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FATIH UNIVERSITY
INSTITUTE OF BIOMEDICAL ENGINEERING

ANALYSIS OF ELECTROENCEPHALOGRAPHY (EEG) SIGNALS TAKEN FROM PATIENTS SUFFER FROM MAJOR DEPRESSIVE DISORDER

SÜMEYRA AGAMBAYEV

MSc THESIS
BIOMEDICAL ENGINEERING PROGRAMME

İSTANBUL, JUNE / 2014

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PROF. DR. SADIK KARA

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FATİH ÜNİVESİTESİ
BİYOMEDİKAL MÜHENDİSLİK ENSTİTÜSÜ

MAJÖR DEPRESYONLU HASTALARDAN ALINAN EEG SİNYALLERİNİN ANALİZİ

SÜMEYRA AGAMBAYEV

YÜKSEK LİSANS
BİYOMEDİKAL MÜHENDİSLİĞİ PROGRAMI

DANIŞMAN
PROF. DR. SADIK KARA

İSTANBUL, HAZİRAN / 2014

T.C.

FATIH UNIVERSITY

INSTITUTE OF BIOMEDICAL ENGINEERING

Sümeyra Agambayev, an **MSc** student of Fatih University **Institute of Biomedical Engineering** student 520112008, successfully defended the **thesis** entitled "**Analysis Of EEG Signals Taken From Patients Suffer From Major Depressive Disorder**", which she prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

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Prof. Dr. Sadık KARA
Director

Date of Submission: 23 May 2014
Date of Defense : 5 July 2013

To my lovely family and my husband,

This study was supported by TÜBİTAK with the project number of 112E317.

ACKNOWLEDGEMENTS

I would like to thank my supervisor Prof. Dr. Sadık KARA for his advises, encouragement, guidence and the times he left for us not only thesis but also during master term. I also would like to thank my co-advisor Yrd. Doç. Dr. Saime AKDEMIR AKAR for her patience and assistance during my thesis. I thank to Yrd. Doç. Dr. Vedat BILGIÇ from Fatih University Psychiatry department for his support about the thesis. I also owe my thank to members of Biomedical engineering department for their help.

Last but not least, I thank to each members of my family for their spiritual support. I also thank to my husband for his motivation and patience during my thesis.

June 2014 Sümeyra AGAMBAYEV

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LIST OF SYMBOLS

Hz	Hertz
Σ	Sum
µV	MicroVoltage

ABREVIATIONS

ANOVA : Analaysis of Variance

BAI : Beck Anxiety Inventory

BDI : Beck Depression Inventory

CIDI : Composite International Diagnostic Interview

CRH : Corticotropin-Releasing Hormone

CTM : Classical Turkish Music

DALY : Disability Adjusted Life Years

DC : Direct Current

DIS : Diagnostic Interview Schedule

DSM-IV-TR : Diagnostic and Statistical Manual of Mental Disorders

ECA : Epidemiology Catchment Area Survey

ECG : Electrocardiography

EEG : Electroencephalography

EMG : Electromyography

EOG : Electrooculography

fMRI : Functional Magnetic Resonance Imaging

HAM-D : Hamilton Depression Rating Scale

HARS : Hamilton Anxiety Rating Scale

HPA : Hypothalamic-Pituitary-Adrenal

KFD : Katz Fractal Dimension

MDD : Major Depressive Disorder

MOIs : Monoamine Oxidase Inhibitors

NCS ; National Comorbidity Survey

NCS-R : National Comorbidity Survey-Replication

PET : Positron Emission Tomography

SPECT : Single Photon Emission Computed Tomgraphy

SSRI : Selective Serotonin Reuptake Inhibitors

TCIs : Tricylic Antidepressants

WHO : The World Health Organization

WN : White Noise

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SUMMARY

ANALYSIS OF ELECTROENCEPHALOGRAPHY (EEG) SIGNALS TAKEN FROM PATIENTS SUFFER FROM MAJOR DEPRESSIVE DISORDER

Sümeyra AGAMBAYEV
Biomedical Engineering Programme
MSc Thesis

Advisor: Prof. Dr. Sadık KARA
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The aim of this study was determination of physiological criteria intended for the diagnosis and grading of depression. Those criteria could be started to use in place of psychiatric scales in clinics. Designation of such criteria was succeeded by evaluating the EEG that reflects the brain activities by means of the wavelet and non linear methods. In this study, EEG signals were recorded from patients who are with major depressive disorder and healthy individuals during resting, disturbing, and relaxing auditory stimulation periods. Recorded signals analyzed with signal processing method were compared to demonstrate the differences between major depressive disorder patients and healthy subjects. In addition, the proposed project with the methods and perspectives may lead to other studies related to different psychiatric disorders.

Keywords: Major depressive disorder, electroencephalography, wavelet decomposition.

ÖZET

MAJOR DEPRESYONLU HASTALARDAN ALINAN EEG SİNYALLERININ ANALİZİ

Sümeyra AGAMBAYEV

Biyomedikal Mühendisliği Programı
Yüksek Lisans

Danışman: Prof. Dr. Sadık KARA
Eş-danışman: Yrd.Doç. Dr. Saime AKDEMIR AKAR

Bu çalışma depresyonun tanı ve derecelendirmesine yönelik fizyolojik kriterlerin belirlenmesini amaçlamaktadır. Bu kriterler kliniklerde psikolojik ölçü olarak da kullanılmaya başlanılabilir. Kriterler beyin aktivitelerini yansıtan EEG sinyallerinin wavelet ve lineer olmayan metodlar ile değerlendirilmesiyle belirlendi. Bu çalışmada, majör depresyonlu hastalar ve sağlıklı bireylerden EEG ve kan hacim sinyalleri sessizlik, gürültü ve dinlendirici işitsel uyaran periyotları esnasında kaydedildi. Kaydedilen sünyaller sinyal işleme yöntemüyle analiz edilerek, sonuçlar majör depresyonlu hastalar ve sağlıklı bireyler arasındaki farklılıkları göstermek amacıyla karşılaştırılmıştır. Ek olarak, önerilen metodlar ve yöntemler ileride yapılacak olan psikiyatrik rahatsızlıklarla ilgili çalışmalara bir örnek teşkil etme amacı taşımaktadır.

Anahtar kelimeler: major depresyon, elektroensefalografi, wavelet bozunması.

CHAPTER 1

INTRODUCTION

1.1 Purpose of the Thesis

To diagnose major depression disorder, there are not any laboratory tests or radiological images. There are some measurement methods which are done by experts called interrater reliability. Experts mostly are grading with different scores, so it causes a problem to decide about disorder for the patient. Therefore, in this thesis it is aimed to look for electrophysiological methods to diagnose mood disorders. It will help to understand the degree, chase, and treatment of mood disorder. It is demonstrated in the litereture that depressed patients had more alpha and beta activity and less delta activity (for alpha activity: [1] [2, 3]; for beta activity: [4]). Additionally, in many frequency bands, brain functions are represented by superimpose multiple brain oscillations [5]. In this thesis, EEG analyses will not be limited just with alpha, beta and delta bands, it will be decomposed to sub bands using wavelet decomposition method. At the same time, almost the only indicator of depression and emotional affect has been shown as the frontal asymmetry ([6-10]; for the review [11]). It is targeted to make Fractal dimension complexity analysis for sub bands of EEG signals taken from multiple regions and to search about differences of neural activity of these regions. To get this target, signals are going to be taken from healthy subjects and major depression patient and they will be compared.

1.2 Thesis Overview

This thesis study includes four steps which details were given in the following chapters step by step.

In **Chapter 1** some rief information about major depression, purpose of the thesis and what chapters include are summarized.

It is described what mental disease is and major depression which is one of its sub branches, some information about depression such as sign and symptoms, diagnosis, treatment, etiology and epidemiology in **Chapter 2**.

Chapter 3 includes the methodology pf the thesis study. How signals were collected from subjects, procedure of data collecting, measurement system, information about EEG, signal processing, transformation, and analysis methods were explained with details.

The results and discussion parts are included in **Chapter 4**. Analysis and statistical results of the study were explained briefly. Graphs and tables were used to give detailed information. In discussion part, some recommendations were given and the thesis were concluded.

CHAPTER 2

2.1 Mood Disorders

Mood disorder is one of the earliest recognized and identified of all disorders [12]. Even Homer defined mental states that can be described as mood disorders[13]. Also Hippocrates became the first physician recognizing that mood disorders are due to brain disease, and he referred to them, along with other mental disorders, as 'brain disorders'[12]. Historically, mood disorders can be either 'organic' or 'reactive' as it is explained in the Diagnostic and Statistical Manual of Mental Disorders-First Edition (DSM-I) (APA, 1952). The same distinction is continued in the second edition using the terms 'psychotic' and 'neurotic' [14]. Mood disorders were conceived in two explanations as either a disease of the mind and neurotic, or organic and a disease of the brain [14].

The Diagnostic and Statistical Manual of Mental Disorders-Third Edition chose a descriptive approach. According to their approach, if the individuals met any clear diagnostic criteria which was based on consjunction of symptoms and specific duration, they are diagnosed with mood disorder.

Mood disorders include the classical syndromes of depression such as Major Depression and Bipolar I disorder. In addition to these classical syndromes, other syndromes with different epidemiology and natural history are included in the group of mood disorders; Bipolar II Disorder, Dysthmia, Cyclothymia, Recurrent Brief Depression, Mixed States, Schizoaffective Disorders.

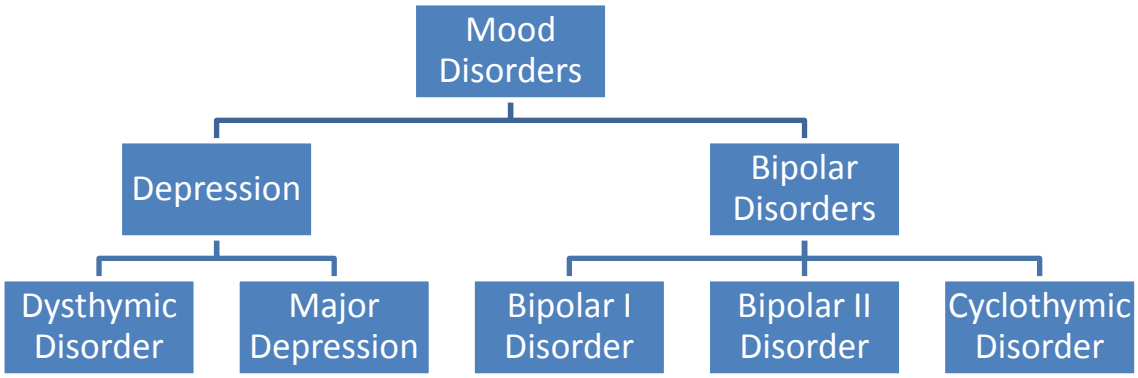

Figure 2.1 Subtypes of mood disorders[15]

2.1.1 Major Depressive Disorder

Major depressive disorder is one of the most prevalent of all psychiatric disorders with a lifetime prevalence of 17% to 21% [16]. It is one of the leading causes of disease worldwide. In some investigations, it is clearly identified that depression is a major public health problem [14]. It is estimated that the rising of MDD will reach to be the second leading cause of disability by the year 2020 [17]

Chronic and recurrent types of major depression can be seen [18]. Between one-half and two-thirds of the people who have ever been clinically diagnosed with depressed can be in episode in any year over the remainder of their lifes [19]. It is indicated that 60-80% of adults who experience one episode undergo at least one recurrence and most of them have recurrences in the first five years [13]. Kraepelin (1921) explained that the episodes of depression are associated with the failure to adapt to life events and this notion is growing by support [20]. There are some deficits in MDD in cognitive domains such as attention, concentration, executive functions as well as learning and memory [21-24] but its underlying neural circuitry and pathophysiology is not completely known [25, 26].

