secure that algorithm has adequate time to converge and clearly separate the two groups of depressive and non-depressive in the 2D visualization of t-SNE.

These settings for key parameters allowed t-SNE to demonstrate its ability to provide a clear and reliable output as well as detect and analyse depression-related patterns in the EEG data, which makes it a valuable tool in depression diagnosis using EEG signals.

3.6 CNN Architecture

In this Phase, a CNN architecture was designed to train the EEG-based model for depression diagnosis. Since CNN is capable to learn hierarchical patterns from the input features, it can effectively process the sequential EEG data. Since CNN needs the data in specific shape, the EEG data was reshaped into a 3D format which includes samples for number of data points, features for input values, and channels for depth of the input. Then the data was divided into training and testing sets with a 70-30 ratio in which it was crucial to have a balanced distribution of depressive and non-depressive cases across both sets. In addition, the class weight was computed during the model training, to ensure this balance.

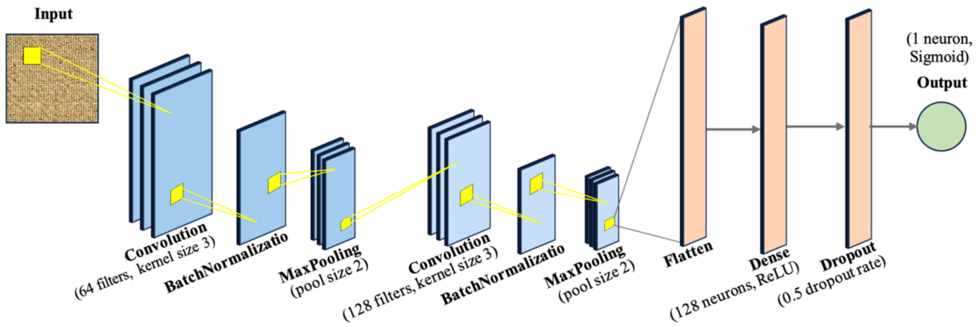

Figure 16. CNN Architecture

The CNN model was designed with multiple layers to ensure the reliability of the result and prevent any overfitting and underfitting. At first, there is a convolution layer as Conv1D, that applies the convolution operation in one dimension of the input data and process the data sequence in EEG data. This layer uses 64 different filters that each filter identifies different features or patterns in the data. Also, it has a kernel size of 3 which is the width of the region is covered at each step of filtering to scan the input data. Second layer is Batch Normalization that stabilizes the training process as well as making it faster. The third layer is MaxPooling with a pool size of 2. This layer checks in input data two by two, and each time takes the maximum value to reduce the input size by half. Next, the fourth layer is another convolution layer as Conv1D with 128 filters and a kernel size of 3. The fifth and sixth layers in order are another Batch

Normalization and MaxPooling with the same pool size of 2. In continuation of these layers, the seventh layer is Flatten that convert the 2D data into the 1D. Eighth, there is a Dense layer that has 128 neurons and ReLU as an activation function that allows model to learn more complex patterns. The ninth layer is Dropout that helps to prevent overfitting and it has a rate of 50% which means it randomly drops 50% of the neurons during each training iteration. Finally, the output layer is a Dense with a single neuron that uses a sigmoid activation for the binary classification task for diagnosing depression.

Table 13

Summary of the CNN Model Architecture and Parameters

Layer Type	Parameters	Description
Conv1D	64 filters, kernel size 3	Extracts features from the input signal using 64 filters.
BatchNormalization	-	Stabilizes and accelerates training.
MaxPooling1D	pool size 2	Reduces the spatial dimension of the feature maps.
Conv1D	128 filters, kernel size 3	Further extracts features using 128 filters.
BatchNormalization	-	Stabilizes and accelerates training.
MaxPooling1D	pool size 2	Reduces the spatial dimension of the feature maps.
Flatten	-	Converts the 2D feature maps into a 1D feature vector.
Dense	128 neurons, ReLU activation	Provides a deep representation of the input features.
Dropout	Dropout rate 0.5	Prevents overfitting, randomly drop 50% of the neurons during training.
Dense	1 neuron, sigmoid activation	Outputs a probability score for binary classification (depressed or non-depressed).

In compilation part, an Adam optimizer with a learning rate of 0.0001 was used as well as binary cross-entropy as the loss function. In training part, the model was trained over 100 epochs with a batch size of 64. Moreover, an early stopping was considered to improve the model's efficiency and prevent overfitting which stops training if the validation loss did not improve for 10 epochs. Eventually, the learning rate was reduced by 0.2 if the validation loss is high and a minimum learning rate was set at 0.00001. The CNN model, designed and tuned to classify patients in two class of depressive and non-depressive using their EEG data.

Table 14

Summary of the key parameters in compilation and training phases

Parameter	Value/Description
Optimizer	Adam
Learning Rate (Initial)	0.0001
Loss Function	Binary Cross-Entropy
Epochs	100
Batch Size	64
Early Stopping (Training)	If validation loss doesn't improve for 10 epochs
Learning Rate Reduction	Factor of 0.2 when validation loss plateaus
Minimum Learning Rate	0.00001

3.6 SHAP

Eventually, the methodology in technical part ends with SHAP as an explainable technique to interpret the model's predictions as well as the contribution and influence of each original feature in decision-making process and the model's output. This phase has four steps:

1. Using Original Features and PCA Loadings: It starts with identifying the original EEG features that were used as inputs for the model and then calculates PCA component loadings to determine the contribution of each feature to the principal components.
2. SHAP Explainer Initialization: In this step, SHAP uses a Kernel Explainer to compute the values. This Kernel Explainer was initialized with a subset of the

training data. This step represents how each feature influenced the model's predictions. After computing these values for a subset of the test data, there will be a detailed examination of the model's behaviour on unseen data.

3. Contribution Calculation: This step is about linking the SHAP values back to the original features. Therefore, the PCA loadings multiplied with the SHAP values to show how much each feature influences the model's predictions. Finally, the results are summarized, sorted, and visualized to highlight the most important features.
4. Interpretation of Top Features: This step is about analysing the visualization which provided a deeper understanding about the most influential features in the model's predictions.

In summary, the SHAP analysis provides a transparent view of how the CNN model predicts which represents the reliability of the ML in diagnosing depression based on EEG data. This process can open a new window to find other biomarkers in EEG signals that are related to depression.

