T.C.
FATIH UNIVERSITY
INSTITUTE OF BIOMEDICAL ENGINEERING

INVESTIGATION OF DEPRESSION, OBSESSIVE COMPULSIVE DISORDER AND THEIR TREATMENT METHODS

MURAT KARA

MSc THESIS
BIOMEDICAL ENGINEERING PROGRAMME

ISTANBUL, AUGUST / 2015

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ASIST. PROF. DR. HAŞİM ÖZGÜR TABAKOĞLU

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FATİH ÜNİVESİTESİ
BİYOMEDİKAL MÜHENDİSLİK ENSTİTÜSÜ

DEPRESYON, OBSESİF KOMPÜLSİF BOZUKLUK HASTALIKLARI VE İLGİLİ TEDAVİ YÖNTEMLERİNİN İNCELENMESİ

MURAT KARA

YÜKSEK LİSANS
BİYOMEDİKAL MÜHENDİSLİĞİ PROGRAMI

DANIŞMAN
YRD. DOÇ. DR. HAŞİM ÖZGÜR TABAKOĞLU

İSTANBUL, AĞUSTOS / 2015

T.C.

FATIH UNIVERSITY

INSTITUTE OF BIOMEDICAL ENGINEERING

Committee Members

Murat Kara**, a** MSc **student of Fatih University** Institute of Biomedical Engineering **student ID 520112024, successfully defended the** thesis/dissertation **entitled "INVESTIGATION OF DEPRESSION, OBSESSIVE COMPULSIVE DISORDER AND THEIR TREATMENT METHODS",** which he prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

Thesis Advisor : Asist. Prof. Dr. Haşim Özgür TABAKOĞLU
Fatih University

Asist. Prof. Dr. Ömer ŞAYLİ
Kocaeli University

Asist. Prof. Dr. Saime AKDEMİR AKAR
Fatih University

It is approved that this thesis has been written in compliance with the formatting rules laid down by the Institute of Biomedical Engineering.

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……**Prof. Dr. Sadık KARA**

Director

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I dedicate my dissertation to my parents. I also devote to this thesis to my friends and project family who have encouraged me during the collecting data process. I will firmly appreciate all they have done, especially Mustafa Selman YILDIRIM for helping me improved my technical abilities and Dr. Haşim Özgür TABAKOĞLU for the many hours of proofreading.

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August 2015 Murat KARA

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LIST OF SYMBOLS

Gy	Gray
mV	Mlili Volt
μV	Mikro Volt
Hz	Hertz
α	Alpha
β	Beta
θ	Theta
δ	Delta
γ	Gamma

ABREVIATIONS

OCD : Obsessive Compulsive Disorder
EEG : Electroencephalography
AP : Action Potential
PSP : Postsynaptic Potentials
ECoG : Electrocorticogram
MS : Multiple Sclerosis
AIDS : Acquired Immune Deficiency Syndrome
SAD : Seasonal Affective Disorder
PET : Positron Emission Tomography
CT : Computerized Tomography
MRI : Magnetic Resonance Imaging
SPECT : Single-Photon Emission Comuted Tomography
fMRI : Functional Magnetic Resonance Imaging
OFC : Orbitofrontal Cortex
rCBF : Regional Cerebral Blood Flow
YBOCS : Yale-Brown Obsessive Compulsive Scale
CBT : Cognitive Behavioral Therapy
SUD : Substance Use Disorder
SSRIs : Selective Serotonin Reuptake Inhibitors
MAOIs : Monoamine Oxidase Inhibitors's
TCAs : Tricyclic antidepressants's
ECT : Electroconvulsive Therapy
TMS : Transcranial Magnetic Stimulation
VNS : Vagus Nerve Stimulation
LINAC : Linear Accelator
FDA : Food and Drug Administration
IV : Intravenous
EBC : European Brain Council
WHO : World Health Organization
ERP : Effective Radiated Power

MMPI : Multiphasic Personality Inventory

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders

DBS : Deep Brain Stimulation

AT : Anterior Commissure

PC : Posterior Commissure

CSTC : Corticostriat Othalamocortical

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SUMMARY

INVESTIGATION OF DEPRESSION, OBSESSIVE COMPULSIVE DISORDER AND THEIR TREATMENTS METHODS

Murat KARA

Biomedical Engineering Programme

MSc Thesis

Advisor: Asist. Prof. Dr. Haşim Özgür TABAKOĞLU

This study is a technique and also a compiler reserach that investigated the nominative case in psychiatric diagnostic illnesses from depression to Obsessive Compulsivve Disorder and their thretament methods. Psychological symptoms related with depression, behavioral disorders and OCD and associated with their old and novel diagnoses threatment methods were historically situated and interpreted. For a long time, a lot of clinical reserach and study have displayed the success of treatment for depression. Antidepressants are useful for decreasing symptoms of illness in lots of teen, especially sadness is severe. Majority physicians prefer to use a combination of psychotherapy and medications in the course of efficacious treatments the millions of people around the World suffering from depression.

There are a number of reserach independently investigated in literature. In this study, their results evaluted especially results of Gamma knife threatment method for OCD patients. Treatment of chronicle OCD have been also in difficulty both for psychiatrist, although Gamma knife has been performed and is seen as a new promising technique for ressisstive OCD patients in majority of countries for more than four decades.

Keywords: Depression, Obsessive Compulsive Disorder, Gamma Knife Treatment

ÖZET

DEPRESYON, OBSESİF KOMPÜLSİF BOZUKLUK HASTALIKLARI VE İLGİLİ TEDAVİ YÖNTEMLERİNİN İNCELENMESİ

Murat KARA

Biyomedikal Mühendisliği Programı

Yüksek Lisans Tezi

Danışman: Yrd. Doç. Dr. Haşim Özgür TABAKOĞLU

Bu tez depresyon ve OKB hastalıklarının psikiyatrik açıdan tanımlanması ve tedavi yöntemlerini araştırmayı konu edinmiş birleştirici ve teknik bir araştırma ürünüdür. Depresyon ve OKB orijinli davranışsal bozukluk ve bunlara yönelik tanı yöntemleri tarihsel bir şekilde yorumlanmıştır. Depresyon tedavisinin başarılı bir şekilde yapılabilmesi için klinik değer taşıyan birçok araştırma uzun zamandır yapılmaktadır. Eğer depresyon şiddetli ise antidepresanlar hastalık belirtilerini azaltmada başarılı sonuçlar sergilemektedir. Doktorların ekseriyeti Dünyada milyonlarca insanın etkilendiği depresyonu etkili bir şekilde tedavi edebilmek için psikoterapi ve ilaç kombinasyonu tercih etmektedirler.

Literatürde birbirinden bağımsız tamamlanmış birçok çalışma yer almaktadır. Bu tezde, araştırmacılar tarafından gerçekleştirilmiş bu çalışmaların sonuçları, özellikle OCD hastalarına yönelik uygulanmış Gama bıçağı kullanımı ve sonuçları değerlendirilmiştir. Gama bıçağı kullanımı özellikle kronikleşmiş OKB hastalarının tedavisi için yeni bir ümit olarak görünmekle birlikte psikiyatristler için kronikleşmiş OKB hastalarının tedavisi birçok ülkede halen zorluğunu uzun zamandır muhafaza etmektedir.

Anahtar kelimeler: Depresyon, Obsesif kompülsif bozukluk, Gama bıçağı terapisi

CHAPTER 1

INTRODUCTION

Mental illness is a expression planted and relate to communally to each one identifiable intellectual sickness. They are expressed precisely by irregulities in awareness, mood or emotion, or the serious supplementary appearance of behavior, such as sociable coactions or programming of coming events. All of the functions of mental diseses are intervened by the central nervous system. Brain is, actually, a central part principle of modem that and our personal mental stateand behavior mirror the generally acting of the brain. Therefore, signs related to conduct or our mental states manifestly mirror changes and abnormal features in brain operate. There may be no hesitation that an single with schizophrenia is gravely ill, however for another intellectual disorders like attention lack, hyperactivity or depression, the marks and indications lives on a continious sequence and there is no luminous sign segregating health from illness. In addition, the indications of mental ilness alter with year, culture and sex of person. The doorsteps of mental disorder have, really, been allocate by treaty, but the reality is that this unclear point is no disparate from any part of medicine.

Some reseracher were believe that level of 200 for a serum cholesterol is really normal ten years ago. Nowadays, this number (200) alert more physicians and may direct to medical therapy.

1.1 Literature Survey

The brain is the collector of concept, feeling, conduct, and wellness. In fact, one of the primary donations of modern intellectual wellness research is the scope to which it has fixed the ruinous divided between physical and mental disorder.

Reseracher have today more knowledge about how to treat mental illness impressively and properly than they know with sureness about how to prevent these illness and assist mental health.

The function of psychological, biological and sociable agents may change beyond human being and on the life span. Among the human being, for instance, depression rouses initially due to exposure to stressful life, since in others the primary factor of depression is genetic sensitivity. The perception generally cross after a moment. But, persons suffer from depression with daily life. For persons suffer from clinical depression, their healthy performance is subverting so much so that both they and those who look out for them are influenced by it. Whereas researchers start to pester excluding study of the causes of the diseases, they commonly begin by disverning mutual relations. A correlation is give a link two or more occurrences connected in some way. Discovering a mutual connection between depression and trying life events would motivate more study on causation. Whether a relative research exhibit in order for a stressful event is connected with an enlarged reasonability for depression and that the stress generally go before depression's attack, then stress is named a "risk factor" for depression [1,2]

There are two major public health problems among aged persons, these are cognitive impairment and depression. Both of them influence more than older people especially aged 65 years and have been connected with loftier limited life span, rapid practical decline and raised use of medical services. Caring cost for patients suffer from dementia and major depression is very huge. Last century aged population in modem societies is increased and health care unions struggle to prevent and treat the cognitive impairment and depression [3,4].

In many cases cognitive impairment and depression exist side by side clinically. If success do not catch, More than half of patients have normal cognition but suffer from major depression can in the end build dementia several years later. Notwithstanding, there are some evidence case show the correlation between the two conditions these are mirrors a emotional connection, a psychological action that is associated with both depression and cognitive impairment like use of antidepressant and other drugs affecting the mental processes or cardiovascular disease [5]. Also in the community, older persons suffer from depression are in many cases stay untreated [6]. Prejudicially because of inadequate proof respecting the harms and benefits of strict antidepressant treatments in late-life illness, particularly in those with minor and mild depression or

with complex medical conditions [7,8]. And so, an explanation of the interconnectedness among depression, antidepressant and other psychotropic use, and cognitive impairment in the aged persons can carry significant overall health of the community [9,10].

Obsessive-Compulsive Disorder (OCD) is a appropriately studied illness. This disease depicted in the literature of psychiatry for more than a hundred years. In spite of OCD treatable disorder, but reseracher did not make a documentation about this illness defining in a formal manner until the pre of the 1900s. At the present time, but, it is a lingering, often debilitating, infrequently curable.

Common indications point out that OCD is a biologic illness. Nowadays a lot of Functional brain imaging studies were completed. Functional brain imaging studies to form a pattern for physiology of disordered function of OCD what includes abnormal activity in definit subcortical and cortical regions [11]. Aligned and partly hostile data processing route appear to be mixed up in order to suitably produce a stable control of concept and motion. The beginning and ability to be supported of the recurrent action is idea to be regulate by the lead route. The finishing of these behavioural practice will then be adjusted by the circuitous route. It is recommended in order for the OCD indications arise from an abnormal, extremely activity in the manage route likened with the circuitous one main to a disrestrained thalamus and the invention of a self-sustaining route among the the orbital cortex and thalamus [12,13]. Protrusions related with corpus striatum also are generally contain glutamic acids, therefore immoderate activity allow cause to the disturbed physiological functions of OCD. Victorious therapy is collaborated with an act of lessening over activity in the neural circuit.

Therefore, researchers has been thought like this,

OCD includes inabilities of two principal suppressive procedure, one of them is behavioral and the other is cognitive [14]. Last study has encouraged two resembling cortex and cerebral mantle links for OCD disease: (a) the frontostriatal cord that liable for defects of behavioural restraint; (b) the prefrontal cortex that liable for defects with perceptive suppressive procedure. These two prohibitive procedure mirror a wide connection of cortico basal ganglia thalamic cords [15-17].

The studies related with concentraions physiology of the nervous system in OCD exhibited reduced intracortical repression of a psychological process on Transcranial Magnetic Stimulation (TMS) and reduced threshold of the motor evoked potential [18].

Diagnosis of mental illness is important subject. The preceding debate has recommended that the presages of cerebral illness descend toward several clear class like psychosis, mood disturbance, anxiety and cognitive impairment. These classification are wide, incongruous, and slightly extending over. Furthermore, every sufferer may show clearly manifestations.

Identification of illness is fundamental in all scopes of wellness for forming and planning therapy and assisting care. identification of illness also tend to as increase communication, comprehensive inquiry, supervision, and compensation for a loss. It is generally believed that it is constraint to diagnos of mental disorders than diagnosis of somatic, or inclusive disorders, because it is not shown any lesion. Whereas the illness or tissue abnormality can identify with laboratory test. The mental illnesses diagnosis have to repose with the doctors' reports of the strength and confident of indications from patients intellectual status investigation, and watching of their behavior. These evidence are gathered together by the clinician into identifiable models named as syndromes. Mainly intellectual and cerebral situations are mentioned as confusions, rather than as diseases, because identification reposes on clinical standard. The term "disease" usually is set for situations with understanded discoverable physical pathology. On the other side the word "disorder" is set for groups of indications linked with defect and extreme danger.

1.2 Purpose of the Thesis

Nowadays, psychiatric disorders become an important problem both in individual and social domain. Depression, which is a frequent disorder, is defined by symptoms such as long-term affliction, calmness, reluctance and pessimism. Negative life events, sudden and deep sadness, hereditary aptitude, serious diseases like epilepsy, aids, cancer, multiple sclerosis, some drugs, major business and family problems, seasonal and hormonal changes are considered as the effective factors in occurrence of the depression even though its exact cause are not known. According to the reports of the

world health organization, as well as being prevalent in women, it is regarded as a serious mood disorder which has a 16-20% lifetime prevalence and accounts for poor quality and short life for 121 million person worldwide. Diagnosis of the depression which has subtypes including major, chronic, postpartum and severity degrees including mild, moderate and serious is made using scales in the form of questions and answers in accordance with the 4th Diagnostic and Statistical Manual of Mental Disorders book (DSM-IV) of the American Psychiatric Association. However, since the occurrence of the symptoms observed as a result of clinical evaluations in other diseases and different points given to the patient by different experts, difficulties are encountered in differential diagnosis and planning treatment process. To get an accurate diagnosis is the most important part of all the disorders. For this aim, a psychiatrist evaluates the patients according to the explanation of the patients of their emotions. In addition, some scales like Hamilton Depression Scale, Beck Depression Inventory which are accepted in all around the world used for diagnose [5].

In developed nations such as United States community today the the process of identifying of depression and Obsessive Compulsive Disorder, especially in women and teens, is taking place at an alarming level. For that reason, it appears as though relavent that a social comprehending of the articulate and identification of these illnesses in people be developed by the layer of psychology. But, the field look like to be needing sufficient comprehensive inquiry in coming out depression and gender combining social and political factors. The best achievable benefit of such an comprehending may guided to novel methods of curing and make an consciousness of the forceful social interaction that design psychiatry this way that prophylactic action may be improved [13].

Additionally, there are directly a few OCD treatment centers in the World, but they are residential, inpatient settings. In these centers the chronicle patients sufferer from OCD are operating using Gamma knife.

The main purpose of this thesis was to investigate basic characteristics, diagnosis techniques and treatment ways of two common psychiatric illnesses such as depression and OCD. In this study, all the treatment techniques of these disorders were discussed and a novel treatment modality that is called as gamma knife therapy was introduced.

Furthermore, the thesis was scientifically supported by important case studies with gamma knife application to OCD patients.

1.3 Hypothesis

Nature of this study was a naturalistic using archival data with a pre-post a few patients outcome. By comapring treatment techniques of Depression and OCD illness, the study can impact future treatment. Additionally, the outcome data of this study can be used in a lot of country, where Gamma knife theaphy technique has not proceed for OCD patients yet. Thus some clinicians will be look to use this study to determine what, if any, changes need to be made in their treatment protocol to ensure treatment success.

CHAPTER 2

HUMAN BRAIN AND ELECTROENCEPHALOGRAPHY SIGNALS

Brain is the chief leader of the human body and the principal portion of the sensory and control system called nevous system. This system controls the dutys of diversified internal part in the person. First of all, following part it is described the the body structure of organism of the brain. Afterwards It will be concentrate to tell about how electrical signals produces. These activities may be inscribe onto a storage medium surface of the brain. It deliveres an entierely concept to comprehend the formation of district electrical current movements through neouron that can be sawn on the screen of the Electroencephalography (EEG) device. In an anatomical manner the brain have three great large sections; They are called, brainstem, cerebellum and cerebrum [19, 20].

These parts of the brain illustrated in Figure 2.1. and in the following paragraphs it can be reach a brief explanation about this sections.

Cerebrum: The cerebrum which develops from the foreword part of the forebrain, is the enormous part of the fully developed brain. It is mostly connect to brain functions identifying with activities of person, concepts, feeling. The cortical cerebrum cortical is composed of nerve-related fabrics. The cerebrum composed of two half of a sphere, these are left and right. One of them may be seperated 4 sections: They are, occipital, parietal, temporal, and frontal lobes [19, 21]. They are liable for a diversity of physical duties.

Frontal Lobe is controls significiant cognitive skills, such as emotional expression, problem solving, memory, programming, reasoning parts of speeking ability and motion.

Occipital Lobe is dependable upon visual discrimination of movement and color.

Parietal Lobe is control center, of the brain and responsible for some sensation, sensory intelligibility, identification, interpretineg of stimuli, movement and orientation.

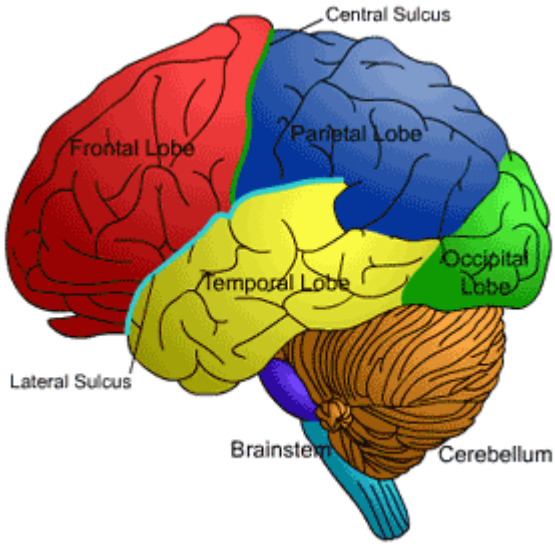


Figure 2.1 Anatomical parts of the brain

(http://web.stanford.edu/group/hopes/cgi-bin/hopes_test/the-hopes-brain-tutorial-text-version/#lobes-of-the-brain)

Temporal Lobe is necessary for the recognition of hearing stimuli, speeking ability, sense and recollection.

Cerebellum: It is a structure situated below backward of the bean and have seperated 2 half a globe. It include over 50% of the total number of neurons in the brain. It is counted amongs the sensory areas of the brain that is receives data from the sensory systems, the spinal cord, and other parts of the brain and then coordinates voluntary movements.

Brainstem: It is placed at the lowest point of the bean and is tied spinal cord. It is the principal supervision band and rules living duty of person, involving respiration, cognition, activities of the mouth and eyes and the pasing of stimuli signals such as noise, warmth, pain, hunger and blood compression [19].

2.1 Brain Neurophysilogy

The human brain composed of aproximetely 100 billion neurons. These neurons provide tiny electrical voltage in the central nervous systm. Neurons transmit neuronal current and there are a message passing between two points. There are three basic parts in the

neuron as shown in Figure 2.2. These three parts called dendrites, soma and axon [19,21,22].

The center of a cell called nucleus is the heart of the cell. The axon is bear electrical nerve impulses away from the cell body. The dendrites are fork fiber in nerve cell. Dendrites suply after synapse ingredient of synapse. By way of from axon through the dendrite, each neuron can transfer data among them. This communication is done could be inward the Action Potential (AP). AP occurs when a neuron sends a stimuli to through following dendrite [23]. Due to this quick change in charge, a voltage is created between inner and external surface of the outer wall of a cell [19,21,24].

These nerve cell send out a substance to start an activity. This chemicals are generally known as neurotransmitters. When neurons are start to active by way of an electrochemical process, particular current stream are manufactured. The electrical pursuit of neurons may be seperated into two subsets; These are named AP and Postsynaptic Potentials (PSP) [23].

During EEG recording, PSP signals record surface of the scalp and from cortex. Neuro AP more than smaller potential field arrangement and are more than little in period of time than PSPs. AP's hence do not give meaningfully intracranial EEG recordings. Alone big quantity of active nerce cell may create tiny signal layer [19,21,24].

In the EEG evaluation, the cerebral layer is the most pertinent building in the condition that it is liable to respond for gretaer request. Because of its exterior viewpoint, the electrical pursuit of the cerebral region has the leading affect on EEG recordings.

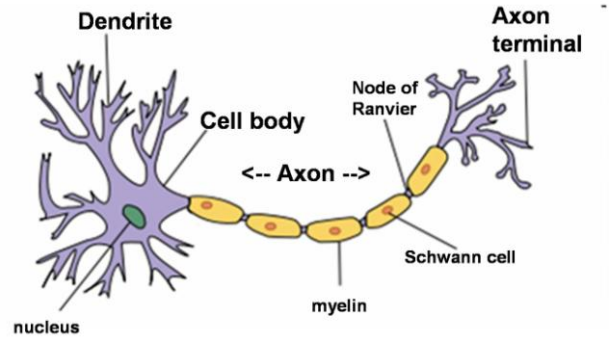


Figure 2.2 A general structure of neuron

(http://paradigmchange.me/wp/wp-content/uploads/2014/09/neuron.png.jpg).

