



BRNO UNIVERSITY OF TECHNOLOGY

VYSOKÉ UČENÍ TECHNICKÉ V BRNĚ

FACULTY OF INFORMATION TECHNOLOGY

FAKULTA INFORMAČNÍCH TECHNOLOGIÍ

DEPARTMENT OF COMPUTER SYSTEMS

ÚSTAV POČÍTAČOVÝCH SYSTÉMŮ

**ELECTROENCEPHALOGRAM (EEG) AND MACHINE
LEARNING BASED CLASSIFICATION OF DEPRES-
SION: UNVEILING HIDDEN PATTERNS FOR EARLY
DETECTION**

ELEKTROENCEFALOGRAM (EEG) A KLASIFIKACE DEPRESE ZALOŽENÁ NA STROJOVÉM
UČENÍ: ODHALOVÁNÍ SKRYTÝCH VZORCŮ PRO VČASNOU DETEKCI

BACHELOR'S THESIS

BAKALÁŘSKÁ PRÁCE

AUTHOR

AUTOR PRÁCE

ADRIANA JURKECHOVÁ

SUPERVISOR

VEDOUCÍ PRÁCE

MUHAMMAD ASAD ZAHEER

BRNO 2023

Bachelor's Thesis Assignment



153450

Institut: Department of Computer Systems (DCSY)
Student: **Jurkechová Adriana**
Programme: Information Technology
Title: **Electroencephalogram (EEG) and machine learning based classification of depression: unveiling hidden patterns for early detection**
Category: Biocomputing
Academic year: 2023/24

Assignment:

1. Study the neural mechanism of depression and its impact on individuals.
2. Learn feature extraction, feature selection, and classification methods for analyzing EEG (Electroencephalogram) data for depression.
3. Identify challenges and limitations in existing methods for early detection of depression through a literature review.
4. Design a machine learning model for extracting relevant features and accurately classifying depression.
5. Implement and evaluate the model using appropriate datasets and evaluation metrics.
6. Critically analyze results, interpret their significance, and discuss their contribution to depression classification.

Literature:

- Based on Supervisor's Recommendation.

Requirements for the semestral defence:

- Fulfillment of items 1 to 4.

Detailed formal requirements can be found at <https://www.fit.vut.cz/study/theses/>

Supervisor: **Zaheer Muhammad Asad**
Head of Department: Sekanina Lukáš, prof. Ing., Ph.D.
Beginning of work: 1.11.2023
Submission deadline: 16.5.2024
Approval date: 30.10.2023

Abstract

This work deals with the pre-processing EEG signals, extraction of the features and classifying depressed patients and healthy control group. For classification, 5 different machine learning models were considered and evaluated. Findings confirm results from prior research and show the importance of a large, diverse dataset. This work utilises a public dataset.

Abstrakt

Táto práca sa zaoberá predspracovaním EEG signálov, extrakciou vlastností a klasifikáciou pacientov s depresiou a zdravou kontrolnou skupinou. Na klasifikáciu bolo zväžených a ohodnotených 5 modelov strojového učenia. Získané poznatky potvrdzujú výsledky z predchádzajúcich výskumov a poukazujú na dôležitosť veľkého a diverzného datasetu. Táto práca pracuje s verejne dostupným datasetom.

Keywords

EEG, depression, machine learning classification, signal pre-processing, feature extraction, depression classification

Kľúčové slová

EEG, depresia, strojové učenie, predspracovanie signálov, extrácia vlastností, klasifikácia depresie

Reference

JURKECHOVÁ, Adriana. *Electroencephalogram (EEG) and machine learning based classification of depression: unveiling hidden patterns for early detection*. Brno, 2023. Bachelor's thesis. Brno University of Technology, Faculty of Information Technology. Supervisor Muhammad Asad Zaheer

Rozšířený abstrakt

Táto práca sa zameriava na spracovanie EEG signálov, odhaľovanie vzorcov na detekciu depresie a klasifikáciou pacientov s depresiou a zdravých ľudí pomocou elektroencefalografie. Motiváciou je využitie dosiahnutých znalostí o zmenenej funkcionalite mozgu depresívneho človeka pri skorej detekcii, diagnostike a liečení depresívnych porúch.

V práci bol použitý verejne dostupný dataset, ktorý obsahoval EEG záznam 68 subjektov. Kvôli poškodeným a opakujúcim sa súborom som vybrala záznamy 25 ľudí trpiacich depresiou a 25 zdravých jedincov. EEG bolo zaznamenané 19 elektródami (Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, C4, P3, Pz, P4, T3, T4, T5, T6, O1 a O2) so vzorkovacou frekvenciou 256 Hz.

Prvým krokom bolo spracovanie neupravených dát. Na tento účel som použila pásmovú priepusť – filter, ktorý prepúšťa len určité frekvencie nachádzajúce sa v želanom rozsahu. Na extrakciu frekvenčných pásem zo signálov som použila Wavelet transformáciu. Frekvenčné pásma som neskôr využila pri výpočtoch asymetrie mozgových hemisfér, pomeru jednotlivých frekvenčných pásem a ďalších EEG vlastností.

Následne som zvolila modely strojového učenia určené na klasifikáciu. Na vstup som vložila extrahované EEG vlastnosti z minulého kroku a ohodnotila výkon klasifikátorov. Najvyššiu presnosť (93%) dosiahol Algoritmus k-najbližších susedov pri klasifikácii segmentovaných dát.

Moje výsledky sa zhodujú s výsledkami z predchádzajúcich štúdií, ktoré skúmali detekciu depresie na základe EEG vlastností. Hodnoty frekvenčného pásma delta boli u depresívnych pacientov nižšie ako u zdravých ľudí. Naopak theta a beta hodnoty boli u skupiny s depresiou vyššie.

Avšak niektoré hodnoty mali opačnú tendenciu ako v predchádzajúcich výskumoch. Tieto odchylky si vysvetľujem rôznou veľkosťou datasetu. Menší dataset môže odhaliť rozdiely medzi depresívnou a zdravou skupinou, ktoré vo všeobecnosti nie sú známkami depresie. Hodnoty mohli byť taktiež rôzne v dôsledku užívania antidepresív.

V budúcnosti by bolo vhodné zamerať sa na získanie väčšieho a rozmanitejšieho datasetu. Demografické informácie, ako sú vek a pohlavie, môžu tiež napomôcť pri klasifikácii depresie. V neposlednom rade by bolo prínosné skúmať efekt antidepresív, ktoré môžu ovplyvniť namerané hodnoty.

Electroencephalogram (EEG) and machine learning based classification of depression: unveiling hidden patterns for early detection

Declaration

I hereby declare that this Bachelor's thesis was prepared as an original work by the author under the supervision of Mr. Muhammad Asad Zaheer. I have listed all the literary sources, publications and other sources, which were used during the preparation of this thesis.

.....
Adriana Jurkechová
May 16, 2024

Acknowledgements

Firstly, I would like to thank my supervisor Mr. Muhammad Asad Zaheer for all the consultations, pieces of advice and guidance throughout the course of this thesis.

Then I would like to express my gratitude to Ing. Jakub Budiský for his consulting and for being my dearest friend through all times.

Warmest thanks to my boyfriend Bc. Ondřej Kinšt for enduring all kinds of my emotions while writing this thesis, spending a "bžundyliardu" on bubble tea and staying up all night, helping with my awful English grammar.

Finally, I want to thank my family for their support, even though my degree took me longer than it should have, and all the people who influenced me in my life.

Thank you all.

Contents

1	Introduction	2
2	Theoretical introduction	3
2.1	Brain anatomy	3
2.2	Neural system	4
2.3	Depression	5
2.4	Electroencephalography	6
2.5	Brain waves	7
3	Literature review	9
3.1	EEG Frequency Bands	9
3.2	EEG Asymmetry	13
3.3	ERP Components	16
3.4	EEG Complexity Metrics	20
3.5	EEG Connectivity Measures	23
4	Proposed methodology	25
4.1	Data acquisition	26
4.2	Pre-processing	26
4.3	Feature extraction	27
4.4	Classifiers	28
4.5	Evaluation	29
5	Implementation	31
5.1	Dataset	31
5.2	Pre-processing	32
5.3	Feature extraction	32
5.4	T-tests	34
5.5	Classifying problem	34
6	Results	35
6.1	Findings	35
6.2	Model Performance	37
6.3	Limitations	38
7	Conclusion	39
	Bibliography	40

Chapter 1

Introduction

Mental disorders are affecting more and more people every year. They don't only affect the life of the person who suffers from any of them, but also their close family, friends and relationships too. Getting the right help is many times really hard for these people. Mental disorders can be hard to diagnose due to their unique symptoms in every person. Diagnostic and Statistical Manual of Mental Disorders provides the most common symptoms based on which a psychiatrist can diagnose the disorder and prescribe medication. However, it can never really be an objective diagnostics. For this reason someone suffering may not get the help they need and this can be fatal for their life.

Studying brain interference is a relatively new science field. Brain is so complex that even in the beginning of the third millennium we still don't know everything about its functioning. We know which area does muscle movements, which area is connected to our memory, speech and behaviour. We also know that neurons (not just the ones in the brain) process their information by electrical signals but we don't know what the information is. With many screening methods we can record these electrical signals and study them. In EEG studies focused on mental disorders, we're trying to correlate the brain activity with some individual symptoms or classify whether the person is suffering from a mental disorder or not.

The main motivation of this thesis is to find patterns in brain activity for early detection of depression. Thanks to its objectivity it could be a helpful tool for prediction, diagnostic and treatment of depressive disorders. And what's the most important, it can save lives in the future.

Understanding the basics about brain anatomy, how the neural system works, causes of depression and the electroencephalography process, is the first thing to start with. These are explained in Chapter 2. This chapter also explains the brain waves that are central to this work.

Furthermore, literature review follows in Chapter 3. In this chapter, more than 35 newest depression-oriented EEG studies are reviewed and summarized. They are divided into five different categories according to the features they've studied.

Later, in Chapter 4, methods to acquire data, pre-process them, extract features from them and classify them are described. In 4.3, the Wavelet transform used for feature extraction is explained. Machine learning classifiers used in this thesis are mentioned in 4.4 and their evaluation metrics are specified in 4.5.

Finally, implementation of the solution follows in Chapter 5 and last but not least, the results and their significance are discussed in Chapter 6.

Chapter 2

Theoretical introduction

This chapter explains crucial knowledge for understanding brain anatomy, neural system, depression and electroencephalography. Further EEG processes and machine learning terms are described in the following chapter Proposed methodology 4.

2.1 Brain anatomy

The brain is a complex organ which controls thoughts, movements, emotion, breathing and so on. Generally, it regulates every bodily process. The brain is divided into two halves – the right and the left hemispheres. The cerebral hemispheres are separated by a Median longitudinal fissure. Corpus callosum is a bundle of fibers that are connecting the hemispheres in the depth of the fissure. The brain contains blood vessels and nerves, including neurons and glial cells.

Grey and white matter

The brain cut in half shows that there's two different types of matter – grey and white [25]. Grey matter is on the outer side of brain and it is primarily composed of neuron somas. White matter is underneath and is mostly made of axons wrapped in myelin.

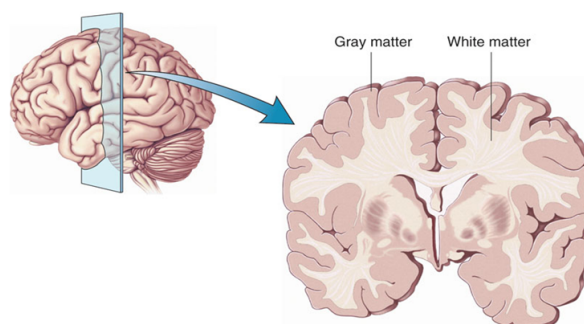


Figure 2.1: The brain cut in half brain showing grey and white matter[6]

Cerebrum, cerebellum, brainstem

The brain can be divided into many different parts depending on the level of detail under discussion. At high level we can say that the brain is divided into the cerebrum, brainstem

and cerebellum [54]. Cerebrum is composed of the right and the left hemispheres. Its functions are speech, emotions, learning, interpretation of touch, vision and hearing, for example [25]. The brainstem connects the cerebrum and the cerebellum to the spinal cord. It performs automatic functions such as breathing, body temperature, sneezing. The cerebellum is located under the cerebrum. It regulates coordination, muscle movements and posture [30].

The lobes of cerebrum

The cerebrum can be divided into six parts - frontal, parietal, temporal, occipital, insular and limbic lobe [30]. The frontal lobe is associated with emotions, speech and judgement [54]. The temporal lobe plays a key role in long-term memory and hearing [25]. Frontal and temporal lobes are divided by the Sylvian fissure. The occipital lobe lies at the back of the brain and is dedicated to visual-related tasks. The parietal lobe processes taste and pain. The central sulcus is dividing the frontal lobe from the parietal lobe, as can be seen in Figure 2.2. The insular and limbic lobes are hidden by the previously mentioned lobes.

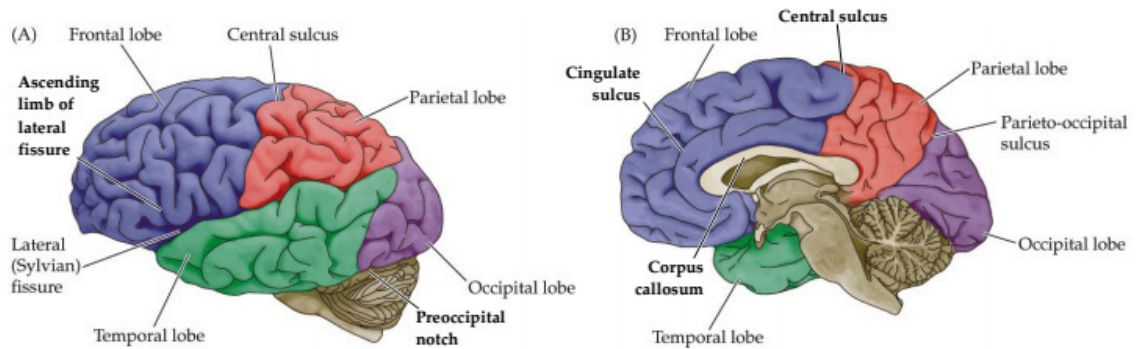


Figure 2.2: Picture showing the lobes of cerebrum[6]

2.2 Neural system

Neural system, or the central nervous system (CNS), consists of nerve cells (neurons) and glia cells (glia) [30]. Neurons help us sense changes in the environment, communicate these changes to other neurons, and command the body's responses to these sensations[6]. Glia contribute to the brain function mainly by insulating, supporting, and nourishing neighbouring neurons.