3.6 Game Theory: A Theorical aspect

While the SHAP analysis highlights the technical aspects of feature importance in model’s prediction, game theory completes this analysis by examining how different brain regions (as players) contribute to influence EEG data transmission, and affect the accuracy of depression diagnosis. Therefore, this part will provide a theorical aspect of the project in which instead of focusing on biomarkers in EEG data, it checks the different brain regions, affected by depression and its impact on EEG data. Hence, a novel coalition game is proposed to model the interactions between different brain regions during the transmission of EEG data in the context of depression. This game involves five key groups to represent for each related region of the brain such as the frontal lobe as Group A, the temporal lobe as Group B, the limbic lobe as Group C, the parietal lobe as Group D, and the occipital lobe as Group E. This part aims to assess the overall impact of each region on the final EEG signal used for diagnosing depression.

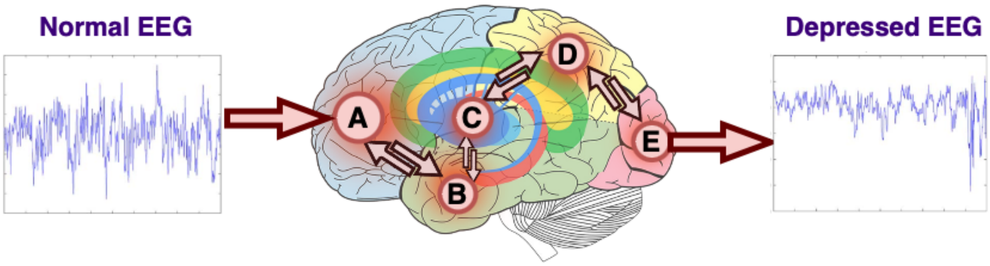

Figure 17. The interaction between groups A, B, C, D, and E as different brain regions and their impact on EEG data and depression.

Table 15

Issues associated with disorder in each region of the brain (G = Group)

G	Region	Issue(s)
A	Frontal	Memory impairment, mood swings, impaired decision-making
B	Temporal	Auditory processing and language issues, emotional instability
C	Limbic	Emotional dysregulation, memory impairment, mood disorders
D	Parietal	Difficulty in attention, spatial awareness and sensory integration
E	Occipital	Visual processing impairments, visual cognitive deficits

In this coalition game, each player is one region of the brain and from now on, the word player will be used. The game operates under the following conditions:

1. Rational Decision-Makers: Each player is assumed to make rational decisions to maximize its contribution to the accurate diagnosis of depression.
2. Probability of Contribution: The probability of each player contributing effectively to the EEG data transition is denoted by specific parameters x_A, x_B, x_C, x_D, x_E), where $x_{i=0}$ means no contribution and $x_{i=1}$ indicates full contribution.
3. Utility Function: The utility of the game for player is determined by several parameters, all dependent on the effectiveness of EEG data transmission and its relevance to depression diagnosis.

4. Cooperative Strategy: The players cooperate to maximize their collective utility, ensuring the EEG data is as accurate as possible for the final diagnosis.
5. Cost and Effectiveness: Each player attempts to minimize the data loss and maximize the effectiveness of the transmitted EEG data.

The interactions between players and their contributions to the EEG data transmission are formalized through the following equations:

$$0 \leq \lambda_i, \rho_i \leq 1 \text{ for } i \in \{A, B, C, D, E\}$$

where λ_i represents the effectiveness rate when the player contributes to the EEG data transition, and ρ_i represents the effectiveness rate when the player does not contribute.

The overall effectiveness of EEG data transmission can be expressed as:

$$C_F = C_I - \sum_{i=A}^{E} C_i$$

Where:

- C_I is the initial EEG data transmission.
- C_i represents the proportion of EEG data handled by each player.

Table 16

Parameters for Initial Data Transition and Each Brain Region's Proportion in EEG Data Transmission During Depression

Parameters	Descriptions
C_I	Initial EEG data transmission in case of depression.
C_A	Frontal lobe proportion in EEG data transition.
C_B	Temporal lobe proportion in EEG data transition.
C_C	Limbic lobe proportion in EEG data transition.
C_D	Parietal lobe proportion in EEG data transition.
C_E	Occipital lobe proportion in EEG data transition.
C_F	Final EEG data transmission in case of depression.

This chapter has detailed all methodological steps taken during the project which includes two parts of technical and theoretical. The technical part represents different phases to prepare data.

Table 17

Parameters for Activation Rates of Brain Regions in EEG Data Transition in Case of Depression

Parameters	Descriptions
λ	Full contribution rate during cooperation
ρ	Partial contribution rate without full cooperation
α	Weight of contribution when fully cooperating
β	Weight of contribution when partially cooperating
C	Cost of contributing
x	Binary variable: 1 for full contribution, 0 for none/partial

The provided coalition game model provides an in-depth analysis of the interactions between brain regions (players) during EEG data transmission in depression. The effectiveness of each region or player is considered in terms of the rates at which they influence various cognitive and emotional processes, ultimately impacting the accuracy of depression diagnosis. The model highlights how these players work together, balancing their contributions to minimize data loss and maximize diagnostic accuracy. Therefore, it offers a robust theoretical framework for understanding EEG data in the context of depression.

3.7 Conclusion

This chapter has detailed all methodological steps taken during the project which includes two parts of technical and theoretical. These parts aim to enhance the precision of depression diagnosis. While AI methods analyse the EEG data to classify the accurately, the game theory focuses on the interactions between brain regions and its overall impact on EEG signal transmission. AI part starts by data preparation, FEX, PCA and t-SNE to simplify the complex EEG data for model training. After designing and implementing the CNN model, the technical part ended with a SHAP explanation to illustrate the most influential EEG features. Moreover, for each phase the key parameter values and the reason of choosing them was explained. The theoretical part focuses on a coalition game to check the influence of each brain region on EEG data in field of depression diagnosis. Next chapter will present the main results obtained in both technical and theoretical part to show the capability and efficiency of each.

Chapter 4

Main Results

This chapter will present the key findings of the study, structured into two primary sections of technical and theoretical. Each section highlights the results derived from the methods applied to diagnose depression using EEG data.

The technical part of this chapter includes three parts of dimensionality reduction, CNN and SHAP. First, it begins with the results from PCA and t-SNE as dimensionality reduction techniques. Due to the complex nature of the EEG data, using these techniques were significant to simplify them to have more effective visualization and analysis. In the result of these techniques, the CNN model achieved an accuracy of over 98% in classifying depression based on the processed EEG data. Lastly, the SHAP analysis provides insights into the interpretability of the CNN model by identifying the contributions of individual EEG features to the model's predictions.