1.4 Electroencephalography (EEG)

EEG gives us electrical brain activity and gives proof of how the brain functions during the next period of the time. It is gretaly may be done by researcher to learn brain work and to examine neurologic confusion of the nervous system. The investigate of the current pursuit belong to brain, by way of the EEG registering is counted amongst the gretest consequential apparatus to identify of diseses of the nervous system, like brain tumour, epilepsy, head damage, abnormal sleep patterns, madness and observing deepness of anaesthesia [25]. It can be advised on account of the care of abnormal feature, conduct unrest, concentration insufficiency, learning and speech difficulty etc.

This device device was present by Hans Berger who was a specialist in neuropsychiatry in Germany in 1929 [26]. He recommended that currents produced brain altered rely upon the practical status like anesthesia, sleep and epilepsy. This was radically new thought that assisted make a new affiliate of physical World named neurophysiology. EEG signals that The first recording are seen Figure 2. 3. [19].

While the EEG recording, several small electrical conductor are put to distinctive place on the layer accompanied by adhesive substance named gel. These electrodes are join to an amplifier. At last, tiny electrical signals from the scalp are send into analog digital converter to converst digital form and to see on a monitor and to inscribe the signals.

During EEG recording it can be use a lot of electrodes (1 to 256) If the recording is done in equidistant this device is named as multichannel device. Every electrode pairs commonly connected up a channel. During an EEG recording every channel yield a tiny signal [19].

There are two types of EEG, these are Scalp or intracranial (Figure 2.4). During the recording of scalp EEG to get valid electrical contact, electrodes are placed on the scalp. If in intracranial EEG specific electrodes established face to face in the brain during the surgery. From the other point of wiev, the EEG recorded openly from the cortical layer utilizing subdural electrodes such as needle electrodes is named the Electrocorticogram (ECoG).

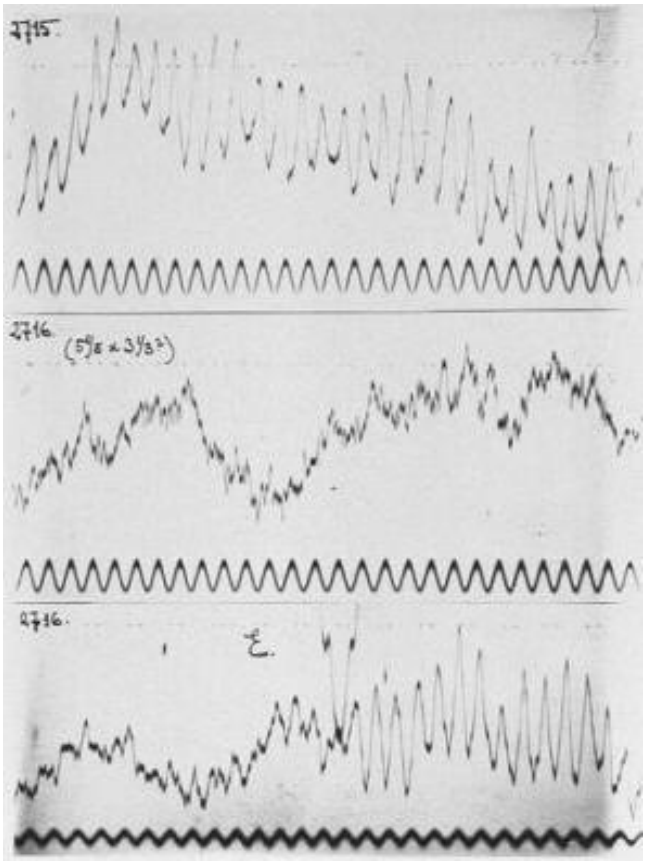


Figure 2.3 First recording of EEG signals made by Hans Berger (https://web.csulb.edu/~cwallis/482/eeg/eeg.html).

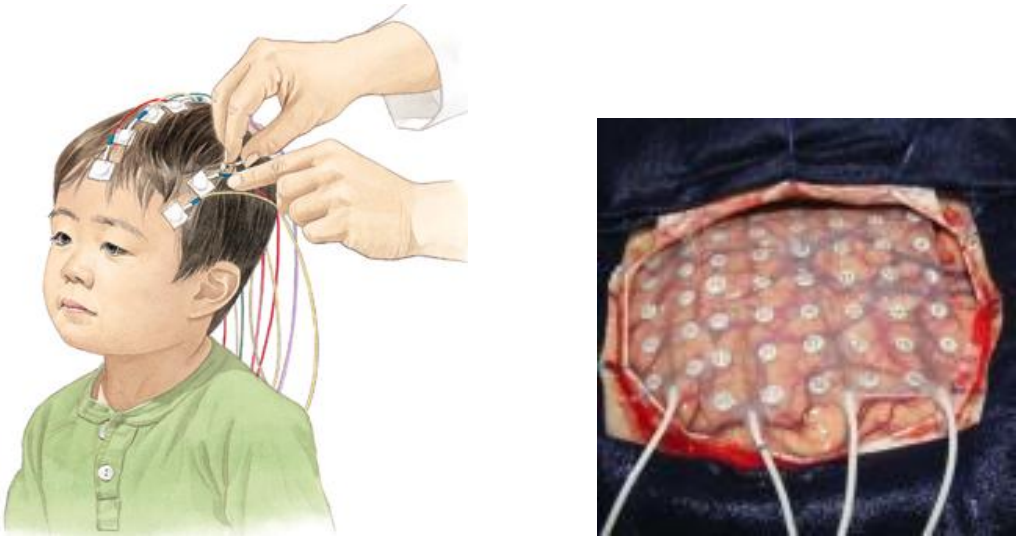


Figure 2.4 Scalp and intracranial EEG recording setup (http://www.fairview.org/healthlibrary/Article/40171) (http://mnepilepsy.org/services/)

In a normal adult an EEG signal has got amplitude ranges from about 1 to 100 μV, but electrocorticogram has got approximately 10 to 20 mV. Because of this building of the brain is not distinctive and the outer layer is usefully arranged, EEG signals pattern may change conditional upon the place of the electrical conductor. Because of the different lobes of cerebral hemispheres are liable for working distinctive pursuit, electrode location is influential. Recordins are done using the norm procedure for restriction of electrode. This method called is the international 10-20 electrode system [27]. 10-20 stand real space among close electrodes of the skull. The positions among close electrodes are settled by the two points; nasion and inon. nasion is the spot between the nose and the forehead. Figure 2.5 show the 10–20 International System of electrode placement [19]

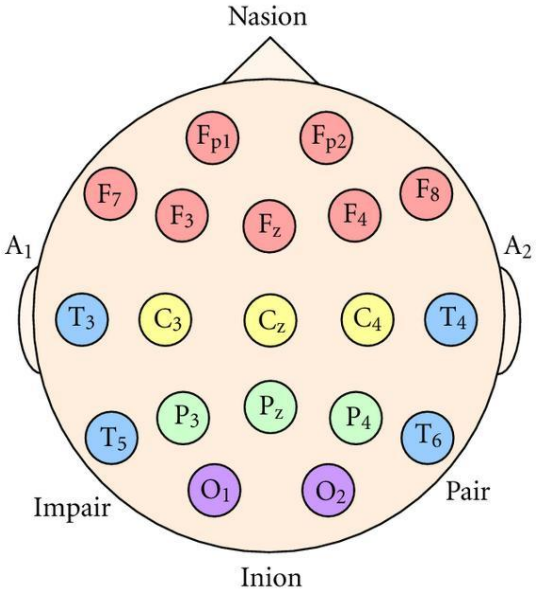


Figure 2.5 The international 10-20 electrode placement system
(http://www.hindawi.com/journals/aai/2011/384169/fig2/)

1.4.1 Nature of the EEG signals and Psychiatric Disorders

Comprehending functional activitiy in perceptive research and estimating irregularity and abnormalities of clinical EEG frequency in EEG trace should be examined. There are billions of fluctuating group of neurons as its sources, EEG signals have unpredictable wavering that are arranged in alterative strip like Delta (0. 2 -4 Hz), Theta

(4-8 Hz), Alpha (8-13 Hz), Beta (13- 30Hz) and Gamma (>30Hz) [1,10]. Figure 2.6 shows patterns of the EEG waves.

Alpha waves have 30-50m μV amplitude and includes the frequency range from 8 to 12 Hz (Moderate), that seem principally in the rear area of the head (occipital lobe) when the patient is in a relaxation state or has eyes closed. Alcohol, relaxant drugs and some antidepressants increase alpha waves. Alpha waves are generally ally with powerful intellectual activity, emphasize and tension. Alpha frequeny is inscribed from sensorimotor layer [19,28].

Beta has high and varying frequency range balanced on two surface in frontal lobe with 13 Hz-30 Hz and low amplitude brain waves. As the cortex is excited and vigorously occupied with intellectual pursuit, it creates Beta waves. These wavesd are attribute of a powerfully occupied brain. It is generally connected to with active possessions, active concentration, and concentration of the solving tangible difficulties [28].

Delta waves are typically created in the right part of the brain and oscillate among the scope of 0. 2 to 4 Hz (cycles per second) and the form is regarded slowest and as the tall in magnitude in waves. It is typically connected profound stages of sleep, acute brain confusion and in the awake condition [28].

Theta wave oscillate between 4 and 8 Hz (cycles per second) accompanied by an magnitude commonly larger than 20 μV. Span of frequency of Theta is mixed up in visionary scheming and sleep. It is linked to us experiencing and perceptive raw and deep sentiments. Extra theta action can make people tending to attacks of depression and may make patients “very amenable” established upon the fact that they are in a profoundly calm, semi-sleep state. T [28].

Gamma waves start from 30 Hz. This wave is occasionally determined as having a greatest frequency approximately 100 Hz. According to a general theory, It is linked with assorted perceptive and motor functions. It is almost always seen artifacts originated from non-cerebral origin in all of the EEG waves. The amplitude of artifacts with contamined EEG signals can be mainly concerning the dimension of magnitude of the cortex gestures of concern. That’s why it takes substantial knowledge to properly explain EEGs clinically [19,28].

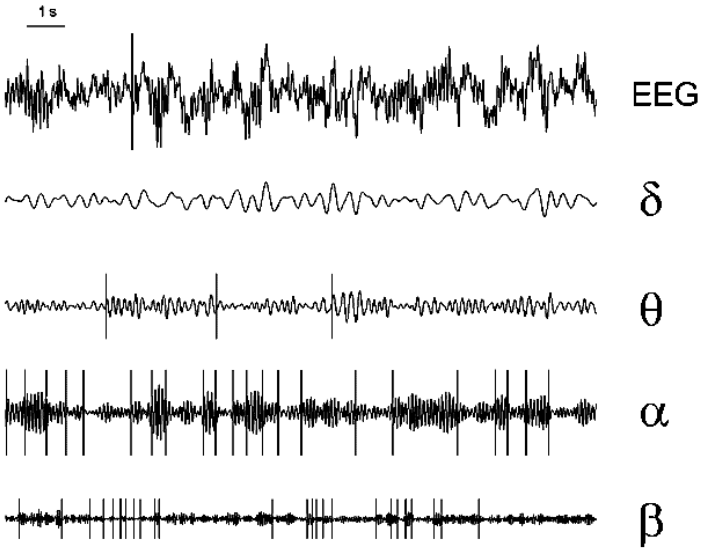


Figure 2.6 Example of different types of normal EEG rhythms
(http://brain.bio.msu.ru/papers/chp2000/7.htm)

To support the diagnosis or to understand the neural dynamics in the brain EEG signals were used frequently in psychiatric disorders. Figure 2.7 display Major diagnostic categories of psychiatric disorders [29].

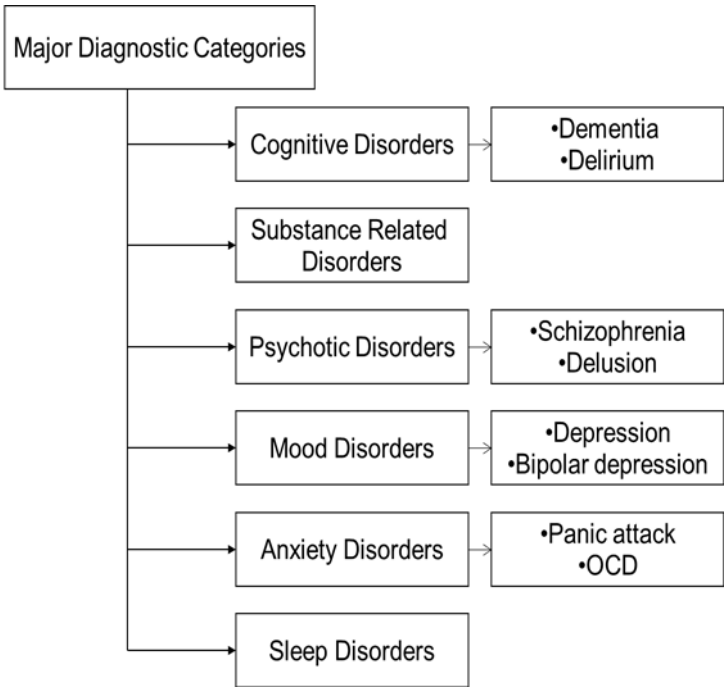


Figure 2.7 Major diagnostic categories of psychiatric disorders [29].

The major advantages of the EEG signals for psychiatric patients can be listed as; It is noninvasive, radiation-free, repeatable, sensitive and multidimensional [29].

Hence, to appraise neural activation in the brain of depressed patients, EEG applications have been widely used in earlier studies. Majority of these studies inspected resting brain activity of patients using traditional linear methods [30]. While some of the previous studies have stated an increased alpha band power over left frontal area that reflects a frontal alpha asymmetry in patients [31], some others have reported raised frontal action in beta band without change in alpha band [32] Moreover, in some other previous works reduced delta and theta band activities in frontal and prefrontal cortex and raised delta action in right occipital area [33] of patients when compared with activities of controls have been reported. However, the findings related to alpha activity in frontal lobe have been accepted contradictory to neurological background due to the origination of alpha waves dominantly only in occipital region [34].

1.5 Overview of EEG Signal Classification

EEG signal classification perform an significant position in biomedical engineering. Grouping these tiny current is extremely prominent in the process of identifying nervous system diseases. An effective classification method aids to recognize EEG fragments, and in the determining on a body of a human health. As EEG signal set include a big quantity of data, importanat difficulty is representing of EEG waves bacause additional investigation, like grouping. It is, first of all, significant to extract functional characteristic from raw EEG waves. The mission of classification happen during everyday life. Sample of grouping missions contain the introductory diagnosis of a patient's disease to choose prompt therapy until awaiting final test results [1]. The aim of the data classification is to allot status tickets through the prominent quality reached starting in watching of a set of medical information in a particular situation. A methodical program in order for executes grouping, particularly in a real execution, is called as a classifier. This sentece occasionally apply to the mathematical duty, executed by a sorting algorithm [19].

CHAPTER 3

DEPRESSION

Depression is neither a sign of weakness nor a temporary change in psychology. Rather, it is a serious medical condition that has behavioral, physical and emotional signs. Depression is one of the most usual illnesses found in human beings. In the brain of the patients suffer from depression there is a condition of mental disturbance and this type patients feel to have low level power and hardship in supporting careful attention or arouse curiosity in their life. Because of depression changes brain metabolism and blood flow frontal cortex. Figure 3.1 and Figure 3.2 displays the increased brain activity patterns in depression condition and changed brain metabolism respectively. That is, brain chemicals are not proper levels or do not work as well as in normal states in the brain of the depressed people, during normally brain chemicals carry messages from one cell to the next in healthy people.

The majority of people who suffer from depression abstain from asking for help (Figure 3.3). Others continue to suffer from depression without taking its symptoms serious. In contrast to what is mostly assumed, depression is not an unavoidable personality imperfection. With a strong feeling of guilt that the disease leads to, depressed people have the abovementioned feelings. Depression is a treatable health problem. However, the sufferer needs to be aware of it and needs to know how to ask for help [35].

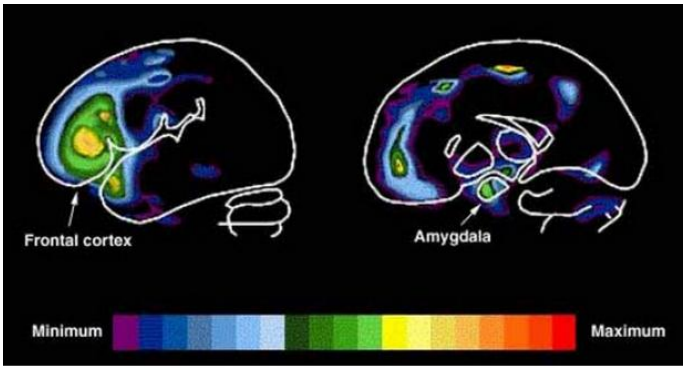


Figure 3.1 The increased brain activity patterns in depression condition (http://bainpictures.org/p/90/depression-brain/picture-90)

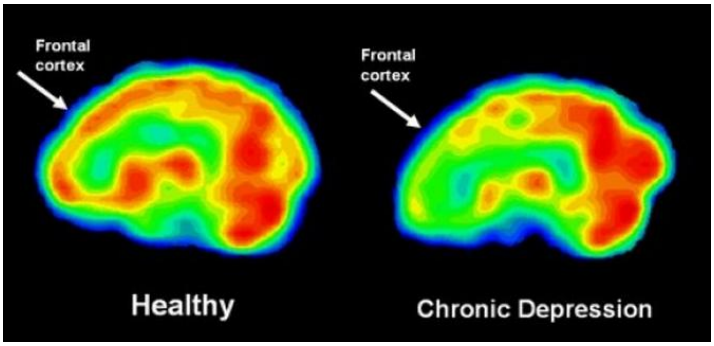


Figure 3.2 The changed brain metobolism in depression condition
(http://brainpictures.org/p/92/brain-functions/picture-92)

The conceptualization of the forms of depression will be done based on the qualitative differences among patients and how patients require different health care based on these differences.

- Heterogeneousness among nosological units
- Heterogeneousness based on related psychiatric features
- Heterogeneousness based on psycho-social and demographic features
- Heterogeneousness based on general health condition

There are different kinds of depression, as mentioned in Fugure 3.3.

Figure 3.3 A representation patient suffer from depression
(http://depressionhurts.ca/en/about/)

3.1 Major Depression

This is the form of depression that has been seen most commonly. This is the symptom of the major depressive disorder that being desperate, unhappy and aimless for at least a 14-day period. Emotional, professional and social areas of life are also under the strong influence of this condition.

The way depression affects people can vary. While some lose weight, others can suffer from sleeplessness. Overeating and feeling guilty and worthless are sometimes added to these symptoms, as well. It is possible for some patients to sustain their functionality and masquerade as 'all is well' towards others. However, when they are alone, they turn to their browned off mood [36].

Among adults, the number of female suffering from major depression is two times more than the number of male suffering from it. The ages between 25 and 44 are the era in which major depressive disorder is most commonly seen. On the other hand, for 65+, the situation is vice versa. Regarding children, depression's effects on female and male children do not considerably differ from each other. As for entire lifetime, while major depression is influential on 10% to 25% of women, this rate is about 5% to 12% for men [36].

Even though the mid-20's is the average era for development of the disease, major depression can emerge at any age. The age, in which the disease mostly occurs, is on the decrease.

The course of repetitive major depression is not stable but may show an alteration in time. The probability for patients to get caught by major depression for the second time, after getting rid of it, is %50-60. %70 of these patients catches the same disease for the third time [37]. While 2/3 of these patients can be totally recovered from major depression, the rest partially can. For those who can be partially recovered from the disease, it is more likely to fall into major depression for the second time.

It is reported that about ten to twenty-five percent of patients with major depression have previously gone through dysthymic disorder (Figure 3.4).

Figure 3.4 A patient with depression in the park. Ten to twenty-five percent of these patients suffer from major depression

(https://www.flickr.com/photos/thomas92/4133269487/in/photostream/)

Regarding the patients with dysthymic disorder, each and every year, ten percent of them succumb to major depression. Some patients have gone through dysthymia previous to major depression.

If these diseases coexist at the same time, then it is named as “double depression”. For those who suffer from both of them are less likely to be totally recovered. In order to cope with the symptoms of both, a longer length of treatment period is needed [38].

There may sometimes be correlation between major depression and some other diseases. About 25% of the patients with diabetes, paralysis or cancer get into major depression. In these cases, it is harder to manage and treat their diseases. The diseases major depression may coexist with are not limited with these. In addition to them, mental health problems such as OCD, alcohol and drug addiction, anxiety and eating disorders may coexist with major depressive disorder [37, 38].

As a result, since major depressive disorder drives 15% of the patients suffering from it suicide, it is a medical condition that should be taken seriously. On the other hand, if patients and people around them are conscious enough, it is possible to take preventive measures to prevent the progression of disease and recover it.

3.2 Minor Depression (Dysthymia)

Compared to major depression, minor depression's symptoms are longer-lasting but they are not as severe as major depression's symptoms. Sufferers from minor depression can barely find the joy of living, if any. Even it is hard for them to recall the happy or exciting moments in their lives. They feel like they have had difficulty all through their lives. Being inactive, dissocial, anxious and guilt-ridden are the typical characteristics of sufferers from minor depression. Additionally, they mostly feel guilty, nervous and have difficulty to sleep [39].

In order to make diagnosis of minor depression, the patient's depressed mood needs to be lasting for at least two year. For children, this process differs a bit. If a child's mood disorder reaches one year, then it is enough for him/her to receive a diagnosis of minor depression. Additionally, the mood of children with minor depression generally shows itself as irritability rather than sadness or depression. Whether it is a child or an adult, people usually seek for treatment of minor depression after they suffer from it for a couple of years. That's because, many people, if *not* most, underestimate feeling continuously depressed. In addition to the patients who realize they have this disease after suffering from it for a while, the number of patients, who have never realized and lived with it, is too big to ignore [39].

People who have immediate relatives with major depression are more likely to get caught by minor depression. The ages that these people usually develop dysthymia are their childhood or early-adulthood. The reason why dysthymia becomes chronic and turns into major depression is mostly because patients do not seek for help for a long time. Developing minor depression increases the patient's chance of developing major depression. 10% of the minor depressive patients get caught by major depression in their future [39].