It is seen that MDD is shown to account for a 23-fold increase in social disability, even after controlling for physical disease, almost 5-fold increase is observed in short term work disability days [17]. In a study conducted with Western Europe, the degree of disability was found to be directly related to severity of depression in patients with MDD [17]. One of the most common symptoms are somatic symptoms for MDD patients such as fatigue, and lack of energy and painful physical symptoms such as headaches and back pain[27]. A.L. Vaccarrino et al. found that 'feeling fatigued, work or tired all over' is the most commonly endorsed somatic symptom (78% reported moderate levels or above) and was rated as the most severe at entry [27].

As a result of having depression people suffer from some cost of this disease. A recent economic review of the cost of depression reports that high healthcare usage is resulted with direct cost of depression. The majority of this is not the result of depression treatment costs, but other healthcare costs. On the other hand, indirect cost of depression is accounted for by economic burden and associated with morbidity such as losses in quality of life, absenteeism and decreased productivity, and functional impairment in many other personal and interpersonal areas of life [14].

2.1.2 Symptoms and Signs

MDD shows variability from person to person. For example, while 67% of people with MDD are experiencing simultaneous symptoms of depressed mood and anhedonia, 28% experience depressed mood without anhedonia, and 5% experience anhedonia without depressed mood. Rates of other symptoms vary among MDD patients and these varistions helps to predict treatment and disease characteristics (e.g. neurotransmitter depletion rates) [28].

According to the some investigators, the three dimensions; anxiety-agitation, depressed mood-motor retardation, and hostility-interpersonal sensitivity can be the characterization of depressive symptoms. Basso et al. reveals that depression does not evince in a unidimensional manner. Depressed individuals possess symptoms which have distinct dimensions, namely negative affect such as agitation and hostility, and lassitude and malaise which are observed in outpatients. Basso et al. also reveals that depressed inpatients present the same symptom dimensions [28]. On the other hand,

while it is certain that there is a heteregogeneity among individuals; it is uncertain whether there is also significant variability of symptoms with individuals over time. In addition, K.L. Minor et al had a result from their research that over the long term course of depressive episode, depressed individuals mostly experience similar symptoms [29].

2.1.3 Diagnosis

Diagnosis of Major Depressive Disorder is decided by psychiatrists by their clinical experiences. There is not any laboratory test or quantitative results to diagnose MDD.

MDD diagnosis is described by The Diagnostic and Statistical Manual of Mental Disorders-4th Edition (DSM-IV-TR) (APA, 2000) based on the presence of a specified number of symptoms with a precise duration [14].

The essential feature to identify MDD is the period keeps at least two weeks. Diagnosing of MDD becomes certain after observing during these two weeks either it is depressed mood or the loss of interest or pleasure in nearly all activities. At least four symptoms included DSM-IV list must be experienced by individuals. The symptoms are needed to persist for most of the day, nearly every day, and for also at least 2 sequential weeks.

2.1.4 Epidemiology

Baltimore Epidemiology Catchment Area Survey (ECA) and the National Comorbidity Survey (NCS) are the two large scale surveys from the U.S. which determine the prevalence of depressive disorder in the general population. They are initially conducted in 1991 and replicated in 2001[14]. It is reported by the ECA that 1-month (5.2%), 6-month (5.8%), 12-month (6.3%), and life-time prevalence (8.3%) of depressive disorder in the population [14]. In ECA survey, data were taken from 18,571 households and 2290 institutional residents aged eighteen years and older. They used the Diagnostic Interview Schedule (DIS) based on the DSM-III (APA, 1980). In general terms, as the result of this survey, 19,5% of the adult U.S. population in any 6-month period, or 1 in every 5 persons eighteen years and above, suffers with a diagnosable mental health disorder[14].

A new National Comorbidity Survey-Replication (NCS-R) was administered using the Composite International Diagnostic Interview (CIDI) based on the publication of DSM-IV (APA, 1994). In the population, it is reported that the prevalence of depressive disorder was 16.2 % for life-time and 6.6 % for 12-month. These epidemiologic studies show thet the frequency of depression in general population of U.S including younger age groups combine with likelihood of recurrence throughout adulthood is clear. Additionally, rank of depression among the leading causes for woman is higher than men [14].

According to demonstration of The World Health Organization (WHO), depressive disorders out of U.S. are one of the most effective causes of diseases worldwide. It is reported that 16 per 100.000 per year for males and 25 per 100.000 per year for females are having depressed syndroms throughout the world. The result of this report shows depression as the fourth leading cause of disease and 4.4% of total disability adjusted life years (DALY) is under effect of [14].

Consequently, depression is a major health problem and it is necessary to develop treatment methods. Also, young generation may need a help to emphasize for early intervention [14].

2.1.5 Etiology

The etiology of major depression is complex with no single risk factor and includes interactions between many sources such as environmental and genetical [30]. Faulty mood regulation by the brain, medications, genetic vulnerability, stressful life events, and medical problems are some of the potential causes of depression. These reasons can interact to cause depression[31].

Stressful life events can cause MDD for people those with a family history of mood disorders since they are referred to as the diathesis-stress theory [32]. Also, some studies suppurted that gene-environmental interaction can cause major depressive disorder. A functional polymorphism in the promoter region of the serotonin transporter (5-HT T) genes determined to presides the effect of stressful life events on depression but depended on the number of events in the previous 4 months. Individuals those have the one or two copies of the short allele of the 5-HT T promoterpolymorphism

displayed more depressive symptoms diagnosable depression, and suicidality than individuals homozygous or the long allele [32].

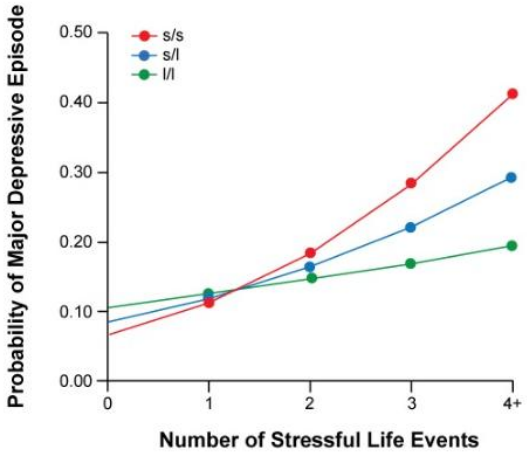

Figure 2.2 Increasing major depressive episedos with increasing stressful life events[32]

Scientists search about genetical causality of depression by finding people with MDD who have a twin. Then they tried to find out if the other twin has also MDD. Genetically, twins who are monozygotic share 100% of their genes, while dizygotic twins saher 50% of their genes. Despite these similarity between twins, according to result of the study, the proportion of total variance due to genetic variation for MDD was estimated at 35%. Although genetic factors are known as playing a significant role, it is found out that MDD can not be defined as a genetic disorder [33].

Some researchers studied about a different gene called as CRHR1 which effects a person's reaction to childhood abuse. This gene affects corticotrophin-releasing hormone (CRH) which is one of the stress hormones. Researchers found that the CRHR1 gene had half of the symptoms of depression among individuals those are suffered with childhood abuse though there was no genetic variation. They found out that the stress impress the CRHR1 genes without a genetic variation [34, 35].

Brain is more understandable using with some imaging methods such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and single photon emission computed tomgraphy (SPECT). These imaging methods make more clear which brain regions regulate mood and how depression may effect the other

functions, such as memory. The amygdala, the thalamus and the hippocampus play important role in depression.

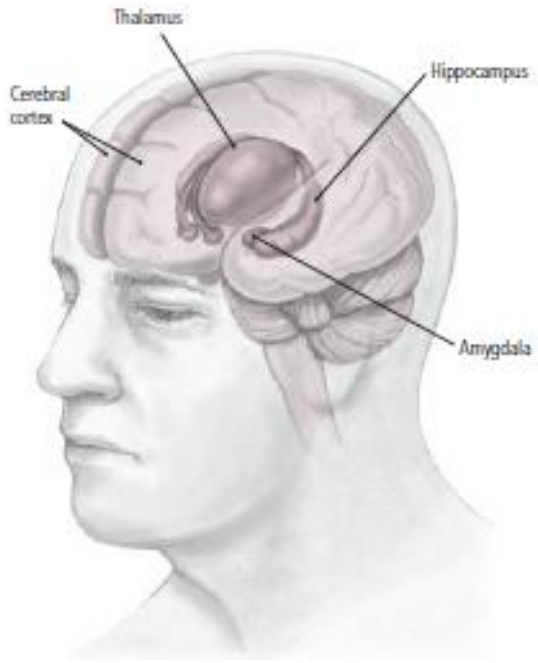

Figure 2.3 Areas of the brain affected by depression[31]

In an fMRI research, it is found that the hippocampus is in same depressed people. On average, hippocampus was 9% to 13% smaller in 24 depressed women than those who were not depressed. Investigators explored that the antidepressants are increasing transmition of neurons in hippocampus. However, people who are depressed don't feel themselves better even if the levels of neurotransmitters increase [36]

Hormones have an important role in depressed life as much as the brain regions or the life style. A signal produced in the part of brain called as hypothalamus triggers the stress response. An then the hypothalamus joins the pituitary and adrenalin glans to form hypothalamic-pituitary-adrenal (HPA) which plays a role in depression.

Corticotropin-releasing hormone (CRH) which is excreted by the hypothalamus influences the cerebral cortex, part of the amygdala, and the brainstem, CRH may play a role in coordinating thoughts and behaviours, unwilled responses, and emotional reactions. While CRH level is increased in people who are depressed, antidepressant and electroconvulsive therapies reduce the high CRH levels [37].

2.1.6 Treatment

The aim of treatment is symptom reduction or extinction if possible [14].

In the treatment of depression, new medications coming to market spread in recent years. Since depression became increasingly viewed as a recurrent or chronic disorder, it became necessary to investigate the effectiveness of long-term treatment with medications. It is resulted in the developments of protocols for continuing and maintaining pharmacotherapy after resolution. According to a research, using of antidepressants for the treatment of depression and outpatient treatment for depression was more than doubled between 1987 and 1997 [38]. At the same time, there is no evidence that new treatments improved outcomes compared to earlier antidepressants. It means that many individuals do not respond –or respond only temporarily- to the new antidepressants. On the other hand, antidepressants can cause some problems. For instance, it could be argued that one of the results of the antidepressant treatment might be the obesity. According to the research of Ohayon (2007), they found that MDD was significantly higher in obese subjects compared to non-obese subjects although they removed all individuals treated with antidepressant drugs [38].

There are several types of antidepressants to treat depression. Major types of these medications include [39];

Tricyclic antidepressants (TCAs) affect the levels of two chemical messengers (neurotransmitters), norepinephrine and serotonin, in the brain. Since they have some side-effects, they are not usually used as the first treatment drugs.

Monoamine oxidase inhibitors (MAOIs) are generally used by the patients who don't respond to other treatment methods. These medications can be in an interaction with some substances in certain foods, beverages like wine, like cheese, and medications. So, those people must adhere to strict dietary restraints. Because of that reason, these drugs aren't used as the first treatment madications.