Neuron

Neuron consists of three main parts: a cell body (soma), dendrites and an axon [30]. The soma is the core of the neuron [6]. It contains genetic information, maintains the neuron's structure, and provides energy to carry out the neuron's work. The axon is a long, thin, cylindrical tube that transmits electrical signal [30]. Many axons are covered in a fatty substance called myelin, which helps the axons conduct an electrical signal. The dendrites help neurons to receive information from other cells [6]. They branch out from the soma, receive and process signals from other neurons.

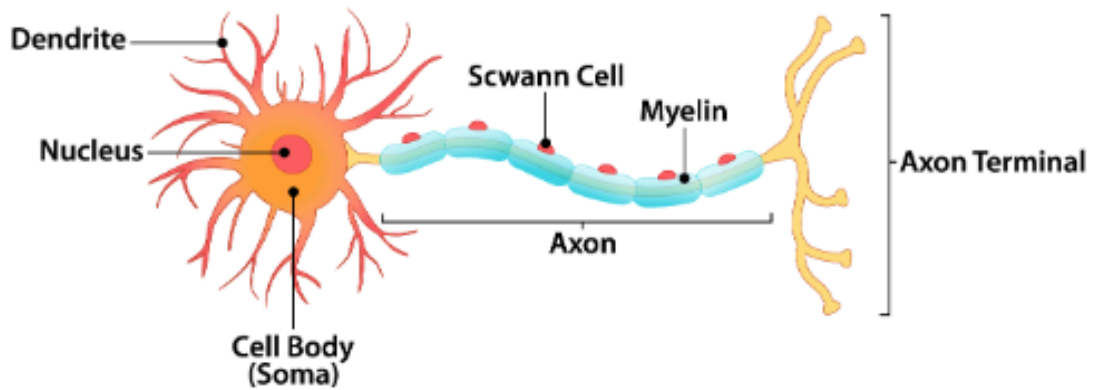


Figure 2.3: Neuron anatomy[6]

2.3 Depression

Depressive disorders, like disruptive major depressive disorder, mood dysregulation disorder, persistent depressive disorder (dysthymia), premenstrual dysphoric disorder and so on, are common mental disorders [4]. They can affect all areas of life including family, school and work. Women are more likely to suffer from depression than men. Approximately 280 million people in the world have depression. A depressed person is twenty times more likely to die by suicide than someone without the disorder. Sadly, more than 800 000 people die due to suicide every year. According DSM-V the common feature of all depressive disorders is the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function. What differs among them are issues of duration, timing, or presumed etiology [4].

Mechanism

Major Depressive Disorder is a familial disorder, and its familiarity mostly or entirely results from genetic influences. Environmental influences specific to an individual are also etiologically significant. Major depression is a complex disorder that does not result from either genetic or environmental influences alone but rather from both. These findings are notably consistent across samples and methods and are likely to be generally applicable [57]. The above-mentioned studies consistently show that the influence of genetic factors is around 30-40%. Non-genetic factors, explaining the remaining 60-70% of variance in susceptibility to MDD, are individual-specific environmental effects[57].

The monoamine-deficiency theory posits that the underlying pathophysiological basis of depression is a depletion of the neurotransmitters serotonin, norepinephrine or dopamine in the central nervous system. Serotonin is the most extensively studied neurotransmitter in depression [24].

Diagnostics

On the internet we can find many self-diagnostic tests that can help determine if one's symptoms require medical treatment. However diagnostics of depression can be done only by a psychiatrist who can prescribe medication. To be diagnosed with depression, symptoms must be present for at least two weeks.

Diagnostics of Major Depressive Disorder

Quoted from Diagnostic and Statistical Manual of Mental Disorders 5th Edition[4]. For additional notes please check the resource.

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either depressed mood or loss of interest or pleasure.
 - 1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful).
 - 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
 - 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
 - 4. Insomnia or hypersomnia nearly every day
 - 5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
 - 6. Fatigue or loss of energy nearly every day.
 - 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
 - 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
 - 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or to another medical condition.
- D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
- E. There has never been a manic episode or a hypomanic episode.

2.4 Electroencephalography

Electroencephalography is a method to observe the electrical activity of brain [26]. EEG can't pick an electrical activity generated by a single neuron [30]. It mostly records neural oscillations generated by large groups of neurons. It is non-invasive, flexible, low cost

and easy to use tool for brain imaging when compared to the other neuroimaging techniques such as the positron emission tomography (PET), magnetoencephalogram (MEG) and functional magnetic resonance imaging (fMRI) [33]. EEG analysis is widely used in studies oriented on detection, classification and prognosis of the Parkinson disease [22], Alzheimer disease [10], emotion state recognition [56] etc.

10-20 system

Electroencephalogram uses the metal electrodes placed over the scalp to record electrical currents [41]. Most used positions to place the electrodes on the scalp follow the International 10-20 system. This system uses anatomical landmarks on the skull - the nasion at the front, the inion at the back and preauricular points in front of ears [30]. 10-20 refers to actual distances between electrodes that are either 10% or 20% of the distance from the front to the back or from the left to the right of the head [32]. This is shown at 2.4.

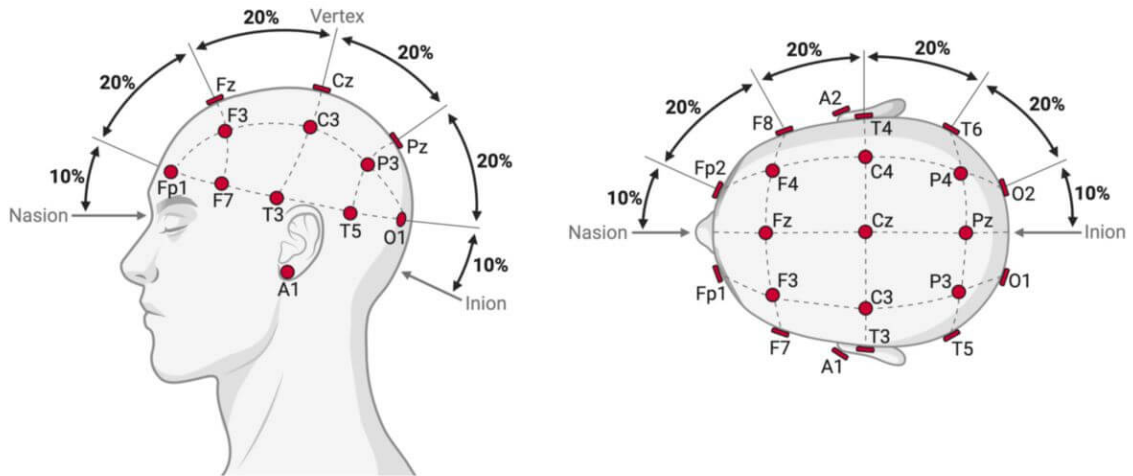


Figure 2.4: Placement layout showing 10% or 20% spacing between electrodes from nasion to inion [51]

International placement system helps researchers to standardize their measurements and reporting [30]. Each electrode has its location labeled with a letter that refers to the area of the brain and a number referring to side of the head - odd numbers for the left side and even for the right side.

2.5 Brain waves

A brain signal consists of various frequencies which were classified into five brain waves - delta, theta, alpha, beta and gamma [33]. These brain waves differ in their frequency ranges and brain state they represent. Their behaviour during 1 second is shown in 2.5.

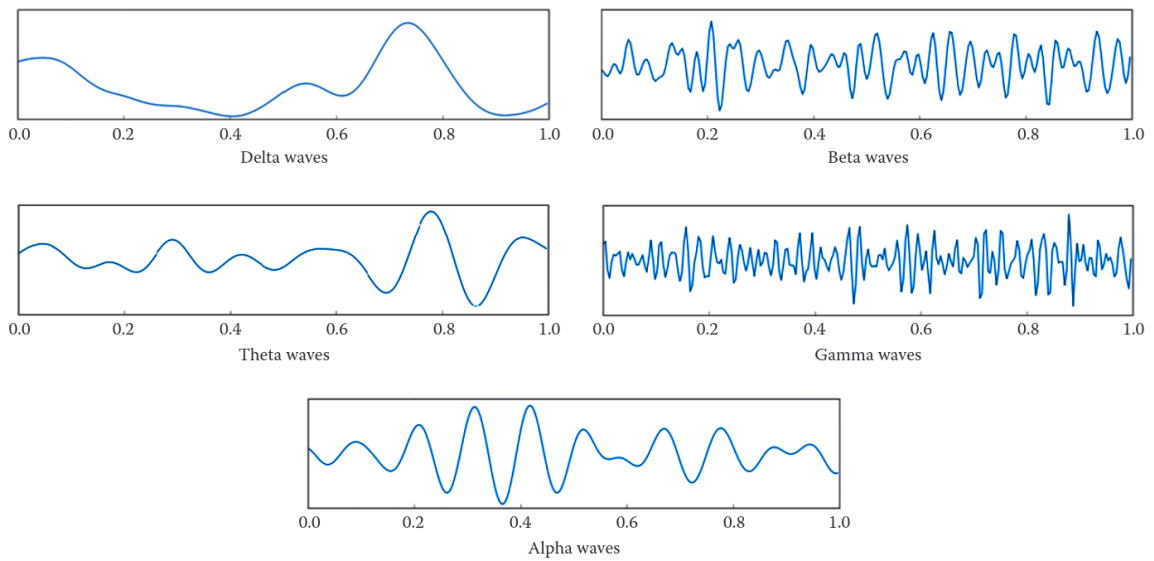


Figure 2.5: Brain waves behaviour [30]

Delta δ

Delta waves are represented within the range of 0.5–4.0 Hz [30]. They have the highest amplitude but the lowest frequency [33]. These waves are mostly associated with deep sleep.

Theta θ

Theta waves are present in the range of 4–8 Hz [30]. They are common for young children [33]. However, they can represent a state of drowsiness, arousal or meditation in adults and older children. They are also present in emotional stress [21].

Alpha α

Alpha waves fall within the frequency range of 8–13 Hz [30]. They are called alpha as they were first discovered brain waves. They occur in relaxed/reflecting mode [21], but are also associated with creativity. Menstrual cycle greatly affects them [33].

Beta β

Beta waves can be found between 14–26 Hz [30]. They are associated with active thinking, problem solving and focusing on the outside world. Low beta occurs in anxious thinking while high beta occurs with low thinking activity [21]. Increased levels can occur in panic [33].

Gamma γ

Gamma waves show in the ranges above 30 Hz [30]. They rarely occur in the human brain. However, they are present during cross-modal processing, when different senses are being combined. Their amplitudes are the lowest but frequency is the highest [33]. Sometimes also referred as fast beta waves.

Chapter 3

Literature review

Biomarkers of Depression

EEG features can provide unbiased information for supporting the MDD diagnosis. It can be a successful and widely used tool, thanks to its cost-effectiveness and availability [23]. A diagnostic biomarker confirms or detects the presence of a disease and identifies an individual with a disease subtype [55]. A biomarker must be specific, meaning accurate in detection of patients who do not have the disease, and sensitive, meaning to be able to identify the presence of the disease in patients who do have the disease. EEG signals already fulfill several criteria to be regarded as a potential biomarker for MDD.

Basis of this chapter is inspired by Greco's systematic review [23]. They identified five EEG biomarker groups: frequency bands power, asymmetry, ERP components, non-linear and functional connectivity measures.

3.1 EEG Frequency Bands

The measured signal by EEG is consisted of brain waves, or neural oscillations [23], that can be observed as different frequencies (see 2.5). Power spectral analysis is the most used analysis method for decomposing and qualifying oscillatory activity of brain waves [5], and through several methods provides information about power, spatial distribution, and frequency change caused by external or internal stimulus. The most common methods are the Wavelet transform method and the Fourier transform method. Both of them create a representation of the signal in the frequency domain, although, the Wavelet method creates representation also in the time domain. The frequency domain was observed by many studies that were trying to find relatable EEG biomarker for detecting depression.

Kristin Koller-Schlauds with colleagues [34] were comparing EEG activity between people with unipolar and bipolar depression. Their study investigated 87 participants, of whom 33 were diagnosed with unipolar, 22 with bipolar and 32 controls without depression (referred to as UD group, BD group and HC group respectively). Patients were diagnosed with a unipolar or bipolar depression according to DSM-IV criteria by the consensus of two psychiatrists. The sample is quite small and subjects were not medication-free. During the procedure, researchers were showing series of sad or happy faces randomized by sex. EEG was recorded from 32 electrodes placed according to 10/20 System. Sampling rate of 500 Hz was used. Koller-Schlauds's team was focused on left (the mean value of F3, F5 and F7 electrodes) and right (the mean value of F4, F6 and F8 electrodes) frontal hemisphere

extracting power for theta (4-7 Hz), alpha-1 (8-10 Hz), and alpha-2 (11-13 Hz) frequency bands for further statistical analysis. For statistical analysis, one-way ANOVA, T-tests and Chi^2 -tests were used. The effect of hemisphere in alpha-1 power was significant for the HC group, but not for the UD group or BD group, meaning alpha-1 power was lower at the left compared to the right side for the HC group. Effect of emotion in theta power was significant for the BD group, but not for UD or HC group, meaning that theta power was lower in the sad condition compared to the happy condition for the BD group. The ROC classification showed the theta score significantly distinguished BD from UD with 85% accuracy, and BD from HC with 74% accuracy. However, UD from HC were not distinguished.

Damborská's research group [16] did a high-density EEG study to observe functional connectivity of the right amygdala in depression. Data were collected from 51 participants - 26 with depression and 25 healthy controls. Depressive participants were diagnosed according to ICD-10 and DSM-V by two board-certified psychiatrists. All patients were medicated. High-density EEG was recorded from 128-channel system with a sampling rate of 1000 Hz during 15 minutes with closed eyes in relaxed position. Five minutes of EEG data were selected and cleaned from components related to ballistocardiogram, saccadic eye movements, and eye blinking. Then recording was down-sampled to 250 Hz. Study used two approaches for evaluation the results - at the population level and at the single-subject level. At both levels, an overall increase in theta (4-8 Hz) and alpha (8-12 Hz) power was found in patients compared to controls. Significantly decreased delta (1-4 Hz) and beta (12-18 Hz) were found in patients compared to controls at the population level. However at the single-subject level, only delta power was significantly decreased comparing patients to controls.