The theoretical part, on the other hand, is about a Coalition Game, which models the interactions between different brain regions as players during EEG data transmission in term of depression. This game-theoretic approach provides a novel perspective on how brain regions work together to influence the diagnosis of depression. The Coalition's game results provide a deeper understanding of the complex dynamics at play and bridge the gap between traditional EEG analysis and advanced AI methods. This chapter will cover the results in detail for both the technical and theoretical aspects of the study.

4.1 PCA and t-SNE

The technical part starts with a combination of PCA for dimensionality reduction and t-SNE for visualization to classify the EEG data in term of depression diagnosis. The EEG data includes 31 features for each patient. Before PCA and t-SNE, the FEX techniques were employed to highlight the significant features. This result was sent to PCA for dimensionality reduction before the EEG data is fed into a classifier, like the CNN, for the actual classification task.

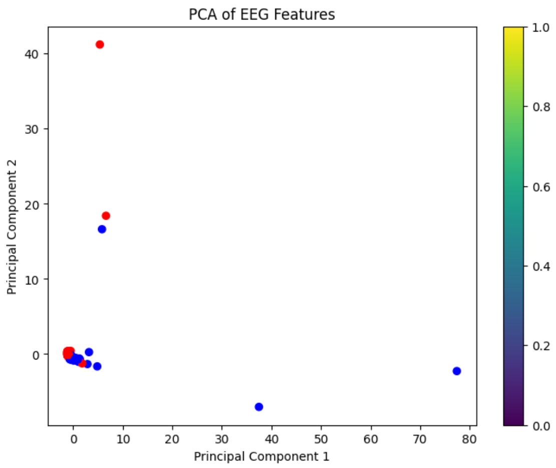

Figure 18. PCA plot

Then, PCA took a big proportion of them, and tried to sort them into two groups based on the characteristic of each to make it easier to see patterns. Figure 18 shows these two components in two different colours of red and blue. PCA tried to illustrate these blocks on a flat surface, therefore the blocks are not well-separated. Therefore, the PCA was combined with t-SNE, offering better arrangement to visualize these two components. As a result, Figure 19 illustrates the data points in two groups clearly.

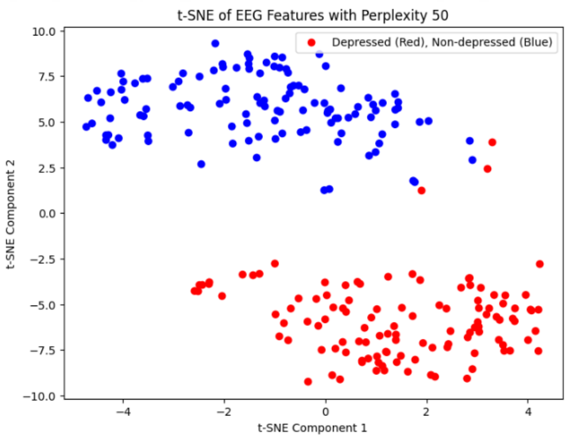

Figure 19. t-SNE plot

4.2 CNN model

After dimensionality reduction using PCA and t-SNE, a CNN model that was trained to classify depression based on EEG data. The model was trained over 100 epochs, with the training and validation loss and accuracy plotted as shown in Figure 20. The left panel shows how the loss value changed over epochs which demonstrates a steady decrease in both training and validation loss, highlighting the model capability in learning to minimize errors. The left panel illustrates the accuracy for both the training and validation set quickly increased over epochs and stabilized at around 98%, indicating the model's performance in classifying the EEG data.

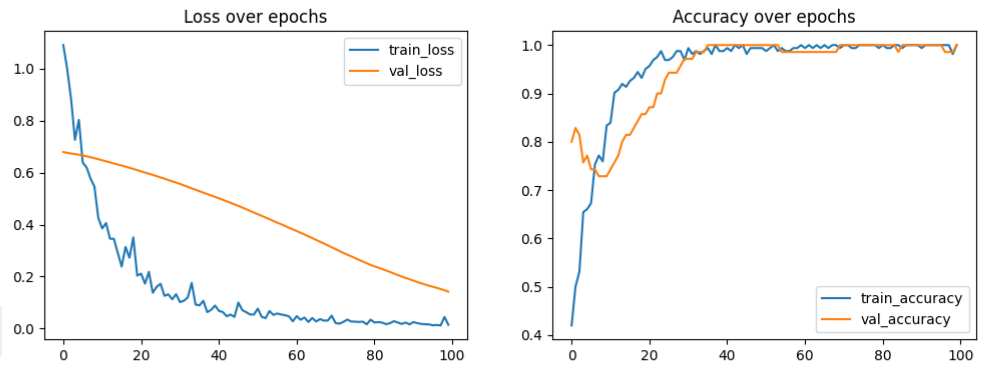

Figure 20. CNN training and validation performance

The CNN model was evaluated on the test set in which achieved an accuracy of 98% (Table 18). In the report, there are three metrics as precision for the model's accuracy of positive predictions, recall for the model's ability to identify the actual positive cases, and F1-score that provides the balance between precision and recall. The table shows these metrics have reached a score of 0.98 for both the depressed (1) and non-depressed (0) classes which is close to perfect. The report indicates that the model was able to correctly identify the vast majority of instances in the test set.

Table 18

The model's classification report

	precision	recall	f1-score	support
0 (non-depressed)	0.97	0.98	0.98	35
1 (depressed)	0.98	0.97	0.98	35
accuracy	-	-	0.98	70
macro avg	0.98	0.98	0.98	70
weighted avg	0.98	0.98	0.98	70

The strong performance of the CNN model indicates that the combination of FEX, PCA, t-SNE and a well-tuned DL model can lead to highly accurate classification results in the context of EEG-based depression diagnosis.

4.3 SHAP

This section represents the results of the SHAP analysis to understand the contribution of each feature in the dimensionality reduction after applying PCA to the model. The results revealed significant insights into the contribution of original features to the model's predictions. The SHAP values were calculated for 21 of the top principal components obtained from PCA, and the impact of these components was traced back to the original EEG features.