Selective serotonin reuptake inhibitors (SSRIs) alter the amount of some chemicals in the brain called seratonin.

Serotonin and norepinephrine reuptake inhibitors (SNRIs) increase availability of the brain chemicals serotonin and norepinephrine.

Table 2.1 Effective medications commonly prescribed [39]

Drug Name		**Type of Medication**	**Potential Side Effects**
Anafril **Adapin** **Aventyl** **Elavil** **Endep** **Norpramin**	Pertofrane Sinequan Surmontil Tofranil Vivactil Zonalon	Tricylic Antidepressants (TCIs)	Dry mouth, blurred vision, increased fatigue and sleepiness, weight gain and muscle twitching(tremors), constipation, bladder problems such as urine retention, dizziness, daytime drowsiness, increased heart rate, sewual problems.
Emsam **Eldepryl** **Nardil**	Marplan Parnate Zelepar	Monoamine Oxidase Inhibitors (MOIs)	Headache, heart racing, chest pain, neck stiffness, nausea and vomiting.
Celexa **Lexapro** **Luvox** **Paxil**	Pexeva Prozac Sarafem Zoloft	Selective Serotonin Reuptake Inhibitors (SSRI)	Sexual problems including low sex drive or inability to have an orgasm are common but reversible, dizziness, headaches, nausea, right after a dose insomnia feeling jittery.
Aplenzin **Buedprion** **Buproban**	Forfivo Wellbutrin	The amounts of the neurotransmitters serotonin and norepinephrine in the brain may be increased by Bupropion.	Weight loss, decreased appetite, restlessness, insomnia, anxiety, constipation, dry mouth, diarrhea, dizziness, seizures.
Cymbalta **Effexor** **Fetzima**	Khedezla Pristiq	The levels of the neurotransmitters serotonin and norepinephrine in the brain can be increased by these drugs.	Drowsiness, blurred vision, lightheadedness, strange dreams, constipation, fever/chills, headache, increased or decreased appetite, tremor, dry mouth, nausea.
Desyrel **Ludiomil** **Oleptro**		Various transmitters are blocked to some degree by these drugs.	Drowsiness, fatigue, tremor, headache, dry mouth, nausea, and vomiting.

There are some interesting findings in some surveys about mental diseases. It is seen that some segments of the population such as older people and non-white individuals underused mental health services. Since 1997, there were little changes on these matters. A possible explanation for this is the improvement of social network substitutes around the world. Another interesting finding from these surveys was that overweight and obese MDD subjects were more leading to be treated for MDD [38]. They are possible using health care services more likely for their physical problems. Therefore, the chances of rcognizing and treatment of depression was increasing.

It is widely assumed that the treatment helps to change improvement in depressive symptoms to an improvement in the quality of life and a decrease in disability. Few studies focus on quality of life in depression over long term. Ormal and colleagues got a decrease of disability after a successful treatment of depression following 201 depressed and anxious patients for 3.5 years. While psychosocial functioning and quality of life are improved by acute pharmacotherapy of depression, significant disability may keep to persist during the course of treatment [17]. In addition, MDD may end completely, or only partially or it does not end.

CHAPTER 3

MATERIALS AND METHODS

In this section, information about subjects, the procedure of research such as designation of experiment, auditory stimuli, EEG registration and the signals which are selected to process and signals processing methods are included.

3.1 Subjects

11 patients from Fatih University Sema Hospital, Istanbul who are diagnosed with major depressive disorder according to DSM-IV criteria were participated. As control group, 11 age-matched individuals were included to study. As standardization, some scales which are used to measure the psychiatric disorders were used such as; Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HARS). The protocol was approved both university and Sema hospital ethics committee. Also, an inform consent was completed and signed by the patients. Information like age, education situation etc. were taken from the psychiatrist Mr.Bilgic.

Table 3.1 Demographics and self-report measures of subjects

	MDD Patients	Controls
Number	11	11
Male/Female	4/7	3/8
Age	30	26

While participants were recruiting, some extension criteria were considered.

Exclusion criteria;

1.Head trauma

2.Epilepsy history about patient or among relatives

3.Having some serious illnesses such as diabetes mellitus, chronic renal insufficiency, hapatic insufficiency etc.

4.Having alcohol or substance abuse disorder

5.Having any other psychiatric disorders

6.Having history of cerebrovascular diseases

7.Having dementia

8.Having multiple medicine usage

Inclusion criteria;

1.Diagnosed with MDD according to DSM-IV criteria

2.Aged between 20-50

3.Applying BDI, BAI, Ham-D, HARS

4.Giving written, informed consent

3.2 Procedure

3.2.1 Trial Design

In order to get the data of good quality, a silent, illuminated, temperature-controlled and airy room was used. Subject was instructed about procedure and proved to adapt to process. During EEG recording, since muscle artifacts are occurred, assuming a comfortable position, avoiding a movement and relax jaw muscles,looking directly in front of her/him even the eyes are closed and avoiding unnecessary eye movements were informed to subject. Additionally, he/she was informed to not move his/her mouth, legs, head or arms during trial because to not to have such artifacts. The behaviors of subject such as movement, sneeze, coughing were observed and recorded as annotations

in EEG BrainAmp recording program. Also, any noises coming from out of subject were recorded. Each subject was exposed to EEG registration, 10 min in duration (eyes closed).

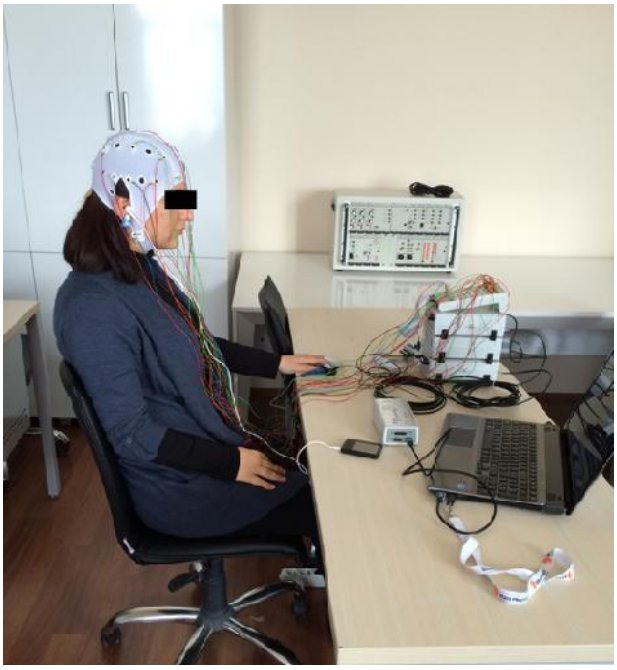

Figure 3.1 Trial design of a control subject

3.2.2 Auditory Stimuli

Auditory stimuli consisted of totally 10 min including five periods each of which 2 min stimulations. Periods were put in an order as the following; 2 min resting period (resting 1), 2 min sedative music, 2 min resting period (resting 2), 2 min alerting stimulation, 2 min last resting period (resting 3). For this stimulation period in this study, stimulations were selected as white noise (WN) for alerting period and classical Turkish music (CTM) for sedative period. White noise was including the sound of a broken washing machine.

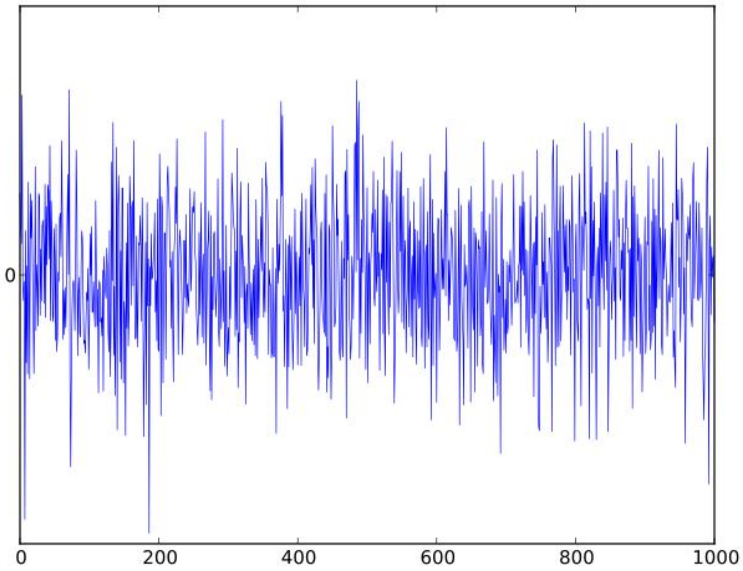

Figure 3.2 Plot of Gaussian white noise signal[40]

For the classical Turkish music, an enstrumantel Rast makam called as ‘Darıldın Mı Cicim Bana’ which is anonym was selected. The history of music in Turkish culture and the place of treatment in classical Turkish music were constructed by Somakci [41]. In the term of 9^{th}-10^{th} century, Farabi who is one of the Turkish scientists expressed that the music is efficient about the treatment, especially for the psychical diseases. He explained the types of makams and the effects of this makams on the soul of human according to their psychological situations. As it is written in the article, there are twelve makams and some of them are as follows: Rast makam make people feel peace and cheer and it helps to feel pleasure; Rehavi makam helps to feel the idea of eternity; Neva makam brings flavor and relief etc. In this study, Rast makam was used to observe the positive emotions during EEG recording. The stimuli with the intensity of 80 dB were listened to the all subjects using headphones binaurally.

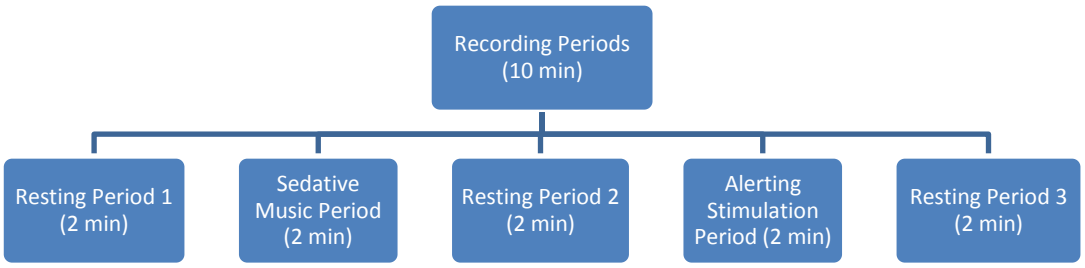

Figure 3.3 Total duration of signal recording periods

3.3 Signal Description and Measurement System

Electroencephalogram measurements were taken from the subjects using the standard V-Amp DC model of Brain Vision Products. V-Amp is enabled to measure different kinds of signals such as EEG, EOG, ECG, EMG and the full range of evoked potentials. Also, auxiliary ports includes sensors for peripheral signals like GSR, blood flow, temperature interface. 16 channels and 2 auxiliary ports are enabled to use.

Figure 3.4 Standard V-Amp

3.3.1 Electroencephalography (EEG)

EEG records the potentials resulted from the communication of brain cells. Brain cells produce tiny signals when they are communicating each other during neural activity. Electrodes placed on the scalp pick up these signals and send them to a machine called as electroencephalogram. EEG records the signals as wavy lines and they can be seen on the computer screen or on the paper. EEG is able to identify the areas of the brain via used electrodes placed on the scalp. The signals of the each brain area can be examined.