Minor depression can be associated with substance-use. People suffering from chronic depression sometimes try to get rid of the symptoms of the disease by consuming alcohol and drugs. Regarding kids, the related mental disorders with dysthymia may be anxiety, learning and attention disorder and hyperactivity. Other than mental ones, physical disorders can also occur related to dysthymia such as Multiple Sclerosis (MS) and Acquired Immune Deficiency Syndrome (AIDS) [39].

3.3 Seasonal Depression

This is the depression type that occurs depending upon lack of enough daylight. It is also named as Seasonal Affective Disorder (SAD). Countries like Canada and Norway are the examples, where people fall into seasonal depression. In Canada, approximately 3-5% of adults are under the influence of seasonal depression. The seasons, in which SAD generally shows itself, are autumn and winter. Starting from spring, it loses its effect [35]. Figure 3.5 displays picture of the seasonal effects on human beings.

Figure 3.5 Representative picture of the seasonal affective disorder (http://www.flickr.com/photos/giesenbauer)

3.4 Postpartum Depression

It is the depression type that develops depending upon the change in hormone levels of a mother with birthing. Some symptoms of postpartum depression are anxiety disorder, crying jag, having difficulty in sleeping and being insensible to their babies. In addition to these symptoms, instability is mostly seen in women's mood and they even can hallucinate [40].

In case of such psychotic features emerge, it is crucial to get medical assistance without loss of time and a close watch should be kept on the patient. Other than psychotic

features, the patient can think of committing suicide, have violent emotions towards her baby and have difficulty in getting concentrated on something [40].

A mother's delusions sometimes show up about her baby. She can see her baby as a creature having supernatural powers or even as evil. Psychotic symptoms can totally take the patient under its control and can make her hurt or kill her baby. These kinds of incidents may even happen in the absence of psychotic symptoms but of course, it is more common in the presence of psychotic symptoms. The patient may hear encouraging voices to kill her baby, which normally don't exist and may hurt the baby, being under the influence of her beliefs about the baby. Psychotic symptoms are seen only one out of 500 to 1000 mothers, who give a new birth. The possibility to be influenced by psychotic symptoms is higher for women, who give birth for the first time. Additionally, once a woman experiences psychotic symptoms after giving a birth, her risk to get caught by them for the second time is 30-50% [40].

Majority of postpartum depression patients keep their depressive thoughts and feelings secret because they see postpartum, when a mother should be happiest [40].

3.5 Symptoms of Depression

Even though symptoms of depression may vary according to patients, it is possible to classify common symptoms as follows:

3.5.1 Physical Symptoms

Depression not only affects human beings mentally but also physically. Depressive people can sometimes suffer from physical pain of unknown origin. They feel like they have no energy. Additionally, poor appetite is another mostly seen physical effect of depression to human body. Since their appetite is not under their control, they cannot control their weights anymore and some antidepressants can also cause either weight gain or weight loss. Headache and backache are the other most common symptoms of depression (Figure 3.6). Waking up in the middle of the night without reason and having difficulty in getting back to sleep can become chronic for depressive people [41].

Figure 3.6 Weight gain while on some antidepresants
(http://fluox.org/losing-weight-while-on-fluoxetine/)

3.5.2 Behavioral Symptoms

Once human beings fall into depression, distinguishable behavioral symptoms generally start showing themselves. They can start behave in the way that they normally don't. Depression can turn someone cheerful into an introvert person by making them indifferent to what is around his/her [41]. Figure 3.7 shows withdrawing of a kid from once-pleasurable activities.

Figure 3.7 Withdrawing of a kid from once-pleasurable activities
(http://www.slideshare.net/monicatana/child-abuse-symptoms-indicators-and-impact)

3.5.3 Emotional Symptoms

People suffering from depression can be unhappy, hopeless, and aimless and they can lose their interest in the things they used to like [41].

For example, for someone who used to like spending time with friends, being friends may turn into something boring once s/he falls into depression (Figure 3.8). Feeling unhappy may become daily routine. The idea that this life is not worth living gets the better of them. Guilt feelings are also strongly effective on them, since they believe that everyone around them is unhappy because of them [40, 41].

Figure 3.8 Depression can swing moods
(http://www.inc.com/magazine/201309/jessica-bruder/psychological-price-of-entrepreneurship.html)

3.5.4 Mental (Cognitive) Symptoms

Since human brain is strongly affected by depression, not only thinking skills but also memory gets its share from depression. As depressive people lose their control on their thinking and memory, it becomes harder for them to change the thoughts depression generate. Additionally, making a decision and concentrating on something get difficult [40, 41].

Depression's effects vary according to people. For example, the risk of women falling into depression is more than men's. The reasons behind this fact are hormonal and

biological factors. The feelings depressive women have are generally unhappiness, guilty and paltriness.

The symptoms of depressed men a bit differ from women's and show themselves as tiredness, anxious and anger. They not only lose their interest in their jobs but also stop enjoying the activities they used to enjoy [40, 41].

The symptoms of elderly patients may not be that realizable, compared to young patients and they mostly try to ignore their unhappiness. Additionally, since the diseases causing depression such as stroke or heart related diseases are more common among elderly people, the risk of depression may increase for them. In addition to diseases, some treatments can also lead to depression because of their side effects. Figure 3.9 displays a representative figure belongs to a homeless person have cognitive deficits.

Children suffering from depression may have different symptoms such as faking a disease in order to skip school or worrying about their parents' health for no reason. Regarding adolescents, they mostly oppose their parents and can easily run in to trouble. However, since these symptoms can also be related to their ages and normal, it should be examined carefully [40, 41].

The very first step of treating depression is to consult a doctor or a professional. In case a drug may cause depressive symptoms, these professionals make sure whether symptoms originate from a drug the patient uses or from depression. In order to understand this, a couple of questions are asked such as when symptoms occur and how powerful they are. Another important thing doctors check is if the patient had the same disease before or not and what kind of treatment performed. Additionally, it is also crucial to know that if any other family members of the patient have had depression or not [42].

Drugs called as antidepressant may help the patient to be recovered from depression. However, in order for them to be influential, there may need to be couple of weeks. The common side effects of different antidepressant are having difficulty in sleeping, sexual problems, anger, queasiness and having headache.

In time, antidepressants' side effects decrease. Even though these drugs are safe for most people, it shouldn't be ignored that they still carry the risk of having bad impacts

on adolescents and children. To illustrate, with the start of using these drugs, these people may get the idea of suicide or they may even try committing it. That's why, a person, who uses antidepressant should be watched closely [42].

Figure 3.9 Majority of people living in the street with mental illness have cognitive deficits
(http://www.psypost.org/2015/01/majority-homeless-adults-mental-illness-high-rates-cognitive-deficits-31153#prettyPhoto/0/)

In addition to medications, psychotherapy is another effective depression treatment way. Psychotherapy is teaching new ways of thinking and acting so that patients can get rid of their behaviors, which drag them into depression. The common thing taught in this therapy is how to deal with problematic relations and conditions. The way psychologists approach to psychotherapy differs and they focus on different approaches. Each and every approach enables psychologists to understand patients' problems and offer solutions for them [43].

The treatment patients get may vary according to some parameters such as the current level of psychological research, psychologist's approach to psychotherapy and patients' exact situation. For example, psychologists, who prefer cognitive-behavioral therapy, approach diseases practically. Psychologists may assign their patients to help them improve their ability to cope with their problems more effectively. For example, they may want patients to write about their feelings and reactions, when something unexpected happens. Additionally, patients may also be assigned to read about a specific topic [43].

Contrary to cognitive-behavioral therapy, psychoanalytic therapy is more about talking to patients than assigning them to do something. In this therapy, the aim of talking to patients is to find out the roots of their problems [43].

Even though different types of psychotherapy are classified as mentioned above, it is not uncommon for psychotherapists to combine different therapies and use them according to patients' needs. What really matters for success and effect of psychotherapy is the experience of psychotherapist [43].

CHAPTER 4

OBSESSIVE COMPULSIVE DISORDER

Obsessive Compulsive Disorder (OCD) is a rather popular topic in terms of disorder research and has been very well studied. Looking into the psychiatric literature, not only can one see how OCD has been pronounced since the 19th century, descriptions referring to cases of OCD are found in written documents from centuries before. For instance, a case of compulsive behavior is documented in Biblical literature with the hand-washing ritual. In the aftermath of Jesus of Nazareth's trail, Pontius Pilot is referred in the biblical text as washing his hands upon releasing Barabbas to the demanding crowd [44]. Lady Macbeth is perhaps the most renowned figure who suffered from compulsive behavior, constantly washing her hands over and over again upon murdering King of Scotland [45]. Precisely speaking, the most common act of compulsion is hand washing. But nevertheless, it wasn't until the beginning of the 20th century that this condition was formally recognized and moved onto being defined and documented [46]. Pointing out to the difference between obsessive and psychotic thinking in late 19th century, Westphalia distinguished obsessive thinking as "abortive insanity" much like the French clinician Esquirol's (1838) [47] term 'insanity with insight". Yet, popular view of OCD in the contemporary world is that it is a highly treatable disease despite being chronic and rarely curable [48].

Everyday life is a stressful one that can easily lead to worry and suspicion, which wouldn't necessarily mean one, is OCD. However, in excess, it can lead to superstitious beliefs of overcoming the cause of suspicion and leading to irrational acts such as hand washing for extended period of time or driving around a block over and over again. OCD is a case by which the brain fails to suppress unwanted thoughts or urges. Thus, it negatively influences the information processing in the brain and the person with OCD cannot be held accountable for the urges. While in the past psychotherapy was ineffective and individuals were left to suffer from this mental disorder, OCD has now become treatable.

The developments in cognitive behavioral therapy and modernmedications have produced positive results; even though it is not curable in all cases, the treatments nevertheless alleviate the negative symptom and provide patients with some kind of relief. Under this light, the recipe for successful treatment includes behavioral changes and occasionally medication [49, 50].

4.1 Heterogeneity of OCD

One topic of research that has been significant is the heterogeneity of OCD. Under these light, homogeneous subtypes of OCD has been heavily scrutinized. The psychiatric literature on OCD portrays this mental disorder as being classified in distinctive ways including emphasis on the time of symptom, the age at which symptoms have emerged, whether tics occur or not, how the disorder progresses, and the existence of insight. The age at which OCD symptoms come about is relevant because of the general belief that the age of onset very much impacts clinical treatment outcome of OCD, whereby the earlier the age, the poorer the response. [51-53]. Furthermore, genetic studies have also given importance to age of onset, where studies show that a familial basis is present in OCD patients with onsets that are relatively early [54]. In OCD classification, the distinction in symptom subtype is also used. Just like age onset, subtype of symptom is also believed to be related to whether a positive clinical outcome will be reached [55]. This notion is very carefully linked with diverse findings in Positron Emission Tomography (PET) data [56]. In the work of Rauch et. al. (1998), the authors propose varying types of OCD symptoms results in distinctions of underlying brain areas; this is without a focus on hoarding symptoms. Furthermore, treatment studies indicate that responses to treatment are heavily based on the typology of OCD symptoms, whereby some symptoms are more likely to show better treatment then others. Under this light, hoarding symptoms are closely related with treatment failure [57].

4.2 Symptoms of Obsessive Compulsive Disorder

Two most significant components of OCD symptoms normally include both obsessions and compulsions. Yet, it is at times possible to come across cases where only obsession symptoms or compulsion symptoms are present. In addition to this, approximately one-third of people diagnosed with OCD also suffer from disorders cause tics, which are

abrupt, momentary, intermittent movements or sounds [58]. The compulsions and obsessions are meaningful source of trouble to the individual.

4.2.1 Obsession Symptoms

OCD obsessions can be identified as mental concepts, reflection and incites that are recurring, constant and undesirable and therefore create distress or anxiety. One may try to overcome these unwanted mental images and urges by performing a compulsion or ritual. The persistency of obsessions typically intrudes in thinking of or engaging in other things. Furthermore, obsessions often form as associated with certain themes. Common themes of OCD obsessions include apprehension of contamination or filth, placing things symmetrically and in order, aggressive thoughts and apprehension from harming oneself or others, and unwanted thoughts of sexuality, aggressiveness, or religious matters. Symptoms and signs of obsessions can vary. For instance, someone with OCD would be fearful of contamination when shaking hands with others or simply touching the objects others have previously touched. Other signs include persisting doubts on certain things such as double checking whether the door is locked, the stove is turned off, etc., intense amount of stress stemming from unevenly placed objects and lack of symmetry, mental images of harming oneself or others, thoughts of inappropriate acts and obscene language usage, avoidance of obsession triggering situations, and distress from inability to control repetitive sexual images [59, 60].

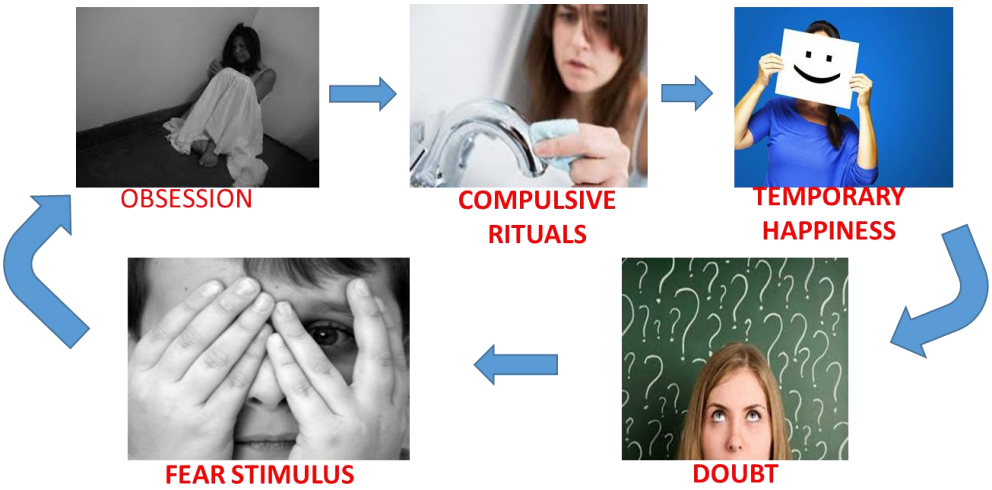


Figure 4.1 The OCD cycle

When an obtrusive thought began, the sufferer carry out an action to prepare the obsessions disappear. Sufferer reaches relief very short time and after obsessions return stronger than before. The compulsive activity goes on. When the time comes, compulsive activities turn into very demanding and disturb to the individual and make happen radical anxiety. Figure 4.1 displays the OCD cycle.

4.2.2 Compulsion symptoms

OCD compulsions, on the other hand, are the action part of this disorder. It is the repetitive behaviors that a patient feels he or she must perform to overcome the anxiety caused by the obsessions or prevent danger that may stem from it. Yet, this act to reduce anxiety many times backfires, and may only offer temporary relief but nevertheless will not bring pleasure or satisfaction with outcome. For instance, patients may create rules or carry out rituals to overcome the anxiety while having obsessive thoughts. Yet, most often these rituals are not rationally created and ineffective in preventing the feared event [61].

Just as is the case with obsessions, compulsions normally possess themes as well. Most common themes include cleaning, counting, double-checking, asking for reassurances, possessing a strict routine, and neatness/orderliness. A few examples of signs and symptoms of a person with OCD include continuous hand-washing up to the point where skin is damaged, double checking doors repetitively to assure they're locked, counting in specific patterns, repeating a prayer/word/phrase silently, arranging books to face the same way, and so on (Figure 4.2). Symptoms normally progress steadily and are usually differing in severity throughout a lifetime. Stress generally works as a trigger to worsen symptoms. Thus, OCD can become disabling with severe and time-consuming symptoms. And although most patients are very well aware that obsessions and compulsions are baseless, this isn’t true in all cases. This is mostly the case in children, who may not recognize what's wrong with them [61].

Figure 4.2 Different obsessions. Obsessive thoughts occur in almost every life from time to time. This type person spend alone much of time having a bath, extreme cleaning, doing homework, etc.
(http://www.ridiculouslife.net/about-ocd.html#.VcMdvPntmHg)
(http://relfc.ism-online.org/files/2013/11/ocd.jpg)
(http://cdn8.steveseay.com/wp-content/uploads/2011/07/Perfectionism.jpg)

4.3 Biological Findings

A lot of studies have now been concluded with both CT, MRI and PET, SPECT, fMRI. All of these techniques have exhibited irregularities in the brain of OCD patients. Pluralities of these researches have implied abnormal features in prefrontal region, anterior cingulate region, basal ganglia and Thalamus. These interconnecting parts are tender to be connected in neuro-anatomical rotes of OCD.

OCD is caused by message distraction between basal ganglia group of nuclei that have been grouped together on the basis of their interconnections which play roles in movements and cognition. Figure 4.3 displays location of the basal ganglia, thalamus, and anterior cingulate gyrus in healthy person. Other functional ciscuits is Prefrontal layer is in the frontal lobe, characterized as be mixed up in emotional and cognitive functions of brain. The thalamus is also a bilateral structure, seperated into many parts of nuclei; It is a relay midpoint, by way of all information about the outside world cross before arriving the striatum, neocortex and amygdala [62, 63].

OCD patients have higher metabolic rate and weak neurotransmitter degrees than healthy persons. They consume high level energy and thalamus dispatches endless distress waves between thalamus and Orbitofrontal Cortex (OFC), therefore increase activity in frontal lobe, caudate and thalamus by increasing anxiety. Due to the recurrent coercions and hostile conduct, what is superior in OCD sufferer is apparently caused by serotonin reduction.

Figure 4.4 shows PET imaging show distinction activity of brain for OCD sufferer against to control group. As the basal ganglia section of the brain of sufferer are activated and he/She are jump to function according to those definite behaviors or activity. These divide of the shape scull route what alters data to concept. If this part is harmed in patients suffer from OCD, so unsuitable sudden desire wave receive inward and they are stunned accompanied by annoying ideas.

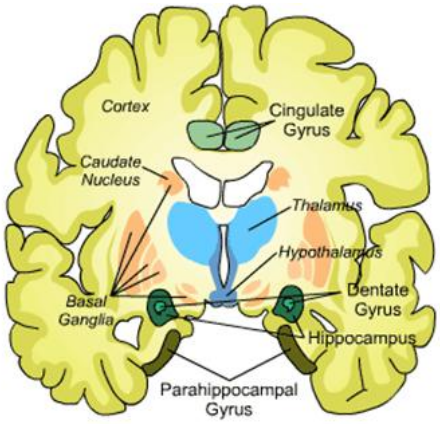
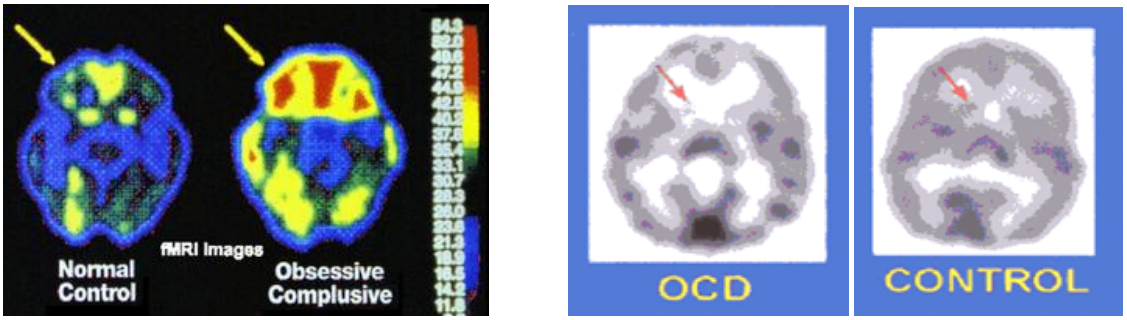


Figure 4.3 Location of the thalamus, anterior cingulate gyrus in healthy person (http://web.stanford.edu/group/hopes/cgi-bin/hopes_test/the-hopes-brain-tutorial-text-version/)



a) **b)**

Figure 4.4 Differences between healthy and OCD patient brain activity

a) High orbital glucose metabolism position of the horizontal slice through the brain in the fMRI image at the left. Red and yellow colors forceful power consume in central nervous system of a sufferer from OCD.

b) OCD sufferer has shallow serotonin degree from healthy person (Alpha [C-11] Methyl-Tryptophan PET)

(http://insidethealcoholicbrain.com/2015/06/22/ocd-a-behavioural-addiction/) (http://www.intechopen.com/books/obsessive-compulsive-disorder-the-old-and-the-new-problems/pathophysiology-of-obsessive-compulsive-disorder-affected-brain-regions-and-challenge-towards-discov)

Scrutinizing this disorder from a biological perspective, various studies have come to conclusions on how this disorder affects the brain itself. For instance, a group of researchers found that patients with early onset of OCD, meaning before the age of 18, had considerably smaller caudate nuclei bilaterally in comparison to the control group [62]. Conducting research among a group of adult-onset OCD only, Aylward and colleagues found that there existed no difference in the size of caudate compared to healthy person [63].

Adding to the literature regarding age of onset, Busatto and colleagues [64] conducted a comparison study on individuals with early-onset OCD, meaning under age 10, and late-onset OCD, meaning over age 12, to control groups by analyzing their brains by single SPECT scans. In this comparative study, the age of onset is defined as the age of the OCD subject at which the subject or those around him/her first observed any kind of OCD symptoms. As a function of age onset, variations in locations and direction of changes were found. For instance, both pre and after onset groups of OCD sufferer differed from the control group in terms of Regional Cerebral Blood Flow (rCBF) in pretofrontal area with OCD groups on decrease. Yet, in comparison to different onset group late and early had significantly lower rCBF in various parts of the cerebrum including the part of the midbrain, the frontal part of cingulate layer and reciprocal subordinate front cortices. Moreover, a positive correlation among the rCBF in left layer and YBOCS degree was also present within early onset bunch [64].