The summary plot illustrates the importance and influence of features in model performance (Figure 21). The result can be categorized into three levels of interest. Firstly, nine features influence the model positively (red color), with the Delta/Alpha ratio and FFT Theta Max Power having the highest impact. Secondly, six features influence the model moderately, and despite their importance, their influence is less dominant. Lastly, six features have little to no contribution to the model's output (blue color). Using this hierarchy helps to find the features that are identified by the model.

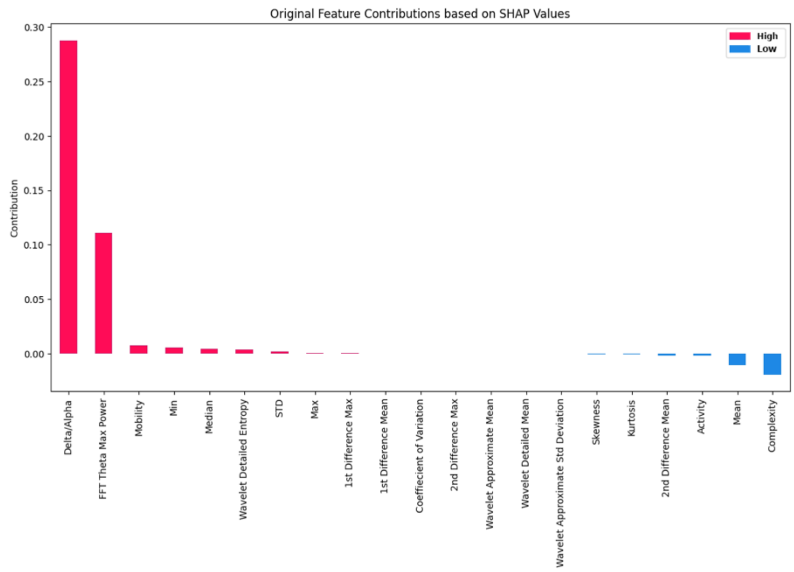

Figure 21. SHAP summary plot

The force plot that shows the contribution of each Principal Component (PC) in model prediction (Figure 22). Each PC is a linear combination of the original features. The base value indicates the expected prediction at 0.488. However, the point of 0.16 represents the result of influences in different principal components. Blue arrows indicate components that lower the prediction, while red indicates the components that push the prediction higher. Based on this fact, PC4 with the highest impact, pushed the prediction strongly in the negative direction. Next PC11 and PC3 had minor positive effects compared to PC4.

Figure 22. SHAP force plot

The summary and force plot help to understand how specific features or PCs influence individual predictions and contribute to the model's performance. However, modeling the contribution between brain regions can provide a deeper insight into this classification.

4.4 The Coalition Game

This section provides the main results related to the theoretical part of the project in which a coalition game how the brain regions or players can work together hardly to increase the risk of depression and affect the EEG data. Therefore, there are payoff function and expected utility function for each player based on the parameters in previous chapter. Also, an optimization model is formulated to analyse how these brain regions contribute to the effective transmission of EEG data during depression. Eventually, the main results determine a unique equilibrium for the brain regions under specific conditions.

4.4.1 Pay-off matrix. First, a pay-off matrix represents the contribution of any two brain regions to the overall transmission of EEG data during depression. The brain regions are considered as players donated as Player i and Player j .

Table 19

Generalized Pay-off matrix for EEG data transmission between any two brain regions (Player i and Player j)

		Player j	
		$x_j = 1$	$x_j = 0$
Player i	$x_i = 1$	$P_{11} = \lambda_i\alpha_i + \lambda_j\alpha_j - C_i - C_j$	$P_{12} = \lambda_i\alpha_i + \rho_j\beta_j - C_i$
	$x_i = 0$	$P_{21} = \rho_i\beta_i + \lambda_j\alpha_j - C_j$	$P_{12} = \rho_i\beta_i + \rho_j\beta_j$

Based on the Pay-off matrix, decision-making processes of each player are formulated by considering their contributions to the EEG data transmission. Four different scenarios will be examined:

1. $x_i = 1$ and $x_j = 1$: Both Player i and j are contributing. It is represented as P_{11} in which the pay-off is the sum of their contributions, minus the associated costs.
2. $x_i = 1$ and $x_j = 0$: Only Player i is contributing. It represents as P_{12} and the pay-off is the non-contribution of Player j.
3. $x_i = 0$ and $x_j = 1$: Only Player j is contributing. It represents as P_{21} and the pay-off is the non-contribution of Player i.
4. $x_i = 0$ and $x_j = 0$: Neither Player i nor j are contributing. It is represented as P_{22} , and the pay-off is the non-contribution for both players.

4.4.2 Expected utility functions. Following by the Pay-off matrix, the utility function will be provided for each brain region's decision-making process during EEG data transmission. The utility function for Player i (e.g., Group A or Frontal Lobe) contributing to EEG data transmission would be:

$$\mathrm{U}_{i_1} = P_{11}x_i + P_{12}\,(\,1 - x_i)$$

The utility function for Player i not contributing would be:

$$\mathrm{U}_{i_2} = P_{21}x_i + P_{22}\,(\,1 - x_i)$$

Therefore, the expected utility function for Player i becomes:

$$\mathrm{U}_i = \mathrm{U}_{i_1} x_i + \mathrm{U}_{i_2}(1 - x_i)$$

Similar utility functions can be established for the other players or brain regions (temporal, limbic, parietal, and occipital lobes).

4.4.3 A Nash equilibrium. This part represents the following optimization model to determine the equilibrium contributions of each player to the EEG data transmission during depression:

$$\max_{0 \le x_i \le 1} U(x_A, x_B, x_C, x_D, x_E),$$

where

$$U(x_A, x_B, x_C, x_D, x_E) = \sum_{i=A}^{E} x_i (\mathrm{U}_{i_1} - U_i)$$

is the utility function representing the collective contribution of all brain regions. For further investigation, the following optimization problem is represented:

$$\max_{0 \le x_i \le 1} \sum_{i=A}^{E} [x_i (1 - x_i)(\mathrm{U}_{i_1} - \mathrm{U}_{i_2})]$$

The strategy of this model is to maximize the sum of the expected utility functions for all players to provide an equilibrium for optimal EEG data transmission during depression.