EEG is mainly use to detect the problems about brain activity it helps to diagnose or manage some brain disorders such as

1.Seizure disorders, including epilepsy

2.Head injury

3.Encephalitis, or inflammation of the brain

4.Brain tumor

5.Memory problems

6.Stroke

7.Sleep disorders

EEG waveforms are defined as frequency, amplitude, and location. During neural activity, scalp EEG shows oscillations at a variety of frequencies depend on the different states of the brain functioning such as being awake and sleep stages [42]. According to these functioning, these oscillations' frequency ranges and spatial distributions are different from each other. Some of oscillations are identified while some are not. The identified frequency range is classified as followed; delta band (0.1 to 3.5 Hz), theta band (4 to 7.5 Hz), alpha band (8 to 13Hz), beta band (14 - 30Hz), and gamma band (30 - 60Hz) . EEG amplitude indicated as the voltage is about 10 to 100 μV.

In our study we recorded the data from different regions; frontal (Fp1, Fp2, F7, F3, Fz, F4, F8), temporal (T7, T8), central (C3, Cz, C4), parietal (P7, P3, P4, P8).

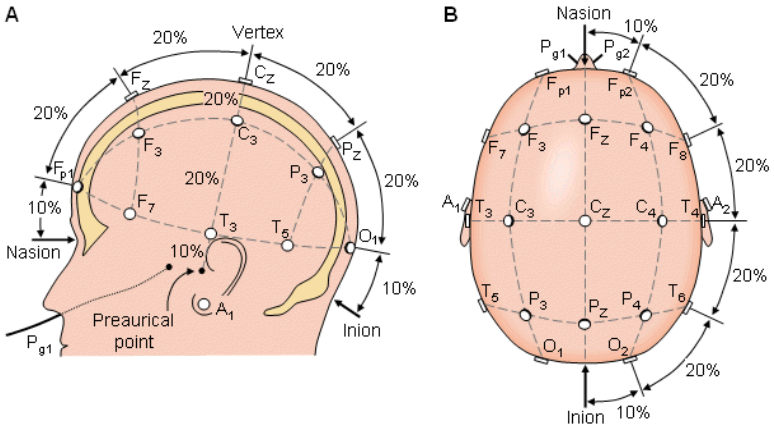

Figure 3.5 The international 10-20 system seen from (A) left and (B) above the head [43]

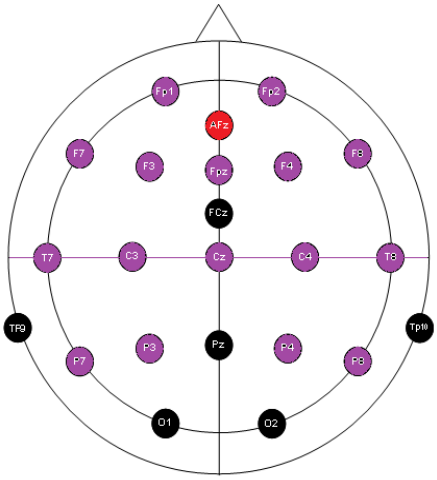

Figure 3.6 16 electrode arrangement on the cap [44]

The signals were recorded using V-Amp DC model of Brain Vision. Reference was taken from both ears to get equal differences between each impedance and ground. So, ground also placed on the Fz region. A lycra stretch 32 channel placed according to 10-20 system cap was arranged on the head and 16 channels we need to get were used. The sampling frequency was set to 250 Hz based on Nyquist theorem, which states that a sampling rate must be at least twice as high as the highest frequency of the EEG signal (50 Hz or 60 Hz), time constant was 10, and data were high pass filtered at 70 Hz. According to Turkish electrical system standard, notch filter was set to 50 Hz.

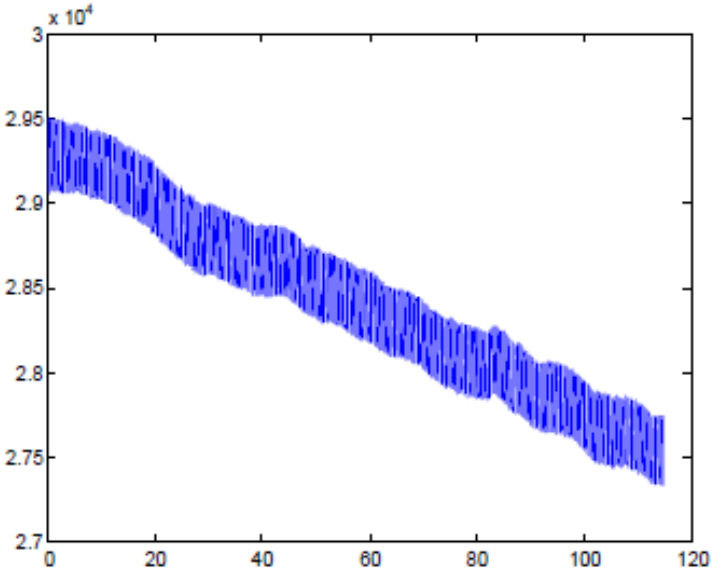

Figure 3.7 EEG signal of a patient

3.4 Signal Processing

3.4.1 Wavelet Decomposition

Signals are not availably understandable when they are first recorded as raw signal. That's why transformations are applied to get further information. Wavelet transformation shows which frequency components exist in what time for non-stationary signals.

The time and frequency informationcan be provided by Wavelet transform simultaneously, so it gives a time-frequency representation of the signal. It helps to know what spectral component exists at any given time instant[45]. Also, it could be known by wavelet transform which different frequencies are analyzed with different resolution since it uses multi resolution technique.

3.5 Discrete Wavelet Transform

Discrete wavelet transform is based on sub-band coding of resources. It is the fast computation way and it easy to implement to transform. Computation time and resources required may be reduced by the wavalet. It is a procedure to decompose the signal to its sub bands. According to the Nyquist's rule, after passing the signal through a half band low pass filter, half of the samples can be eliminated. After subsampling the

signal by to discarding every other sample, it will have half the number of points and the scale of the signal is doubled. Resolution is halved by the lo pass filtering but the scale doesn't change. While the frequency reaolution is doubled, the time resolution is doubeled by the discrete wavelet transform since the entire signal is characterized by the half the number of the samples..

Transformation procedure starts with passing the signal (sequence) through a half band digital low pass filter with impulse response h[n]. Filtering signal corresponds to convolution operation of the signal with the impulse response of the filter. The convolution operation in discrete time is as followed;

$$x[n] * h[n] = \sum_{k=-\infty}^{\infty} \mathrm{x[k]} \cdot \mathrm{h[n-k]} \qquad (3.1)$$

where x[n] is the sequence.

In the figure 3.8 x[n] is the original signal to be decomposed and h[n] and g[n] are low pass and high pass filters, respectively. The f is showed at each level as the bandwidth of the signal[45].

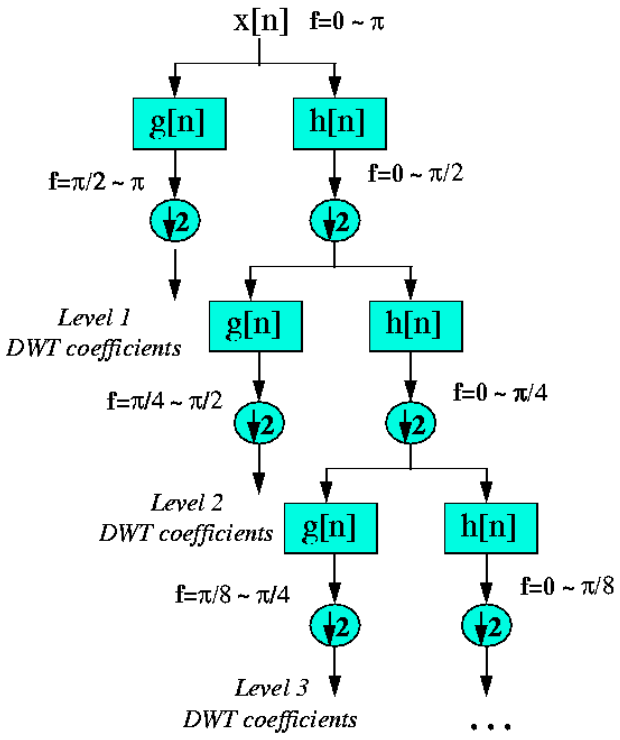

Figure 3.8 The subband coding algorithm [45]

3.5 Statistical Analysis

3.5.1 Analysis of Variance (ANOVA)

Analysis of variance is a statistical technique used to determine inequality among population means. ANOVA can be used to analyze variability in data in order to infer the differences of more than two population means. It helps to save time doing in a short time and to have the control of the probability of falsely declaring significant differences among means. In the honor of Sir R.A. Fisher who conceived the idea of ANOVA, the statistic of its name is called as *F statistics [46]*.

3.5.1.1 Two Way Analaysis of Variance

Two way ANOVA is useful when we desire to compare effects of one dependent variable on two or more independent variables or in other words factors. These two factors must be independent and the variances of populations must be equal. The size of independent groups must be the same and populations are normally distributed [47].

Three sets of null hypothesis are included in the results of a two way ANOVA. The first hypothesis is the population means of first variable or factors are same, the second is the population means of second factor are same and the third is that there is no interaction between the two factors [48].

Total sum of squares is

$$SS_{Total}=SS_{between} + SS_{within} = \sum X^2 - \frac{(\sum X)^2}{N} \tag{3.2}$$

The sum of squares between groups is

$$SS_{between} = \frac{(X_1)^2}{n_1} + \frac{(X_2)^2}{n_2} + \cdots + \frac{(X_{ac})^2}{n_{ac}} - \frac{(\sum X)^2}{N} \tag{3.3}$$

The sum of squares within group is

$$SS_{within} = SS_{total} - SS_{between} \tag{3.4}$$

The sum of squares of independent variables is

$$SS_A = \sum \frac{(\sum for\ each\ row)^2}{n\ for\ each\ row} - \frac{(\sum X)^2}{N} \tag{3.5}$$

$$SS_C = \sum \frac{(\sum for\ each\ column)^2}{n\ for\ each\ column} - \frac{(\sum X)^2}{N} \quad (3.6)$$

The interaction sum of squares is

$$SS_{AC} = SS_{between} - SS_A - SS_C \quad (3.7)$$

Degrees of freedom, *df*, for each sum of squares[49]

$$df_{total} = N - 1,\ \ df_A = a - 1,\ \ df_C = b - 1, df_{AC} = (a-1)(b-1) \quad (3.8)$$

The mean squares of total, A factor, C factor and interaction mean square are as followed

$$MS_A = \frac{SS_A}{df_A}$$

$$MS_C = \frac{SS_C}{df_C}$$

$$MS_{AC} = \frac{SS_{AC}}{df_{AC}} \quad (3.9)$$

-

CHAPTER 4

RESULTS

In this chapter, analyzing results of electrophysiological data are reported. EEG signals recorded from major depressed petients and control subjects are processed using algorithms for each signal which are eveloped in MATLAB to generate discriminating features between groups and between periods of auditory stimuli.