A resting-state EEG study was conducted by Dell'Acqua et al. [18] observing alpha and theta frequency bands in dysphoria. 26 female participants with dysphoria and 38 female healthy controls, both groups in undergraduate age, were included in this study due to the stronger association between alpha asymmetry and depression in females and a high female preponderance of dysphoria. Depressive symptoms were evaluated according to the paper-and-pencil version of the Beck Depression Inventory-II and the module A of the SCID-I. The research team used 32-channel EEG to record data with a sampling frequency of 500 Hz while participants were seated for 4 minutes with open eyes and task to gaze at a fixation cross. Individuals with dysphoria showed increased connectivity between the right frontal and central areas, and between the right temporal and the left occipital areas in the theta band (4-8 Hz). The alpha band (8-12 Hz) in individuals with dysphoria had increased connectivity between right and left prefrontal cortex and between frontal and central-occipital areas bilaterally. These results may be associated with the rumination and excessive self-focus.

Another resting-state EEG data were recorded by Zhang's research group [60], focusing on major depressive disorder analysis and classification. Results of 48 subjects were included in the study, of whom 24 patients with MDD and 24 healthy controls. Patients were diagnosed by a psychiatrist and their PHQ-9 score was greater than or equal to 5. 128-channel sensors recorded data with 250 Hz sampling rate for 5 minutes positioned according to the 10-20 System, while participants were sat in their comfortable, resting position. Later, researchers selected 64 electrodes to ensure the effectiveness of the study and reduce the amount of calculation. To evaluate if there's correlation between specific biomarker and an MDD patient, researchers used 4 classification tools: random forest (RF, numTrees=20), support vector machine (SVM, Linear Kernel), K-nearest neighbors (KNN, K=3) and an

artificial neural network (ANN, activation function is Sigmoid). It was found that theta (4-8 Hz) and alpha2 (10-13 Hz) power is significantly increased in MDD patients.

Resting-state EEG study by research group around Wu [59] was trying to find patterns in the brain of patients with late-life depression. 60 or older patients were examined by an advanced psychiatrist, diagnosed by DSM-IV and evaluated with Hamilton Rating Scale for Depression. Study included results of 41 patients with depression and 41 healthy controls. All participants were right-handed with normal or corrected vision. EEG data were recorded for 3 minutes in a resting state with eyes open and for 3 minutes in a resting state with eyes closed. 22 electrodes were according to the 10-20 system, four of them for horizontal and vertical electrooculograms. Results showed an increased alpha and beta power over patients with late-life depression. There was no significant difference in alpha asymmetry found between the depressed and the healthy subjects. No correlation between the EEG and the severity of depression was found.

Lin et al. [42] studied MDD patients comorbid with anxiety disorders or anxiety symptoms. The primary diagnosis of MDD was based on DSM-V. Beck Depression Inventory-II and Beck Anxiety Inventory results of patients must have been higher than 14 and 8 respectively. The participants filled self-report questionnaires (including demographic data), the BDI-II and the BAI. To record the EEG, 19 electrodes were placed according to the 10-20 system. The participants with eyes closed went through five procedures, each 5 minutes long: baseline, depressive recall, depressive recovery, happiness recall and happiness recovery. During baseline, depressive and happiness recovery, the participants were asked to rest in a sitting position. In recall sections, participants were asked to think of a memory of an event that made them feel depressed in depressive recall and happy in happiness recall. The analysis of EEG power at rest showed lower total delta, lower total theta and higher total beta in the group with MDD in the whole brain area. At F4, healthy group showed higher total alpha. No other significant differences were found.

Kaushik's team [31] compared resting-state and task-based EEG to predict vulnerability to depression in a non-clinical population. Participants were invited to fill in the Perseverative Thinking Questionnaire (PTQ) measuring repetitive negative thinking, Rumination Response Scale (RRS) measuring depressive rumination and the Center for Epidemiologic Studies Depression Scale (CES-D) for the severity of depression. The top and bottom 20 participants were selected based on total score obtained. 10-20 EEG cap with 32 electrodes and 6 loose electrodes was used with a sampling rate of 512 Hz. For resting-state EEG, participants were asked to sit quietly and be relaxed for 5 minutes with closed eyes. The SART procedure was used for task-based EEG. The resting-state EEG data showed increased activity in the right temporal channel, and decreased activity in the left fronto-central and right occipital channels in the more vulnerable participants. Task-based data showed that the less vulnerable participants had increased activity in the central part of the brain and the more vulnerable individuals had increased activity in the right temporal, occipital and parietal regions.

Study	Publish year	Number of subjects	Limitations	Results
Koller-Schlaud et al. [34]	2020	87	Participants on medication. 32 electrodes.	Theta power (4-7 Hz) distinguished group with unipolar depression from the group with bipolar depression with 85% accuracy.
Damborská et al. [16]	2020	51	Small sample size. Participants on medication. 128 electrodes.	Depressed group showed increased theta (4-8 Hz), increased alpha (8-12 Hz) and decreased delta (1-4 Hz). Beta (12-18 Hz) was decreased only at the population level for the depressed.
Dell'Acqua et al. [18]	2021	64	Only young females. 32 electrodes.	In participants with dysphoria, Theta (4-8 Hz) was increased between the right frontal and the central areas and between the right temporal and the left occipital areas. Alpha (8-12 Hz) increased for this group between the right and the left prefrontal cortex and between the frontal and the central-occipital areas bilaterally.
Zhang et al. [60]	2021	48	Small sample size. 64 electrodes.	Theta (4-8 Hz) and alpha2 (10-13 Hz) power is increased in MDD patients.
Wu et al. [59]	2022	85	Participants on medication. 22 electrodes.	Alpha (8-12 Hz) and beta (12-30 Hz) increased in patients with LLD.
Lin et al. [42]	2021	270	Participants on medication. 19 electrodes.	Total delta and theta decreased and total beta increased in the depressed group in the whole brain area. Higher total alpha in the healthy group at F4.
Kaushik et al. [31]	2023	40	Small sample size. 32 electrodes + 6 loose electrodes.	More vulnerable subjects for depression showed increased activity in the right temporal channel, decreased activity in the left fronto-central and the right occipital channels in resting-state EEG. And increased activity in the right temporal, occipital and parietal regions in task-based EEG.

Table 3.1: Article review of changes affected by depression in the frequency domain

3.2 EEG Asymmetry

Human brain consists of two hemispheres, the left and the right, which are not completely symmetrical neither in structural, nor functional aspects [23]. Abnormalities in asymmetry (mostly frontal alpha asymmetry) are associated with MDD in many EEG studies. However, the newer ones claim that frontal alpha asymmetry isn't empirically grounded as an EEG biomarker for depression detection.

Lateral asymmetry index

„A laterality index is computed by dividing the differences between left and right hemispheres by their sum

$$A = (P_{left} - P_{right}) / (P_{left} + P_{right})$$

where P_{left} and P_{right} are relative power of the corresponding frequency band at the appropriate brain region.“ [29] A positive result can be understood as the dominant brain activity is in the left hemisphere, a negative result means that the dominance of brain activity is in the right hemisphere. A zero indicates that both hemispheres are equivalent in brain activity.

Koller-Schlaud's study [34] mentioned before found pattern in alpha asymmetry too. For post-hoc analysis they used Bonferroni-corrected t-tests, analyzed Pearson correlations for the difference scores with BDI-II and HDRS-17-scores. A significant difference was showed in the asymmetry between patients with unipolar depression and healthy controls. No significant difference was found between healthy controls and patients with bipolar depression. In Face-Affect scores the researchers were able to find pattern in alpha-1 asymmetry to distinguished depressed patients from healthy controls with accuracy of 0.69. The alpha asymmetry was decreasing. With combination with theta power, unipolar and bipolar depression could be classified with an accuracy of 0.83.

Kustubayeva's team [36] was looking into asymmetry in decision-making task with negative and positive feedback with 120 participant, of whose 60 have Major Depression. Participants were medication-free, right-handed with normal or corrected vision. All participants filled the Inventory of Depressive Symptomatology I. Then they were asked to complete Hamilton Rating Scale for Depression and interviewed by psychologist and psychiatrist. 30 trials had been done by participants on the decision-making task. After every 10 trials researchers obtained mood and confidence ratings. For decision-making task the „search-and-rescue“ task was used. EEG was recorded by 17 electrodes posited by 10-20 system and two additional electrodes for vertical and horizontal electrooculogram recording. Research team was able to define that left lateralization (i.e., higher alpha power in the right hemisphere) was showed in healthy patients and otherwise in depressed patients, or with minimal lateralization. The strong difference in healthy and depressed participants by asymmetry was found in parietal alpha early in decision-making.

Mahato et al. [46] found that depression affects temporal-parietal brain region. Study was done on 24 depressed participants diagnosed by DSM-V with severity of depression rated by HAM-D score and 20 healthy subjects. EEG was recorded using 128 electrodes placed using the 10-5 system. Recording took 15 minutes in resting state with sampling frequency 512 Hz. EEG data were selected for 6 channels in frontal and parietal lobes. For classification they used Support Vector Machine (SVM) classifier with polynomial, Gaussian and Sigmoid kernel functions. Gamma2 power was increased in patients with depression

and gamma1 and gamma2 asymmetry was ranked on top 2 biomarkers to detect depression. Accuracy for detection of depression was 96.02% and for severity scaling 79.19%.

Jang et al. [28] compared frontal alpha asymmetry among schizophrenia and MDD patients. 54 participants were recruited, 20 of them with MDD. They were diagnosed by DSM-IV and Hamilton rating scale. All of them had normal vision and hearing. 62 electrodes were placed by 10-20 system and recorded EEG with sampling rate of 1000 Hz. EEG recording took 5 minutes with open eyes and 5 minutes with closed eyes. Researchers found significant difference in F4-F3 between schizophrenia patients and healthy controls, but no difference in F4-F3 was found in MDD patients. Results are suggesting that frontal alpha asymmetry can't work as biomarker to differentiate between patients with MDD and healthy controls.

Kolodziej et al [35] analyzed five independent studies. 388 medication-free participants in total were included in the analyses. Participants were diagnosed based on Beck Depression Inventory I and II and Patient Health Questionnaire-9. Researchers did channel-pair analyses, cluster-based analyses, cluster-based analyses on standardized data, source level analyses and analyses on aggregated data. In channel-pair analyses only 3 out of 60 analyses gave significant results. However, single channel analyses are not good approach according to Kolodziej. In cluster-based analyses, only one significant result of 30 was found. However, after age, gender and education controlling the significant result is no longer present probably due lower education in depressed group. Conclusion of their research is that FAA as a biomarker of depression is not sufficiently empirically grounded.

Lin et al. [42] study previously mentioned in 3.1 didn't find significant differences at the frontal and parietal alpha asymmetry. The results revealed 58 patients (42.96%) with FAA and 77 (57.04%) without FAA among the participants in the MDD group, 42 participants (31.11%) with FAA, 92 (68.15%) without FAA among the participants in the HC group. There were 62 patients (45.93%) with PAA and 73 (54.07%) without PAA in the MDD group, and 71 participants (53.79%) with PAA, 61 (46.21%) without PAA in the HC group. Conclusion stated that possible reason why FAA and PAA were not confirmed as a biomarker for detection of depression, could be that this study was focused on participants diagnosed with MDD comorbid with anxiety and not MDD alone.

Roh et al. [52] compared frontal alpha asymmetry in MDD patients with suicidal ideation with FAA in healthy controls. The study recruited 44 MDD patients, 23 MDD patients with suicidal ideation and 60 healthy controls. Patients were diagnosed based on DSM-IV and severity was determined by the Hamilton Rating Scale for Depression (HAM-D). Suicidal ideation had to be experienced during the ongoing depressive episode. All participant were right-handed. 62 electrodes were places according to 10-20 system and EEG was recorded in resting state for 3 minutes with eyes closed and 3 minuets for eyes open. MDD group had higher FAA than healthy group which means that patients with MDD have more activity at the front of right hemisphere. However, patients with MDD without suicidal ideation had significantly higher FAA that patients with suicidal ideation in F7-F8. This means that patients with suicidal ideation have more left frontal activity.

Resting-state EEG study by research group around Wu [59] was trying to find patterns in brain of patients with late-life depression. 60 or older patients were examined advanced psychiatrist, diagnosed by DSM-IV and evaluated with Hamilton Rating Scale for Depression. Study included results of 41 patients with depression and 41 healthy controls. All participants were right-handed with normal or corrected vision. EEG data were recorded for 3 minutes with in resting state with eyes open and for 3 minutes in resting state with eyes closed. 22 electrodes were placed by 10-20 system, four of them for horizontal and ver-

tical electrooculograms. Results showed increased alpha and beta power over patients with late-life depression. There was no significant difference in alpha asymmetry found between depressed and healthy subjects. No correlation between EEG and severity of depression was found.

Study	Publish year	Number of subjects	Limitations	Results
Koller-Schlaud et al. [34]	2020	87	Participants on medication. 32 electrodes.	Alpha-1 asymmetry decreasing.
Kustubayeva et al. [36]	2020	120	17 electrodes 2 additional electrodes for EOG. Resting FAA varies with phase of the menstrual cycle.	Parietal alpha asymmetry decreasing in depressed participants. Alpha asymmetry increasing in healthy participants.
Mahato et al. [46]	2020	44	Small sample size. 128 electrodes.	Higher gamma1 and gamma2 asymmetry in temporal region.
Jang et al. [28]	2020	54	Small sample size No information about medication. 62 electrodes.	No significant differences in FAA between patients with MDD and healthy controls.
Kolodziej et al. [35]	2021	388	64 electrodes.	FAA as a biomarker of DD is not sufficiently empirically grounded.
Lin et al. [42]	2021	270	Participants on medication. 19 electrodes.	The FAA and PAA (parietal) indices between the two groups showed no significant differences.
Roh et al. [52]	2020	127	Small sample size of MDD patients with suicidal idealization. Participants on medication. 62 electrodes.	FAA was higher (increased alpha power in the left frontal region) in the MDD group than in the HC group. The FAA was lower (reduced alpha power in the left frontal region) in MDD patients with suicidal idealization than in MDD patients without suicidal idealization. Our results suggest that suicidal idealization is a clinically important moderator of frontal alpha asymmetry in patients with MDD.
Wu et al. [59]	2022	85	Participants on medication. 22 electrodes.	No significant differences in frontal alpha asymmetry.

Table 3.2: Article review of changes affected by depression in hemispheric asymmetry

3.3 ERP Components

An event-related potential (ERP) is change in EEG voltage amplitude due to a sensory or cognitive event. An ERP component is a specific part of the more complex ERP waveform. ERP components can be classified by timing, polarity, scalp distribution, sensitivity to stimuli type and task manipulation [23]. For example N100 is ERP component that occurred 100 milliseconds from the stimulus onset. The N in N100 indicates Negative deflection. P would be used for Positive deflection.