Theorem: In this game, the dynamic system $U(x_A, x_B, x_C, x_D, x_E)$ defines a unique equilibrium when the following inequalities are satisfied:

$$\lambda_i \alpha_i > \rho_i \beta_i + \mathrm{C}_i, \quad for\ i \in \{A, B, C, D, E\}.$$

The equilibrium contributions for each brain region are given by:

$$x_i^* = \frac{1}{2} \quad for\ i \in \{A, B, C, D, E\}.$$

Proof: Since

$$U\ (x_A, x_B, x_C, x_D, x_E\ ) = \sum_{i=A}^{E} x_{\mathrm{i}}\ (\ 1 - x_i)\ (\lambda_i \alpha_i - \rho_i \beta_i - \mathrm{C}_i)$$

It can be indicated that the utility function is strictly concave. This concavity implies that there is only one critical point where the function is maximized, resulting in a unique equilibrium decision for each brain region at $x_i^* = \frac{1}{2}$

Therefore, the theorem establishes a unique equilibrium where each player a a brain region contributes equally to the EEG data transmission. This equilibrium is achieved when the benefits of each brain region's contribution outweigh the associated costs, ensuring effective and balanced EEG data transmission for depression diagnosis. This approach completes the SHAP analysis by bridging the gap between feature importance and interactions of different brain regions.

4.5 Conclusion

This chapter reveals significant insights into both the technical and theoretical aspects of diagnosing depression using EEG data. On the technical side, the study demonstrates the effectiveness of dimensionality reduction techniques such as PCA and t-SNE, which were required in simplifying the complex EEG data, enabling more accurate classification through a CNN model that achieved an impressive accuracy of 98%. Additionally, SHAP analysis provided interpretability to the CNN model by identifying the contributions of specific EEG features, further validating the model's predictions. On the theoretical side, the Coalition Game offers a novel approach to understanding the interactions between different brain regions during EEG data transmission in depression. This game-theoretic perspective bridges traditional EEG analysis with advanced ML and DL methods and provides a comprehensive understanding of how brain regions collaborate to influence depression diagnosis. These results collectively highlight the potential of integrating technical ML approaches with theoretical game models to enhance the accuracy and interpretability of depression diagnosis through EEG data.

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Chapter 5

Numerical Simulations

This chapter will present the numerical results obtained from both the technical and theoretical approaches employed in this study. Numerical simulations are crucial for validating the proposed methods as they offer a controlled environment to rigorously test the models' capabilities. These simulations help to observe how the models perform with different parameters, on various subsets of data, and under different levels of complexity.

The chapter is structured into two main sections. At first, it focuses on the technical results derived from ML techniques, including dimensionality reduction, CNN classification, and SHAP analysis. These results showcase the performance and accuracy of the models used to diagnose depression based on EEG data, providing a quantitative assessment of their effectiveness. The second section delves into the theoretical results, specifically the outcomes of the Coalition Game model. This game-theoretic framework explores the interactions between brain regions during EEG data transmission in the context of depression, offering a deeper understanding of how these regions contribute to the diagnosis.

Together, these numerical results provide a comprehensive view of both the practical performance and the theoretical underpinnings of the methods used in this study, highlighting their combined potential in advancing the field of EEG-based depression diagnosis.

5.1 The EEG-based model

This section provides the numerical results obtained from the CNN model applied to the processed EEG data for depression diagnosis. The CNN model was evaluated on a set of four test samples, which were previously transformed using PCA for dimensionality reduction (Table 20). The data was fed to the CNN model without any label as depressed or non-depressed.

Table 20

Input EEG data consist of two samples for each group of depression and non-depression

Feature	Patient 1	Patient 2	Patient 3	Patient 4
Depressed	No	No	Yes	Yes
Wavelet Detailed Entropy	0.8	0.7	-0.3	-0.4
Mobility	-0.2	-0.1	0.4	0.5
Complexity	0.1	0.15	-0.1	-0.15
FFT Theta Max Power	-0.4	-0.35	0.5	0.45
Delta/Alpha	0.3	0.25	-0.25	-0.3
Min	0.2	0.25	-0.2	-0.25
Max	-0.1	-0.15	0.1	0.15
STD	0.05	0.07	-0.06	-0.07
Mean	-0.03	-0.02	0.04	0.05
Median	0.02	0.03	-0.03	-0.04
Activity	0.01	0.015	-0.02	-0.03
Kurtosis	-0.05	-0.04	0.05	0.04
2nd Difference Mean	0.04	0.03	-0.04	-0.03
2nd Difference Max	-0.06	-0.05	0.06	0.05
1st Difference Mean	0.07	0.06	-0.07	-0.06
1st Difference Max	0.03	0.025	-0.03	-0.025
Coefficient of Variation	-0.02	-0.015	0.02	0.015
Skewness	0.01	0.02	-0.01	-0.02
Wavelet Approximate Mean	-0.01	-0.01	0.015	0.01
Wavelet Approximate Std Deviation	0.02	0.015	-0.02	-0.015
Wavelet Detailed Mean	0.03	0.025	-0.03	-0.025

The model was capable of diagnosing depression among these patients and the results was exact same as the actual situation for each patient. Although the accuracy for the model was high, the results came by a confidence score which was between 0.41 to 0.59. These confidence scores suggest that the model was reasonably confident in its predictions, distinguishing between depressed and non-depressed states based on the processed EEG features.

To provide a visual representation of the CNN model's performance, a bar chart was generated to display the confidence scores for each of the four samples (Figure 23). As shown in the chart, the bars are color-coded to indicate the predicted class: blue for non-depressed and red for depressed. The height of each bar corresponds to the confidence score, and the specific score is displayed on top of each bar, alongside the predicted label.

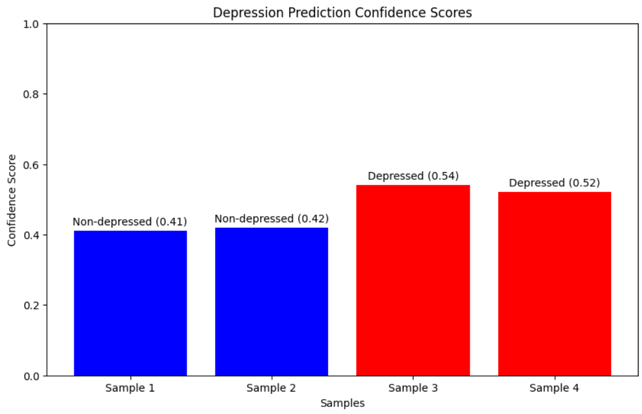

Figure 23. Confidence scores of the CNN model

This visualization underscores the model's ability to classify the samples with varying degrees of confidence, demonstrating the effectiveness of the CNN in processing the EEG data and identifying depression-related patterns.