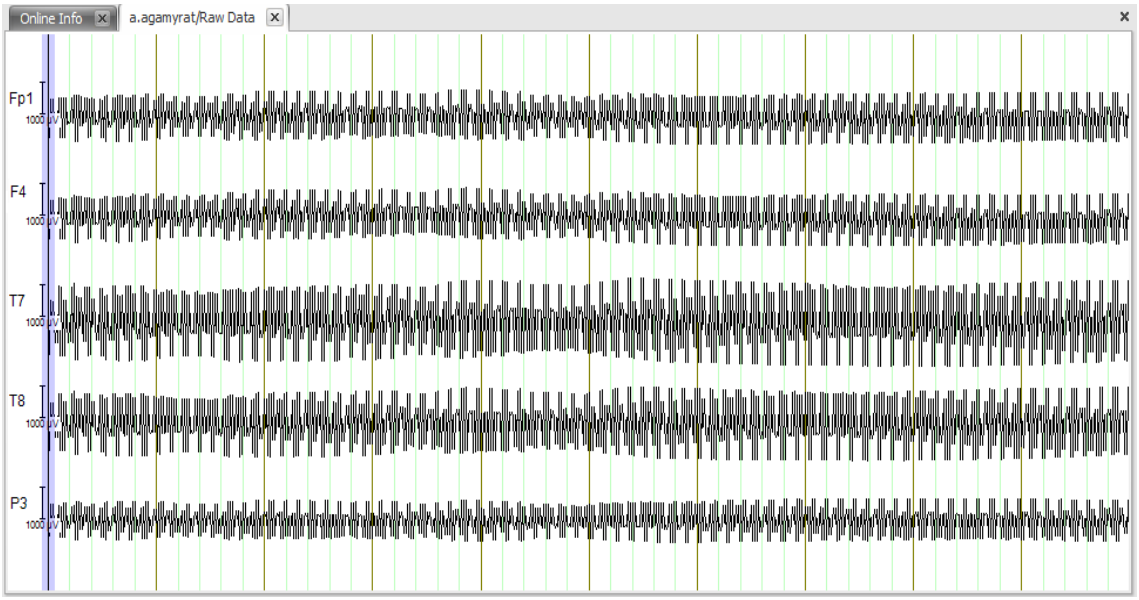

Figure 4.1 A sample EEG data recording on the BrainVision Analyzer

Figure 4.1 shows a sample EEG data recording on the BrainVision Analyzer. Further more, data are analyzed by the SPSS (v.20.0) statistical package (SPSS Inc., Chicago, IL) to detect differerences in features between patients and controls, between periods, and the results of statistical analysis are reported in this chapter.

EEG signals recorded from Fp1, F4 frontal, T7, T8 temporal, and P3, P4 parietal regions analyzed using nonlinear methods. The nonlinear analysis was done using MATLAB 7.6.0®. Raw EEG signals of a patient in the Fp1 region during different recording periods are shown in Figure 4.2.

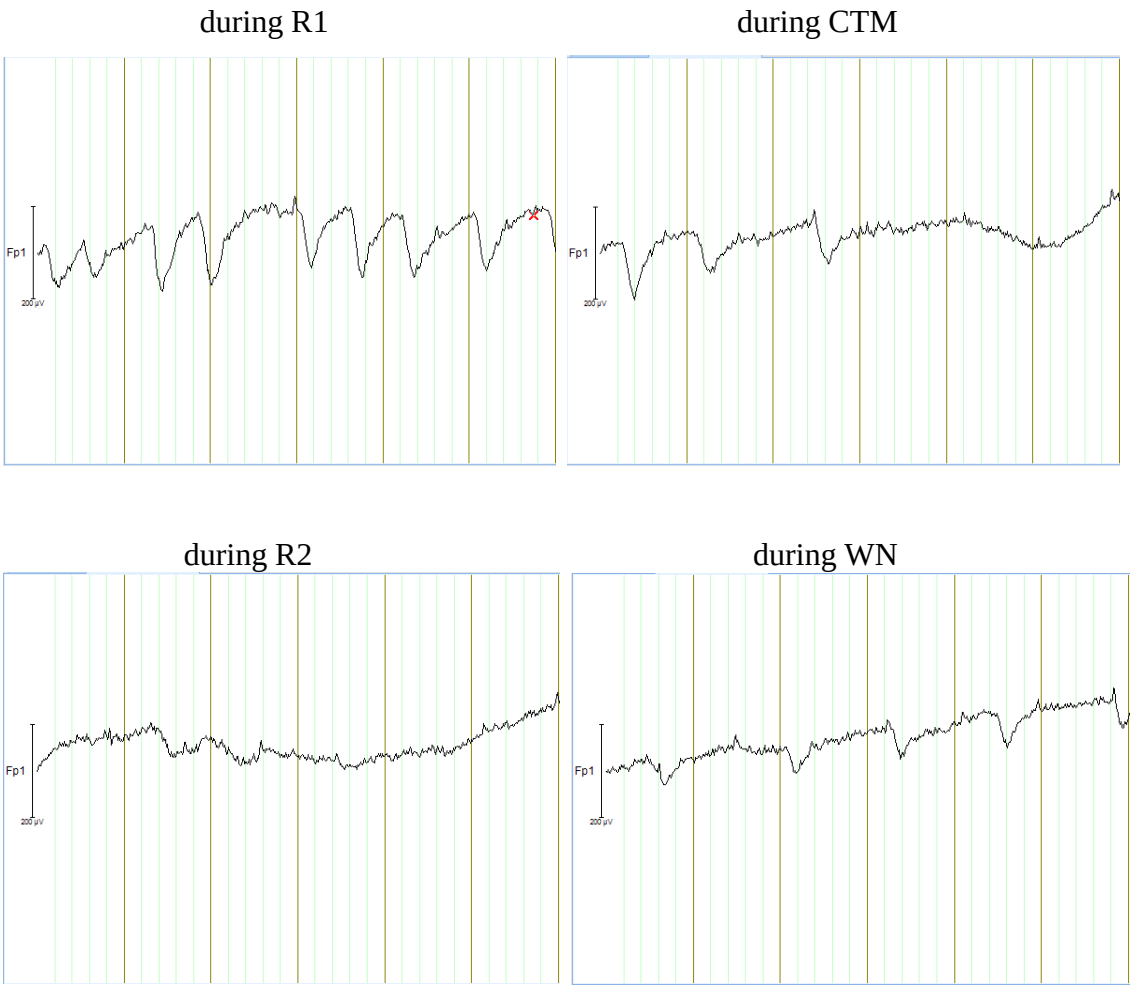

Figure 4.2 Raw Fp1 region EEG signal of a patient during R1, CTM, R2, and WN

Both Higuchi and Katz fractal dimensions were investigated for MDD group and control goups. Since Higuchi fractal dimensions were almost same within both groups, KFD were considered to analyze significant differences. The mean and standard deviation results of the KFD of EEG subbands in each channel of control subjects and depressed patients are summarized in Tables 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8, 5.9, 5.10, 5.11, 5.12 .

Table 5.1 The Fractal Dimension of EEG signal in each period for the control subjects for Fp1 region

Control Group	The Fractal Dimension				
Fp1	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,025±0,026	1,027±0,038	1,017±0,018	1,013±0,014	1,017±0,025
Theta (mean ± SD)	1,025±0,026	1,027±0,038	1,017±0,018	1,013±0,014	1,017±0,025
Alpha (mean ± SD)	1,71±0,047	1,703±0,046	1,711±0,047	1,704±0,014	1,695±0,057
Beta (mean ± SD)	1,84±0,014	1,844±0,017	1,852±0,019	1,844±0,017	1,828±0,071

Table 5.2 The Fractal Dimension of EEG signal in each period for the control subjects for F4 region

Control Group	The Fractal Dimension				
F4	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,018±0,028	1,022±0,027	1,035±0,039	1,028±0,031	1,037±0,053
Theta (mean ± SD)	1,018±0,028	1,022±0,027	1,035±0,039	1,028±0,031	1,037±0,053
Alpha (mean ± SD)	1,692±0,040	1,687±0,039	1,692±0,040	1,689±0,040	1,689±0,043
Beta (mean ± SD)	1,852±0,015	1,842±0,011	1,848±0,019	1,845±0,015	1,848±0,019

Table 5.3 The Fractal Dimension of EEG signal in each period for the control subjects for T7 region

Control Group	The Fractal Dimension				
T7	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,009±0,012	1,012±0,020	1,014±0,017	1,018±0,025	1,034±0,036
Theta (mean ± SD)	1,009±0,012	1,012±0,020	1,014±0,017	1,018±0,025	1,101±0,218
Alpha (mean ± SD)	1,648±0,218	1,711±0,041	1,718±0,043	1,710±0,043	1,713±0,045
Beta (mean ± SD)	1,847±0,218	1,852±0,020	1,857±0,022	1,847±0,021	1,850±0,021

Table 5.4 The Fractal Dimension of EEG signal in each period for the control subjects for T8 region

Control Group	The Fractal Dimension				
T8	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,016±0,028	1,018±0,044	1,018±0,025	1,018±0,028	1,038±0,396
Theta (mean ± SD)	1,016±0,028	1,082±0,210	1,018±0,025	1,018±0,028	1,038±0,039
Alpha (mean ± SD)	1,717±0,048	1,714±0,045	1,719±0,048	1,713±0,045	1,714±0,049
Beta (mean ± SD)	1,849±0,048	1,845±0,016	1,852±0,022	1,845±0,020	1,846±0,016

Table 5.5 The Fractal Dimension of EEG signal in each period for the control subjects for P3 region

Control Group	The Fractal Dimension				
P3	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,034±0,039	1,014±0,017	1,035±0,041	1,021±0,026	1,037±0,044
Theta (mean ± SD)	1,034±0,039	1,014±0,017	1,035±0,041	1,021±0,026	1,037±0,044
Alpha (mean ± SD)	1,703±0,046	1,701±0,041	1,706±0,046	1,702±0,044	1,704±0,040
Beta (mean ± SD)	1,839±0,013	1,838±0,013	1,846±0,013	1,837±0,013	1,843±0,015

Table 5.6 The Fractal Dimension of EEG signal in each period for the control subjects for P4 region

Control Group	The Fractal Dimension				
P4	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,020±0,023	1,011±0,014	1,018±0,021	1,026±0,039	1,027±0,030
Theta (mean ± SD)	1,020±0,023	1,011±0,014	1,018±0,021	1,026±0,039	1,027±0,030
Alpha (mean ± SD)	1,694±0,043	1,693±0,039	1,701±0,041	1,697±0,041	1,699±0,043
Beta (mean ± SD)	1,842±0,007	1,837±0,007	1,846±0,010	1,836±0,009	1.840±0,010

Table 5.7 The Fractal Dimension of EEG signal in each period for the depressed subjects for Fp1 region

Depressed Group	The Fractal Dimension				
Fp1	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,019±0,018	1,016±0,022	1,013±0,023	1,014±0,021	1,011±0,016
Theta (mean ± SD)	1,018±0,017	1,016±0,022	1,013±0,023	1,014±0,021	1,011±0,016
Alpha (mean ± SD)	1,700±0,017	1,696±0,048	1,706±0,047	1,700±0,050	1,702±0,052
Beta (mean ± SD)	1,846±0,016	1,840±0,014	1,852±0,016	1,839±0,011	1,847±0,016

Table 5.8 The Fractal Dimension of EEG signal in each period for the depressed subjects for F4 region

Depressed Group	The Fractal Dimension				
F4	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,017±0,017	1,014±0,014	1,015±0,022	1,021±0,025	1,019±0,021
Theta (mean ± SD)	1,017±0,017	1,014±0,014	1,015±0,022	1,021±0,025	1,019±0,021
Alpha (mean ± SD)	1,698±0,050	1,692±0,047	1,700±0,049	1,693±0,052	1,693±0,049
Beta (mean ± SD)	1,842±0,017	1,838±0,014	1,850±0,017	1,836±0,013	1,846±0,016