Component name	Description
Mismatch Negativity (MMN)	Arises in response to an odd stimulus in a sequence of standard ones
Late Positive Component (LPC)	Differs new or previously experienced stimulus
Contingent Negative Variation (CNV)	Slow negative potential occurring prior to the onset of a stimulus
Error-Related Negativity (ERN)	Consists in a negative deflection occurring approximately 80-150 ms after an individual responds incorrectly during a task or responds when a response should be withheld
Correct-Related Negativity (CRN)	Same latency as ERN, is usually smaller and occurs after the individual correctly responds to a trial task
Feedback error-related negativity (FRN)	A variant of the ERN, occurs approximately 250 ms after an individual receives external feedback indicating that the performance is worse than expected

Table 3.3: ERP components

Dell’Acqua et al. [19] recruited 117 participants, of those 75 with current depressive disorder and 42 healthy subjects. Depressed group scored equal or greater than 13 on the Beck Depression Inventory-II and was diagnosed according to DSM-V. Healthy controls scored less than 13 on BDI-II. EEG data were collected by 32-channel system with a sampling rate of 1000 Hz. During EEG recording participants were viewing 60 color pictures; 30 pleasant images and 30 neutral images. The cluster-based analysis showed a significant larger delta power on positive centro-parietal cluster on event-related delta power in healthy group. Logistic regression showed that smaller residual LPP and residual delta power were related to increased probability of depression disorder.

Investigation of ERP in pediatric MDD was done by Dell’Acqua et al. [17]. 63 early adolescents (age 11-14) were part of this study that recorded EEG data with 34 electrodes placed according the 10-20 system. 29 participants had been diagnosed with MDD and 34 participants were in healthy control group. Patients were asked to fill the Children’s Depression Inventory(CDI) and diagnosed according to DSM-IV. Study found that the ERN was larger (more negative) than the CRN across the whole sample. The ERN_{resid}

was more positive in depressed group. Study found several time-frequency differences between error and correct trials; greater delta power, greater theta power, decreased alpha power, decreased beta power to error trials relative to correct trials. Error-related theta was reduced more in depressed than healthy controls and error-related beta power was greater in MDD group. There were no significant error-related delta and error-related alpha differences between depressed and healthy group.

Miao Li et al. [37] tried to cover deficit in facial emotion intensity recognition. 62 subjects (of them 31 depressed) were asked to complete the emotion intensity recognition task while their EEG was recorded using 64 channel system placed according to 10-20 system. Patients were diagnosed according to DSM-IV and had 18-65 years of age. The severity of depression was given by the Hamilton Depression Rating Scale. The emotion intensity recognition task (EIRT) consisted of 6 face pictures for each of basic emotions (sadness, disgust, happiness, surprise, anger, fear) and 3 neutral faces. Participants were asked to assess the intensity of emotion presented by picture of face on scale from 0 (no emotion) to 5 (very strong emotion). The study aimed on some ERP components in time-window: P100 (80-130 ms), N170 (130-200 ms), P200 (150-300 ms) and P300 (300-600 ms). The Mann-Whitney U-test and chi-square test were used for demographic analysis. For EEG data analysis, the ANOVA, Spearman correlation coefficient and Bonferroni corrections were used. It was found that P100 and P300 is higher in depressed group. They also had higher N170 amplitude in the occipital lobe than in the temporal and the central lobe, and P200 amplitude was higher in the central and temporal lobe.

Above mentioned 3.2 study of Kustubayeva et al. [36] was also analysing ERP components in Decision-Making Task with Negative and Positive Feedback. Study measured two ERP components in time-window: P300 (200-500 ms), P100 (50-150 ms). ERP power spectrum for alpha was calculated during 200-500ms after each event. Parietal ERP amplitudes during decision making were significantly larger in healthy group. Higher response amplitude in the frontal and central areas.

Pengchen Li's reaserch group [38] was interested in depressive states in healthy subjects. For study they recruited 43 participants who had not been diagnosed with depression. Their depressive states were evaluated by the BDI-II with maximum score of 20. Participants were rating the pleasant and the unpleasant images on scale from 1 (pleasant) to 9 (unpleasant). For recording they used 21 electrodes placed in 10-20 system with a sampling rate of 500 Hz. There were no significant differences in the latencies of P100 and P200. The LPP peaked at around 500 ms for less depressive state group. LPP of this group also showed larger responses to the negative and positive images and relatively small response to the neutral images. High depressive state group had slower response in LPP and peaked at around 600 ms. ANOVA¹ showed significant differences at around 250 ms to 380 ms for negative images, at around 180 ms to 300 ms for neutral images and at around 160 ms to 380 ms for positive images. From 100 to 200 ms, the differences were in the frontal region after stimulus caused by negative images and in the central and parietal region for stimulus caused by negative and positive images. After application of ERS² they observed increase in the delta (0-4 Hz) and theta (5-8 Hz) and decrease in the alpha band (8-12 Hz). The more depressed group shows a stronger decrease in the alpha amplitude starting at around 250 ms. In the delta and theta amplitudes, the low depressive group showed a stronger increase.

¹Analysis of variance

²Event-related changes in the power spectrum

Liu et al. [43] looked at correlations between ERP and self-referential processing and their ability to predict depressive symptoms in late childhood. For study, researchers recruited 65 children from age 9 to 12 and their caregivers. Children first watched a three-minute sad movie clip to introduce dysphoric mood, next they completed an SRET while EEG was being recorded. For that, the researchers used 64-channel net with a sampling rate of 250 Hz. SRET consisted of 60 personal trait words (30 positive, 30 negative). In the meantime, caregivers filled a parent-report version of Child Depression Inventory which consisted of 26 items for assessing depressive symptoms (The item „I want to kill myself“ was excluded). The higher positive SRET score and greater LPP in processing positive words were associated with lower depressive symptoms.

Chen et al. [13] recruited 52 participants to make aesthetic judgements on faces and landscapes. 25 of them were diagnosed with depression according to DSM-V. All participants filled Beck Depression Inventory before the experiment. For the main experiment, 66 pictures were selected (22 for each category; „beautiful“, „ugly“, neutral face pictures) and 22 pictures for landscape experiment. During EEG recording, the researchers presented picture for 2 s and the participants were asked to evaluate whether the picture is beautiful, ugly or neutral. EEG was recorded with 32 electrodes placed according 10-20 system with a sampling frequency of 1000 Hz. Researchers performed ANOVA on response bias that showed a stronger reaction bias towards ugly face in depressive group. The depressive group showed longer ERP latencies than the healthy group. In face experiment, the amplitude of N170 was more negative in depressed towards ugly and neutral face in occipital region but no towards beautiful face. For ugly faces, there was also decrease N200 negativity in depressed.

Jang et al. [27] observed 31 drug-naïve participants diagnosed with MDD and 31 healthy controls. The patients were diagnosed according to DSM-V. All participants filled Beck Depression Inventory and patients filled also the Hamilton Depression and Anxiety Rating Scale. For EEG recording, 62-channel head cap was used. The electrodes were placed by 10-20 system. They recorded resting-state EEG (REEG), the loudness dependence of auditory evoked potentials (LDAEP) and P300. For classification, researchers used linear discriminant analysis (LDA) and support vector machine (SVM) with t-test based feature selection. Depressed group showed higher P300 and lower LDAEPs. They also showed decreased absolute power in high alpha and delta bands in resting state EEG. For multiple paradigms, study was able to classify depression with 94.52% (P300 amplitudes and LDAEP features).

Study	Publish year	Number of subjects	Limitations	Results
Dell'Acqua et al. [19]	2022	117	Mostly female participants. Participants on medication. 32 electrodes.	Smaller LPP_{resid} and $delta_{resid}$ power were related to increased probability of depression disorder.
Dell'Acqua et al. [17]	2023	63	Mostly female participants. 34 electrodes.	MDD group showed a smaller (i.e., more positive) ERN. MDD group had reduced error-related theta. MDD group had greater error-related beta power.
Miao Li et al. [37]	2023	62	Small sample size. Larger age range. Participants on medication. 64 electrodes.	P100 higher in depressed. N170 amplitude in the occipital lobe higher than in the temporal lobe and the central lobe. P200 amplitude higher in the central lobe and temporal lobe. Higher P300.
Kustubayeva et al. [36]	2020	120	17 electrodes 2 additional electrodes for EOG.	Parietal ERP amplitudes during decision making were significantly larger in healthy group. Higher response amplitude in the frontal and central areas.
Pengcheng Li et al. [38]	2023	43	Mostly male participants. Small sample size. 21 electrodes.	The high depressive group showed a stronger decrease in the alpha amplitude. The low depressive group showed a stronger increase in the delta and theta amplitudes.
Liu et al. [43]	2023	65	64 electrodes.	The higher positive SRET score and greater LPP in processing positive words were associated with lower depressive symptoms.
Chen et al. [13]	2023	52	Small sample size. 32 electrodes.	N170 more negative in depressed towards ugly and neutral face in occipital region. Decreased N200 negativity in depressed for ugly faces.
Jang et al. [27]	2023	62	Small sample size. 62 electrodes.	Depressed group showed higher P300 and lower LDAEPs. Decreased absolute power in high alpha and delta bands in resting state EEG.

Table 3.4: Article review of changes affected by depression in ERP components

3.4 EEG Complexity Metrics

It is hard to understand such a complex system as the human brain by decomposing it into simpler components [23]. Because of this problem, we use some techniques and concepts from Nonlinear Dynamical Systems theory. Predicting system's behaviour in future depends on the amount of information generated by this system [23]. For this phenomenon exists term entropy in information theory. Some of entropy measures are the Approximate Entropy (ApEn) and the Sample Entropy (SampEn). The Lempel-Ziv Complexity (LZC), the analysis of fractal dimension (FD), Katz fractal dimension (KFD) and Higuchi's fractal dimension (HFD) are closely related to entropy.

Large data pool was recorded by Brian Lord and his colleague John J. B. Allen [45]. 306 subjects participated in their study, with 163 non-depressed and 143 with history of depression. Of depressed group, 62 had a current major depressive episode, and 81 were previously depressed but currently didn't have a depressive episode. For recording they used 64-channel system with electrodes placement according to 10-20 system. Data were filtered by bandpass filter at 0.5-50 Hz and epoched to five-second epochs. Depressed group showed lower HFD in PO3 and PO4 with eyes closed and lower SampEn in FC4 with eyes open. Previously depressed group showed slight increases only with open eyes in some frontal leads. Women had much higher complexity scores than men in frontal and occipital brain locations.

Akbari's group [3] were investigating recording from 22 healthy controls and 22 depressed participants. Only 2 channels were used to obtain EEG data (bipolar recording). EEG was recorded with eyes closed and eyes open for 10 minutes. Sampling rate was 256 Hz. Records were divided into 2 s segments. Features were extracted by two methods - empirical wavelet transform and discrete wavelet transform. For classification, they used support vector machine (SVM) and K nearest neighbour (KNN). The mean of centered correntropy was more significant in depression rhythms and centered correntropy was lower in depressed. The std value of the extracted features in depressed was lesser for both hemispheres.

21 depressed participants and 20 healthy participants were examined by Čukić's research group [14]. All depressed patients were medicated and both groups were right-handed. For EEG recording was used 10-20 system placement of 19 electrodes. Subjects were sitting in the comfortable chair with closed eyes. Recorded data were epoched to 5 s long segments and for every person and every electrode 3 artifact-free epochs were selected. For classification of depressed patients, researchers calculated Higuchi's Fractal Dimension and Sample Entropy. HFD in depressed patients were higher than in healthy controls. SampEn was also higher in depressed group.

Zhao and colleagues [61] focused on frontal alpha complexity. 69 depressed and 14 healthy subjects participated in this study. Patients were diagnosed according to International Classification of Diseases (IDC-10) and evaluated according Hamilton Depression Rating Scale. Based on depression severity, three groups of depressed patients were formed - patients in nondepressive state, patients with mild depression and patients with confirmed depression. EEG was recorded from Fp1, Fp2 and Fz electrodes with sampling frequency of 1000 Hz. In data pre-processing signals were resampled to 200 Hz and artifact were removed by wavelet threshold filter. Alpha signal was extracted by Butterworth filter. Entropy was significantly higher in depressed groups than healthy control group but wasn't significant enough between depressed groups. Frontal alpha complexity was increased in patients with depression and was increasing as the depression deepens.

Cukic et al. 2019 [15] did a nonlinear analysis in episode and remission phase of recurrent depression. Dataset consisted of 22 participants with recurrent depression (11 in remission, 11 in the episode) and 20 healthy participants. Patients with depression were diagnosed according to ICD-10 scale. All of them were on medications. EEG was recorded with 19 electrodes placed according to 10-20 system in the resting state. Sampling rate was 1 kHz. HFD and SampEn were lowest in healthy controls. Patients with depression in remission had the highest HFD and SampEn. ANOVA showed that SampEn can differentiate between all three groups - healthy, in episode, in remission.

Minkowski et al. [48] extracted EEG features to identify depression and anxiety. Study used public dataset of 119 subjects. 45 diagnosed with depression and 64 healthy controls. Participants have been asked to fill Beck's Depression Inventory to assess depression severity and the Spielberger Trait Anxiety Inventory to evaluate anxiety. All depressed participants also met the anxiety criteria. For EEG recording was used 66 electrodes placed according to 10-20 system with a sampling frequency of 500 Hz. For each frequency band, 6 features was extracted. ANOVA II showed that CD in delta band is lower in healthy participants between the hemispheres. CD in theta band is lower in depressed group in prefrontal cortex. LE is lower in healthy participants between hemispheres. ApEn is lower in healthy controls in prefrontal cortex.

Zhao et al. 2022 [62] observed features of subclinical depression. 40 female students with subclinical depression and 38 healthy controls were participating in this study. All participants were right-handed. EEG was recorded with eyes closed and eyes open for 4 minutes through 32 electrodes placed according to 10/10 placement system. To preprocess data, researchers applied 0.5-45 Hz bandpass filter and 50 Hz notch filter. Data were then epoched to 2 s long segments. Omega complexity was decreased in depressed in the theta, beta-2 and gamma bands and may be associated with attention deficits.