Another study that used SPECT scans for biological examination of OCD subjects completed by Pogarell and colleagues [65]. By comparing the SPECT scans of OCD subjects and a control group, the purpose of their research occur to examine the availability of neurotransmitter in individuals' sufferer from OCD. The OCD participants were further divided into subtypes as onset bunch. Further research was conducted in order to understand whether these two groups of OCD subjects differed from one another in terms of their transporter availability. The "Early" age onset was conceptualized as seventeen years older or earlier. Outcome showed in order for in comparison to the healthy subject, those with OCD possessed considerably higher mean binding ratios in the midbrain pons region. In terms of binding in the striatal regions, there is was not found any distinction among OCD and healthy subject. And OCD

severity as indicated by the YBOCS scores was found not to be related to binding in the midbrain-pons region. In comparisons of OCD subtypes as onset group was found to have the highest mean midbrain-pons binding ratios. On the other hand, no difference could be found [65]. Just as can be seen with the abovementioned results, the biological patterns of OCD depend heavily on the age at which OCD signs and symptoms initially emerged. Ergo, it is possible to suggest that age onset of OCD explains the differences present in brain mechanisms.

4.4 Neuropsychological findings

All of us have some different chemicals named Serotonin, Dopamine, Oxytocin and Endorphin ın our brain. When our brain releases one of these chemicals, we feel good. These chemicals have a special work to do and it shut off when the job is complete. In the serotonergic system, key neurotransmitter is serotonin highly common throughout nature. It is manufactured from the tryptophan and amino acid and is discovered in base ganglia, hypothalamus, front layer and limbic system. It regulates and helps control many functions such as pain, sleep, sexual function, sensitivity and appetite. Majority of the antidepressants influence serotonin levels. It is not known a method to assess the levels of serotonin in human being brain. Figure 4.5 displays the serotonergic system of the brain. Its working is unbelievably frugally.

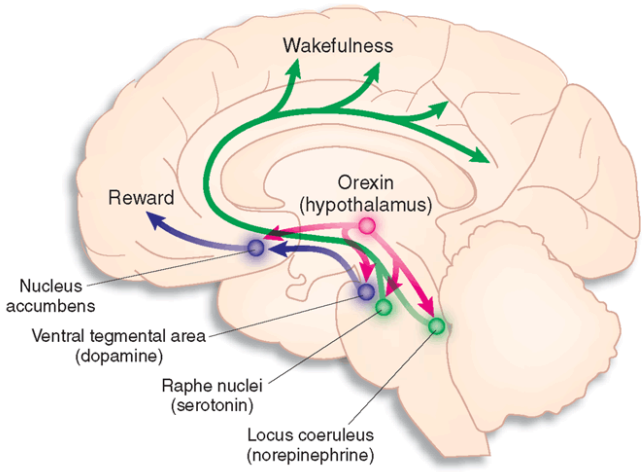


Figure 4.5 The serotonin system. It is play a role in mood, social character, emotion, sleep time, imagining, alertness and appetite. (http://derekwmeyer.blogspot.com.tr/2010/12/safety-and-freedom-only-solution-to-any.html)

Neurons communicate by synapses tiny gaps between neurons very close together. Messages move from one neuron to another as chemical or electrical signals. Neuronal connections built from life experience and the electricity among the neurons moves along smoothly like fluid in a storm, finding the paths of least effortful. There are more than a billion neurons in the nervous system. Figure 4.6 shows as basic picture of the scene where this exchange occurs. The first nerve cell drop abruptly neurotransmitters into the space and the second nerve cell on the other side have receptors respond correspondingly.

Studies include Neuronal imaging have exhibited raised pursuit in the base of the brain with OCD patients. But age of OCD onset and its impact on neuropsychological findings has been rarely studied and therefore only a few studies can be found in the literature until the 2000. For example, under this light, a study carried out by Henin and colleagues (2001) looked into the association of age onset with episodic memory impairment. In this study, adult OCD subject's reports for neuropsychological test analysis were collected. The study design included driving the 68 OCD subjects into two groups based on age onset; one group divided as before age eighteen and the second group as age onset at age eighteen or older. Information regarding the age of OCD onset was determined by a structured interview, and double-checked a few weeks later by asking the same question on age onset to 28 of the 68 participants. When asked a second time, all but one of the 28 participants gave the same answer.

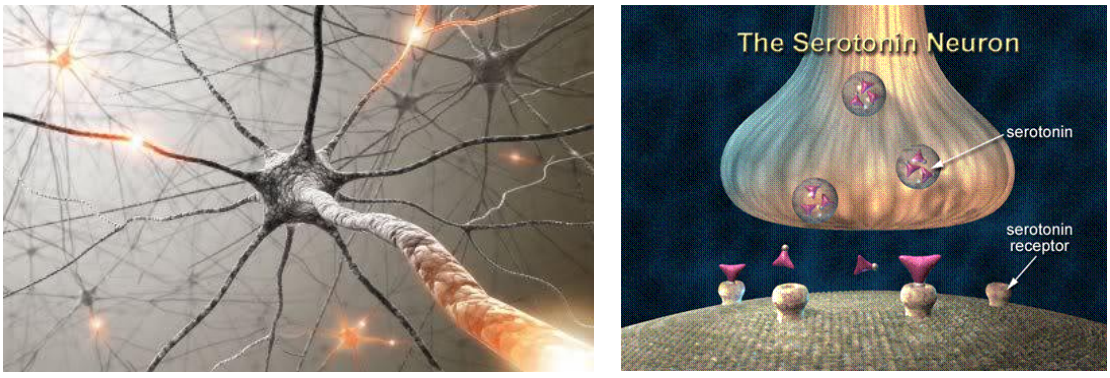


Figure 4.6 Neuronal information and Neurotransmitter firing system (https://www.emaze.com/@AOFWOCLF/Neurotransmitter-Substance-P-and-Norepinephrine-copy1) (http://scicurious.scientopia.org/2010/08/25/back-to-basics-3-depression-post-4-the-serotonin-system/)

Results of this study show that although OCD subjects performed worse in compared with control groups, no differences amongst the two groups of different age of onset exist for any of the measures considered [66].

4.5 Clinical Symptom Subtypes and OCD

Components of OCD include obsessions and compulsions. While most OCD patients do have both obsessions and compulsions, a small group of individuals do possesses either a compulsion or obsession. According to the Y-BOCS checklist in DSM-IV field trial, 1.7% of participants with OCD reported having only compulsions and 2.1% only obsessions [67].

The various types of obsessions and compulsions that exist have called for a need to categorize and describe these symptoms. Thus, several different measures have been developed and The YBOCS checklist is just one example. Based on content, this checklist divides the obsessions and compulsions into sixteen different categorical groupings of symptoms; eight of which are obsessions and the other eight compulsions. Religious, sexual, contamination, aggressive, symmetry, hoarding/saving, somatic, and miscellaneous obsessions are all a part of the obsession category. Counting, hoarding/collecting, repeating rituals, cleaning/washing, ordering/arranging, checking compulsions, mental and miscellaneous compulsions are all part of the compulsion category. And each category is further divided to individual items. For instance, the category of somatic obsession is further divided to two items, which include the interest accompanied by sickness and excess interest accompanied by impression of the body

In early 50s, OCD illness was thought as a unitary sickness [68]. Yet an analysis of the YBOCS found that only one factor underlay the items and concluded that it measured only a singular construct [69]. Rasmussen and Eisen (1988) further added to the literature by questioning the extent of symptom heterogeneity in OCD by pointing out that OCD patients often present multiple obsessions and compulsions [70]. Yet, other researchers like Hodgson and Rachman (1977) continued to view OCD as a disorder having heterogeneous clinical symptom subtypes. Hodgson and Rachman reported OCD complaints were made up of four main problems of checking, cleaning, slowness,

and doubting. Nevertheless, an OCD patient may have complaints from more than one category [71].

Later research attempts to shed some light on the issue of OCD symptom heterogeneity focused on the single objects of the Y-BOCS list and clinical manner extracted symptom categories. Summerfeldt and colleagues (1999) [72] conducted a study using a confirmatory factor analytic method to test how well the different models of OCD fit. They included the one-, two-, three-, and four-factor models and concurrently compared these independently-developed models conceptualizing the agent construction of the Y-BOCS checklist. Analyzed at the individual item level, the pattern of Leckman (1997) [73] showed the best fit. Additionally, the results indicated the relative distinctness of the symmetry/ordering and hoarding factors from the other two categories. Yet, checking, in particular was concluded to be a heterogeneous entity, which overlaps with other symptoms. All in all, this study suggests that the four-factor solution doesn't necessarily provide a satisfactory record for the dimensional structure of OCD symptoms [72]. Feinstein's (2003) study provided further evidence in support for the notion that these categories aren't entirely exclusive. He examined the YBOCS checklist items and found that heterogeneity among items in the contamination factor. When examined at the item level, symptom fit showed variances; for instance, some fit better in the obsessions/checking compulsions factor while other items were part of the disgust with contaminants/cleaning compulsions [74].

4.6 Neuroanatomical Basis of OCD

Other researchers have focused on the neuroanatomical underpinnings of OCD by using various methods of neuro photographing like the Functional Magnetic Resonance Imaging fMRI, PET, computed X-ray tomography and MRI. Under such investigations, scans of patients' brains were taken before and after treatment for analysis. And while some studies were carried on during symptom provocation, others were conducted during resting states.

Many studies in the literature of OCD suggest that disturbance in the frontal-striatal-thalamic circuits is what underlies the symptoms of OCD. Many reports that in the orbitofrontal gyro, there is hyper metabolism and those abnormalities exist in the

caudate nuclei. Nevertheless, there are other areas implicated in the brain such as the anterior cingulate, striatum, and thalamus. In fact, positive correlations among the activity of different front striatal-thalamic areas were found and that these correlations are argued to have disappeared following successful treatment response. What this presumably meant is that the abnormalities in the brain are due to the OCD state [75]. Such patterns in the brain were found to be unique to OCD with differences located between the metabolism of OCD and depression subjects. Further evidence of these brain areas involvements is provided by research on OCD-specific measures like OCD severity and OCD improvement and its relation to the metabolic activity in these areas [76]. Additionally, research shows that differential relationship to neuroanatomical findings in OCD symptom subtypes [77].

4.7 Neuropsychological Testing and OCD

The neuropsychological testing of patients has been the main focus on OCD researchers. While findings have been rather inconstant across many studies, consistency in neuropsychological deficits was found across several domains including visuospatial skills, nonverbal memory, and executive functioning. In fact, several studies have concentrated completely on executive functioning. Executive functioning can be defined as the ability to respond adaptably and appropriately under diverse conditions, efficient use of behavioral/attentional resources, controlling unfitting reactions, using methods to enhance memory function, and planning new action [78]. In their work on executive functioning, Bryan and Luszcz (2000) [79] discuss what it is and how refers to cognitive actions like responding to newness, planning and executing strategies for action, monitoring performance, creating response based on feedback, attentiveness and inhibiting irrelevant inputs.

Various explanations have been proposed to shed light on the deficits that make daily life difficult. For example, Behar and colleagues (1984) [80] propose that individuals with OCD have issues with mental rotation in space along with recognizing and following tacit rules. Tallis (1997) [81] suggested that OCD patients have difficulty on tests of ‘set shifting’ and Savage’s work (1998) [82] supports this notion by stating problems caused by “shifting mental set” Veale, Sahakian, Owen, and Marks (1996)

[83] hypothesized OCD deficits result from issues of obtaining and sustaining cognitive sets along with difficulty in producing and checking responses.

Studies show that in areas of visuospatial functioning, nonverbal memory, and executive functioning, OCD patients perform significantly worse in comparison to control groups. Taking a look at the studies, universal deficits across different parts of functioning are not found. Instead, deficits are noticed on a study base for a selection of tests administered. Nonetheless, inconsistency in findings prevails with replication of study when the sample is different. A front striatal circuits that is normally functioning are claimed to be central for these abilities. For normal test performance, the neuroanatomical areas and circuitry are specifically the most significant cerebral areas; it is in these areas of OCD subjects that abnormal metabolism are found. These mechanisms could be the explanation behind the relationship between the OCD and neuropsychological deficits.

CHAPTER 5

TREATMENT OF DEPRESSION AND OBSESSIVE COMPULSIVE DISORDER

5.1 Overview of Treatment

Therapy is not efficient everytime. In Twentieth century, scientiests did not get achievement to prevention patients from chronically illness. In the a lot of countries, during period of World War II, the number of the people suffer from depression and population are increased and also this situation brought financial problem to these countries. During World War II, a lot of researcher in the mental health services of the military begun to think as mental health problems can treat [84, 85]. Figure 5.1 display a psychiatric interview between doctor and a soldier in a base hospital During World War II.

Treatments can be together under two main categories impending pharmacological and psychosocial. Besides combination of them known as, nultimodal therapy that it could occasionally be always impressive than each of them [84, 86].

Figure 5.1 A psychiatric interview is shown between doctor and a soldier in a base hospital During World War II

(http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2089086/) Date of access 03.08.2014

5.2 Psychotherapy

Psychotherapy, tends to provide an individual emotional and behavioral problems and it is the general name of technology aimed at the promotion and protection of mental health. Psychotherapy is not always the subject of individual members only, sometimes takes the whole family interactional issues examined [87].

Psychotherapy provide an appropriate purpose of the mental and spiritual balance of science and art therapy carried out by establishing the exchange of thoughts and feelings that shows patients with emotional disorders. To put under a very general headings, psychotherapy can be increase the level of spiritual harmony, matures interpersonal relationships, solutions that emotional conflicts [87].

Psychotherapy, to decide what is right on behalf of the therapist is not to say or how to change. Not just people living with psychological problems, anyone who wants to continue to make life more meaningful way may enter the therapeutic process [87].

Psychotherapist using their theoretical knowledge and practical skills; keep light to his clients, to enhance the awareness and recognition on the life and develop new solutions. There are a few psychotherapy types in use following;

5.2.1 Cognitive Behavioral Therapy (CBT)

Behavioral therapy is to ensure outcomes such as behavior modification or reduction in the frequency behavior as a result of learning, such as automatic modeling in behavior. Clinical applications and observations in psychotherapy indicate that effective results reveal that the use of a combination of cognitive behavioral methods [83, 88]

Due to the negative and positive force, environmental factors are very prominent for behavior therapists. Therefore, forming environment for the needs of the individual pathways are important for the behavior therapy [83, 88].

Despite CBT may be used in almost any emotional state, therapists often tend to achieve success in people who suffer from addiction can branch out in the various parts of actions. Figure 5.2 shows a useful image to help us see some of the ways of addiction.

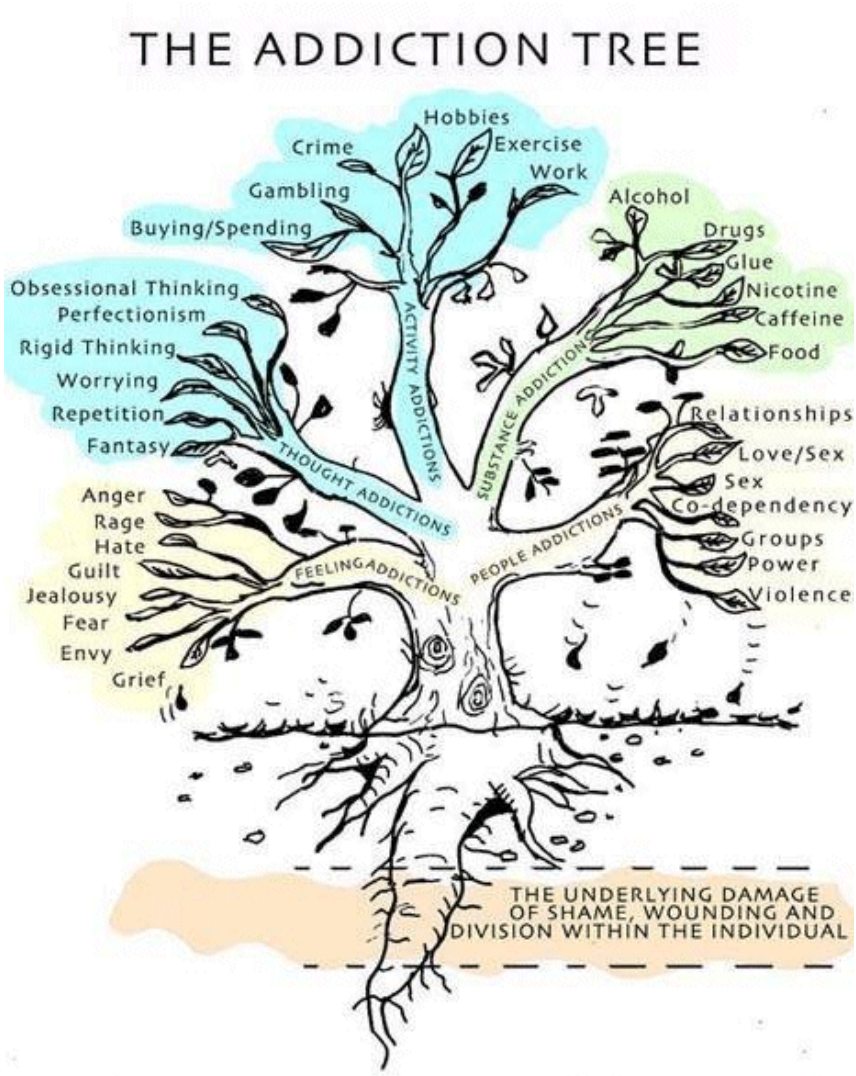


Figure 5.2 The addiction tree
(http://www.straightpathtorecovery.com/?page_id=254) Date of access 01.09.2014

Substance Use Disorder (SUD) is a clinical word that defines extremism or continued use of certain substances that cause distress or physical disorder (Figure 5.3). In cases due to drug addiction disorder, some connection changing among the cell, making variation in the usefulness of the brain. All these changes may prevent ability to think clearly and implement valid attitude, while influenceing memory and comprehension together with the ability to check on the behavior. Drug or alcohol addiction is recognized as a long-term condition. As in other health-related problems, the drug addicts must be continuously managed for recovery.

Figure 5.3 In substance use disorder people, several synaps circuits are being changed. (http://akuamindbody.tumblr.com/) Date of access 08.09.2014

CBT sometimes can be a useful instrument for care of intellectual sickness like sadness and anxiety. But cognitive behavioral therapy does not yield positive results in all patients. It may help people in a stressful to learn how to manage stress and can be an effective tool.

Behavior therapists can teach new behaviors to the patient using learning strategies and teach ways to stay away from undesirable behavior. So behavioral therapy must be very focused in order to get results. CBT teaches new behaviors to minimize the harm to customers.

5.2.2 Humanistic Therapy

Humanistic psychology, behaviorism and psychoanalytic theory has been developed in response. Philosophical roots of the humanistic therapy theory was started with 19th century philosopher, Soren Kierkegaard. Humanistic therapy to bring a sense of meaning to life and helps individuals themselves that is it encourages us to see ourselves as a whole person. This form of therapy helps to achieve the belief that all people are innately good patient. In psychotherapy, it is used in various ways as experimental, humanistic existential or Gestalt therapy. It was rooted in everyday personal experiences with people who need help shape this therapy [89].

The main benefit of humanistic treatment to create a growing awareness in the minds of patients. Instead of reactionary attitudes of patients, they are directed to develop in a manner that is self-aware approach. During treatment provided to patients regarding

their awareness of inner goodness and and unlimited potential. Therapists in all states to respect the patient and make empathy is advised. Humanistic therapy may be helpful in tretament of anxiety, depression and various types of addiction.

5.3 Pharmacological Therapies

Pharmacologic treatment involves the use of drugs is a health care style, used individually or in combination with other modalities of treatment.

In recent years, novel medications marketed for the intellectual sickness treatment were outpoured. Most of these drugs have been those used to treat depression and schizophrenia stocked by neuroscience and molecular biological research. Through a procedure known as reasonable drug design by manipulating the chemical building of the drug has become increasingly sophisticated. The purpose of these accomplished studies to produce new drugs have low side effect and provide more effective treatments for mental disorders [90].

The most important medical treatment for depression is antidepressant use. There is a wrong information about the use of antidepressants and although there is no simple explanation about how it works. Antidepressants can be very useful in the rehabilitation of severe or moderate depression.

Antidepressants may be prescribed during the treatment of psychological disorders, when when patients had moderate or severe attacks. In some moments, antidepressant are engaged in cases where other treatments have failed or when the psychological treatment is impossible because of the severity of the disease.

People who get severely depressed such as psychosis and bipolar disorder often need to do medication. This drug may comprise one or a union of anti-psychotic drugs, antidepressants and mood stabilisers.

Many different types of antidepressant commercially available, but their effectiveness varies from patient to patient. Antidepressants begin to show the effects minimum two weeks later, and doctors needed extra time to find the right dose and most fitting combination. The antidepressants of late are more than permited and connected to less narcotic actions than the former sort of antidepressants. Interactions and side effects

decrease success of treatment. Most of side effects disappearance in the course of time and with dose reduction [91].

Physicians frequently use Selective Serotonin Reuptake Inhibitors (SSRIs) to raise the quantity of the neurochemical matter in the brain. Reseracher thought that, serotonin levels are often to be low in the brain of the depression patients. The SSRIs effect by discriminativly barring serotonin retake among the synapsis. Serotonin is transmits electrical signals across among the synapses [91].

The SSRIs act by holding serotonin existent in high density among the synapses by averting the consuming of serotonin again. This proces is accountable for shut off the assembly of new serotonin. It is thought that this, helps activate cells thus the depression symptoms are decreased [91].

Side effects of the SSRIs are very low level than the TricyclicA antidepressants's (TCAs) and Monoamine Oxidase Inhibitors's (MAOIs). Hence, Physicians prefer at the beginning SSRIs drug as first type of theraphy for depression illness. Some of SSRIs contain Paxil (Paroxetine), Zoloft (Sertraline), Fluvoxamine-Luvox, C-Celexa, and Lexapro (Escitalopram), Fluoxetine-Prozac [91].

Patients may feel better using antidepressants, but they does not alter their personality or make them happy all the time. As seen with other drugs, antidepressants may also have side affects. Taken drugs and depending on the patient the most most seen common side effects, contain headaches, dizziness, anxiety, nausea, sweating, agitation, dry mouth, weight gain, and sexual difficulties. These symptoms can sometimes take short time and the side effects vary between individuals and medications and from patient to patient.