Table 5.9 The Fractal Dimension of EEG signal in each period for the depressed subjects for T7 region

Depressed Group	The Fractal Dimension				
T7	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,018±0,025	1,016±0,021	1,012±0,018	1,012±0,017	1,013±0,021
Theta (mean ± SD)	1,018±0,025	1,016±0,021	1,012±0,018	1,012±0017	1,013±0,021
Alpha (mean ± SD)	1,720±0,062	1,704±0,042	1,712±0,042	1,706±0,044	1,708±0,045
Beta (mean ± SD)	1,855±0,023	1,845±0,019	1,853±0,018	1,841±0,017	1,847±0,015

Table 5.10 The Fractal Dimension of EEG signal in each period for the depressed subjects for T8 region

Depressed Group	The Fractal Dimension				
T8	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,014±0,024	1,017±0,030	1,008±0,012	1,008±0,008	1,048±0,121
Theta (mean ± SD)	1,014±0,024	1,074±0,188	1,081±0,012	1,075±0,022	1,084±0,022
Alpha (mean ± SD)	1,714±0,049	1,706±0,050	1,715±0,052	1,714±0,063	1,709±0,056
Beta (mean ± SD)	1,843±0,025	1,838±0,025	1,848±0,022	1,866±0,114	1,840±0,018

Table 5.11 The Fractal Dimension of EEG signal in each period for the depressed subjects for P3 region

Depressed Group	The Fractal Dimension				
P3	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,018±0,027	1,015±0,013	1,010±0,010	1,008±0,007	1,010±0,009
Theta (mean ± SD)	1,018±0,027	1,015±0,013	1,010±0,010	1,008±0,007	1,010±0,009
Alpha (mean ± SD)	1,702±0,049	1,641±0,208	1,707±0,048	1,700±0,051	1,700±0,053
Beta (mean ± SD)	1,872±0,115	1,816±0,056	1,843±0,010	1,830±0,030	1,834±0,009

Table 5.12 The Fractal Dimension of EEG signal in each period for the depressed subjects for P4 region

Depressed Group	The Fractal Dimension				
P4	R1	CTM	R2	WN	R3
Delta (mean ± SD)	1,006±0,009	1,006±0,010	1,012±0,025	1,014±0,025	1,014±1,066
Theta (mean ± SD)	1,070±0,219	1,069±0,209	1,012±0,025	1,074±0,223	1,066±0,170
Alpha (mean ± SD)	1,716±0,06	1,699±0,049	1,712±0,049	1,703±0,053	1,725±0,050
Beta (mean ± SD)	0,115±1,872	1,831±0,010	1,840±0,010	1,825±0,006	1,831±0,008

KFDs' of both control and MDD groups were compared for each periods in each channels. The values of KFDs of each group are shown in Figure 4.3, 4.4, 4.5, 4.5, 4.6, 4.7, 4.7, 4.9, 4.10, 4.11, 4.12, 4.13, 4.15, 4.16, 4.17, and 4.18. In this way, the differences in between groups are much available in these graphs to have a clear result.

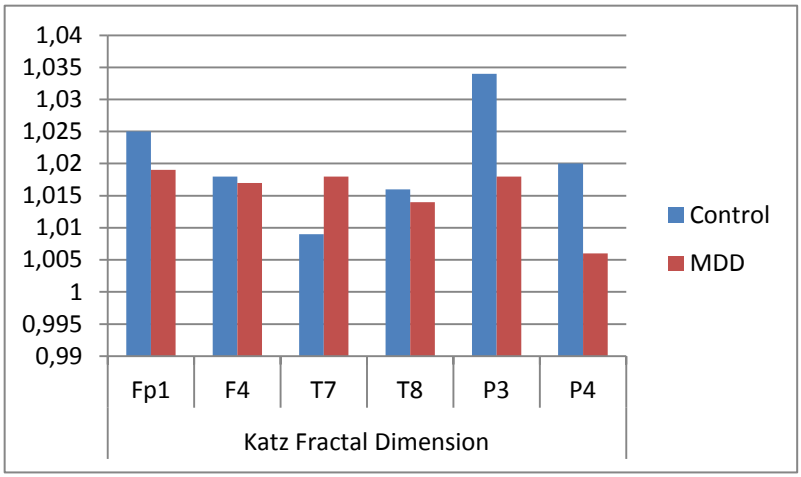

Figure 4.3 Comparison of KFD values' of delta band from all channels in R1 position

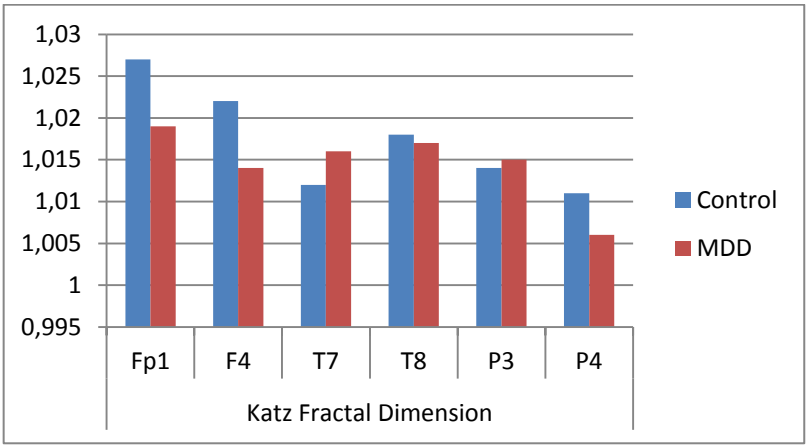

Figure 4.4 Comparison of KFD values' of delta band from all channels in CTM position

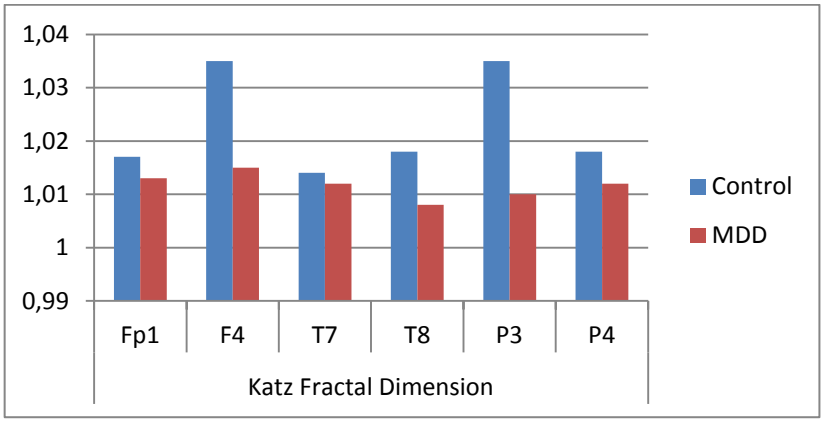

Figure 4.5 Comparison of KFD values' of delta band from all channels in R2 position

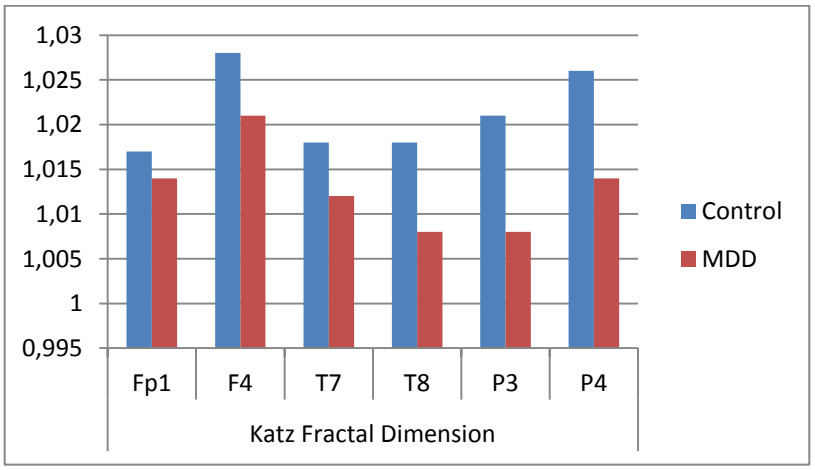

Figure 4.6 Comparison of KFD values' of delta band from all channels in WN position

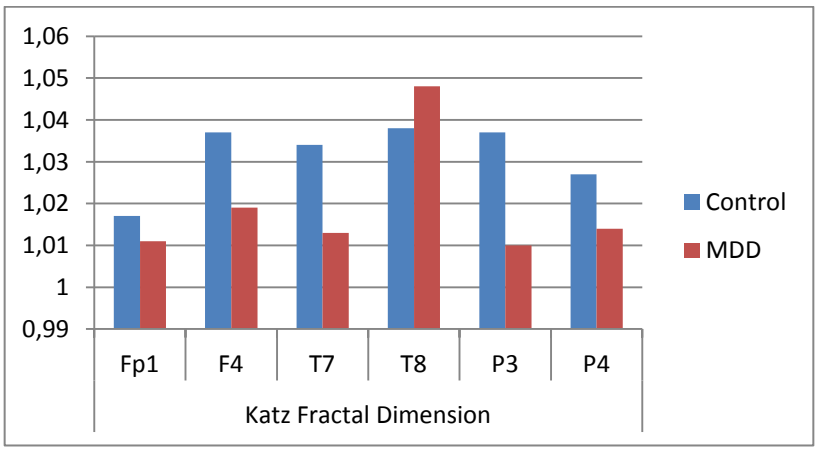

Figure 4.7 Comparison of KFD values' of delta band from all channels in R3 position

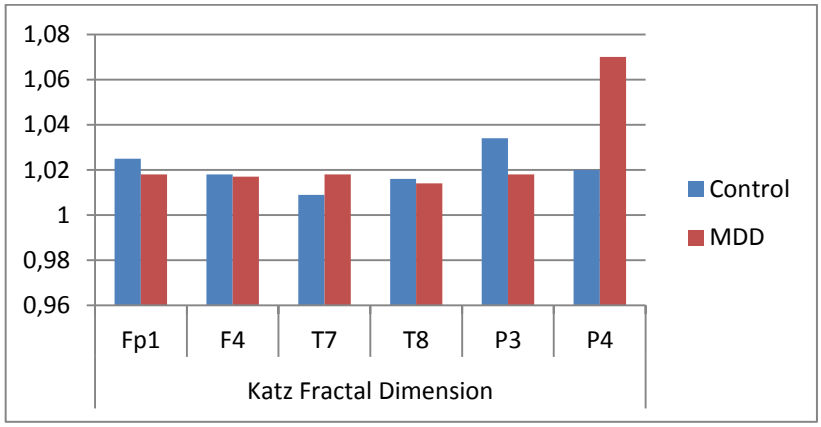

Figure 4.8 Comparison of KFD values' of theta band from all channels in R1 position

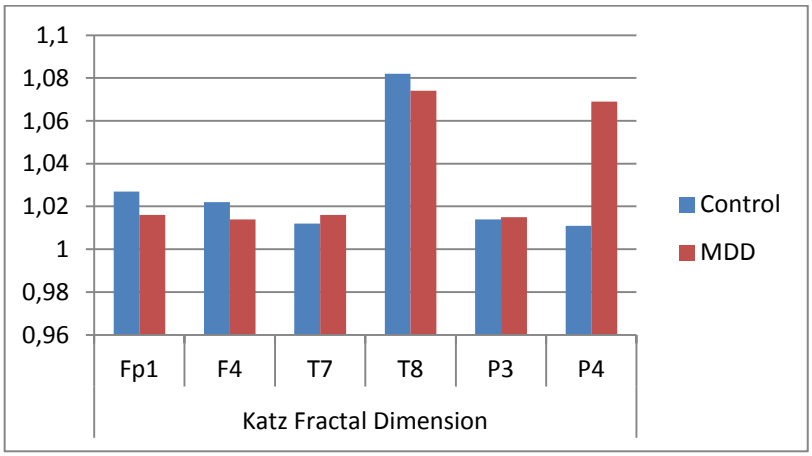

Figure 4.9 Comparison of KFD values' of theta band from all channels in CTM position