Study	Publish year	Number of subjects	Limitations and specifics	Results
Lord et al. [45]	2023	306	Young age range. 64 electrodes.	Lower HFD in PO3, PO4 in depressed. Lower SampEn in FC4 in depressed.
Akbari et al. [3]	2021	44	Small sample size. Bipolar montage.	Lower centered correntropy in depressed.
Čukić et al. [14]	2020	41	Participants on medication. 19 electrodes.	Higher HFD in depressed. Higher SampEn in depressed.
Zhao et al. [61]	2020	83	6 electrodes.	Higher ApEn, SEn and LZC in depressed.
Chen et al. [12]	2022	61	No information about medication. 3 electrodes.	Higher sample entropy (SEn) and fuzzy entropy (FEn) in alpha band in depressed.
Čukić et al. [15]	2019	42	Participants on medication. 19 electrodes.	Higher HFD and SampEn in depressed.
Minkowski et al. [48]	2021	119	66 electrodes.	CD in delta band is lower in healthy controls. CD in theta is lower in depressed in prefrontal cortex. ApEn in alpha band is lower in healthy group.
Zhao et al. 2022 [62]	2022	78	32 electrodes.	Global omega complexity reduction in the beta-2 and gamma bands in depressed.

Table 3.5: Article review of changes affected by depression in complexity metrics

3.5 EEG Connectivity Measures

Brain activity is can also be viewed through the interactions between different brain regions [23]. A graphic representation of a complex systems contains node and edges in mathematics. In brain studies, we can represent nodes as brain regions and edges as connections among them. The connectivity can be structural and functional. Structural connectivity is physical connections between individual brain regions. Functional connectivity can be defined as statistical dependencies among remote neurophysiological events [23].

Liu et al. [44] researched functional connectivity recorded on ongoing EEG during music perception. 20 patients with MDD and 19 healthy controls participated. EEG was recorded with 64 electrodes placed in 10-20 system. Significant connections were found in delta and beta bands in right central areas and between right temporal and left parietal regions. The connectivity in depressed was decreased in delta band and increased in beta band.

Li's research group [39] studied recognition of mild depression based on functional connectivity. 51 participants were recruited, 24 of them depressed. 128-channel sensor was used to record EEG data with sampling frequency of 250 Hz. The alpha was significantly higher in mild depressed group. In the parietal-occipital region, mild depressed showed lower clustering coefficient in beta band. Results were mainly found in right hemisphere.

Study of Damborská et al. [16] found altered functional connectivity of the right amygdala. 26 patients with depression and 25 healthy subjects were monitored with 128-channel system with sampling rate of 1 kHz. The global and local efficiency, clustering coefficient, outflow and strength were significantly higher in depressed subjects. The global efficiency was higher in depressed, but showed no correlation with depression. However decreased with increasing medication intake.

Dell'Acqua et al. [18] did a resting-state EEG study. Only female participants were recruited in this study. 26 with dysphoria and 38 healthy subjects were monitored by 32-channel sensor. Patients with dysphoria showed increased connectivity in theta band between right frontal and central areas and right temporal and left occipital areas. Increased connectivity was also found in alpha band between right and left prefrontal cortex and between frontal and central-occipital areas.

Lian's study [40] was focused on spatial functional connectivity during sleep. 51 participants were recruited. 25 patients with depression were diagnosed by psychiatrists based on DSM-IV. Hamilton Depression Scale and Self-Rating Depression Scale were used to rate depression in all participants. Data collecting lasted 9-10 hours while all participants underwent polysomnography. 16 electrodes were placed by 10-20 system. Study used several support vector machine (SVM) classifiers with linear, polynomial and Gaussian kernel functions. A leave-one-out cross-validation procedure was used for binary classification between normal controls and depressed participants. Significant differences were found in WPLI between controls and patients with depression. There were higher average cortical inter-hemispheric functional connectivity intensities in patients. Also lower intra-hemispheric FC intensities were found in patients. The cortical FC was increased in depressed participants. Discriminative connections were mostly found in the delta band between the left and right temporal lobes, in alpha and theta band in frontal and temporal lobes.

Remitted depressed patients participated in Benschop's study [7]. In total 37 subjects, 20 of them with remitted depression, were recruited to record EEG data with 128-channel sensor. Higher default mode network (DMN) EEG connectivity was found in remitted depressed subjects. Thanks to this finding, EEG DMN connectivity may be used to identify potential risk of depression.

Study	Publish year	Number of subjects	Limitations and specifics	Results
Liu et al. [44]	2020	39	Small sample size. 64 electrodes.	Decreased connectivity pattern in delta band in depressed. Increased connectivity pattern in beta band in depressed.
Li et al. [39]	2020	51	Small sample size. 128 electrodes.	Larger characteristic path length and lower clustering coefficient in beta band in depressed.
Damborská et al. [16]	2020	51	Small sample size. Participants on medication. 128 electrodes.	Increased functional connectivity in the right amygdala in depressed.
Dell'Acqua et al. [18]	2021	64	Only young females. 32 electrodes.	Increased connectivity in theta and alpha bands between frontal and occipital areas in depressed.
Lian et al. [40]	2021	51	Small sample size. 16 electrodes.	Increased the cortical FC in depressed.
Benschop et al. [7]	2021	37	Small sample size. Only remitted patients. 128 electrodes.	Higher DMN connectivity in depressed.

Table 3.6: Article review of changes affected by depression in functional connectivity measures

Chapter 4

Proposed methodology

To be able to detect or predict the major depressive disorder from EEG brain recordings, we need to process them first. Recorded EEG is a raw signal from all the channels we used for the recording. Raw signal must go through pre-processing which includes removing saccadic eye movement and eye blinking. The clean EEG signal is then transformed and features are extracted. This process is represented by the diagram in figure 4.1. Then the data are split into training and testing datasets. Training dataset is used as an input for the machine learning model. After training the model, the testing dataset is used to evaluate the performance of the model. This process is drafted in figure 4.2.



Figure 4.1: Pipeline of data processing

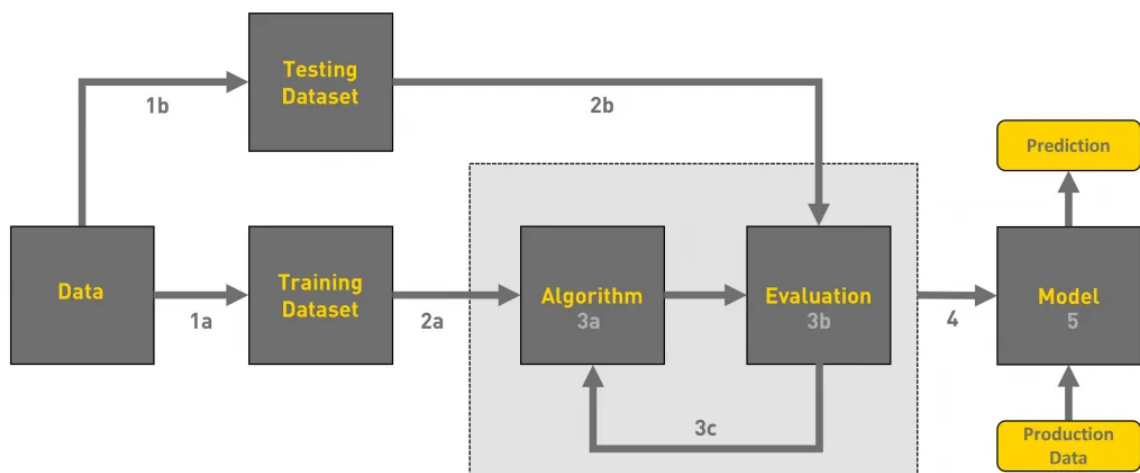


Figure 4.2: Machine learning workflow [50]

4.1 Data acquisition

Electroencephalogram is safe and painless [47]. The process of EEG signals acquisition starts with a technician who measures the patient's head and marks where to attach the electrodes. Then electrodes are attached to the patient's scalp and connected to an amplifier which amplifies the brain waves and records the EEG. The patient is asked to relax in comfortable position with their eyes closed or open and EEG signals are recorded. After recording, the electrodes are removed and patient should be able to return to their typical routine.

4.2 Pre-processing

EEG artifacts

EEG artifacts are signals that invaded the brain signal during its recording [20]. Artifacts can be extra-physiologic (created by external environment or equipment) and physiologic (created by the body from sources other than the brain).

Extra-physiologic artifacts are problems that should be avoided as much as possible. They are mostly human errors. Wrong technical preparation can cause the 60-Hz alternating artifact, when there's no sufficient grounding of the electrodes on patient's head. Electrode artifacts are also caused by an incorrect placement of an electrode on the patient's head. These mistakes change the impedance. Artifacts can be generated by the movements of other persons around the patient and by the interference of other equipment. Radio, cell phone, television high-frequency radiations can overload EEG amplifiers and in this case the EEG signal cannot be recorded.

Physiologic artifacts cannot be avoided as they are generated by the patient's body and are essential to living. Electrooculography (EOG) is an artifact caused by eye movements, electrocardiogram (EKG or ECG) is caused by the interference of the heart beats, skin artifacts caused by sweat and hairy head, glossokinetic artifact caused by the movement of the tongue and artifact signal generated by the movement of muscles - electromyogram (EMG).

Artifact removal

Artifact removal should begin prior to the start of recording. Extra-physiologic artifacts should be avoided by proper placement of electrode cap on the patient's head and a suitable environment for acquisition. Physiologic artifacts are removed in pre-processing step. Probably the most common way to clean raw EEG data is the application of linear filtering. High-pass linear filtering removes EOG artifacts and low-pass linear filtering removes most of the EMG artifacts. Linear adaptive filter has two major processes - filtering and an adaptive process. In the filtering process, FIR filters are mostly used. Quantum neural network-based filter, spatial filter and Cauchy-based filter can be also used.

ICA artifacts removal

Independent Component Analysis (ICA) is used to remove muscle, eye blink, or eye movement artifacts without removing the affected data portions. An experienced researcher can identify components containing such artifacts. I decided not to use ICA as I am not expe-

rienced enough to identify whether its artifact or not. In figure 4.3 are shown components of Independent Component Analysis and ICA006 represent eye blink artifact.

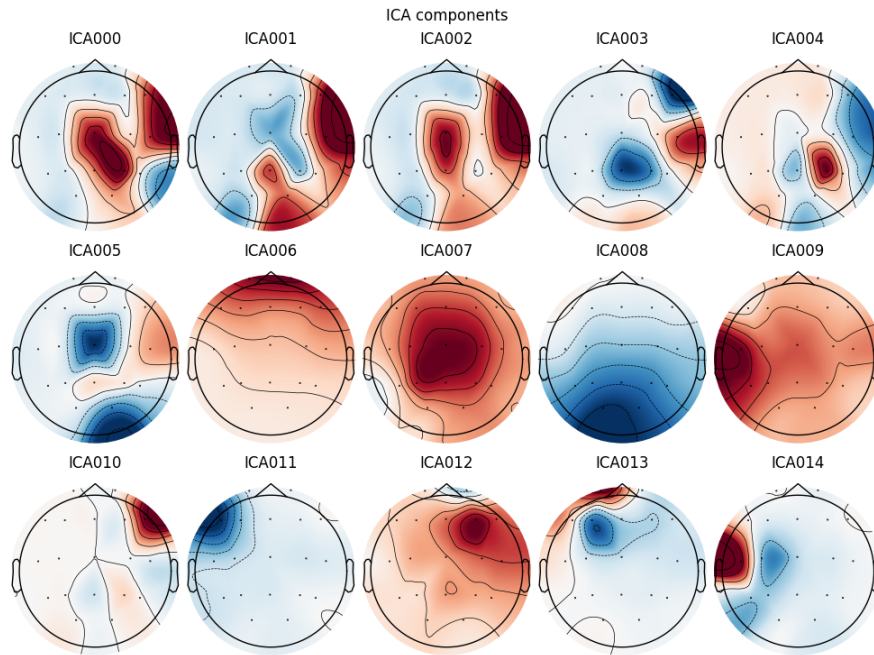


Figure 4.3: ICA components

4.3 Feature extraction

For feature extraction, Fourier transform and Wavelet transformation is mainly used. Multilevel wavelet decomposition can be used to extract frequency bands from an EEG signal. For each level, the signal is passed through the high-pass $h[n]$ and a low-pass $g[n]$ wavelet filters followed by downsampling by a factor of 2 [9]. Approximation coefficient is again used in next level decomposition. After the desired level decomposition we obtain an approximation coefficient of level order and all detail coefficients. Individual coefficients are mapped to frequency bands.

Wavelet transform

Wavelet transform was primarily created to solve the limitations of the Fourier transform [1]. Fourier analysis decomposes a signal into sine waves of specific frequencies, while wavelet analysis decomposes a signal into a wavelet. Wavelet is different from sine wave in rapidly decaying and wave-like oscillation. Thanks to that, wavelets can represent data on multiple scales.

Multilevel one-dimensional discrete wavelet transform can be used for signal analysis, de-noising and compression of signals. For extracting individual frequency bands from EEG signal, a wavelet discrete decomposition can be used. Multilevel decomposition starts on the first level, the signal is passed through a low-pass filter g and a high-pass filter h . The output from the high-pass filter is called a detail coefficient and approximation coefficient is a result of the low-pass filter. Coefficients are downsampled by factor 2 and another level

continues with the approximation coefficient of the previous level. This continues to the state in which the required frequency range is achieved.

Thanks to decomposition, we are able to extract individual frequency bands. Extracted frequency bands are then used to compute statistical data, total power, relative powers, asymmetry, complexity features and connectivity measures.

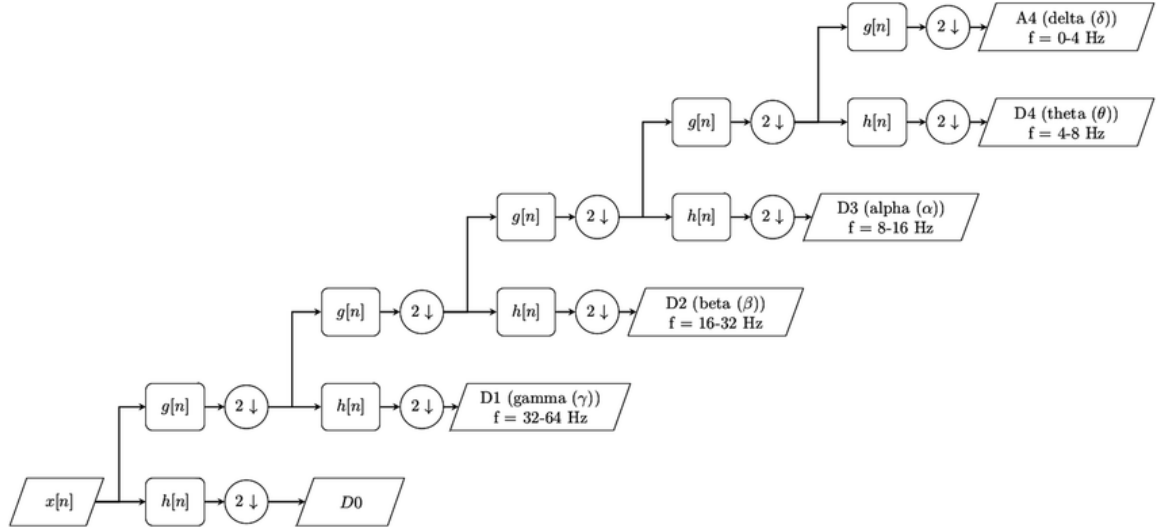


Figure 4.4: A 4-level wavelet transform based decomposition of an EEG signal $x[n]$ to obtain the typical EEG rhythms in the sub-band signals. [9]

4.4 Classifiers

Random Forest

The random forest consists of an ensemble of decision trees, trained with the bagging method¹. Firstly, training data are split into multiple subsets of features. For each subset, a decision tree is constructed. Each tree results in a prediction and the final prediction is an aggregation of all these predictions.