5.4 Electroconvulsive Therapy (ECT)

It is really hard to treat patients with deep depression by giving medication or psychotherapy. Once it is realized that medication does not work for relieving symptoms of major depression, other possible options should be tried. For major depression cases, which cannot be treated with standard treatment methods, brain stimulation techniques should be tried such as Electroconvulsive Therapy [92]. (Figure 5.4).

Before electroconvulsive therapy, patients are anaesthetized and also specific amount of neuromuscular blocker is given to them. Then, electrodes are positioned to pre-determined places on the head to apply controlled electrical current. The electrical current leads to seizure of the brain. Since prior to the therapy, neuromuscular blocker is given to patients, the effect of the seizure only seems as slow shake of hands and feet. After a while, patients come out of anesthesia confusedly. This confusion lasts for a while. ECT is applied 3 times a week and the total time of the therapy generally lasts 2 to 4 weeks.

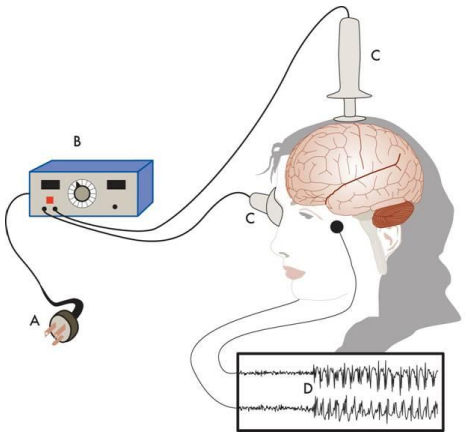


Figure 5.4 Electroconvulsive therapy has been an efficient technic for treatment-resistant mood mess patients

(http://academicdepartments.musc.edu/psychiatry/research/bsl/ect.htm) Date of Access 10.09.2014

5.5 Transcranial Magnetic Stimulation (TMS)

The brain stimulation technique with the smallest amount of side effects is TMS, (Figure 5.5). In this type therapy, forehead is exposed to magnetic wave generated by a medical device. The reason why forehead is stimulated in this technique is because it is the part of the brain related to mood.

Practice span takes generally 30 to 60 minutes and physcians does not use anesthesia in this technique. A coil produced electromagnetic field is held against the forehead that is thought to be engaged in mood regulation. Then, during the coil produce short electromagnetic pulses, these pulse train continously reach to the skull, and stimulate nerve cells in the brain [92].

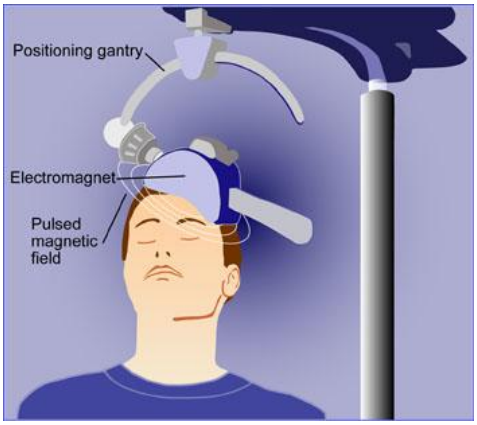


Figure 5.5 Stimulating of the brain sclap by TMS. (http://www.nimh.nih.gov/health/topics/brain-stimulation-therapies/brain-stimulation-therapies.shtml) Date of access 10.09.2014

5.6 Vagus Nerve Stimulation (VNS)

Another alternative treatment method for depression is VNS (Figure 5.6). In this theraphy, a device surgically placed to the brain in order to stimulate the related nerve, which is called as vagus nerve. On the other hand, for mild depression, easier methods can also be used such as hypnosis or yoga, for treatment.

In this technique generator continuously produce electrical pulses that last about 30 seconds and these pulses are sent to the vagus nerve about each five minutes. Physcian program the frequency and duration of the cycles properly. After this the vagus nerve sends these puls train to the brain. The generator is operated by a battery that lasts about 10 years, after it can be replaced. During operation, patients does not feel any pain, but raerly it may provoke coughing or the hoarse voice [92].

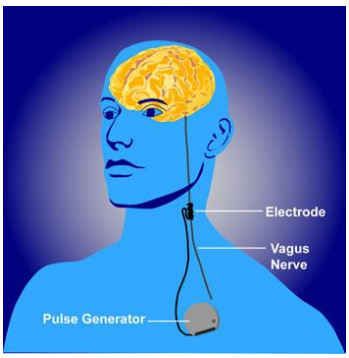


Figure 5.6 Vagus Nerve Stimulation is an alternative treatment method for depression (http://www.nimh.nih.gov/health/topics/brain-stimulation-therapies/brain-stimulation-therapies.shtml) Date of access 12.09.2014

Comparing all these methods, electroconvulsive therapy is the safest and the most influential one for depression treatment. Before getting the therapy, patients are anaesthetized. Then, through electrodes positioned to the forehead, certain amount of electrical current is given. After the therapy, most patients can get easily and quickly get rid of depression symptoms. Electroconvulsive therapy is not only used for depression but also other psychologic illnesses. Even though ECT is that effective against major depression, it is the last method used, if patient does respond to other treatments.

Even though electroconvulsive therapy has been used since 40s, it is still misunderstood by considerable number of people. The risks and side effects of the therapy, if any, are because of the misuse of the device or unexperienced health personnel, not because of the therapy itself [92].

5.7 Complementary and Alternative Treatment

Interest in recent years in abundance in innate goods have beared demands connected to presumed results on intelectual health. There are some reports show enhanced memory of the people using the herb, ginseng and some flowers as an antidepressant (Figure 5.7). There are importanat struggle to estimation the part of mental health safety and the alternative rehabilitation used in the improvement of mental disorders. On the market, preparations consist of an active ingredient or a mixture of some. Some factors such as bioavailability, purity, amount and timing of doses could not be possessed for answered to with nature goods. But these are set basic rules for traditional pharmaceutical agents prior to testing [93,94].

Complementary and Alternative Medicine surrounds diversity of access. They contain all from exercise and diet to lifestyle changes. Examples of Complementary and Alternative treatment comprise: Acupuncture, aromatherapy, hypnosis, meditation, biofeedback, dietary supplements, guided imagery, massage therapy and relaxation.

Figure 5.7 Aromatherapy uses natural oils extracted from flowers

(http://www.postpartumprogress.com/the-best-complementary-alternative-medicine-treatment-options-postpartum-depression) and (http://www.healthline.com/health-slideshow/beating-depression-naturally) Date of access 14.09.2014

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5.8 Neurosurgical Treatment

Neurosurgery is a surgical field treating spinal cord, peripheral nerves and brain sickness. For the first time psychiatric illness treatment cases have been depicted by Egas Moniz first who neurosurgeries. In the 50s lack of alternative therapies that it has encouraged neurosurgeries. At that time, the pre- frontal leucotomy has been used in some neurosurgical centers. However, Personality changes and frontal lobe disorders could be seen in patients who have operated. The negative impact of the use of surgery gave decline in the psychosurgery at that time [95].

The first stereotactic neurosurgeries reduced post-operative side effects in 1947 [96]. From that time until today, several stereotactic techniques were used as front cingulotomyt [97] capsulotomy [98] subcaudate tractotomy [99] and limbic leucotomy [100] cingulotomyt in a lot of different health centers. Later, Leksell made a simulation study. In this instance, Cobalt-60 radioactive isotope send out gamma beam toward the focused lesions. From now on, It was invented lateral central thalamotomy was a new technique [101].

In the last 20 years, neurosurgeries was born again especially in the treatment of mental disorders such as OCD. Neurosurgeries with special attention to the input for use in patients who do not respond to treatment and stereotactic technique reduces

complications were much lower level with a promising way. Also with the use of the latest techniques such as Gamma- Knife radiosurgery also remove the necessity skull opening.

5.9 Neurosurgical Techniques

Functional neuroimaging findings in OCD patients supports the theoretical infrastructure of surgery [102]. A number of studies using SPECT and PET showed that an raise activitiy of metabolism in the resting state OCD within the caudate nucleus and inside the cingulate and in the orbitofrontal cortex differently from healthy individuals. As well as some findings, in these patients after the use of drugs or behavioral therapy It was observed in these regions to normalize metabolic activity [103]. As a result of these findings results attained that cortical regions, the medial dorsal thalamus and basal ganglia have considerable importance in the pathophysiology of OCD [104].

When using a multi-method for surgical treatment of obssessive compulsive disorder, most reliable and most efficient four procedures carried out bilaterally are applied. All of them controlled by stereotactic situations to permit for exact lesioning of target cells. These ones: Subcaudate tractotomy, Subcaudate tractotomy, Anterior cingulotomy, Anterior capsulotomy and Limbic leucotomy [104].

5.9.1 Subcaudate Tractotomy

In 1964, Subcaudate tractotomy was presented in UK. The goal of this technique was to discontinue white matter area in the mids of the lower part of cortex constructions and orbital layer by creating a wound around the substantia innominata. In patients suffer from OCD and sadness (depression), total recovery was clinically observed in 2/3 of the people who requires medical care [105]. The position of the Subcaudate tractotomy lesion is shown In Figure 5.8.

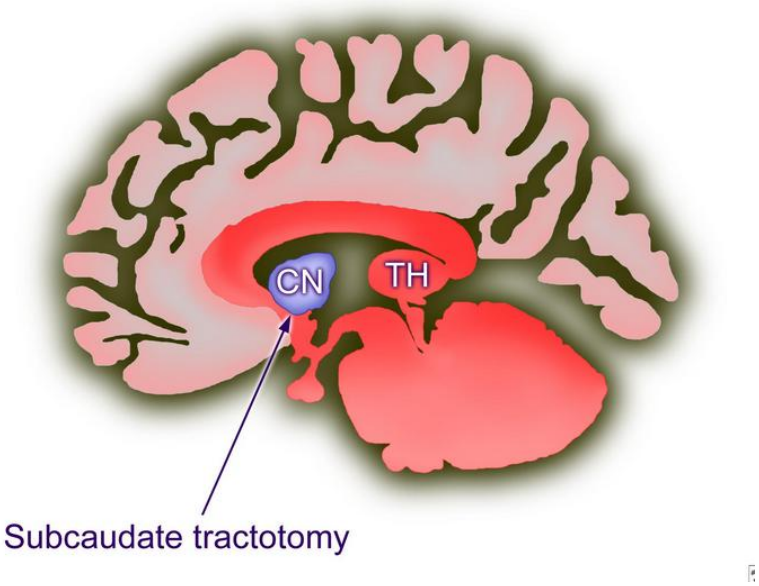


Figure 5.8 The position of the Subcaudate tractotomy lesion (http://emedicine.medscape.com/article/1343677-overview#a5) Date of access 17.10.2014

5.9.2 Anterior Cingulotomy

The anterior cingulum were identified as target with the recommendation of the Fulton an cingulotomy was at first performed as an open surgery. At first, these operations were achieved respecting with cerebral ventriculography than MRI guided stereotactic techniques started to use. and thermocoagulation method was used to create lesion [105, 106]. The position of the cingulotomy lesion is shown in Figure 5.9.

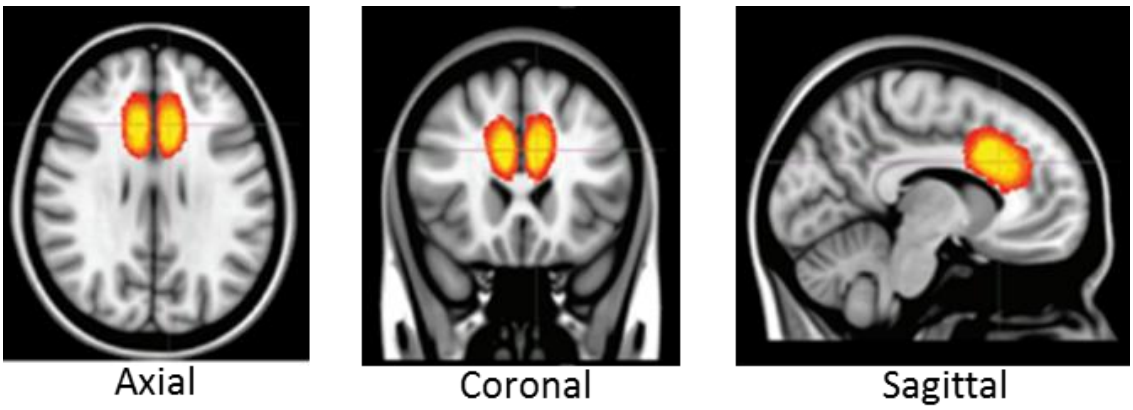


Figure 5.9 An anterior cingulotomy lesions are seen as T1-weighted template and heat maps. Yellow color show more lesion accordance and red show less lesion. (http://thejns.org/doi/pdf/10.3171/2013.9.JNS13839) Date of access 20.11.2014

5.9.3 Limbic Leucotomy

In 1973, The Limbic leucotomy was came out by Kelly and anterior cingulotomy and subcaudate tractotomy was come together using this technique. The goal of this technique was to discontinue connection between former lession and orbital-frontal-thalamic pathways. These two lesions or lesion alone may goes to a better outcome for the indications for obsessive compulsivve disorder [105, 106]. A representative Limbic leucotomy lesions are seen in figure 5.10.

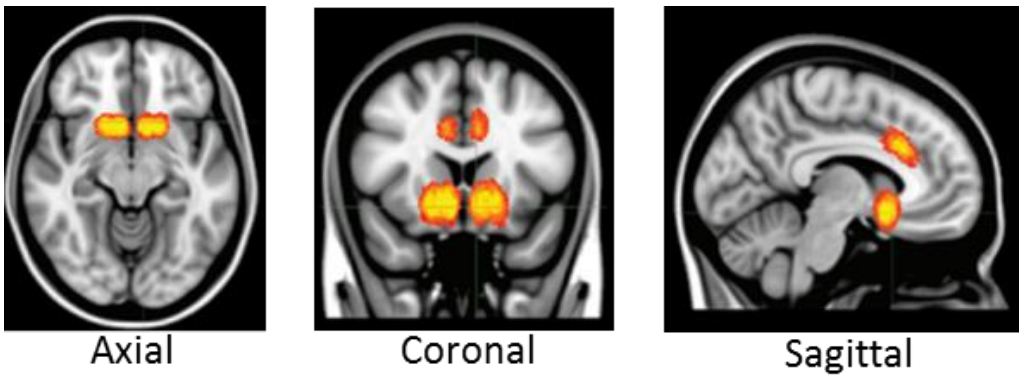


Figure 5.10 An Limbic leucotomy lesions are seen as T1-weighted template and heat maps. Yellow color show more lesion accordance and red show less lesion. (http://thejns.org/doi/pdf/10.3171/2013.9.JNS13839) Date of access 20.11.2014

5.9.4 Anterior Capsulotomy

Although anterior capsulotomy initially defined by Talairach, The procedures implemented for psychiatric illness was popularized by Leksell. It was targeted to cut the connections of the fronto-thalamic in the anterior limb in the operations achieved. In this operations Gamma knife used to create lesion for capsulotomy comprised depression, anxiety etc. In tests performed on 250 patients after operation, not found any evidence related cognitive dysfunction. Today, in some psychiatric disorders like especially chronic OCD, anterior capsulotomy and cingulotomy techniques are used. Positive results obtained from Gamma capsulotomy in the treatment of suicidal patients suffer from OCD increase and encourage the use of these techniques [107].

Synapses in some regions in OCD patients is always electrically active and behavioral therapy and drug use may reduce the electrical transmissions. However chronic patients are responding negatively to this type of treatment. Therefore in these patients, cutting

ties with the gamma knife is preferred. Where a specific area is targeted, the healthy tissue is protected [107].

Gamma Knife is also used in the care of some ilnesses like Parkinson's ilness and some type of Neurological confusions. In the treatment of chronic Anxiety disease states and severe OCD The Surgical treatment may be useful. Such operations must be carried out by specialist experienced teams and it should begin and continue psychiatric rehabilitation after surgery. The great majority of post-operative health of the patient are achieved and therefore gamma knife theraphy has become the most pre-engineered form of treatment for disabling psychiatric patients [107].

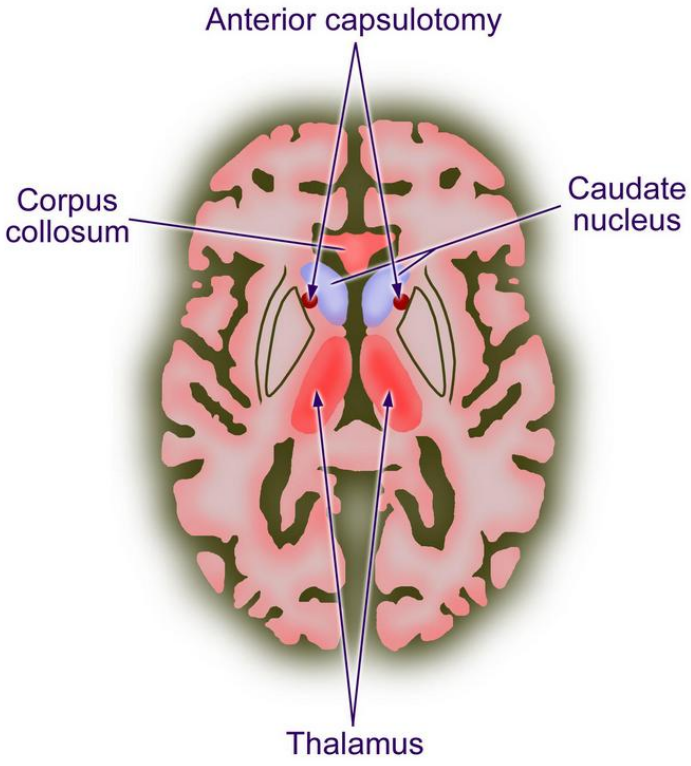


Figure 5.11 The red signed division represent the characteristic position of the Anterior capsulotomy lesions. (http://emedicine.medscape.com/article/1343677-overview#a5) Date of access 22.11.2014

Theoretical elements that support surgical operations for patients with OCD relates to one or more selective section of the roads that connect these structures. For instance, in anterior cingulotomy conductor are reciprocal acquainted, by way of stereotaxy, in the prior to part of the cingulate, presenting warmed wounded cell by radio waves in the brain part.

Anterior capsulotomy, be based on in the reciprocal stereotactic wounded cell of the white matter structure. Than, the fibers divided among the subgenual anterior cingulate and the middledorsal thalamus [107]. A representative Anterior capsulotomy lesions in Figure 5.11.

5.10 Treatment of OCD Patients by Stereotactic Radiosurgery

Radiosurgery is the use of a non-invasive technology to treat lesion on the target. It is an alternative to standard open surgery in some patients. This quite high and focused radiation dose is transfered with a single short term and prevents possibly injurious energy to encircling structures of brain. Radiosurgery is different from the radiation therapy in some ways. using regular outer radiation therapy methods, tumors or target cell are cured to the similar portion of radiation.

Surgeons use three types of technology to deliver radiation during stereotactic radiosurgery that can be perform without using the knife. These technologies be mentioned as Gamma knife, Cyber knife is also to be mentioned as Linear Accelator (LINAC) and Proton beam is charged particle radiosurgery is available in only a handful of some research centers. All of them have robotic radiosurgery machines technology that give painless treatment possibility for patients. Robotic surgery is allow automatically correction of the patient position [107-110].

Before using the Gamma Knife, stereotactic radiosurgery procedures created Dr. by Lars Leksell who inventor of the Gamma Knife, at the University of Upsala. This university had a convincing physics department, to meet the all needs such as the cyclotron used in stereotactic radiosurgery. In Figure 5.12 shown First stereotactic radiosurgical procedure [107-110].

Gamma knife machine was invented in Karolinska institute in Stockholm by Lars Leksell, a Swedish neurosurgeon was born in Fassberg on November 23rd 1907. First patient was treated by Dr. Lars Leksell is seen in Figure 5.13 with the first Gamma Knife patient at the Karolinska Institute, Stockholm, Sweden in 1968 [107-110].

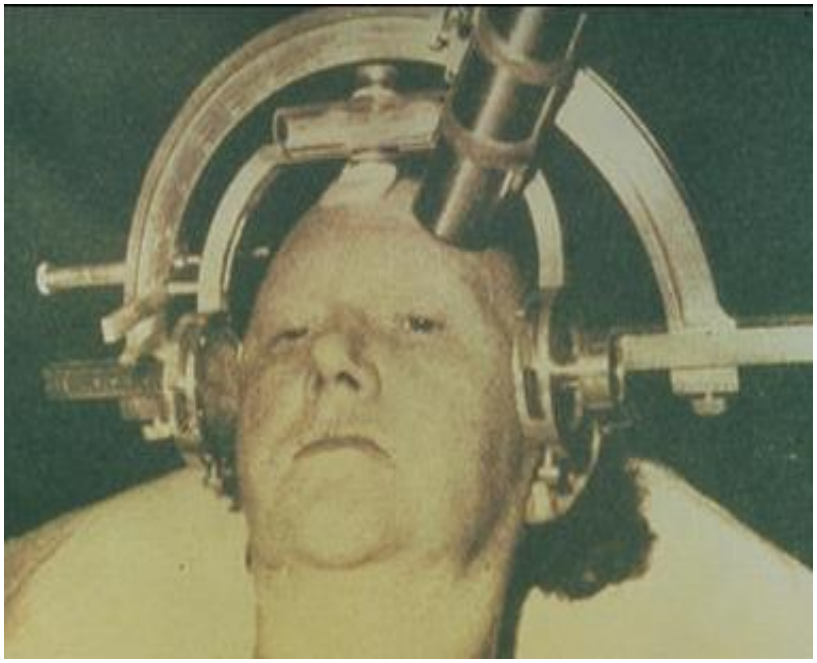


Figure 5.12 First stereotactic radiosurgical operation
(http://www.lowback-pain.com/gammaknife.htm) Date of access 01.12.2014

Figure 5.13 The first Gamma Knife and patient with Dr. Lars Leksell in 1968.
(http://www.lowback-pain.com/gammaknife.htm) Date of access 01.12.2014

During radiosurgery, a Gamma knife deliver high dose Cobalt radiation toward a spesific target in the internal capsule in brain while delivering minimal dose to surrounding tissues for several hours. A Gamma knife concept is shown in Figure 5.14.