The chart is an essential tool for interpreting the model's predictions, offering a clear and concise summary of how the CNN evaluated the test samples. This aids in understanding the model's decision-making process and provides insights into its overall performance in the context of depression diagnosis using EEG data.

5.2 The Coalition Game model

In this section, we present numerical simulations conducted on sample EEG data to validate the proposed coalition game model's key results. The simulations utilize Sequential Least Squares Programming (SLSQP) to solve the payoff functions and expected utility functions established in the previous section.

The coalition game model involves five key players representing the different regions of the brain including the frontal lobe as player A, temporal lobe as player B, limbic lobe as player C, parietal lobe as player D, and occipital lobe as player E. Each player contributes to the overall EEG data transmission during depression, and their interactions are modelled to find an optimal equilibrium that maximizes the utility for each brain region.

Table 21

Sample parameter values for equilibrium scenario

Parameter	Frontal (A)	Temporal (B)	Limbic (C)	Parietal (D)	Occipital (E)
λ	0.7	0.6	0.5	0.8	0.7
ρ	0.2	0.3	0.4	0.2	0.3
α	50	45	40	60	55
β	20	25	30	15	25
C	10	12	14	8	11

Using the parameters outlined in Table 21, the payoff functions were established to represent the contributions of each brain region. The optimization process aimed to find the equilibrium where each brain region's contribution maximizes the overall utility.

The optimal values for each brain region's contribution were found to be $x_A = x_B = x_C = x_D = x_E = 0.5$ which corresponds to the equilibrium point where the utility is maximized. The maximum utility achieved at this equilibrium point is 19.875.

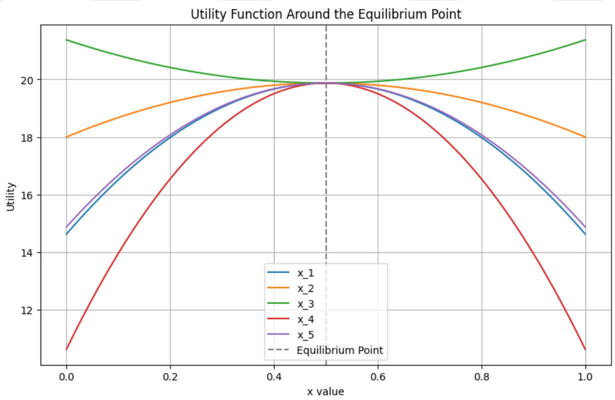

Figure 24. Utility function around the equilibrium point for each brain region. The dashed line indicates the equilibrium point at x = 0.5

Figure 24 shows the utility function around the equilibrium point for each brain region. As depicted in the figure, the utility function is concave, with the highest utility occurring at the equilibrium point $x = 0.5$ for all brain regions. This result indicates that equal contributions from all brain regions lead to the optimal transmission of EEG data during depression.

The results confirm that the coalition game model effectively captures the interactions between brain regions during EEG data transmission, and the identified equilibrium represents the optimal state for depression diagnosis based on EEG data. The use of game theory in this context provides a robust framework for understanding the contributions of different brain regions and their collective impact on EEG-based depression diagnosis.

5.2 Conclusion

In this chapter, the numerical results from two distinct approaches were thoroughly examined to validate the efficacy of the models used in depression diagnosis via EEG data. The CNN model, which was applied to processed EEG data, successfully classified patients as depressed or non-depressed with a high degree of accuracy. However, the model's confidence scores, ranging between 0.41 and 0.59, indicate a moderate level of certainty in its predictions, necessitating further refinement or complementary approaches to enhance reliability.

Furthermore, the coalition game model was introduced as a theoretical framework to analyse the interactions among various brain regions during EEG data transmission in the context of depression. By simulating this model with the Sequential Least Squares Programming (SLSQP) optimizer, it was determined that an equilibrium state is reached when all brain regions contribute equally $x_A = x_B = x_C = x_D = x_E = 0.5$, maximizing the overall utility to 19.875. This finding underscores the significance of balanced brain region activity in the optimal transmission and processing of EEG signals, a critical factor in accurate depression diagnosis.

The results presented herein affirm the utility of combining ML techniques with game theory to advance the understanding and diagnostic capabilities of EEG-based analysis for depression. This integrated approach not only highlights the strengths of each method but also paves the way for more comprehensive and accurate diagnostic tools in the field of mental health. Using the insights gained from these numerical simulations, future work can focus on refining these models and exploring their applications in broader clinical settings, potentially leading to more effective and personalized treatment strategies for people with depression.

Chapter 6

Discussions

This chapter will discuss the concepts and importance of the findings presented in the previous chapters to provide a critical analysis of both the technical and theoretical aspects of the study. The discussion will explore how the use of dimensionality reduction techniques like PCA and t-SNE, combined with CNN models, contributed to the successful classification of depression based on EEG data. Moreover, it will examine the accuracy of the models in the context of existing literature and discuss the interpretability of the results provided by SHAP analysis. Furthermore, the theoretical insights obtained from the coalition game model will be analysed to understand the interactions between brain regions during EEG data transmission and their impact on depression diagnosis.

This chapter will also address the potential limitations of the study, suggest improvements for future research, and explore the broader implications of these findings for neurological case as well as using ML techniques and EEG-based diagnostic tools. Finally, the discussion aims to provide a comprehensive understanding of the study's contributions and their relevance in advancing the diagnosis of depression using EEG data.

6.1 Technical Analysis

The use of dimensionality reduction techniques such as PCA and t-SNE is essential in handling high-dimensional and complex EEG data. After reducing the complexity of the data, these techniques enabled more effective visualization and analysis, paving the way for the high classification accuracy of the CNN model. The PCA results, though limited in their ability to completely separate the data into two groups, provided a simplified representation of the EEG features that was further modified by t-SNE. The t-SNE visualization offered a more understandable separation of depressed and non-depressed individuals. However, the FEX process effectively captured the most relevant information as well.

The CNN model's performance, with an accuracy of 98%, underscores the effectiveness of combining dimensionality reduction with a DL approach. This accuracy suggests that the model was able to generalize well from the training data to unseen test data that makes it a reliable tool for diagnosing depression based on EEG signals. Despite the high accuracy, the model showed an unreliable confidence score around 50 %, which can be dure to several reasons, such as limited dataset, dimensionality reduction and using unsupervised learning.