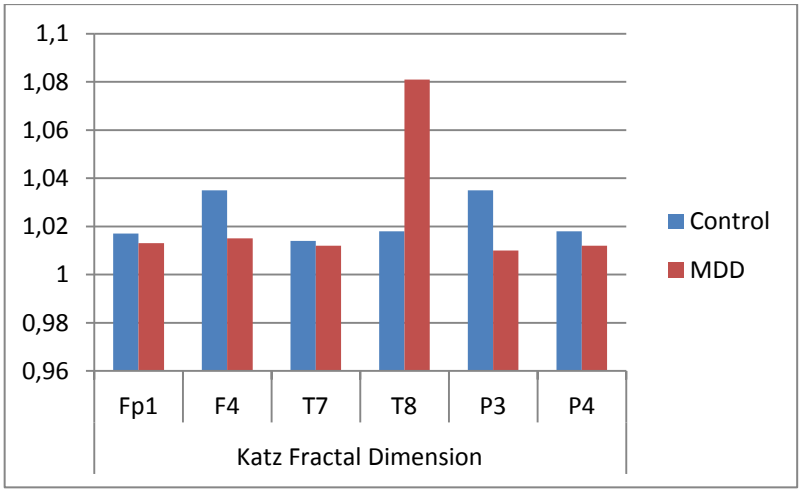

Figure 4.10 Comparison of KFD values' of theta band from all channels in R2 position

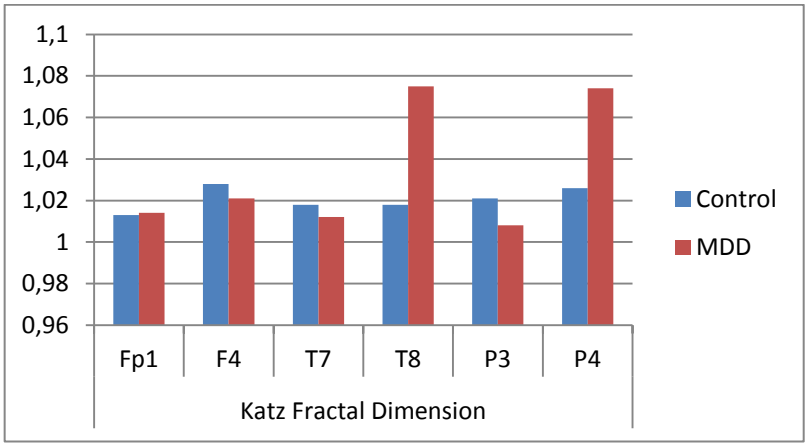

Figure 4.11 Comparison of KFD values' of theta band from all channels in WN position

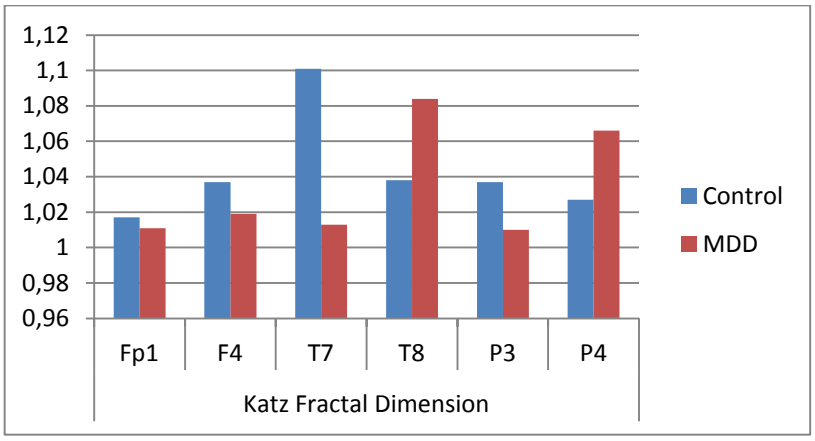

Figure 4.12 Comparison of KFD values' of theta band from all channels in R3 position

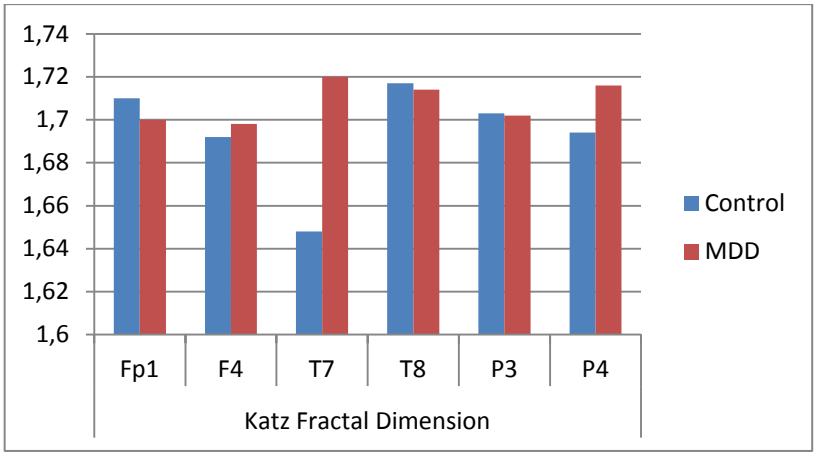

Figure 4.13 Comparison of KFD values' of alpha band from all channels in R1 position

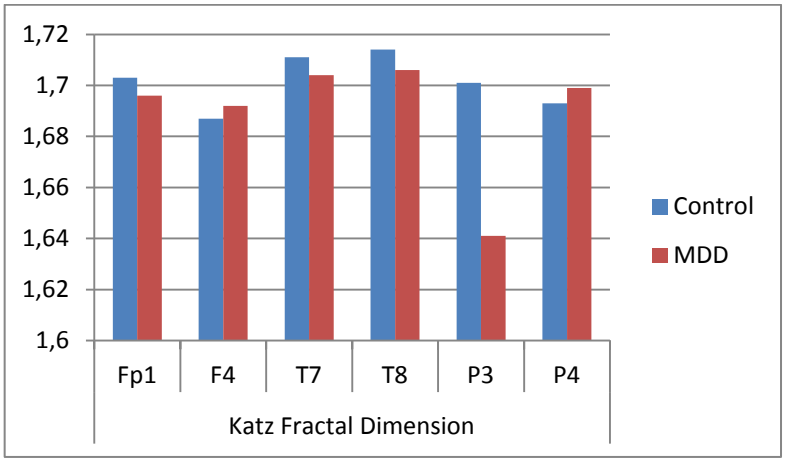

Figure 4.14 Comparison of KFD values' of alpha band from all channels in CTM position

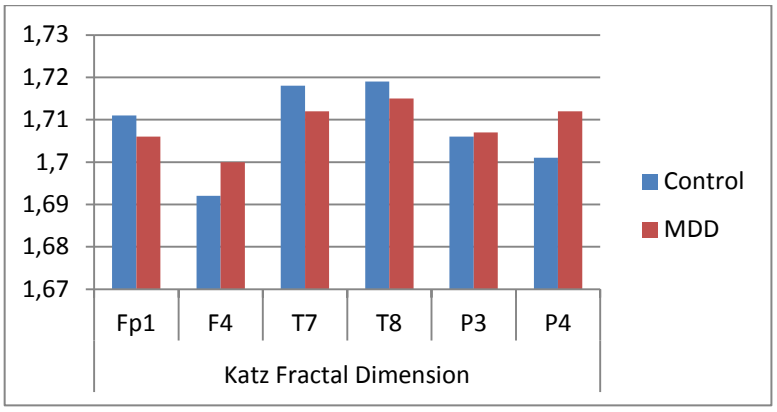

Figure 4.15 Comparison of KFD values' of alpha band from all channels in R2 position

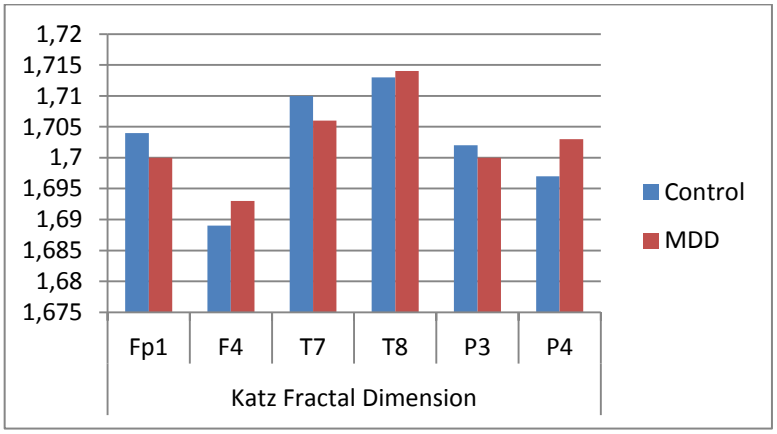

Figure 4.16 Comparison of KFD values' of alpha band from all channels in WN position

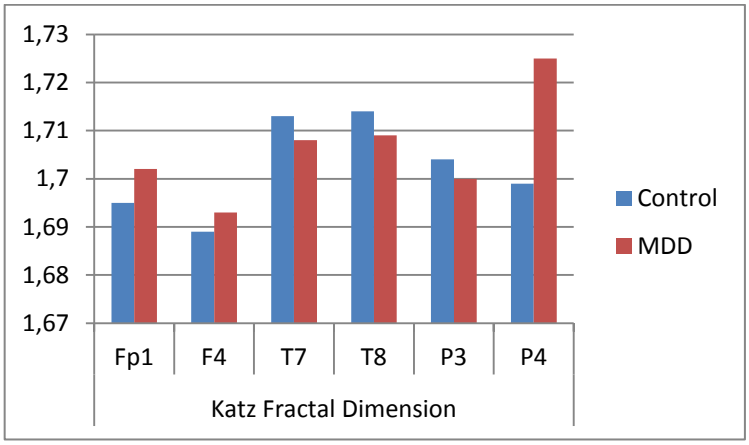

Figure 4.17 Comparison of KFD values' of alpha band from all channels in R3 position

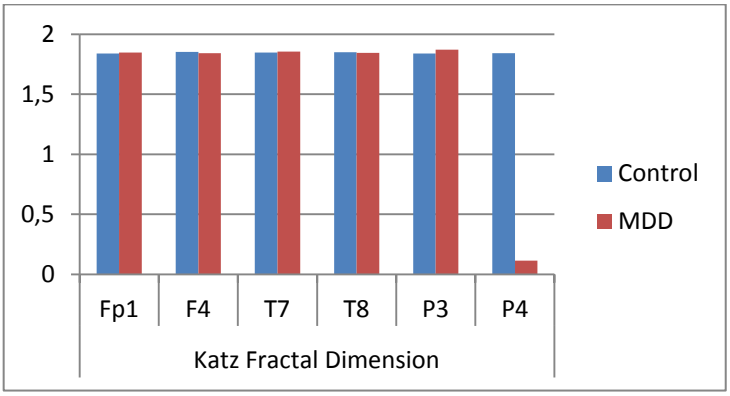

Figure 4.18 Comparison of KFD values' of beta band from all channels in R1 position