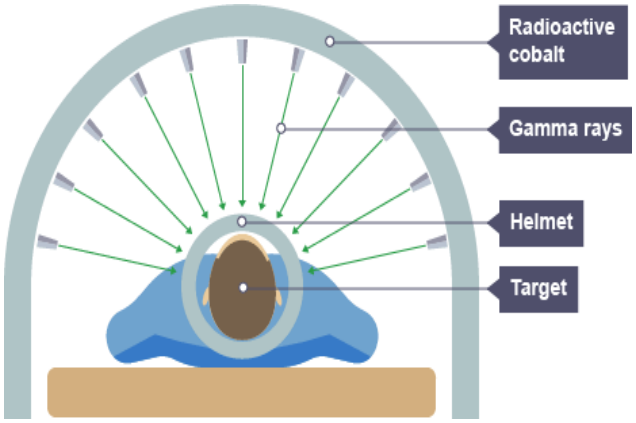


Figure 5.14 Gamma Knife concept (http://www.bbc.co.uk/schools/gcsebitesize/science/triple_edexcel/ionising_radiation/radiation/revision/3/) Date of access 12.12.2014

Gamma Knife unit, uses the most energetic rays produced by a radioactive source. This rays have shortest wavelength ranged from 0,003 to 0,0003 nm. Gamma rays can travel very far in air at the same of the speed of light and with high energy level 10,000 times more than visual scope of the electromagnetic spectrum. Gamma beams pass through all items and not capable of reflection from any materials or capturing with reflector [107-110].

Gamma rays are manufactured using Cobalt-60 is not unaffectedly encounter in universe and produced by neutron vivacity of Cobalt-59 for purposeful of therapy. If a reseracher a radioactive beam to be used as therapeutic, have to consider some significant facets such as high level energy and high particular pursuit [107-110]

This device affects the tissues as other stereotactic radiosurgery methods. Gamma Knife is not remove the tumor or diseased tissue, instead of produces damage in the DNA of cells. Thereupon diseased cells lose their normal characteristics and this targeted cells die as nutrition division functions are impaired.

This machine has high precision, high accuracy ($\leq$ 1 mm) and minimizes dose to normal tissues in proximity to the target and the biggest benefit of using this technique that it is nt an obligation opening the skull [111, 112].

There are some parts in the Gamma knife unit such as the radiation unit, the focusing unit, the control console and the computer using tratment planning.

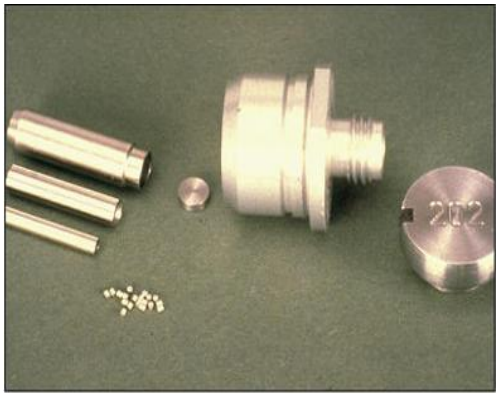


Figure 5.15 Cobalt 60 Radiation source for the Gamma knife
(http://www.lowback-pain.com/gammaknife.htm) Date of access 15.12.2014

Gamma knife typically contains 201 narrow, collimated gamma beams emitted by a Cobalt-60 is a stereotactic teletherapy machine. In Figure 5.15 Cobalt 60 elements is shown.

Sources of Gamma beam are arranged in a half of a sphere and directed into a collimator to catch the focal zone. The metalic head is situated within the Gamma unit in order that the marked cell is in the focal zone of the gamma beams. Figure 5.16

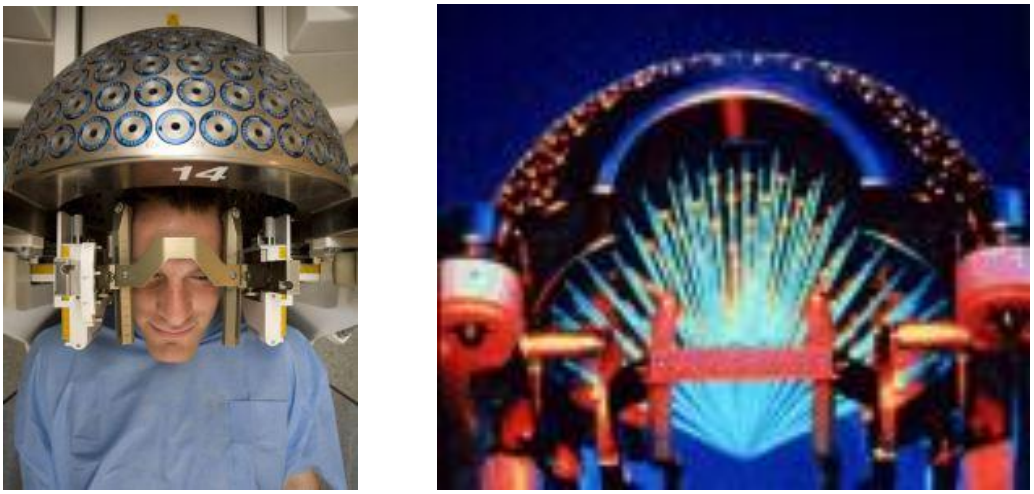


Figure 5.16. Gamma knife collimators and beam focusing. The beams are focused by the focal point of the Gamma knife collimators

(http://strength-in-numbers.co.uk/tag/cancer/ and
http://www.virtualtrials.com/gamma.cfm), Date of access 09.01.2015

Point of intersection of the rotational axis of radiation is called isocenter. The tissue encircling the isocenter absorb beam in ratio to the number of ray of light crossing through it, in addition to the spread from photons that are partially absorbed. Once you've targeted lesions with stereotactic localization, patient is delivered to a covered private area of the Gamma Knife unit and the destruction is carried out. Radyosurgery generally preferred without general anesthesia, so doctors finds the opportunity to talk with patients during the operation. According to the complexity of the treatment process revealed processing time and generally this process may take up to 60 minutes [105]. In Figure 5.17, It is seen a modern Gamma knife machine.

Figure 5.17 Gamma Knife Radiosurgery unit with a treatment-ready patient (http://www.jlgh.org/Past-Issues/Volume-2---Issue-1/7-Years-of-Gamma-Knife-Radiosurgery.aspx) Date of access 10.01.2015

The Cyber Knife robotic radiosurgery system was developed by John Adler, a doctor at Stanford. In 1994, the first patient was treated at Stanford using the Cyber Knife. It was approved by the Food and Drug Administration (FDA) in 2001. When the Gamma Knife uses radioactive cobalt to generate the gamma ray, all newer generation machines such as Cyber Knife is made up of a radiation delivery device (LINAC) attached to a robotic arm utilize X rays instead of gamma rays. The Cyber Knife is the world's first and only intelligent robotic radiosurgery system [105, 113, 114].

In the radiosurgery process using the LINAC, beam is revolved through set of arcs nearby the targeted cell or an arc. When transmitted beam reaches the target cells is

irradiated until the end of the treatment by the way just beam passes through inclosing the tissue. LINAC machine has a part called the gantry moves around the patient. It sends beam at different angles to the patient. (Figure 5.18) [113, 114].

Because the LINAC is cleaner and and doesn't require the disposal of radiaoctive cobalt by the hospital, it is generally preferred. Cyber Knife robotic radiosurgery combines computer controlled robotics and image guidance technology. Computer controlled robotics allow the system to send high doses of radiation without a metal head frame while preserving sub-millimeter accuracy. This part of system depend on skeletal territorial markers or firmly established markers that are put percutaneously in the process of fluoroscopic guidance to place treatment targets. [113, 114].

The CyberKnife be composed of an progressive, slight linear accelerator, embedded on a robotic arm together with and few x-ray cameras to follow position of patient. Cameras record sequential photographs of the patient during treatment and utilize this data to target the radiation beam emitted by linear accelerators. If the patient is acting during operation, position change is detected by the camera and the robot will redefine the objectives of the linear accelerator before administering the radiation beam before radiation is applied. This control and correction process is continually done. This process guarantee precise radiation during treatment [113, 114].

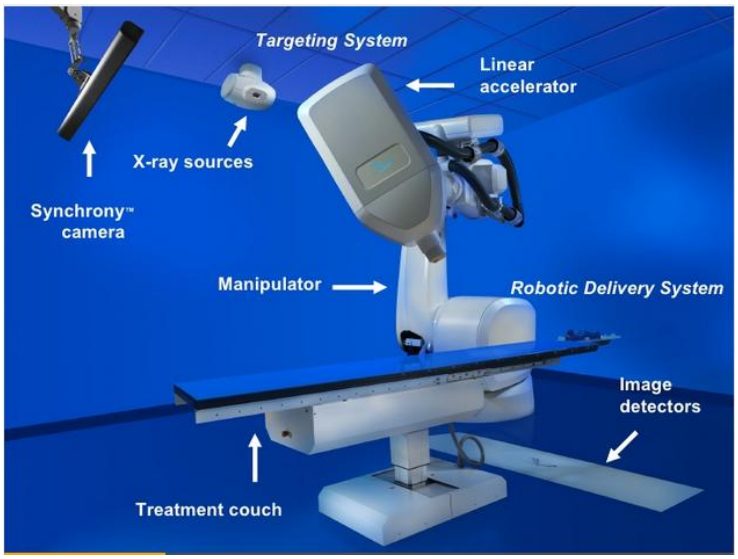


Figure 5.18 A modern Cyber Knife unit inclusive LINAC radiation delivery device (http://www.slideshare.net/fovak/cyber-knife?next_slideshow=1) Date of access 11.01.2015

Until the end of the beginning of the operation in stereotactic radiotherapy, some important apparatus used suc as fixation apparatus containing frameless technology and masks immobilizers are employed.

In the frameless technology, it is used embedded gold fiducial markers, which are easily added to the head to supply a arrange system. In the mask systems there is a mask molded for each patient. Head of patients put in a U-shaped frame, and maxilla and the forehead are protected with polymer band.

The mask system reduces the patient's variation less than 1-mm with helper patient and less than 2-mm for a non-helper patient. In the head immobilizers system vacuum-attached markers used to ensure the maxilla and the rear section of the skull into a steady condition [113, 114].

Because of the using of fractionated stereotactic radiotherapy provide excellent control of the target cell, fractionated stereotactic radiotherapy may prefer to manage the radiation treatments of small children who un-helped. At the same time fractionated stereotactic radiotherapy releases the brain from such cognitive side effects [113, 114].

Stereotactic radiosurgery has also been used to tretment of OCD. As others, in this technique an abrasion is producing in the anterior capsule. The anterior capsule is linked to producing neural activities that account for OCD in the patients brain [115-117].

In these days, technology of the gamma knife has been modernized to be more strict without the need to drill in neurosurgery and how is this, it is started to prefer mainly [118, 119]. Some sections of the brain picture with capsulotomy lesions are shown in Figure 19 [120].

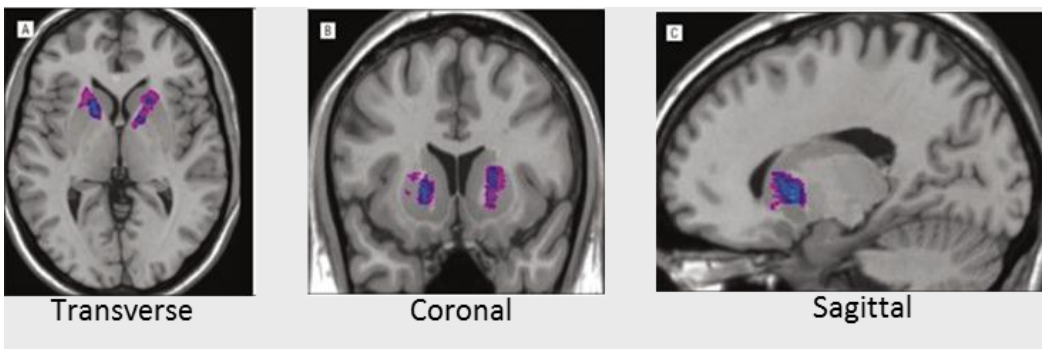


Figure 19 Some sections of the brain picture with capsulotomy lesions. (http://archpsyc.jamanetwork.com/article.aspx?articleid=210096)

5.10.1 Procedures of Gamma Knife Application

5.10.1.1 First Step: Head Frame Placement

During head frame fixation, lightweight aluminum frame put on the patient's head by the neurosurgeon using local anesthesia and intravenous, conscious sedation. Local anesthetic injected at pin sites. This protocol quick and well beared. The frame work as a remark point for the ensuing planning of target cell arranges in the brain using images. Until the end of the treatment process the frame stay on the patient's head [121-123]. (Figure 5.20)

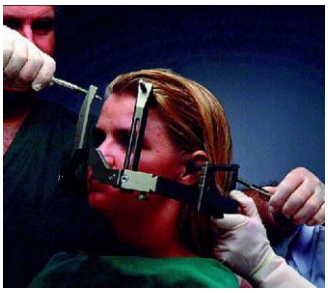


Figure 5.20 Application of the Gamma knife head frame placement (http://www.gams.com/presentations/or01/brainshort.pdf) Date of access 12.02.2015

5.10.1.2 Second Step: Diagnostic Location Imaging

After frame fixation, the patient then undergoes a head scan to take CT or MRI. That is head is imaged using CT ot MRI while the patient wears the stereotactic frame. If the patient with vascular abnormalities, at that time an angiogram is required. CT or MRI images taken from patient are used purpose of the treatment planning. A patient preperation to get the head image is shown in Figure 5.21 and angiographic picture and CT scan picture are shown in Figure 5.22. [122-124].

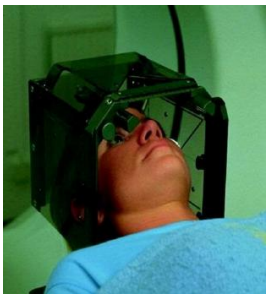


Figure 5.21 A preperation to get the head image using an computerized tomography or Magnetic resonance imaging devices from patient weared the stereotactic frame (http://www.gams.com/presentations/or01/brainshort.pdf) Date of access 13.02.2015

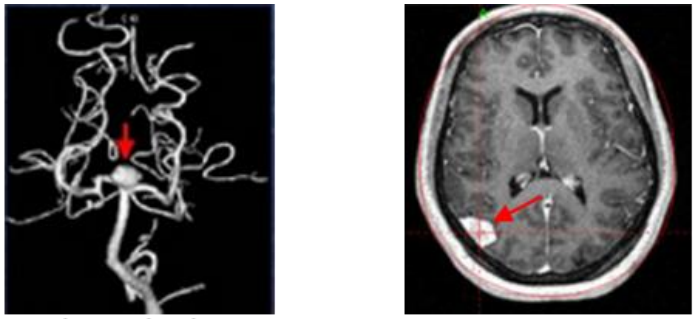


Figure 5.22 Some diagnostic imaging pictures (http://gammaknifeindia.com/gammaknife-treatment-procedure.html) Date of access 17.02.2015

5.10.1.3 Third Step: Radiation Dose Planning

Radiation oncologist, neurosurgeon and physicist need to develop a reliable conformal treatment plan using the images. The while, CT or MR images and powerful computer and software are used to precisely calculate the radiation dose and These systems give a 3-D image of the brain belong to patients waiting to operate to highlight the area to be treated. To day, surgeons are allow of treating intracranial illnesses owing to high speed data processing and using computer techniques. (Figure 5.23 and 5.24).

Before the operation, experienced surgeon team have to assay and determine the shot sizes, the quantity and weights of shots, target cell locations [121-123].

Figure 5.23 The surgeon team are developing a treatment from the images (http://www.sd-neurosurgeon.com/practice-gamma-knife.php) Date of access 18.02.2015

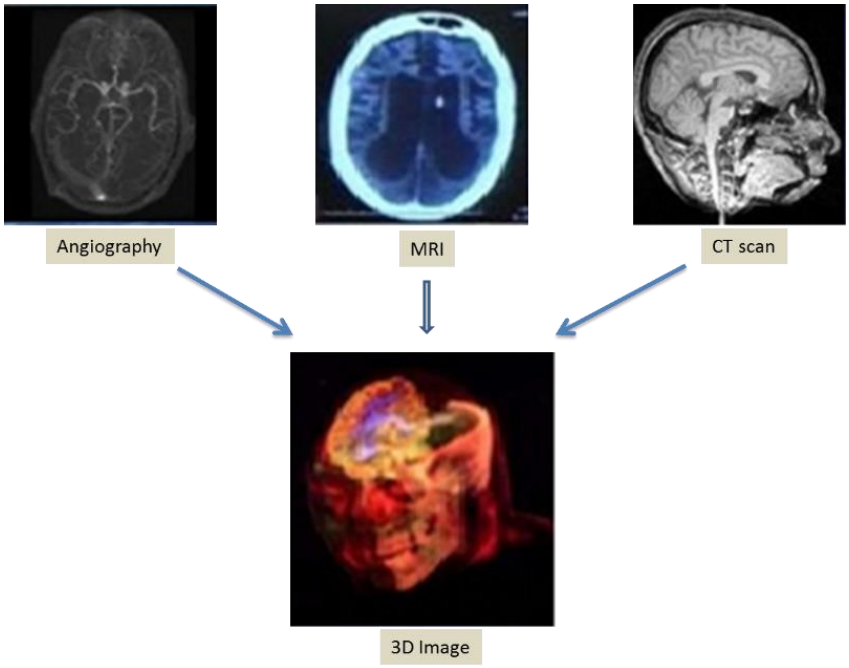


Figure 5.24 Generation of 3D image (http://www.sd-neurosurgeon.com/practice-gamma-knife.php) Date of access 18.02.2015

5.10.1.4 Fourth Step: Actual Radiation Treatment

At first, the patient will be operated is doll up an Intravenous (IV) device and deliver intravenous liquids to avert loss of water due to the fact that the patient not able to drink and eat up to the therapy is finish. During the operation the patient under generalized or local anesthesia. If a localised anesthetic is prefered, it is an obligation to give a sedative drug by way of the IV in to reduce motion along the the operation.

Before the patient is adapted accompanied by a steriotactic frame, the anesthesic agent transferred to the patient. The frame is used to catch accurate position as an assessing guide.

At first, gamma knife bed properly situated, afterward the frame is bound to a collimator helmet. Steriotactic frame and Collimator Helmet are shown in Figure 5.25. After this, the patient is put in gently across a surface into the gamma knife cavity including the radiation generator, the treatment starts and the 201 seperate radiation light pass over at the through a single target point, that being the target cell. Figure 5.26 display the Schematic of the actual treatment position in Gamma knife couch [122-124].

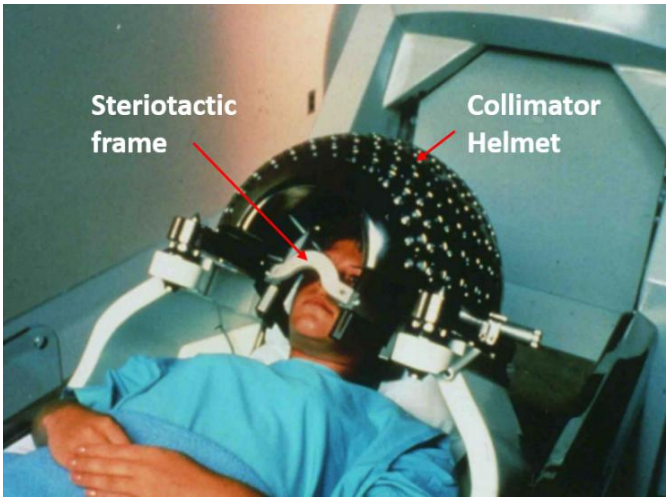


Figure 5.25 Some major componenets of Gamma knife
(http://www.gams.com/presentations/or01/brainshort.pdf) Date of access 22.02.2015

Figure 5.26 Schematic of the actual treatment position in Gamma knife couch
(http://gammaknifeindia.com/gammaknife-treatment-procedure.html)
Date of access 12.03.2015

During Stereotactic radiotherapy, small spherical lesions or nonspherical lesions may be considered for these procedures. In some condition, the shape of a lesion requires more than one treatment isocenter. When multiple isocenter are required, attention should be taken to recognize and minimize the volume of dose overlap. Very strict appliance are used for limiting to a certain location of the isocenter during on its own treatment [124]. Sufficient dose homogeneity to nonspherical area with lenient of regular cell is possible by utilizing various cones and isocenters [125].

The total amount of ionizing radiation is deposited at the target cell by implementing one of the “globe” of portion at a distinctive requested place. Radiation amount determines by the tenet of Superposition and various such shots as mentioned by Gamma Knife users. Nonspherical shaped target volumes exposed different shooting are shown in Figure 27.

When new shots are supplemented, computer refigures the dose allocation in real time. This arithmetical refigures of dose allocations, distinguished normalization, is applicable because all portions inside the computation matrix are display as ratio assess.

When dose delivery level calculated and approved by operation team, the scheduled beam to be managed. During treatment, the one of team ceaselessly confirm if the treatment plan are set correctly [125].