However, while the technical success of the CNN model is evident, it is crucial to consider the model's interpretability which is a common challenge in DL. This is where the SHAP analysis played a vital role, offering insights into how specific EEG features contributed to the model's predictions.

6.2 SHAP Analysis

Using SHAP is one of the significant contributions of this study, which values to interpret the CNN model's predictions. SHAP analysis allowed for a detailed examination of how individual EEG features influenced the model's decisions, providing transparency that is often lacking in DL models. The analysis revealed that features such as the Delta/Alpha ratio and FFT Theta Max Power were among the most influential in predicting depression.

This interpretability is critical not only for validating the model's predictions but also for gaining clinical insights into the EEG patterns associated with depression. This identification features most strongly influence the model. Thus, healthcare professionals can better understand the biomarkers of depression which potentially leads to more targeted and effective treatments.

Despite the strengths of the SHAP analysis, it is important to recognize its limitations. Firstly, there are other depression-related biomarkers that was not captured by SHAP. Secondly, SHAP values provide a post-hoc explanation of the model's behaviour, meaning they do not influence model’s training or predictions. So, this form of interpretability does not alter the underlying black-box nature of the CNN model. Future research should integrate interpretability directly into the model design, potentially leading to even more transparent and trustworthy AI tools.

6.3 Coalition Game Model

The theoretical aspect of this study, centred around the coalition game model, and offers a novel perspective on how different brain regions interact during EEG data transmission in depression. In this process each brain region was considered as a player. The model provides a framework for understanding how these regions collectively influence the EEG patterns used to diagnose depression.

The pay-off matrix and expected utility functions developed for each brain region highlight the complex interplay between different parts of the brain during depression. The results suggest that a contribution of all brin regions may have a more significant impact on EEG data transmission during depressive episodes. This insight aligns with neurobiological theories that emphasize the role of these regions in mood regulation and emotional processing.

The Nash equilibrium derived from the coalition game model indicates that under specific conditions, the brain regions reach a state of balance where their contributions to EEG data transmission are optimized. This theoretical finding is particularly valuable as it provides a comprehensive aspect of the neural dynamics in depression, and offers a bridge between traditional EEG analysis and advanced ML and DL methods. Combining game theory with EEG data analysis opened new avenues for research that could lead to more sophisticated diagnostic tools and treatment strategies.

Although the Nash equilibrium represents a state of balance in this interaction, this approach has some limitations. First, brain regions are part of a highly interconnected network, so simplifying their complexity limits the model's ability to capture the full dynamics of brain activity during depressive episodes. Secondly, the coalition game model and Nash Equilibrium has a theoretical nature, and their predictions have not been directly validated with real-time or experimental EEG data.

6.4 Limitations and Future Directions

While the study presents promising results, it is essential to acknowledge its limitations in each phase of project:

- The EEG data used in this research, may not fully capture the diversity of depression manifestations across different populations. Future studies should aim to include more diverse datasets to improve the generalizability of the findings.
- The CNN model showed an unreliable confidence score around 50%, possibly due to factors such as a limited dataset, dimensionality reduction, and the use of unsupervised learning.
- SHAP analysis did not capture all depression-related biomarkers.
- SHAP provides post-hoc explanations that do not influence model training or predictions, leaving the CNN model's black-box nature unaltered.
- The coalition game model oversimplifies the complex interconnections between brain regions and other parts of brain, limiting its ability to capture the full dynamics of brain activity during depression.
- The coalition game model and Nash equilibrium are theoretical constructs that have not been directly validated with real-time or experimental EEG data.

Table 22

limitations and future directions

Limitation	Future Direction
EEG data may not capture the full diversity of depression.	Include more diverse datasets to improve generalizability.
CNN model shows low confidence scores (~50%).	Improve confidence with supervised learning and larger datasets.
SHAP missed some depression-related biomarkers.	Explore additional biomarkers.
SHAP provides post-hoc explanations without influencing model training.	Integrate interpretability into model design.
Coalition game model oversimplifies brain region interactions.	Use more detailed models to capture complex brain dynamics.
Coalition game model lacks real-time validation.	Validate with real-time EEG or experimental data.

By addressing these limitations, future research could focus on expanding the dataset to include a broader range of depression cases, improving model confidence by integrating supervised learning techniques, exploring other biomarkers that SHAP analysis might miss, incorporating interpretability directly into the model design, and validating the coalition game model through real-time EEG experiments to better capture the complex interactions between brain regions and enhance the robustness of the theoretical framework.

6.5 Comparative studies

This study presents a multi-technique approach for diagnosing depression using EEG data, which offers noticeable improvements in accuracy, efficiency, and explainability (Figure 25), compared to previous studies. Earlier studies often use AI techniques separately, such as PCA or wavelet-based analysis for classifying EEG signals, leading to limitations in analysing complex patterns in high-dimensional EEG data (Gajic et al, 2014). This study used both PCA and t-SNE for dimensionality reduction which allows in-depth identification of depression biomarkers. EEG data and t-SNE both have non-linear characteristics, so using t-SNE for EEG data offers a better clustering to separate depressed and non-depressed states (Hamid et al, 2020).

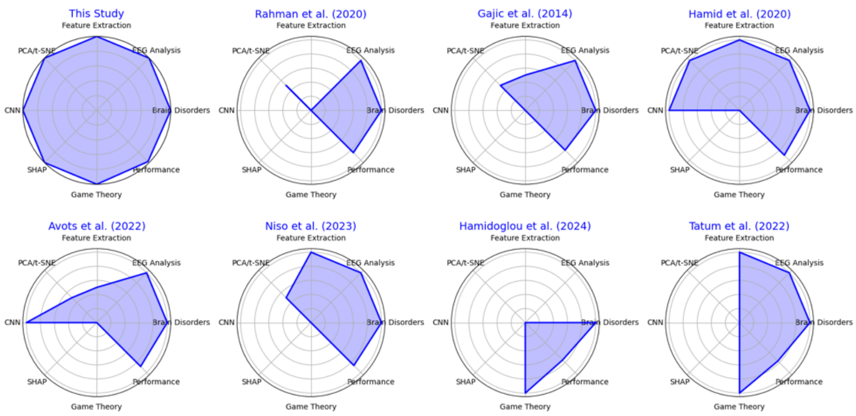

Figure 24. Comparative studies

To compare model accuracy, this study uses a combination of CNN and SHAP to classify EEG signals and interpret the model's performance. In comparison with existing research like the ensemble method for diagnosing depression using EEG data (Avots et al, 2022) and wireless EEG classification systems (Niso et al, 2023), the strength of this study is not only achieving higher accuracy but also offering greater transparency in the model decision-making process. The SHAP explanation highlights the most influential EEG features, which are important in clinical uses. In addition, this study used game theory to model the interactions between brain regions during EEG data transmission. Compared to other studies that use game theory and AI techniques separately (Hamidoglou et al, 2024; Tatum et al, 2022}, this study used a combination of them to improve both feature selection and the model's accuracy in diagnosing depression using EEG data.