Support Vector Machine (SVM)

The SVM tries to find the best hyperplane that separates data points into different classes. Margin is the distance between hyperplane and the nearest data point. The bigger margin, the clearer separation. For non-linear data, SVM uses „kernel trick“ that transforms data into a higher-dimensional space where a linear separation can be performed.

Gradient boosting (GB)

Gradient boosting, like random forest, is an ensemble of decision trees. New decision trees are sequentially added and try to correct the mistakes made by previous series of trees. Gradient boosting is very accurate when the parameters are carefully set.

¹Bagging method is used to improve accuracy by training multiple models on random subsets of the training data and then combining their predictions.

K-Nearest Neighbours (KNN)

The KNN classifies data based on its neighbours. For assigning class to a data point, KNN looks at the class of „K“ closest data points and assigns that class. The accuracy of KNN depends on choosing the right number of neighbours and suitable distance metric.

Adaptive Boosting (AdaBoost)

Similarly as random forest and gradient boosting, AdaBoost combines multiple weak learning models, usually decision stumps (one-level decision trees). It adjusts data weights based on error rate of the weak learner. Final prediction combines predictions of all weak learners weighted by their individual accuracies.

4.5 Evaluation

Confusion matrix

A confusion matrix is an $N \times N$ matrix² used as a performance evaluation tool in machine learning, representing the accuracy of a classification model [8]. It compares the actual (true) values with the values predicted by the classifier. This can help in identifying misclassifications and improving predictive accuracy.

The classification problem in my work is binary (two target classes - depressed and healthy) so a 2×2 matrix is created, as shown in figure 4.5 with 4 values:

- True Positive (TP): A depressed subject is predicted as depressed by classifier
- True Negative (TN): A healthy subject is predicted as healthy by classifier
- False Positive (FP): A healthy subject is predicted as depressed by classifier
- False Negative (FN): A depressed subject is predicted as healthy by classifier

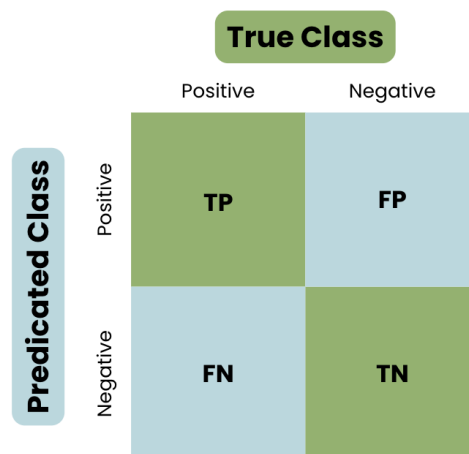


Figure 4.5: Confusion matrix in Machine Learning [2]

²N is the total number of target classes.

Accuracy

Accuracy is the proportion of correct predictions out of the total predictions. Accuracy tells how well can a binary classifier identify the different classes. It's best used when data from both classes are balanced.

$$Accuracy = \frac{TP + TN}{TP + FP + FN + TN} \quad (4.1)$$

Precision

Precision is the proportion of true positive predictions out of all positive predictions. It tells how many of the predicted positive instances are actually positive. A high precision indicates that the model has a low false positive rate.

$$Precision = \frac{TP}{TP + FP} \quad (4.2)$$

Sensitivity (Recall)

Sensitivity is the proportion of true positive predictions out of sum of true positives and false negatives. It tells how well a machine learning model can detect positive instances. A high sensitivity indicates that the model is good at identifying positive instances. In medical field it is a crucial metric as missing a positive case (false negative) can have fatal effect.

$$Sensitivity = \frac{TP}{TP + FN} \quad (4.3)$$

Specificity

Specificity is the proportion of true negatives out of sum of true negatives and false positives. It tells how well a machine learning model can identify negative results. A high specificity indicates that the model is good at identifying most of the negative results. Similarly as sensitivity, it is crucial metric in the medical field.

$$Specificity = \frac{TN}{TN + FP} \quad (4.4)$$

F1-score

F1-score is the harmonic mean of precision and sensitivity. F1-score can provide a more balanced evaluation of a machine learning model's performance, especially in imbalanced datasets. In those cases, it is better to use F1-score than accuracy.

$$F1\text{-score} = 2 \times \frac{Precision \times Sensitivity}{Precision + Sensitivity} \quad (4.5)$$

Chapter 5

Implementation

In this chapter, an implementation of the proposed solution from the previous chapter is described. Everything was written in `Jupyter notebooks`, due to its ease of working with signal and visualizing signals and matrices.

5.1 Dataset

I used a public dataset [49]. The dataset contains EEG recordings of 64 subjects. 34 of them with a major depressive disorder and 30 healthy subjects. The MDD patients met the criteria for depression according to DSM-IV. They were assessed using the Beck Depression Inventory-II and Hospital Anxiety and Depression Scale (HADS). Involved MDD patients were without any psychotic symptoms. EEG sensor placement followed the 10-20 system. 19 channels were used to record brain waves (Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, C4, P3, Pz, P4, T3, T4, T5, T6, O1, and O2) with sampling frequency of 256 Hz. The EEG was recorded for 5 minutes with eyes open and for 5 minutes with eyes closed.

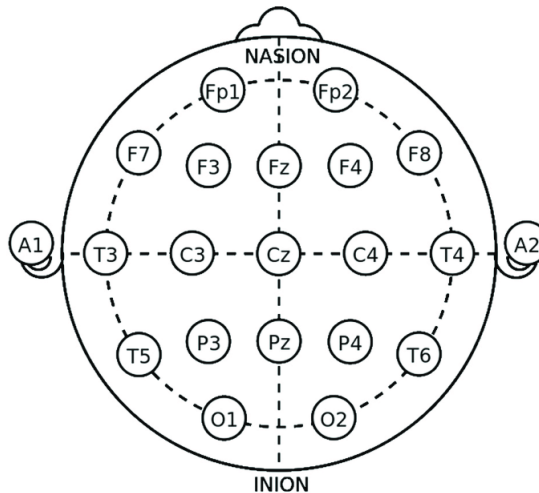


Figure 5.1: 10-20 system electrode placement [53]

5.2 Pre-processing

The dataset contained EEG data from 64 subjects. However, some EEG recordings were missing or corrupted. Due to this issue, I decided to use EEG data from 25 MDD patients and 25 healthy controls. Data were band-passed from 0.5 to 40 Hz with use of the function `filter()` from the Python library `mne`. The filtering process can be seen in pseudo-algorithm 1.

Algorithm 1 An algorithm for filtering EEG recording

Input: Raw data in `.edf` files

Output: Filtered data in `.edf` files

```
for every raw file do
    mne.io.read_raw_edf()
    filter(0.5, 40)
    mne.export.export_raw
end for
```

Some studies used the whole recording and some segmented data to smaller chunks. I decided to try out both options. In my first take I used the first three minutes of the recordings, in my second take I divided the first three minutes into 30 second long segments to get more data for classifying purposes.

5.3 Feature extraction

Filtered data were read with `EdfReader` from `pyedflib` library. For feature extraction I used Discrete wavelet decomposition. After decomposition, coefficients need to be reconstructed back to get individual frequency bands. Both for decomposition and reconstruction, Daubechies wavelet `db4` was used as it was marked as the best wavelet for EEG frequency bands extraction. Level 5 was suitable since the dataset was recorded with the sampling frequency of 256 Hz. Signals were divided into individual frequency bands within the ranges in Table 5.1.

Wavelet coefficient	EEG Frequency bands	Frequency range
D1	Higher gamma and noise	64 - 128 Hz
D2	Gamma	32 - 64 Hz
D3	Beta	16 - 32 Hz
D4	Alpha	8 - 16 Hz
D5	Theta	4 - 8 Hz
A5	Delta	0 - 4 Hz

Table 5.1: 5-level wavelet decomposition coefficients

Frequency band extraction algorithm

The pseudoalgorithm 2 for extracting absolute powers from `.edf` files is quite simple. Wavelet and the level of wavelet transform was set. Every `.edf` file contains an EEG

recording from one subject. The recording has signals from all channels - electrodes that were used in the recording. In a for loop, take every channel from every subject and call `wavedec()`. Reconstruct its output with `upcoef()`, compute powers and save them to a `.csv` file.

Algorithm 2 An algorithm for extracting frequency band powers

```
Input: Preprocessed .edf files
Output: Matrix of absolute powers and subjects in .csv file
    wavelet = 'db4'
    level = 5
    for every subject do
        for every channel do
            frequency_bands = wavedec()
            for every frequency band do
                individual_frequency_band = upcoef()
                compute_powers()
                add powers into matrix of features and subjects
            end for
        end for
    end for
return matrix of absolute powers and subjects
```

Asymmetry and Ratios

Another feature extracted was asymmetry. Asymmetry was calculated as subtraction of natural logarithms for absolute power on the left and the right hemisphere. Ten values for every frequency band were obtained - the asymmetry of individual electrodes Fp1-Fp2, F7-F8, F3-F4, C3-C4, P3-P4, T3-T4, T5-T6, O1-O2, whole frontal area asymmetry (between the mean value of Fp1, F7, F3 and the mean value of Fp2, F8, F4) and whole temporal area asymmetry (between the mean value of T3 and T5 and the mean value of T4 and T6). For the frontal, temporal and parietal brain areas, the theta/beta, alpha/theta and beta/alpha ratios were also calculated.

Non-linear features

Due to the high time complexity needed to compute non-linear features, I selected only four complexity metrics - Sample Entropy, Approximate Entropy, Katz fractal dimension and Higuchi's fractal dimension. In their implementation I used functions defined in `Antropy` library - `sample_entropy()`, `app_entropy()`, `katz_fd()` and `higuchi_fd()`. Their values were calculated for the signals from every electrode.

Data labelling

In the end we have 5*19 absolute power features, 5*10 asymmetry features and 3*3 ratio features - 154 extracted linear features. With 76 (4*19) non-linear features, it is 230 different features used for classification. All features were saved into a `.csv` file. For classification purposes, the column `'label'` was added with a Depressed/Healthy value based on the status of the subject.

5.4 T-tests

`ttest_ind()` from `scipy` library was used for evaluating the significance of extracted features. Alpha was set to 0.05 and null hypothesis for every feature was that there is no significant difference between depressed and healthy subjects.

5.5 Classifying problem

Classifying was done in file `classifiers.ipynb`. I used 5 different classifying algorithms - Random Forest, Support Vector Machine with rbf kernel, Gradient boosting, k-nearest neighbours and AdaBoost. All were implemented with use of functions from the Python library `sklearn` - namely `RandomForestClassifier()`, `SVC()`, `GradientBoostingClassifier()`, `KNeighborsClassifier()` and `AdaBoostClassifier()`.

Data splitting

Before classification, data were split into training and testing data. I used 80% of data for training purposes and 20% for testing purposes. For this, the function `train_test_split` from `sklearn` was used.

Evaluation

Confusion matrices were plotted with the `ConfusionMatrixDisplay()` function. For printing the F1-score, accuracy, sensitivity, specificity and precision metrics I implemented my own function `printMetrics()`. Input argument is a 2x2 confusion matrix from which I am calculating and printing the metrics. The confusion matrix 4.5 contains True Positive (TP), True Negative (TN), False Positive (FP) and False Negative (FN) results of the applied machine learning algorithm. All metric calculations are based on these values.

Chapter 6

Results

This chapter shows the results found through my EEG study and talks about the trends found in absolute powers, asymmetry, ratios and non-linear features. Machine learning model performance and evaluation of classification is the main output of my work.

6.1 Findings

One of the main contributions to depression classification is identifying trends that can detect depressive symptoms in a person. Significant differences in brain functioning between depressed patients and healthy controls could show us how the brain is affected by depression.

T-tests

T-tests showed significant differences in many features. First 10 of them with the most significant difference between patients with MDD and healthy subjects are listed in Table 6.1. P-value showed that the most significant difference between the two groups was in the central and temporal brain areas. The significant difference was in the alpha and theta asymmetry in the central area and in the theta asymmetry in the occipital brain area. Absolute delta and theta were significantly different in the temporal area. Significant difference was also observed in the theta/beta and the beta/alpha ratios in the parietal brain area. Significant differences were also found in SampEn, ApEn and Katz fractal dimension.

Frequency band powers

Relative delta was decreased in patients with MDD in the whole brain area, except the Fz electrode. These results were mentioned in many studies [16], [42]. Relative theta was increased in patients with MDD in the frontal, central and right temporal lobe. Relative beta was increased in patients with MDD in the occipital, right temporal and right parietal lobe. Increased theta and beta were also observed by [18], [60], [59], Alpha was decreasing in the whole brain area in the depressed group. This result was completely different than results from literature review [16], [42], [59]. Most studies report increasing alpha in the frontal area, in my case the opposite results may be caused by the decision not to apply the ICA artifact removal to remove eye movements, eye blinks and muscle movements. Artifacts linked to eyes are present in the frontal brain signals which could affect trends in

Order	Feature	p-value
1	Central alpha asymmetry	4.9552791932304955e-06
2	Central theta asymmetry	9.132802533154552e-06
3	Parietal theta/beta ratio	1.0521274760786547e-05
4	Absolute delta in T6	7.182013157286067e-05
5	Absolute theta in T6	9.94545081312008e-05
6	Occipital theta asymmetry	0.00011002802264469505
7	Absolute theta in O1	0.00013071800351326912
8	Absolute delta in T5	0.00015358278193523318
9	Absolute theta in T3	0.00018157416609035034
10	Parietal beta/alpha ratio	0.0002019089263186193

Table 6.1: Top 10 most significant features and their p-values

powers. I also used a dataset with data recorded with open eyes. Holding your eyes open without blinking for 3 minutes is very difficult and eye artifacts are more present than in a dataset with eyes closed.