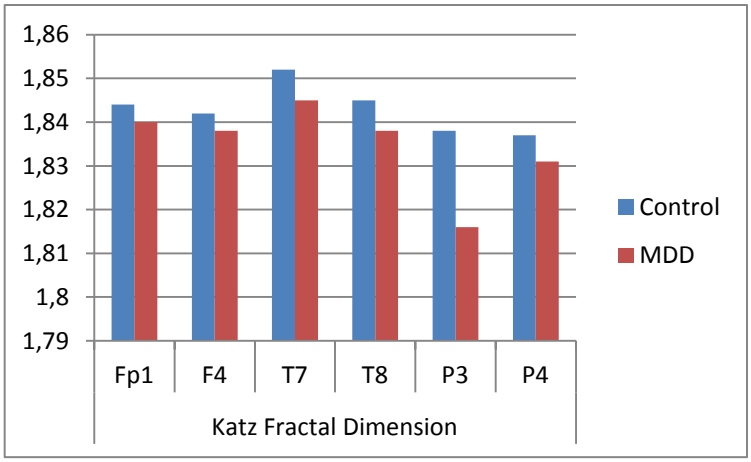

Figure 4.19 Comparison of KFD values' of beta band from all channels in CTM position

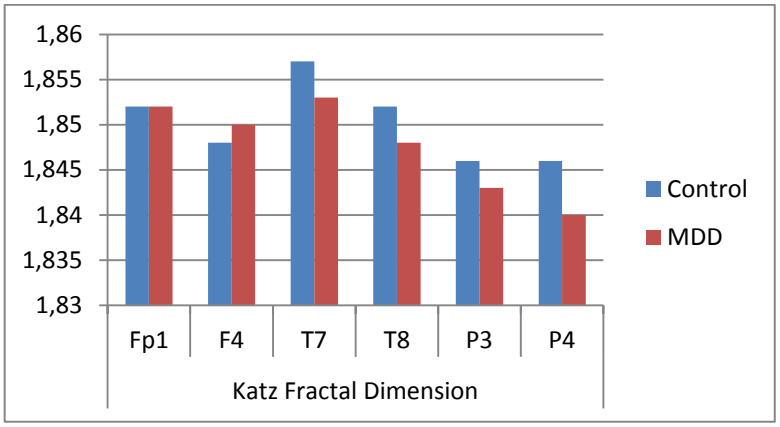

Figure 4.20 Comparison of KFD values' of beta band from all channels in R2 position

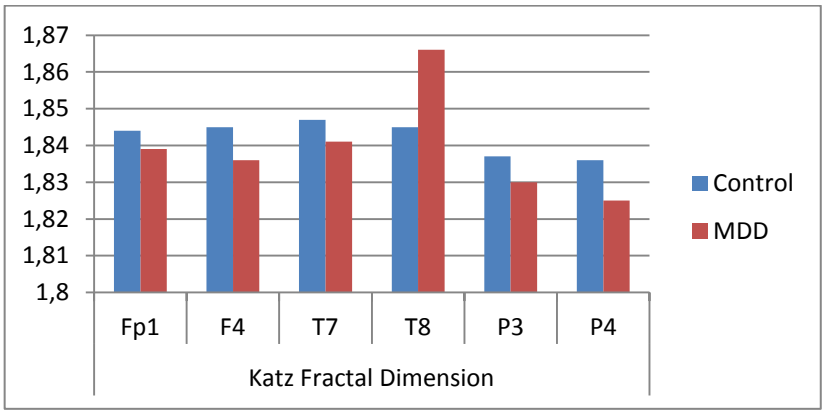

Figure 4.21 Comparison of KFD values' of beta band from all channels in WN position

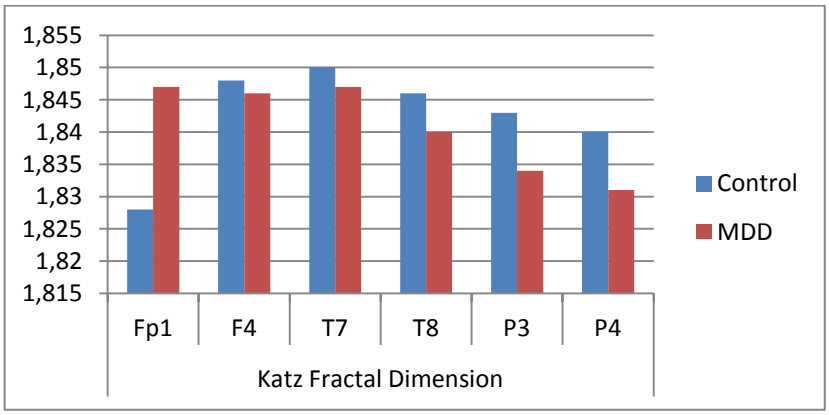

Figure 4.22 Comparison of KFD values' of beta band from all channels in R3 position

EEG signals were analyzed using the SPSS (v.20.0) statistical package. The values of fractal dimensions of each sub bands during each period were compared between groups and within groups using two way ANOVA for each channel. Two way ANOVA was chosen to study the two independent categorical variables (groups and periods) on the one dependent variable (fractal dimension values) and to look if there is any interaction between independent variables. It was assumed that there was a significant difference between and within groups, when p <0,05.

Table 5.13 The p values of KFD's of left end right frontal lobes of EEG sub-bands in discriminating MDD and contol groups.

	Left frontal lobe	Right frontal lobe
Beta band	0,748	0,130*
Alpha band	0,692	0,548
Theta band	1,367	,0056*
Delta band	0,408	0,056*

Table 5.14 The p values of KFD's of left end right temporal lobes of EEG sub-bands in discriminating MDD and contol groups.

	Left temporal lobe	Right temporal lobe
Beta band	0,599	0,969
Alpha band	0,533	0,693
Theta band	0,230	0,528
Delta band	0,479	0,757

Table 5.15 The p values of KFD's of left end right parietal lobes of EEG sub-bands in discriminating MDD and contol groups.

	Left parietal lobe	Right parietal lobe
Beta band	0,867	0,974
Alpha band	0,403	0,132*
Theta band	0,003**	0,137*
Delta band	0,003**	0,030**

*close value to significance p-value of 0,05.
**less than fignificance p-value of 0,05.

As the results of two way ANOVA test, we looked if there is a significant difference between control subjects and depressed groups and also, if there is a significant difference between periods. Table 5.13, 5.14, 5.15 shows the p values of in between groups. In some regions any significant difference was seen. On the other hand, the results of within periods were not have significant difference. The values which belongs to analysis of within periods were almost same. It means the effects of different stimuli has similar effects on the subjects. According to analysis results in between MDD and control groups there were siginificant diferences in some regions for some sub bands. While frontal and parietal regions show differences between groups, temporal regions, theta sub band obviously show there is difference between depressed and healthy groups. For beta sub band of F4 region and for theta and alpha sub bands of P4 region, the effect of auditory stimuli is similar since the p values (0.130, 0.137, 0.132) are greater than 0,05. It doesn't mean that if the number of subjects increases, there won't be any significant difference. For delta and theta sub bands of F4 region, there is close significant difference between groups. The p value (0,056) is pretty much close to 0,05. So, we can't say the effects of auditory stimuli is same in this region for both groups. On the other hand, if the number of subjects increases, probably the results will show a significant difference clearly. For the beta and theta bands of P3 region, there is a high significant difference between groups, since the p value (0,003) is much less than p value of 0,05. We can conclude that, for P region of subjects, effects of stimuli can be seen exactly in the beta and theta sub bands.

CHAPTER 5

DISCUSSION AND CONCLUSION

Major depression is one of the most spreaded diseases around the world [18]. Sadness, volnurebility, suicidality, loss of energy, sleep disturbances are some of the main symptoms. MDD people also have deficits about cognitive domains such as attention, concentration, and executive functions [21-24]. MDD is diagnosed by the clinical experiences of psychiatrists with the criteria based on American Psychiatric Association's Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR) in the case of having at least four symptoms for two weeks [14]. So, there is no other diagnosing method like laboratory tests or electrophysiological methods. Treatment methods os MD are using antidepressants and electroconvulsive therapy which is rarely ud\se. number os using antidepressants is increasing day by day although tey have some important side effects [38].

Some researchers found differences about brain of MDD patients using some imaging methods such as fMRI, PET, and SPECT [23] Also, some investigators are searching about brain signals of MDD using EEG an in some them found some change in the frontal activity of the brain [50].

In his thesis, we studied about the analysis of EEG signals belongs to MDD patients using nonlinear methods. 11 MDD patients and 11 control subjects who are in the age of between 20 to 50 were recruited to collect the signal data. Patients who have epilepsy history in their family or among relatives, dementia, alcohol or substance abuse disorder were elected. Also, they were diagnosed with DSM-IV criteriato be included to study. Signlas were recorded from 6 regions of brain (Fp1, F4, T7, T8, P3, P4). Participants were exposure to auditory stimuli which keeps 10 minutes. Auditory stimuli has 5 periods consist of R1, CTM, R2, WN and R3 periods.

Recorded EEG signals were analysed in MATLAB using wavelet decomposition which is one of the nonlinear methods and then signals were decomposed to sub bands (alpha, beta, delta, theta). Fractal dimensions of each sun bands were calculated using Katz and

Higuchi fractal diemension methods. Since there was almost no differences among the alues of Higuchi fractal dimension calculations, KFD were used for this study. Two way ANOVA were applied to obtain statistical results in SPSS. Using this method, it is aimed to investigate significant differences between MDD patients and healthy subjects and also differences within the periods.

As the result of this study, it is supported that there are some changes about MDD patient's brains and it is obviously can be analyzed using EEG. We recorded signals only from 6 channels and parietal and temporal regions have differences between MDD and healthy subjects. Especially, theta and delta bands includes high significant differences that can be discriminate both groups from each other. Research can be done with more channels to have detailed information about brain changes of MDD patients. According to our research, if the number of each group members increase, the results would be more clear. The other regions and sub bands of these regions may show significant differences. For example, alpha and theta bands of parietal region, beta, thete, and delta bands of frontal region have close values to significancy. It is highly possible to see significant difference if the number of individuals increase. On the other hand, we couldn't see a siginificant difference within the periods. But, it is possible to have better results with more crowded research group.

There are some researches which are similar to our study. One of them was investigated about effects of mucical stimuli on 16 healthy subjects [51]. They were listened three types of music which are neutral, positive or negative moods when their eyes are opened. Researches found that there is a frontal asymmetry between right and left frontal electrode sides. Acording to another research there are significant differences about three frequency sub bands of MDD and healthy subjects. Theta and alpha activity at parietal and occipital regions is higher for MDD which causes decreased cortical activation and enhancement of beta power may cause anxiety symptoms which play important role for depression[52]. Frontal abnormality is studied in another research, too. 12 MDD and 12 healthy subjects were recruited for this study at the age of between 20 and 28. They were sat a quite room for 3 minutes recording EEG signals without any stimuli. They used wavelet-chaos methodology to analyze results and calculated the Katz and Higuchi fractal dimensions and used Higuchi for statistics. ANOVA is chosen

to have a statistical result for the investigation. It is found differences between MDD and healthy subjects in frontal lobe for beta and gamma band [50].

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