6.6 Broader Implications

The findings of this study have significant implications for the field of neurological disorders, particularly in the context of mental health diagnostics. The successful application of DL techniques, coupled with game theory, demonstrates the potential for ML and DL to revolutionize how depression is diagnosed and understood. By providing both accurate classification and interpretability, the methods developed in the field of explainable AI, which is crucial for gaining trust in ML and DL models, especially in clinical settings.

The Coalition Game model, in particular, offers a new lens through which to view brain activity during depression, potentially leading to more targeted therapies that address the specific neural mechanisms involved. As AI continues to evolve, integrating technical advances with theoretical models like the Coalition Game will be key to developing holistic approaches that improve patient outcomes.

6.7 Conclusion

The discussion chapter has critically analysed the technical and theoretical findings of this study, highlighting the effectiveness of the applied methods in diagnosing depression using EEG data. The successful combination of dimensionality reduction techniques, CNN modelling, and SHAP analysis not only yielded a high classification accuracy but also provided crucial insights into the interpretability of the model, making it more trustworthy for clinical application.

The introduction of the Coalition Game model added a novel theoretical perspective that offers a deeper understanding of how different brain regions interact during depression. This game-theoretic approach bridges the gap between traditional EEG analysis and advanced ML/DL techniques that help in having a more comprehensive understanding of the neural dynamics in depression.

While acknowledging the study's limitations, this discussion sets the stage for future research, emphasizing the importance of integrating technical innovations with theoretical models to enhance the accuracy, interpretability, and clinical relevance of AI-driven diagnostics.

Chapter 7

Conclusions

This thesis was focusing on depression diagnosis in patients with neurological disorders. The reason for this research was that patients with neurological problems are more at risk of depression due to drug interactions and the treatment process. These patients mostly undergo EEG tests, so this study decided to use the EEG as a tool to diagnose depression in this patient population.

7.1 Key Findings

The technical part of this research focused on the use of PCA and t-SNE for dimensionality reduction, followed by the implementation of a CNN for classifying depression based on EEG signals. The study demonstrated that these techniques, when used together, can effectively handle the complexity of EEG data, leading to a model with an impressive accuracy of 98%. This level of performance suggests that the proposed approach is highly capable of distinguishing between depressed and non-depressed individuals, making it a valuable tool for clinical diagnostics.

In addition to the high classification accuracy, the study emphasized the importance of model interpretability through the use of SHAP analysis. By linking the CNN's predictions back to the original EEG features, SHAP provided a transparent view of how specific features influenced the model's decisions. This interpretability is crucial in a clinical context, where understanding the underlying factors driving a diagnosis is as important as the diagnosis itself. The SHAP analysis identified key EEG features, such as the Delta/Alpha ratio and FFT Theta Max Power, as significant contributors to the diagnosis, reinforcing findings from existing literature.

On the theoretical side, the introduction of the Coalition Game model offered a novel framework for understanding the interactions between different brain regions during EEG data transmission in depression. By treating each brain region as a player in a game, the model provided a structured approach to analysing how these regions work together to influence EEG patterns associated with depression. The theoretical results demonstrated that brain regions play a more significant role in EEG data transmission during depressive states. The model also established a unique equilibrium point, suggesting optimal conditions under which these brain regions contribute to depression diagnosis.

7.2 Contributions and Implications

This thesis contributes to the field of mental health diagnostics by integrating advanced ML techniques with theoretical models, providing both high accuracy in depression diagnosis and a deeper understanding of the underlying neural mechanisms. The use of SHAP for interpretability addresses a critical challenge in AI-driven healthcare, ensuring that the models not only perform well but are also transparent and trustworthy. The Coalition Game model introduces a new way of thinking about brain region interactions, which could have broader implications for understanding and treating neurological conditions beyond depression.

The findings of this study suggest that the combination of technical and theoretical approaches can lead to more effective and interpretable diagnostic tools, which are essential for clinical adoption. The success of the CNN model, combined with the insights from SHAP and game theory, demonstrates the potential of ML and DL to enhance traditional diagnostic methods and offer a more comprehensive approach to understanding and managing depression.

7.3 Limitations and Future Directions

Despite the promising results, this study is not without its limitations. The EEG dataset used, while robust, may not fully represent the diversity of depression manifestations across different populations. Future research should aim to validate these findings using more diverse and larger datasets to ensure the generalizability of the models. Additionally, while SHAP provides valuable post-hoc interpretability, there is a need for developing models that integrate interpretability directly into their structure, potentially leading to even more transparent DL systems.

The theoretical framework introduced by the Coalition Game model, while innovative, requires further empirical validation. Future studies could explore the use of neuroimaging techniques to observe and quantify the interactions between brain regions during depressive episodes, providing more concrete evidence to support the theoretical model.

7.4 Broader Impact

The integration of ML, DL and game theory in this study represents a step forward in the development of AI-driven diagnostic tools for mental health. As the field of healthcare AI continues to evolve, the methods and insights presented in this thesis could serve as a foundation for future innovations. By combining technical precision with theoretical depth, this research contributes to a more holistic approach to mental health diagnostics, with the potential to improve patient outcomes and advance our understanding of neurological disorders.

7.5 Final Thoughts

In conclusion, this thesis has demonstrated that the fusion of ML and DL, interpretability techniques, and game theory can provide powerful tools for diagnosing depression using EEG data. The high accuracy and interpretability of the models developed, along with the theoretical insights gained, highlight the potential of these methods to transform mental health diagnostics. As ML and DL continues to be integrated into healthcare, the approaches outlined in this thesis offer a promising pathway towards more effective, transparent, and theoretically grounded diagnostic tools.

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