Asymmetry

Temporal theta and delta asymmetry was more negative in the depressed patients. Occipital alpha and theta asymmetry was more negative in the depressed group. Central alpha, beta and theta asymmetry was more negative in the depressed subjects. Parietal alpha asymmetry was more positive in the depressed participants. Frontal delta asymmetry was more negative in the depressed patients. Fp1-Fp2 alpha asymmetry was more negative in the depressed group. F7-F8 delta asymmetry was more negative in the depressed individuals. Literature review suggests alpha asymmetry decrease [34], [36] in frontal area what agrees with my results.

Ratios

Previous studies showed decreasing alpha/theta ratio at the parietal cortex (Pz) [58], [11]. This aligns with my observation of decreasing alpha/theta ratio in the frontal, parietal and temporal area in depressed patients. Beta/alpha ratio in temporal and parietal is increased in the depressed patients.

Non-linear features

According to the t-test, 32 non-linear features were significantly different between depressed group and healthy group. Higuchi's fractal dimension wasn't significantly different in any electrode. SampEn, ApEn and Katz fractal dimension were significantly decreasing in depressed patients. This is the complete opposite to the results from literature review 3.4. Only in one study [45] was found lower SampEn in F4 channel in the depressed group.

The hypothesis is that the non-linear features are heavily affected by medication. Different sample size could also influence these results.

6.2 Model Performance

Five different classifiers were used to classify the features extracted from EEG recordings. Three different groups of input data were given to the machine learning models - frequency power features, asymmetry and ratio features, and non-linear features. Model performances can be seen in Table 6.2.

Metric	Classifier	Frequency powers	Asymmetry + Ratios	Non-linear features
Accuracy (%)	Random Forest	80	60	60
	SVM (rbf kernel)	70	40	70
	GB	80	70	70
	KNN	60	30	50
	AdaBoost	60	60	50
Specificity (%)	Random Forest	75	75	67
	SVM (rbf kernel)	60	50	100
	GB	67	80	71
	KNN	50	33	67
	AdaBoost	50	75	57
Precision (%)	Random Forest	83	75	50
	SVM (rbf kernel)	67	75	100
	GB	67	75	50
	KNN	50	50	75
	AdaBoost	67	75	25
Sensitivity (%)	Random Forest	83	50	50
	SVM (rbf kernel)	80	38	57
	GB	100	60	67
	KNN	75	29	43
	AdaBoost	67	50	33
F1-score (%)	Random Forest	83	60	50
	SVM (rbf kernel)	73	50	73
	GB	80	67	57
	KNN	60	36	55
	AdaBoost	67	60	29

Table 6.2: Evaluation of classifiers when input data were from 3 groups - frequency power features, asymmetry + ratio features and non-linear features

To choose the best algorithm for depression detection I followed a simple rule - Accuracy, specificity and sensitivity must be really high. As mentioned in the Evaluation section 4.5, sensitivity and specificity are a crucial metric in the medical field. The best results in these metrics were achieved by the Random Forest algorithm when the frequency band features were on its input. This model was able to classify depressed patients and healthy subjects

with an accuracy of 80%, specificity of 75%, and sensitivity of 83%. By selecting features with the best importance scores, Random Forest got a 90% accuracy score and an 83% specificity score.

As I mentioned in Chapter 4, I was also running classification with 30 s long segmented data. The best results were achieved by classifying asymmetry and ratio features with the KNN model. The model reached an accuracy of 93%, specificity of 96% and sensitivity of 90%. It's confusion matrix can be seen in Figure 6.1.

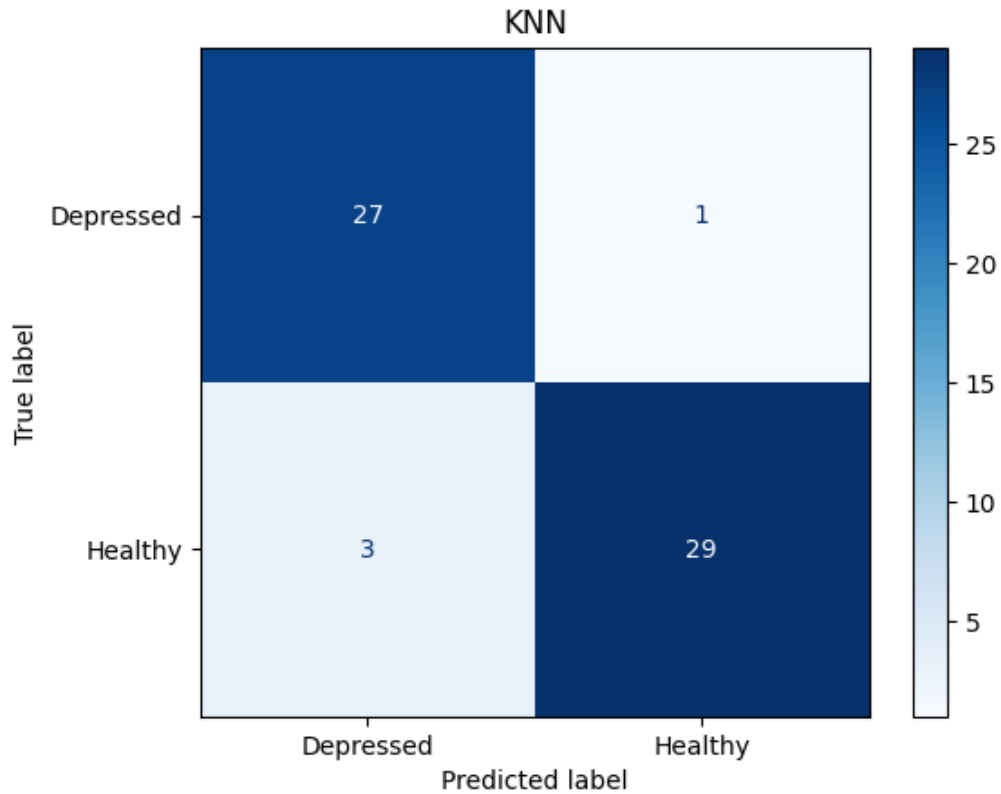


Figure 6.1: Confusion matrix of K-Nearest Neighbours classifier

6.3 Limitations

There are some limitations that could've impacted my work. The key limitation is a small sample size. Medication could also be a problem. Even when subjects had gone through a washout time period of two weeks prior to the recording, some medication could have a longer effect.

Chapter 7

Conclusion

The main aim of this thesis was to design a model for feature extraction and classifying depression. I studied brain waves, EEG recording, processing signals and machine learning classification processes.

I conducted a comprehensive review of articles that studied this topic, summarizing their results and limitations. In the proposed methodology, I chose to extract features using the Discrete wavelet decomposition and considered different machine learning algorithms. I have implemented a solution to extract features and used multiple algorithms for classification of healthy and depressed individuals.

My findings confirm that band powers and hemisphere asymmetry can be used for detecting depression. Using the K-Nearest Neighbours algorithm, I was able to classify depressed patients and healthy controls with an accuracy of 93%. Additionally, I discovered several other features that show significant differences between the two groups.

Some of my findings were contrary to the findings in the literature review. This can be attributed to differing sample sizes and the lack of consideration for the effects of medication in some studies. Moreover, variations in demographic factors, such as age and gender, could also contribute to these discrepancies.

The results of this thesis highlight the potential of machine learning in improving diagnostic accuracy. Future work should focus on providing a large, publicly available dataset, including more diverse populations, and investigating the impact of various factors, such as medication, on EEG features and classification performance.

Bibliography

- [1] *What Are Wavelet Transform?* online. Available at: <https://www.mathworks.com/discovery/wavelet-transforms.html>. [cit. 2024-04-23].
- [2] AHMED, N. A. *What is A Confusion Matrix in Machine Learning? The Model Evaluation Tool Explained* online. 2023. Available at: <https://www.datacamp.com/tutorial/what-is-a-confusion-matrix-in-machine-learning>. [cit. 2024-04-20].
- [3] AKBARI, H.; SADIQ, M. T. and REHMAN, A. U. Classification of normal and depressed EEG signals based on centered correntropy of rhythms in empirical wavelet transform domain. *Health Information Science and Systems*, Feb 2021, vol. 9, no. 1, p. 9. ISSN 2047-2501. Available at: <https://doi.org/10.1007/s13755-021-00139-7>.
- [4] AMERICAN PSYCHIATRIC ASSOCIATION. *DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS*. 5th ed. American Psychiatric Publishing, 2013. ISBN 978-0-89042-554-1. Available at: [https://repository.poltekkes-kaltim.ac.id/657/1/Diagnostic%20and%20statistical%20manual%20of%20mental%20disorders%20_%20DSM-5%20\(%20PDFDrive.com%20\).pdf](https://repository.poltekkes-kaltim.ac.id/657/1/Diagnostic%20and%20statistical%20manual%20of%20mental%20disorders%20_%20DSM-5%20(%20PDFDrive.com%20).pdf).
- [5] BAŞAR, E.; GÖLBAŞI, B. T.; TÜLAY, E.; AYDIN, S. and BAŞAR EROĞLU, C. Best method for analysis of brain oscillations in healthy subjects and neuropsychiatric diseases. *International Journal of Psychophysiology*, 2016, vol. 103, p. 22–42. ISSN 0167-8760. Available at: <https://www.sciencedirect.com/science/article/pii/S0167876015000483>. Research on Brain Oscillations and Connectivity in A New Take-Off State.
- [6] BEAR, M.; CONNORS, B. and PARADISO, M. A. *Neuroscience: Exploring the Brain*. 4th ed. Jones & Bartlett Learning, 2016. ISBN 978-1-28421-128-3. Available at: <https://link.springer.com/article/10.1007/BF02234670>.
- [7] BENSCHOP, L.; POPPA, T.; MEDANI, T.; SHAHABI, H.; BAEKEN, C. et al. Electrophysiological scarring in remitted depressed patients: Elevated EEG functional connectivity between the posterior cingulate cortex and the subgenual prefrontal cortex as a neural marker for rumination. *Journal of Affective Disorders*, 2021, vol. 281, p. 493–501. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S0165032720331712>.
- [8] BHANDARI, A. *Understanding & Interpreting Confusion Matrix in Machine Learning (Updated 2024)* online. 2024. Available at: <https://www.analyticsvidhya.com/blog/2020/04/confusion-matrix-machine-learning/>. [cit. 2024-05-05].

- [9] BISWAS, S. and SINHA, R. Wavelet filterbank-based EEG rhythm-specific spatial features for covert speech classification. *IET Signal Processing*, september 2021, vol. 16.
- [10] CASSANI, R.; ESTARELLAS, M.; SAN MARTIN, R.; FRAGA, F. J. and FALK, T. H. Systematic Review on Resting-State EEG for Alzheimer’s Disease Diagnosis and Progression Assessment. *Disease Markers*. Hindawi, Oct 2018, vol. 2018, p. 5174815. ISSN 0278-0240. Available at: <https://doi.org/10.1155/2018/5174815>.
- [11] CHANG, J. and CHOI, Y. Depression diagnosis based on electroencephalography power ratios. *Brain and Behavior*, 2023, vol. 13, no. 8, p. e3173. Available at: <https://onlinelibrary.wiley.com/doi/abs/10.1002/brb3.3173>.
- [12] CHEN, F.; ZHAO, L.; CAI, Z.; LI, Y.; ZANG, X. et al. Different Sub-bands Assessment of the Resting-state Prefrontal EEG in Depression Patients. In: *2022 International Conference on Sensing, Measurement & Data Analytics in the era of Artificial Intelligence (ICSMD)*. 2022, p. 1–6.
- [13] CHEN, Z.; WANG, Z.; SHEN, Y.; ZENG, S.; YANG, X. et al. Face-specific negative bias of aesthetic perception in depression: Behavioral and EEG evidence. *Frontiers in Psychiatry*, 2023, vol. 14. ISSN 1664-0640. Available at: <https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsy.2023.1102843>.
- [14] ČUKIĆ, M.; STOKIĆ, M.; SIMIĆ, S. and POKRAJAC, D. The successful discrimination of depression from EEG could be attributed to proper feature extraction and not to a particular classification method. *Cognitive Neurodynamics*, Aug 2020, vol. 14, no. 4, p. 443–455. ISSN 1871-4099. Available at: <https://doi.org/10.1007/s11571-020-09581-x>.
- [15] ČUKIĆ, M.; STOKIĆ, M.; RADENKOVIĆ, S.; LJUBISAVLJEVIĆ, M.; SIMIĆ, S. et al. Nonlinear analysis of EEG complexity in episode and remission phase of recurrent depression. *International Journal of Methods in Psychiatric Research*, 2019, vol. 29. Available at: <https://onlinelibrary.wiley.com/doi/10.1002/mpr.1816>.
- [16] DAMBORSKÁ, A.; HONZÍRKOVÁ, E.; BARTEČEK, R.; HOŘÍNKOVÁ, J.; FEDOROVÁ, S. et al. Altered directed functional connectivity of the right amygdala in depression: high-density EEG study. *Scientific Reports*, Mar 2020, vol. 10, no. 1, p. 4398. ISSN 2045-2322. Available at: <https://doi.org/10.1038/s41598-020-61264-z>.
- [17] DELL’ACQUA, C.; HAJČAK, G.; AMIR, N.; SANTOPETRO, N.; BRUSH, C. et al. Error-related brain activity in pediatric major depressive disorder: An ERP and time-frequency investigation. *International Journal of Psychophysiology*, 2023, vol. 184, p. 100–109. ISSN 0167-8760. Available at: <https://www.sciencedirect.com/science/article/pii/S0167876023000053>.
- [18] DELL’ACQUA, C.; GHIASI, S.; MESSEROTTI BENVENUTI, S.; GRECO, A.; GENTILI, C. et al. Increased functional connectivity within alpha and theta frequency bands in dysphoria: A resting-state EEG study. *Journal of Affective Disorders*, 2021, vol. 281, p. 199–207. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S0165032720331049>.