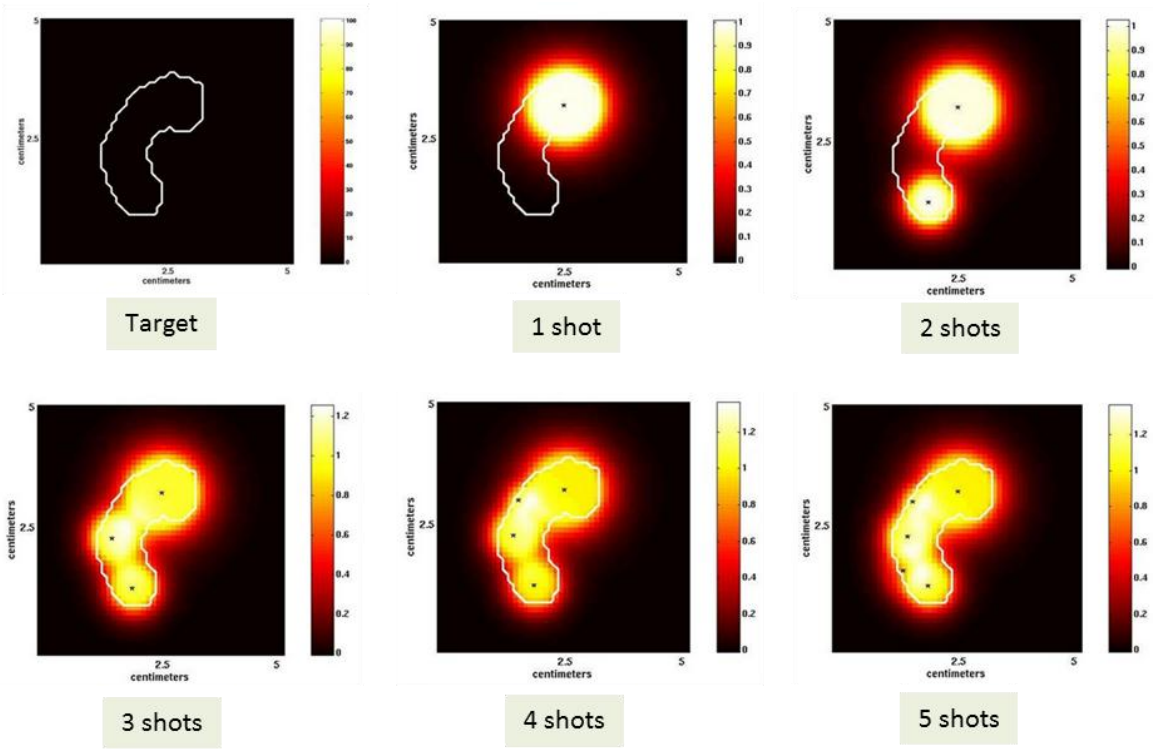


Figure 5.27 Nonspherical shaped target volumes exposed different shooting (http://www.slideshare.net/radiotherapist90) Date of access 15.03.2015

5.11 Side Effects of the Gamma Knife Treatment

In this type of operation meticulous radiate from the gamma unit through the targeted cell by a lot of different angles for a little lenght of time. Because there is no real knife engaged in this treatment, It may be useful for some special patients who are suffer from chronic OCD that can't be treated with using drug.

During operation, a few patients may be disturbed wherefore some symptoms such as, vomiting, nausea, local pain and swelling in the scalp and headaches. But tehese are also uncommon. Sometime, drugs can help alleviate this type matters.

If big areas of the brain is affected from radiation, a few patient can forfeit some brain function depending on the treated area and how much radiation is delivered, These functions are maybe character changes, mind loss and problem centralizing.

CHAPTER 6

RESULTS

In this thesis frame, we studied two different but closed ilnesses named depression and OCD and their treatments. This thesis gave a depiction about depression and OCD and in shortly surveys the conceptual interpretation and treatment of the sickness.

A great number of patients who have OCD also encounter precept for extra conclusion like mood, anxiety and personality disorders. The present and advanced treatment methods particularly for depressed OCD patients are exemplified with some case example.

According to the results of World Health Organization studies in 2012, clinical depression is the mortally giver to the universal volume of disease. In the World, approxiamtely 350 million human for all ages feel ill wherefore depression, and in a tragic manner, 1 million patients cease living by self destruction every year [126].

The most prevalent treatment methods for depression are medicinal treatment using antidepressant and psychotherapy. Antidepressant medications ambrace a lot of new agents such as SSRIs, TCAs and MAOIs. Customarily, prefering of antidepressant drug are frequently retained to deal with major depressions, during psychotherapies are often prefered for the moderately depressed patients and in these days, newer antidepressants such as SSRIs have low side-effect portraits and greater tolerability acquired new consequence [126].

One of forty adults in the World suffer from OCD known as the fourth most public psychiatric sickness. OCD patients mostly live tenacious, interfering idea or misgivings that drive them to carry out comfort rites. Patients wsuffer from OCD generally know that their compulsive ideas and conducts are radical or not reasonable, but this consciousness does not assist them rule their disorders [126]. The procedure of estimation for OCD depicts an significant function in determining a curative connection with outpatient and distinguishing therapy targets.

The assignation of OCD may be lead on utilizing produced organized disputation apparatus, involving a norm indication list and seriousness rank scale[126].

OCD has biological origin and drug therapy performs an fundamental function in medical care. The symptoms of this disease has been attributed to the irregularity of the serotonin in brain and using SRIs may be reduce the symptoms of ilnesses. Aproximately 50% of patients suffer from OCD get considerable recovery using SRIs such as, sertraline, fluoxetine, fluvoxamine, etc. All of this type drugs exhibited the ability to produce the desired result in decreasing OCD symptoms [126].

6.1 Social and Economic Impact of Brain Disorders

Financial costs of illnesses have become a significant factor for not only research but also health policies. However, it is generally hard to estimate them. For policy analysis (the prime purpose of cost estimate it is advantageous to take neurologic and mental diseases together under the scope of brain diseases, as cardiovascular illnesses are examined together in spite of different etiology. Additionally, researches show that neurologic and mental diseases have really similar, if *not* equal, significant mechanisms. According to WHO, one third of all illnesses in developed parts of the world are mental and neurological disorders. Cost estimates of brain diseases supplement volume of sickness estimates, by giving info regarding the financial effects of illnesses. The European Brain Council (EBC) is an association of European organizations interested in brain and its diseases [127, 128].

Regarding impaired life quality and loss of money, OCD was ranked among the top ten diseases, which adversely affect people most. [127, 128].

Obsessive Compulsive Disorder places a significant burden not only to patients but also to their families, health care services and the general public. Since the economic cost of OCD is not limited to treatment expenses, it is hard to measure it. For example, OCD patients' absenteeism to their work is another cost. This kind of costs is not only arose from patients but also from their families and friends who look after them [127, 128].

In comparison to other anxiety-related diseases, people with OCD are more likely to have work-related impairment as well as social [127, 128].

According to a US-based research report, the annual cost of Obsessive Compulsive Disorder in United States is more than 8 billion dollars. Also in the UK, mental illnesses' costs are at a significant level. To illustrate, more than one-third of physically and mentally disabled people had become disabled because of mental illnesses in the UK. Regarding the financial costs of mental illnesses in the UK, UK loses is approximately 1% of its total annual income because of absenteeism right of mental illness sufferers. Additionally, the cost of mental illnesses to British taxpayers is approximately 7 billion Sterling due to the incapacity benefit and tax immunity of sufferers from mental diseases [127, 128].

The average time an OCD sufferer spends without having a job is 3 years. In addition to economic loss due to the unemployment, there are others, such as opportunity losses to build a career and the cost to family [127, 128].

Even though OCD's financial and social costs are mostly taken lightly, they still show the significance of early intervention. That's because, by providing early intervention, the adverse impacts of OCD, whether they are financial or social, can be kept minimum [127, 128].

6.2 Case Report 1

Ms. Sarah came to a specialized hospital to take OCD treatment with her family. She was a fifteen years old. Her ebeveyn had look for therapy giver in a big cities for a long time, but did not take positive precursory response from physicians because of the seriousness of their daughter's OCD disorder. Sarah did not desire to keep busy in care because of the chance of was abandoned at the hospital. At the beginning, an initial agreement was signed between patient and authorized person in hospital. At the moment of treatment, OCD symptoms belongs to Sarah were high level and she was suffer from compulsions and obsessions such as sexual and harming obsessions and continously checking. Sarah had lost her capability of sleeping and could not generally go into her own bedroom and consequently she had quit school because of her OCD indications. Other difficulty for her

showering, and wearing could take minimal 2 hours from her time. She always emotionally sensed to complete these procedure to avert damage to herself and her parents. Whereas she reach 13, she was continuing to her school, get a lot of fans, and took part in assorted pursuits suc as exercises. Then she started to stay very long time in the bathroom and heard warning from her mother. She struggled to get out of this rituals but failed [129].

At the attack of illness, she met some obsessions such as contamination, harm, morality, numbers and colours and she met some compulsions such as extreme washing, intellectualarituals and avoiding "bad" numbers, letters, and colors. She felt herself contaminated and always believed that some numbers like 6, 18, 2, 3 were bad but she would not be able to change this thought at heaps of time. She believed digit seven was constantly a pleasant value. She interpreted that the digit seven was excellent due to the fact that God made the world in seven days in accor with her religious beliefs [129].

Because of escaping some these numbers, colours and letters and Sarah was incapable of wearing dress with some colours. At the beginning of care, her recording points on the CY-BOCS was to a very great degree range (36 out of 40). She was extremely worried regarding the treatment plan, but was not pressed down and had pleasant perception through her OCD [129].

At first, physcians endeavored to get a relation treaty inward learning concerning the perceptive conduct cure example and to make a distributed structure for directing to the OCD signs by assembling an revealing rule [129].

Sarah quickly seized her medical care. After the initial prosperous Effective Radiated Power (ERP), she realized the deserve of the therapy. Before starting theraphy, she physically sensed complete alone, understand incorrectly and embarrassed of her compulsive thought [129].

She continuosly took 2 hours of ERP day by day throughout six weeks, she given back to her ebevyn occupied with patient exercis and her CY-BOCS point had descended through 4 as an 89% act of decreasing. She did not used any drug whenever during the theraphy and was very pleasur in her performance that was as a result of ERP process. She was worried

about going back her house and begining again slumbering in her home, what had been a start for some compulsions and obsessions [129].

She could exercise imaginative denouncements and different another methods and did actually perform healthy on her come back house. One year later, her illness stayed in the observable level and she was getting no drug and going to school entire time [129].

6.3 Case Report 2

Mr. V is worked as an engineer. He is 62-year-old man living in Karnataka and had a dominating personality that was reserved and anxious, with strong determination but short-tempered. After the death of his father in 1990, Mr. V became depressed. A year after treatment for depression, his symptoms turned to anxiety and became very much-subjugated obsession and compulsion. His OCD behavior's severity slowly increased, causing him to retire. He hasn't worked in the last 15 years and the fact he cannot sign for himself makes him unable to withdraw his pension. His obsessive behavior included continues checking and verification of document and money. His compulsive behavior was continuous hand washing that is between 80 to 100 times, spending around 3 to 4 hours in the bathroom, and continuously asking the same questions to gain verified answers. He had no ideas in reference to persecution and had no hallucinations. The severity of his case severely affected quality of his life and his caregiver's lives, and caused him to be inside the house most of the time. In terms of medication, he has been given selective SSRIs in maximum doses; His medication was Escitalopram, Sertraline, Fluvoxamine, Clomipramine, Fluoxetine and etc. In addition to being on medication, Mr. V had also behavioral therapy with more than 20 out-patient sessions. Yet, despite the use of both medication and behavioral therapy, no significant improvement was detected in his symptoms. When admitted, his medication dose included Fluoxetine-100 mg, Risperidone-2 mg, Alprazolam-0.5 mg, Escitalopram-10 mg, Quetiapine-75 mg. Mr. V was found to be adequate to establish intractability by psychiatrist, the one referring and the one independently assessing for surgery. Furthermore, both were also pleased with the period of his treatment [130].

When examined, Mr. V was found to be a clever individual who was anxious but nevertheless well oriented with normal memory. Although co-operative, he was rather repetitive but had preserved insight. And although his though process reflected at times tangentially, one could assist him to think rationally and no other central neurological deficits could be found [130].

Two psychiatrists conducted Mr.V's independent evaluation of OCD. Upon concurring with a neurosurgeon, an offer to follow a surgical option was put on the table. Mr. V took two neuropsychological testing; Minnesota Multiphasic Personality Inventory (MMPI) and Rorschach. The results of the MMPI indicated "Fake Bad" rules of behavior; where the F% was at the rate of 66.67%, which suggests a weakening tie with reality. The results were taken to be reported indicators of OCD and psychoses. Furthermore, the Mr. V was identified to be very tired and also defensive when taking the neuropsychological tests. On the YBOCS, Mr.V scored a 38/40 and had a score of 24 on the Hamilton depression exam. Mr. V showed a moderate level of anxiety with a score of 26 on the Beck's Anxiety Inventory. He had a cognitive profile that is considered normal with a score of 30 on the Mini-Mental State Examination. The team of psychiatrists concluded that Mr. V had intractable OCD and was found fitting for surgical intervention when considering his clinical history, subject interview, and results of neuropsychological tests. DBS and ablative surgery (lesion) were the two available for surgery options. But because Mr.V's home was far and traveling was difficult, he opted for lesion [130].

To double check before surgery, the patient was also send to the brain surgery team that included a neurologist, neurosurgeon, and psychiatrist. The board reached the conclusion that surgical treatment was a reasonable option to improve Mr. V's case [130]. Because OCD made Mr. V incapable of signing consent, his sister and wife gave an informed consent on his behalf, where Mr.V had his consent recorded on video [130].

A day before the surgery, a preoperative planning MRI was taken. To identify the internal capsule, IR and T2-weighted coronal images were utilized. 3 mm anterior to the posterior line and 2 mm inferior to the AC-PC surface commissure is choosed as the surgical area. This location indicated was the bottom of the target. A stereotactic CT scan taken on the

day of the surgery was fused with the preoperative MRI. Using a bit anesthetic agent the location through which the target was approached. Neurophysiological response was noted around the targeted area. Area scrutinized for response included 15 mm above. When getting closer to the targets, the neurophysiological response notes indicated the response as decrease in anxiety, with more calmness and pseudo smile. At 75°C, Radiofrequency lessoning was done on both sides for 60 seconds [130].

The suitable target location was confirmed with a Post-operation CT [Figure 1]. Although Mr.V's OCD symptoms had significantly improved, he suffered from stark confusion and disorientation in the three days following the operation. Furthermore, although no apparent reason could be found, Mr.V suffered from high-grade fever and hyponatremia. His psychotropic medication was reduced in dosage upon consultation with the psychiatrist. When released to go home a week after the surgery, he had a good amount of relief from his OCD symptoms and no anxiety, along with a decreased score of nine on the YBOCS and six on the depression test. During the follow-up session 3 months after the surgery, Mr.V's family noted that he had less anxiety and depression in comparison to before surgery and that that his obsession was well controlled and that apathy had reduced. To gain a better understanding on the surgical option, the referring psychiatrist of Mr.V keeps a close eye on the medical management and progress of him [130].

The evidence converges on that note that in pathophysiology of OCD, basal ganglia, the corticostriat othalamocortical loop, ACC and OFC is key. Even back in the early 1950s, the treatment of intractable OCD had included practices in the anterior capsulotomy. In Sweden, Lars Leksell nevertheless popularized the target of the anterior capsulotomy by aiming at interrupting the fronto-thalamic fibers. He operated on 117 patients between the years of 1952 to 1957 alone, where 78% of his patients reported good or fair outcome in long-term follow-up. Comparison of capsulotomy and cingulotomy has been done by several authors and general conclusion has been that among the two, capsulotomy was more effective. Additionally, another review pointed at the importance of correct placement, where correlations showed better outcome with placement on right AC lesion in comparison to that housed near the AC [130].

In 1990, Dr. Nuttin displayed a result induction of beneficial effects in an intractable OCD subject is possible with exciting of the anterior wings of capsules using electrical signals in 1999. Following from this, a multicenter trial reported that in 27 patients, an improvement of YBOCS occurred with a change from a mean of 34 to 20. With the average 31 months follow-up, the researchers found that the lot of sufferer answering had raised to 75% as their experience improved. Furthermore, they found increasing effectiveness with the more ventral contacts. In the latest follow up, 21 of 25 patients rated their functioning's of study, housekeeping as either good or fair. Additionally, 20 of the 25 patients rated their ability to live independently as fair or good. Yet, it is important to note that simulation in patients required high voltage and that over 12-18 months was the average pacemaker life. Ergo, one should be cautious with using DBS for OCD treatment because the price can substantially raise [130].

Figure 6.1 Axial image lesions belongs to bilateral anterior capsule by CT (http://www.indianjpsychiatry.org/viewimage.asp?img=IndianJPsychiatry_2011_53_3_270_86823_f1.jpg)

With stimulation-evoked responses, intraoperative confirmation of the target location can be attained. With intraoperative stimulation, reduction of anxiety and tension had been present in 20% of the patients [130].

Another important aspect is the presence of care under a psychiatrist who will take on the responsibility to provide the proper psychiatric support that is needed after surgery. [130].

Overall, capsulotomy is a procedure that is quite safe. Yet, the side effects should be considered. Another complication is lack of initiative or apathy, which can last for some weeks after surgery. Furthermore, fatigueness can last for a few weeks but other than that there are no significantly visible complications [130].

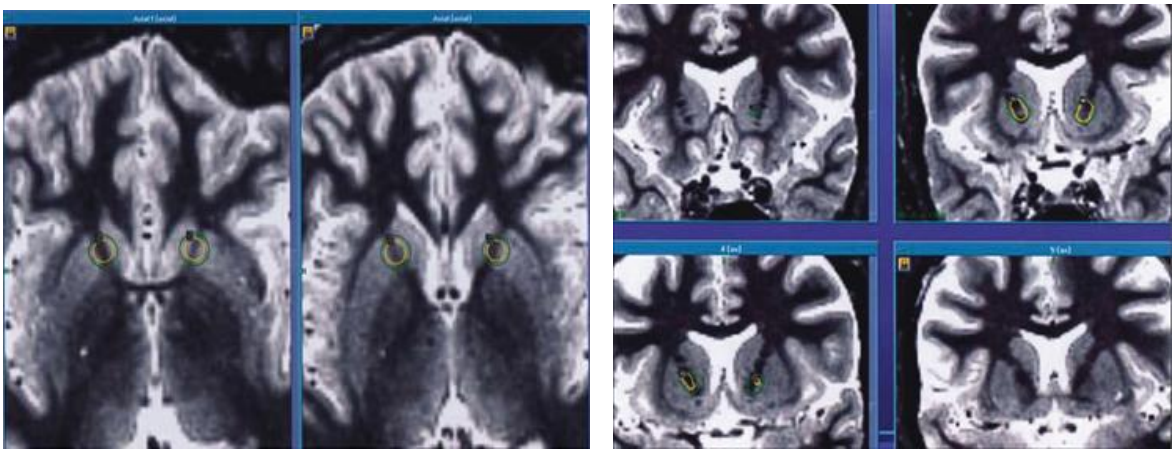
For over five decades now, the practice of surgical treatment of OCD is present. Intractable OCD makes daily life difficult for both the patient and their loved ones. OCD symptomatology and pathophysiology studies recent advancements of knowledge have had significant contributions to further understanding target refinement and reduction of post-surgery complications. Although the surgical option to OCD treatment is currently underutilized, more research should be conducted to create advancement to heal the unwanted results and enhance the wanted ones [130].

6.4 Case Report 3

The third patient was female and she was 37 years old. She was diagnosed with obsessive compulsive disorder, when she was only 12 years old. Since that time, she had been hospitalized approximately 40 times because of OCD. The patient had to drop out of school in one year, after she was diagnosed with OCD, even though academic success was the first thing she became obsessed with. Later on, obsession started showing itself as cleaning herself for hours. Additionally, academic-success related obsessions did not leave her in peace by waking her up at the middle of the night to prepare for school, even though she dropped out of it. She hadn’t been able to leave her home, in the year prior to the surgical operation [130].

Fluvoxamine, clomipramine, clonazepam and ziprasidone were among the medications used. Symmetry, contamination, and religious thoughts were her main obsessions with compulsive behavior of continuous cleaning, inspection, numbering, and organazing things. Thoughts of suicidal and engagement in triming conducts are present in her medical history. Before the radiosurgery, her YBOCS score was 34/40 [6].

A 5-month time period existed between her first neurosurgical assessment and procedure. At a follow up session six months after the GKAC with the dose of 140 Gy, MR imaging exhibited signal changes in the target volume along with areas of contrast enhancement. In Figure 6.2, the dose plan can be found [130].



a) b)

Figure 6.2. Dose projection on the a) Axial, b) Coronal image for anterior capsulotomy

(http://ovidsp.tx.ovid.com/sp-3.16.0a/ovidweb.cgi?S=EDDEFPLICPDDHEOANCKKJHIBKIBOAA00&Graphic=00006123-201101000-00005%7cFF1%7cM%7cjpg)

30 months after the radiosurgery, significant change and improvement could be seen in the patient's obsessive compulsive behaviors. For example, while the time she took bathing and hair care was four hours before surgery, now she spent two carrying out this compulsive behavior. Furthermore, the patient did throw out items she had been keeping since age 18 up until the surgery. She could now leave the house for shopping and arrange appointments. Her social life got in order with her ability to date, visit friends, and take

college classes. No more hospitalization was required, especially since her suicidal thought disappeared and cutting behavior ended. She continues to take medication for her OCD including lithium, clomipramine, clonazepam, and fluvoxamine. Her YBOCS score dropped to 24, 55 months after radiosurgery. And she found her life to be more stable since the surgery took place. In Figure 6.3, one can find parts of the letters she wrote at her last follow-up [131].