- [19] DELL'ACQUA, C.; BRUSH, C.; BURANI, K.; SANTOPETRO, N. J.; KLAWOHN, J. et al. Reduced electrocortical responses to pleasant pictures in depression: A brief report on time-domain and time-frequency delta analyses. *Biological Psychology*, 2022, vol. 170, p. 108302. ISSN 0301-0511. Available at: <https://www.sciencedirect.com/science/article/pii/S0301051122000448>.
- [20] ELSAYED, N.; ZAGHLOUL, Z. S. and BAYOUMI, M. Brain Computer Interface: EEG Signal Preprocessing Issues and Solutions. *International Journal of Computer Applications*, July 2017, vol. 169. Available at: https://e-tarjome.com/storage/panel/fileuploads/2019-03-16/1552738023_E11935-e-tarjome.pdf.
- [21] FUAD, N.; JAILANI, R.; OMAR, W.; JAHIDIN, A. and TAIB, M. Three dimension 3D signal for electroencephalographic (EEG). In: *2012 IEEE Control and System Graduate Research Colloquium*. 2012, p. 262–266.
- [22] GERAEDTS, V. J.; BOON, L. I.; MARINUS, J.; GOUW, A. A.; HILTEN, J. J. van et al. Clinical correlates of quantitative EEG in Parkinson disease. *Neurology*, 2018, vol. 91, no. 19, p. 871–883. Available at: <https://www.neurology.org/doi/abs/10.1212/WNL.0000000000006473>.
- [23] GRECO, C.; MATARAZZO, O.; CORDASCO, G.; VINCIARELLI, A.; CALLEJAS, Z. et al. Discriminative Power of EEG-Based Biomarkers in Major Depressive Disorder: A Systematic Review. *IEEE Access*, 2021.
- [24] HASLER, G. PATHOPHYSIOLOGY OF DEPRESSION: DO WE HAVE ANY SOLID EVIDENCE OF INTEREST TO CLINICIANS? *World Psychiatry*, 2010. Available at: <https://doi.org/10.1002/j.2051-5545.2010.tb00298.x>.
- [25] HINES, T. *Anatomy of the Brain* online. 2018. Available at: <https://mayfieldclinic.com/pe-anatbrain.htm>. [cit. 2024-04-02].
- [26] HOSSEINFARD, B.; MORADI, M. H. and ROSTAMI, R. Classifying depression patients and normal subjects using machine learning techniques and nonlinear features from EEG signal. *Computer Methods and Programs in Biomedicine*, 2013, vol. 109, no. 3, p. 339–345. ISSN 0169-2607. Available at: <https://www.sciencedirect.com/science/article/pii/S0169260712002507>.
- [27] JANG, K.-I.; KIM, S.; CHAE, J.-H. and LEE, C. Machine learning-based classification using electroencephalographic multi-paradigms between drug-naïve patients with depression and healthy controls. *Journal of Affective Disorders*, 2023, vol. 338, p. 270–277. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S016503272300753X>.
- [28] JANG, K.-I.; LEE, C.; LEE, S.; HUH, S. and CHAE, J.-H. Comparison of frontal alpha asymmetry among schizophrenia patients, major depressive disorder, and healthy controls. *BMC Psychiatry*, 2020. Available at: <https://www.researchsquare.com/article/rs-37400/v2>.
- [29] JIN, S.-H.; NA, S. H.; KIM, S. Y.; HAM, B.-J.; LEE, D. H. et al. Hemispheric laterality and dimensional complexity in schizophrenia under sound and light stimulation. *International Journal of Psychophysiology*, 2003, vol. 49, no. 1, p. 1–15.

ISSN 0167-8760. Available at:

<https://www.sciencedirect.com/science/article/pii/S0167876003000783>.

- [30] KAMEL, N. and MALIK, A. S., ed. *EEG/ERP Analysis: Methods and Applications*. 1st ed. CRC Press, 2014. ISBN 9780429170836.
- [31] KAUSHIK, P.; YANG, H.; ROY, P. P. and VUGT, M. van. Comparing resting state and task-based EEG using machine learning to predict vulnerability to depression in a non-clinical population. *Scientific Reports*, May 2023, vol. 13, no. 1, p. 7467. ISSN 2045-2322. Available at: <https://doi.org/10.1038/s41598-023-34298-2>.
- [32] KHAZI, M.; KUMAR, A. and J, V. M. Analysis of EEG Using 10:20 Electrode System. *International Journal of Innovative Research in Science, Engineering and Technology*, 2012, vol. 1. ISSN 2319 – 8753. Available at: <https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=317e34d0f91fdc569af4160df35e06ccaf5d7132>.
- [33] KHOSLA, A.; KHANDNOR, P. and CHAND, T. A comparative analysis of signal processing and classification methods for different applications based on EEG signals. *Biocybernetics and Biomedical Engineering*, 2020, vol. 40, no. 2, p. 649–690. ISSN 0208-5216. Available at: <https://www.sciencedirect.com/science/article/pii/S0208521620300231>.
- [34] KOLLER SCHLAUD, K.; STRÖHLE, A.; BÄRWOLF, E.; BEHR, J. and RENTZSCH, J. EEG Frontal Asymmetry and Theta Power in Unipolar and Bipolar Depression. *Journal of Affective Disorders*, 2020, vol. 276, p. 501–510. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S0165032720324150>.
- [35] KOŁODZIEJ, A.; MAGNUSKI, M.; RUBAN, A. and BRZEZICKA, A. No relationship between frontal alpha asymmetry and depressive disorders in a multiverse analysis of five studies. *eLife*. eLife Sciences Publications, Ltd, may 2021, vol. 10, p. e60595. ISSN 2050-084X. Available at: <https://doi.org/10.7554/eLife.60595>.
- [36] KUSTUBAYEVA, A.; KAMZANOVA, A.; KUDAIBERGENOVA, S.; PIVKINA, V. and MATTHEWS, G. Major Depression and Brain Asymmetry in a Decision-Making Task with Negative and Positive Feedback. *Symmetry*, 2020, vol. 12, no. 12. ISSN 2073-8994. Available at: <https://www.mdpi.com/2073-8994/12/12/2118>.
- [37] LI, M.; ZHANG, J.; JIANG, C.; WANG, J.; SUN, R. et al. The Neural Correlates of the Recognition of Emotional Intensity Deficits in Major Depression: An ERP Study. *Neuropsychiatric Disease and Treatment*. Dove Medical Press, 2023, vol. 19, p. 117–131. Available at: <https://www.tandfonline.com/doi/abs/10.2147/NDT.S393264>.
- [38] LI, P.; YOKOYAMA, M.; OKAMOTO, D.; NAKATANI, H. and YAGI, T. Depressive states in healthy subjects lead to biased processing in frontal-parietal ERPs during emotional stimuli. *Scientific Reports*, Oct 2023, vol. 13, no. 1, p. 17175. ISSN 2045-2322. Available at: <https://doi.org/10.1038/s41598-023-44368-0>.
- [39] LI, X.; LA, R.; WANG, Y.; HU, B. and ZHANG, X. A Deep Learning Approach for Mild Depression Recognition Based on Functional Connectivity Using Electroencephalography. *Frontiers in Neuroscience*, 2020, vol. 14. ISSN 1662-453X.

Available at: <https://www.frontiersin.org/journals/neuroscience/articles/10.3389/fnins.2020.00192>.

- [40] LIAN, J.; SONG, Y.; ZHANG, Y.; GUO, X.; WEN, J. et al. Characterization of specific spatial functional connectivity difference in depression during sleep. *J Neurosci Res*. United States: [b.n.], october 2021, vol. 99, no. 11, p. 3021–3034. Available at: <https://onlinelibrary.wiley.com/doi/full/10.1002/jnr.24947>.
- [41] LIGHT, G. A.; WILLIAMS, L. E.; MINOW, F.; SPROCK, J.; RISSLING, A. et al. Electroencephalography (EEG) and Event-Related Potentials (ERP's) with Human Participants. *Current Protocols: Neurosciece*, 2010. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909037/#>.
- [42] LIN, I.-M.; CHEN, T.-C.; LIN, H.-Y.; WANG, S.-Y.; SUNG, J.-L. et al. Electroencephalogram patterns in patients comorbid with major depressive disorder and anxiety symptoms: Proposing a hypothesis based on hypercortical arousal and not frontal or parietal alpha asymmetry. *Journal of Affective Disorders*, 2021, vol. 282, p. 945–952. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S016503272100001X>.
- [43] LIU, P. and TAN, J. X. Y. Incremental validity of ERP correlates of self-referential processing in predicting emerging depressive symptoms in late childhood: Evidence from a community-dwelling sample. *Psychophysiology*, 2023, vol. 60, no. 11, p. e14382. Available at: <https://onlinelibrary.wiley.com/doi/abs/10.1111/psyp.14382>. E14382 PsyP-2022-0438.R2.
- [44] LIU, W.; ZHANG, C.; WANG, X.; XU, J.; CHANG, Y. et al. Functional connectivity of major depression disorder using ongoing EEG during music perception. *Clinical Neurophysiology*, 2020, vol. 131, no. 10, p. 2413–2422. ISSN 1388-2457. Available at: <https://www.sciencedirect.com/science/article/pii/S1388245720304168>.
- [45] LORD, B. and ALLEN, J. J. B. Evaluating EEG complexity metrics as biomarkers for depression. *Psychophysiology*, 2023, vol. 60. ISSN 0048-5772. Available at: <https://onlinelibrary.wiley.com/doi/full/10.1111/psyp.14274>.
- [46] MAHATO, S.; GOYAL, N.; RAM, D. and PAUL, S. Detection of Depression and Scaling of Severity Using Six Channel EEG Data. *Journal of Medical Systems*, May 2020, vol. 44, no. 7, p. 118. ISSN 1573-689X. Available at: <https://doi.org/10.1007/s10916-020-01573-y>.
- [47] MAYO CLINIC STAFF. *EEG (electroencephalogram)* online. 2022. Available at: <https://www.mayoclinic.org/tests-procedures/eeg/about/pac-20393875>. [cit. 2024-04-23].
- [48] MINKOWSKI, L.; MAI, K. V. and GURVE, D. Feature Extraction to Identify Depression and Anxiety Based on EEG. In: *2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*. 2021.
- [49] MUMTAZ, W.; MALIK, A. S.; MOHD AZHAR MOHD YASIN; ALI, S. S. A. and LIKUN XIA. *EEG-based Diagnosis and Treatment Outcome Prediction for Major Depressive Disorder*. figshare, 2016. Available at: <https://figshare.com/articles/dataset/EEG->

based_Diagnosis_and_Treatment_Outcome_Prediction_for_Major_Depressive_Disorder/
3385168/1.

- [50] PANT, A. *Workflow of a Machine Learning project*. 2019. Available at: <https://towardsdatascience.com/workflow-of-a-machine-learning-project-ec1dba419b94>.
- [51] REH, F.; ANTWERPES, F. and HÖFEL, N. van den. *10-20-System* online. 2023. Available at: <https://flexikon.doccheck.com/de/10-20-System>. [cit. 2024-05-13].
- [52] ROH, S.-C.; KIM, J. S.; KIM, S.; KIM, Y. and LEE, S.-H. Frontal Alpha Asymmetry Moderated by Suicidal Ideation in Patients with Major Depressive Disorder: A Comparison with Healthy Individuals. *Clin Psychopharmacol Neurosci*. Korea (South): [b.n.], february 2020, vol. 18, no. 1, p. 58–66. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7006982/>.
- [53] ROJAS, G.; ALVAREZ, C.; MONTOYA MOYA, C.; IGLESIA VAYA, M. de la; CISTERNAS, J. et al. Study of Resting-State Functional Connectivity Networks Using EEG Electrodes Position As Seed. *Frontiers in Neuroscience*, march 2018, vol. 12.
- [54] SCANLON, V. C. and SANDERS, T. *Essentials of Anatomy and Physiology*. 5th ed. F. A. Davis Company, 2007. Available at: [https://repository.poltekkes-kaltim.ac.id/1144/1/Essentials%20of%20Anatomy%20and%20Physiology%20\(%20PDFDrive%20\).pdf](https://repository.poltekkes-kaltim.ac.id/1144/1/Essentials%20of%20Anatomy%20and%20Physiology%20(%20PDFDrive%20).pdf).
- [55] SIMMATIS, L.; RUSSO, E. E.; GERACI, J.; HARMSSEN, I. E. and SAMUEL, N. Technical and clinical considerations for electroencephalography-based biomarkers for major depressive disorder. *Npj Mental Health Research*, 2023. Available at: <https://www.nature.com/articles/s44184-023-00038-7>.
- [56] SUHAIMI, N. S.; MOUNTSTEPHENS, J. and TEO, J. EEG-Based Emotion Recognition: A State-of-the-Art Review of Current Trends and Opportunities. *Computational Intelligence and Neuroscience*, 2020. Available at: <https://www.hindawi.com/journals/cin/2020/8875426/>.
- [57] SULLIVAN, P. F.; NEALE, M. C. and KENDLER, K. S. Genetic Epidemiology of Major Depression: Review and Meta-Analysis. *The American Journal of Psychiatry*, 2000, vol. 157. Available at: <https://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.157.10.1552>.
- [58] WANG, S.-Y.; LIN, I.-M.; FAN, S.-Y.; TSAI, Y.-C.; YEN, C.-F. et al. The effects of alpha asymmetry and high-beta down-training neurofeedback for patients with the major depressive disorder and anxiety symptoms. *Journal of Affective Disorders*, 2019, vol. 257, p. 287–296. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S0165032719301454>.
- [59] WU, Z.; ZHONG, X.; LIN, G.; PENG, Q.; ZHANG, M. et al. Resting-state electroencephalography of neural oscillation and functional connectivity patterns in late-life depression. *Journal of Affective Disorders*, 2022, vol. 316, p. 169–176. ISSN 0165-0327. Available at: <https://www.sciencedirect.com/science/article/pii/S0165032722008230>.
- [60] ZHANG, B.; YAN, G.; YANG, Z.; SU, Y.; WANG, J. et al. Brain Functional Networks Based on Resting-State EEG Data for Major Depressive Disorder Analysis and

Classification. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 2021, vol. 29, p. 215–229.

- [61] ZHAO, L.; YANG, L.; LI, B.; SU, Z. and LIU, C. Frontal Alpha Complexity of Different Severity Depression Patients. *Journal of Healthcare Engineering*, 2020, vol. 2020. Available at: <https://www.hindawi.com/journals/jhe/2020/8854725/>.
- [62] ZHAO, S.; NG, S.-C.; KHOO, S. and CHI, A. Temporal and Spatial Dynamics of EEG Features in Female College Students with Subclinical Depression. *International Journal of Environmental Research and Public Health*, 2022, vol. 19, no. 3. ISSN 1660-4601. Available at: <https://www.mdpi.com/1660-4601/19/3/1778>.