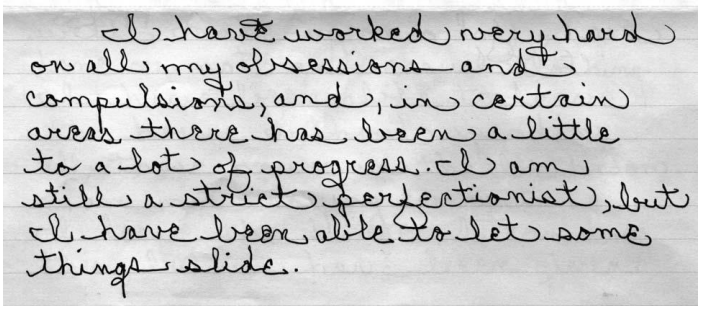


Figure 6.3. A letter from OCD patient, a few months later than radiosurgery operation. (http://ovidsp.tx.ovid.com/sp-3.16.0a/ovidweb.cgi?S=EDDEFPLICPDDHEOANCKKJHIBKIBOAA00&Graphic=00006123-201101000-00005%7cFF2%7cM%7cjpg)

6.5 Case Report 4

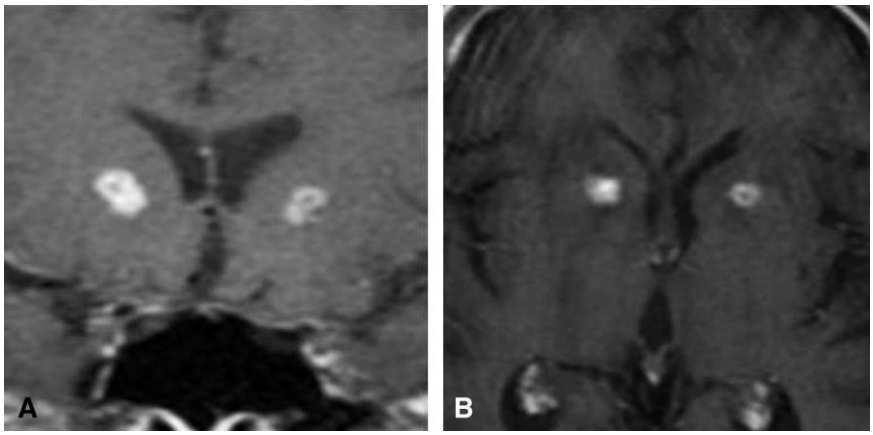
Patient number 4 was a 55-year-old male. He was an engineer who had obsessive dermis tearing out. He went through GKAC. Looking at his medical history, he had used high-dose medication and took behavioural treatment to alleviate his symptoms. Yet, he had four dermis tissues. Additionally, he used various tools to slice the skin [132].

When brought in for care, patient 4 had his whole front part of the neck grafted. Moreover, large fraction of his upper back also consisted of severe skin picking. Before the patient requested the procedure, a medical treatment option was taken as a result of other mental request upon estimation, where four months trial of high level chlorimipramine took place. The time frame between the neurosurgical examinations was 56 weeks, where YBOCS record was 40. Just as in case 1, Gamma knife radiosurgery was performed with the biggest portion of 140 Gy. His results of MRI are portrayed in Figure 4 [132].

Three months after the procedure, his wife described him as more agreeable, interactive, and appreciative than before procedure. He was now able to enjoy family meals and became less argumentative about his OCD care treatments. Medications showed better results by the 7th month, where he performed ritualistic behavior a lot less. Testing indicated a reduction of his YBOCS score to 32. By month 17, this score dropped to as low as 8. Comparison of neuropsychological testing results at 14 months and before radiosurgery baseline revealed patient 4 as carry out higher than his starting line. Although he had some impulsive behavior and showed perseveration, his frontal lobe performance was normal. His wound s had healed by the 18th month and the area grafted by the 30th. [132].

His YBOCS scores were 4 and 7 at 30 and 42 months respectively. At roughly 36 months, the patient had felt well and wanted to reduce the fatigueness side effect of his medication.

Thus, he reduced his quetiapine and stopped taking fluvoxamine without psychiatrics knowledge. Such behavior became very much linked to the return of picking behavior of a tiny area behind his right ear. And once medication was reinstituted, his symptoms improved once again. Images of his healing wounds can be found in a separate report [132].



a) b)

Figure 6.4. MR images belong to a patient after radiosurgery, a) Coronal and b) Axial

(http://ovidsp.tx.ovid.com/sp-3.16.0a/ovidweb.cgi?S=EDDEFPLICPDDHEOANCKKJHIBKIBOAA00&Graphic=00006123-201101000-00005%7cFF3%7cM%7cjpg)

6.6 Case Report 5

Patient number 5 is a 39-years old female who had early-onset of OCD with compulsive and obsessive behavior beginning at age six. She was hospitalized at various centers across the nation numerous times. Her obsessions were revolving around cleanliness, alignment, bad luck, thoughts of frightenment and things like ‘‘is my life real.’’ Her compulsive behavior included rituals such as avoidance, writing, counting, grooming, and so on. Fluvoxamine, escitalopram, quetiapine and lorazepam were the drugs she took as part of her medical treatment. She scored a 39 on the YBOCS test. With the GKAC executed to a biggest portion of 150 Gy, her YBOCS level was lessened to 18 in the follow up at 28 months after the procedure [8]. 4 months after surgery, she was able to live and work independently. She referred to her OCD as “manageable,’’ and indicated that its interference in her daily life was significantly lower. But nevertheless, her medical treatment continues and she takes pregabalin-150mg per day, quetiapine-200mg per day, lorazepam-2mg per day and fluvoxamine-300mg per day [133]. In her case, it is not displayed bad effects raised from the protocol. In Figure 5, the line plots for all three patients OCD scores can be found. [133].

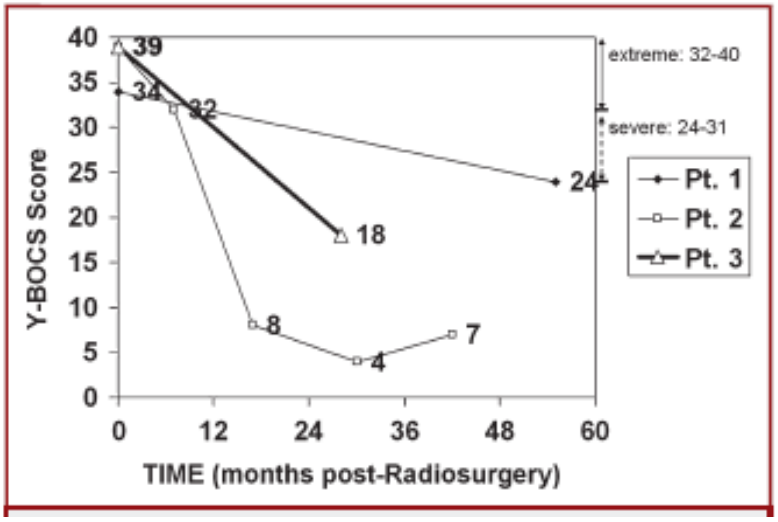


Figure 6.5. Y-BOCS OCD scores belong to the 3 patients before and after radiosurgery. (http://ovidsp.tx.ovid.com/sp3.16.0a/ovidweb.cgi?S=EDDEFPLICPDDHEOANCKKJHIBKIBOAA00&Graphic=00006123-201101000-00005%7cFF4%7cM%7cjpg)

Hyper metabolic changes in the cingulate cortex, orbital frontal cortex, caudate and thalamus region are noted in the imaging studies conducted on OCD subjects. The patterns of cortico striato thalamo cortical dysfunction is widely supported by the literature on OCD and thus giving room to explanations of modulation or effects present on this circuitry. Thus, the brain region that should be targeted for modulation is the ventral anterior internal capsule [133].

Earlier studies conducted in the Karolinska Institute provide information regarding the presence of effectiveness of radiosurgery in targeted areas, such as the anterior section. Yet, no thorough information regarding the clinical outcomes is found. A report published in 2008 show that on 25 sufferer endure capsulotomy with three different surgical methods including 9 gamma knife radiosurgery patients, 12 bilateral radiofrequency lessoning patients and 4 unilateral radiofrequency lessoning patients, the mean YBOCS score dropped to 18 at a long term follow up from the initial score of 34 before the surgery. And among the surgical methods, no difference was found in response rates [8]. But despite the positive effects of decrease in YBOCS scores, 10 of the patients in the sample experienced unfavorable outcomes such as disinhibition, apathy or issues in their executive functioning capabilities. In some, such adverse effects were recognized to be part of large lesion volumes, and six of the patients had to receive various surgeries or take in high radiation doses of 200 Gy with 3 isocenters. [133].

Using the conservative response criteria, research conducted at the Brown University portrays effectiveness with achievement of lowering the YBOCS level by 35% in the subjects with OCD. Ergo, a recommendation to use bigger oval-shaped radio surgical volume that is with two 4-mm isocenters was made [133].

The mean YBOCS score of 32.2 before the surgery dropped to 20.2. Minor side effects covered temporary pain in the head, dizziness, changes in heaviness, and queasiness. With a DBS electrode, the simulation volume may be imitated by the radiosurgical volume's oval shape. Normally, the effect of the radiosurgery is one that progresses over several months, and tissue necrosis of the targeted area is to occur in two to four months. After 2

months upon radiosurgery, all of the patients under scrutiny started to show improved behavior [133].

The FDA has recently given approval for the use of bilateral anterior internal capsule DBS in OCD management. And while reversibility and adjustability are some of the benefits of using the DBS systems, some noteworthy problems have been reported, mostly due to battery failure stemming from the fact that current use is typically high. While a long-lasting procedure that is not dependent on the hardware is the preferred and better option to OCD management, the relative price of radiosurgery must nevertheless be examined excellently to enhance the options that is currently at hand. Furthermore, no comparison of DBS and radiosurgery on safety and efficacy has taken place in any clinical study. When a lesion is created by radiofrequency techniques, the effect tends to be permanent but not adjustable. In this study, in comparison to ventral striatum DBS target, the radiosurgery target was a bit more superior and anterior. Knowledge on whether radiosurgery would be even more effective. Furthermore, is has symptoms that are vary much similar to and at times overlap with many other psychiatric illnesses, like OCD, body dysmorphic disorder, and trichotillomania. This disorder can cause great harm like scarring and dermatologic infections. To manage pathological skin picking and similar illnesses like self-mutilation, medications and behavioral therapy that is consistent with OCD is applied. Although done rarely, with surgery such as limbic leucotomy may be used for treatment in intractable OCD. The FDA humanitarian device exemption for ventral striatum DBS does not cover skin picking is due to potential issues in healing [133].

OCD treatment continues to be challenging in many ways, where it can be refractory to multimodal pharmacologic. Use of medication is vital where termination or reduction without psychiatric supervision may cause side effects to exacerbate. While whether improvement is solely caused by surgery or the combination of medication and surgery is unknown, the researchers suspect the dominant role of surgery since patients had been medication refractory. Out of the 3 patients, only 1 patient had gone through detailed neurocognitive testing. Nevertheless, usefulness of obtaining such testing in all patients following such procedure is unquestionable for adding to the literature in this area. Still,

the finding that radio surgical anterior capsulotomy is beneficial to patients with extreme OCD is very significant [133]. In addition to improvements in both social and thinking behaviors, development in the physical demonstrations of the disease occurred with no adverse events present. Based on the set criteria, subject selection should be done cautiously and judiciously. In this light, a necessity for research that compares DBS to stereotactic radiosurgery comes to surface [133].

CONCLUSION AND RECOMENDATION

In this thesis, It is niggled respecting depression and OCD ilnesses. Depression is a grave and common situation and is characterized as one of the most disqualifying illnesses in the World by WHO. It is affecting approximately a lot of people in their lifetime. This illness does not discriminate patients Is that so; they are women or men or their age and instructive position, and social background.

A main problem is that the majority of the patients suffer from depression are never diagnosed and they alone treated. But the others is swiftly recognized and cured, and their symptoms are controllable.

Treatment of depression rely on severity of illness as well as the uniq and duration. Main treatment type for depression. Basic types of treatment for depression contain psychotherapy, ECT, antidepressant drugs or their combination. Antidepressants correct the neurotransmitter level in the brain and are successful in 70% of patients. Generally, antidepressants show their efficacy taking several weeks and up to months.

Second issue in this thesis was OCD. A few inequalities in familiarity concerning the influence emotional stress has on OCD have been emphasized in some part of the thesis. More extensive investigation toward the inside neurological predilection, retrospective causes, sort and topic of trauma, and care of particular OCD is essential. In spite of the need of heuristic proof, impersonal final decisions can be attracted from the combining of the existent research.

The treatments such as exposure and response/ritual prevention were largely formulated by the knowledge taken from learning theory models. In learning theory, the key point is that stimulus and response are connected to form a habit. The insight learning theory has provided in creation of behavior therapy is immense. Majority of individuals who suffer from OCD enjoy lasting benefits from such behavioral intervention.

The success rate of this therapy has been well documented with around 90% of patients showing initial improvement, and 70% to 80% maintaining it for the 1-year follow-up

Behavior therapy exposes the OCD patient to the obsessional fears, which is the stimuli, and response prevention of the rituals occurs. While with exposure the patient is brought to contact with the feared object, and the response prevention is done to prohibit the compulsive behavior. To illustrate, the patient touched garbage cans (exposure to stimulus), but omits washing hands after in contact with contaminant (response prevention). The goal of the therapy is to reach habituation that is until the Patients continue to be exposed to the feared object until the need to respond to the fear by rituals is gone. This therapy is believed to work because obsessions represent fear and compulsions represent reactions to fears. And for the OCD treatment to be a success, the fear/response schemas that support the obsessive and compulsive symptoms must be targeted.

Contemporary OCD treatment manuals include what is called the Exposure and Response Prevention (ERP) procedure. This procedure is made up two components: firstly the exposure, that is the daily treatment sessions by which the patient is deliberately exposed to the discomforting stimuli until habituation occurs, and the response prevention, that is the strict prohibition to perform rituals.

As the treatment such as Cognitive behavioral therapy (CBT) and ERP allow for intervention of obsessive thoughts and compulsive behaviors, individuals with OCD are becoming more productive citizens and able to have a functioning daily life. And as they become more functional, they can be employed.

In spite of the progress in behavioral and pharmacologic therapy for the cure of OCD, there is quiet a set of patients that formal treatment is unsatisfactory for them. Therefore, neurosurgery should be shown. Before the realization of the protocol different features should be consider as well.

In addition to the customary technical skill in which diseased cell are excited using radio frequency, other smaller invasive ones, like radiosurgery or possibly overturned, like DBS are tend to reduce the procedure risk. In the near future, Physcians will have a lot of knowledge about the neurobiological substratum of OCD and the development of these methods it may be awaited the finding of increasingly exact targets, with less view

of side-effects. Mutually, the consequence of the cure using these methods will create nowel information for the OCD pathogenesis.

A lot of scientist have worked to obtain new opening approaches about Gamma knife technology for 50 years. Gamma knife capsulotomy, a type of ablative technique, gives a hope in the treatment of severe OCD.

The researchers explain that the surgery using this technique was mostly well tolerated. It may be seen a few side effectss were self-limited. It is slightly seen an adverse event like radiation-induced cyst in a patient But after short time, memory deficits will descend.

DISCUSSION

The findings of this thesis are the more inform about the treatment of clinical depression and OCD. These findings forexample have special suggestions for researcher to use new tretment technique such as Gamma knife for severe and chronic OCD patients or this thesis shown that woman or man may gain selfcontrol over their illness and recover.

Living through major depression may be considerably more complicated than patients realize. Until treating the issue of this illness, relationships can be lasted, suitable and financially manageable treatment may be time consumption are enough to avert patienets from accepting treatment. Even well into the late 1970s, the dominant thought in clinical psychology had been that OCD was untreatable OCD symptom severity couldn't be reduced. The conceptualizations of OCD development had been based mainly on the psychodynamic models [134].

These psychodynamic models were derived from Freud's theories. According to Freud, obsessive thinking is unconscious mental processes that are created by the childhood sexual activity that is prohibited yet pleasurable [135]. His treatment of obsessive thinking and compulsive behavior were through free association, but treatments formulated from his theory did not lead to substantial improvement in OCD subjects. As a result, OCD was seen as an intractable disorder up until the 1960s and 1970s, when the newly developed intensive behavioral treatments showed the contrary and showed considerable promise [136].

There are some limitations of neuroanatomical and Neuropsychological studies: Similarities and differences exist among studies, and the differences are mostly found in the study-specific characteristics. For instance, the simplest difference could be the way patients are scanned in studies conducted in resting states; while most studies scan subjects with eyes and ears open, Forexample Swedo and colleagues have had their patient's ear's plugged and eyes closed during scanned [137].

Another difference in studies is taking scans when subjects are medication free. Some studies add to this difference by scanning patients in groups as taking medication and medication free and in such studies, further difference results form variation in type of drug treatments used, where some studies even place multiple medications in the same trial. A study conducted by Baxter and colleagues [138] is interesting in the sense that

they studied patients taking medications that are not for treatment of OCD. While some studies did include patients with comorbid affective and anxiety disorders [138]. There were others with subjects that didn't meet the clinically significant criteria of OCD as measured by the Y-BOCS [139]

Another difference among the studies is the variation in the criteria to define what clinical improvement means. For instance, while some studies have taken clinical improvement as at least a "much improved" status on the CGI scale and a change in Y-BOCS scores [140], others have only considered the CGI scale and not the Y-BOCS scores [138]. Additionally, there are studies that haven't even referred to what their basis is for defining clinical improvement [137] And some have used other criteria for it [137]. Such differences in methodology are what make it challenging to compare anatomical findings across studies and reach a conclusive finding.

Age onset is another inconsistency across studies; some studying childhood-onset [137] and others adult [141]. Such difference in age onset becomes even more complex with studies that do not specify the OCD onset age of their subjects. This difference is significant by the simple fact that age onset is one of the ways to subtype OCD and significant findings may be unintentionally overlooked when heterogeneity of age onset is ignored as can be seen in the work of Pogarell and colleagues [142].

Because inconsistency of findings across studies prevail, the growing consensus that OCD patients have neuropsychological deficits becomes hard to discuss conclusively, specifically the true nature of these deficits. Several explanations have been proposed to clarify inconsistencies in early works investigating neuropsychological functioning and OCD. For example, Christensen, Kim, Dysken, and Hoover [143] point to several reasons as to why inconsistencies exist such as the IQ differences among the samples of OCD and control groups, the lack of controlling for type I error in studies, the existence of significant levels of depression in OCD subjects, and that OCD subject selections not by complete diagnostic criteria but by isolated.

Nevertheless, other methodological problems could also be causing issues and inconsistencies in finding such as participants being on psychotropic medications or medication free, presence or absence of comorbid conditions and failure to use a control

group. Differences in sample selection are another salient factor that makes it difficult to compare results.

Issues of study design are also critical in overcoming inconsistencies among findings. While some studies use the same measures formed and used in earlier studies to distinguish among OCD subjects and the control group, others use new tests that haven't been administered in OCD investigations of neuropsychological studies. And even in cases where the common test is administered, lack of uniformity in examination of outcomes from the tests creates room for inconsistency.

Further issues arise in attempts to draw conclusions on the nature of neuropsychological OCD deficits. For example, contrary results can come about where using the same test; some provide evidence to OCD display impaired performance while others shows no impairment in performance. Such difference is clearly exemplified in the literature with the Wisconsin Card Sort Test, which is used as a measure of set-shifting ability; while some studies find deficits in performance of OCD subjects [144].

Lastly, problems in relation to neuropsychological tests specificity also exist. Little agreement is present as to which underlying constructs and abilities are selected to be tests in the various tests. This is an important factor that plays a role in drawing conclusions on the deficit types that exist make it difficult to reach a consensus regarding the neuropsychological literature.

One limitation of this study was also that at the beginning of this study there is no any application using Gamma knife to treat for severe and chronic OCD patients at any hospiatl in Istanbul in Turkey. If I have any possibility to access to patient files and treatment plans, as well as progress notes, I may give more detailed side effects and clinical ultimate results belong to patients treated with Gamma knife.

Noninvasive stereotactic radiosurgery has been improving over the past 50 years is now reachable more than 100 cities all over the world. In the future, this technique may be applied a lot of patients have got many types of disorders in the all over the body. To reach to this purpose, reseracher are in need of more funding for clinical trials and more knowledge of the possible capabilities of stereotactic radiosurgery.

There are some advantages prefering Gamma Knife Surgery. Forexample; it is performed without general anesthesia and surgical cutting as conventional neurosurgery have a lot of different risks such as infection, losing blood and neurological deficit. After Gamma knife performed, patients go back to preoperation activities in a few days.

Gamma Knife unit known as unharmed system and over 400,000 patients worldwide received benefit from this treatment until this day. Because this unit gives continously reach to target areas of the brain and reach through the cervical spine level using future fixation apparatus.

As standard radiation therapy impose more chemotherapy interruption, Gamma knife system provides less interruption increasing patient comfort using most accurate stereotactic radiosurgical procedures for the brain.

Inoperable and untreatable lesions can be cured with Gamma knife without high risk during treatment unlike open skull surgery and the cost of the operation is in many cases approximately 30% less than traditional neurosurgery. But sometime Gamma knife surgery can take some simple risks and can see temporary side effects while conventional types of brain surgery has more serious risks. These usually minimal and temporary side effects can occur as a result of gamma knife treatments. These all contain headaches, nausea, instability, physical feebleness and numbness.

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CURRICULUM VITAE

Name Surname: Murat Kara

Place and Date of Birth: Kayseri, 1985

Address: Ata Sitesi, Kamelya Apartmanı, Daire No: 22, Çankaya Caddesi, Beykent, Beylikdüzü, İstanbul

E-Mail: unifat1385@gmail.com

B.Sc.: Department of Economics, Faculty of Economics and Administrative Sciences at Erciyes University

Professional Experience and Rewards: Murat Kara completed his primary and high school education in Kayseri. He was graduated from Department of Economics, Faculty of Economics and Administrative Sciences at Erciyes University in 2012. After this he received his master degree on Biomedical Engineering from Institute of Biomedical Engineering at Fatih University in 2015.

He had work experiences at two projects as a managerial stuff and project assitant receiving a scholarship respectively. One of them is titled "University and Industry together from Production through R&D and from R&D through product in the biomedical sector" supported by Republic of Turkey, Istanbul Development Agency.

The other project title is "The investigation of the relationship between brain activation and autonomic nervous system activity using EEG and heart rate variability signals during different auditory stimuli for diagnosis of depression" supported by The Scientific & Technological Research Council of Turkey.

He speaks English fluently also attended an English intensive course for academic purpose arranged by Kaplan international centers in Boston in 2014.

He has unmarried yet and has also interested in music besides his business and academic studies. His amateur music life started in 2000s. On those days, he had learned to make various music types from his mother and father.