Libyan International Medical University

Faculty of Pharmacy

Obsessive Compulsive Disorder (OCD):

“A battle with unwanted thoughts”

Submitted by:

Safaa Omar Abbas

Heba Farag Zainoba

Under the supervision of

Dr . Narges Kablan

Supervisor's Approval: ----------Date: ----------

A thesis submitted to Libyan International Medical University in partial fulfillment of the require ments for the Bachelor of Pharmacy degree.

Declaration

This is to certify the research work embodied in this thesis entitled (Obsessive compulsive disorder) has been written by both of us and under the supervision of Dr. Narges kablan

Safaa Omar Abbas

Heba Farag Zainoba

Abstract

Obsessive compulsive disorder (OCD), one of the anxiety disorders, is a potentially disabling condition that can persist throughout a person's life. The individual who suffers from OCD becomes trapped in a pattern of repetitive thoughts and fears (obsessions) and behaviors (compulsions) that are senseless and distressing but extremely difficult to overcome.

OCD occurs in a spectrum from mild to severe, but if severe and left untreated, can destroy a person's capacity to function at work, at school or even in the home.

The causes of the OCD are still unknown, but there are factors that may increase the risk of developing or triggering the disorder which include:(Neurobiological, behavioral, cognitive, environmental, infection or genetic factors)

The most effective treatments for OCD are Cognitive Behavior Therapy (CBT) and/or medication. More specifically, the most effective treatments are a type of CBT called Exposure and Response Prevention (ERP), and/or a class of medications called serotonin reuptake inhibitors (SSRIs). In severe cases of OCD and in individuals who do not respond to medical and behavioral therapy, more drastic options might be useful such as brain surgeries.

OCD is a chronic disease that requires long-term treatment with frequent follow up and a regular behavioral therapy. OCD needs more attention and awareness especially in the Arab world,

an aim that is intended to be reached in this study by spotting the light on the concept, signs and symptoms and the treatment of this disease.

Table of contents

List of tables

List of figures

List of abbreviations

OCD	Obsessive Compulsive Disorder
WHO	World Health Organization
CBT	Cognitive Behavioral Therapy
SSRI	Selective Serotonin Reuptake Inhibitor
UK	United Kingdom
NA	Not asked magical thought
Y-BOCS	Yale Brown Obsessive Compulsive Scale
HSERT	Human Serotonin Transport Gene
NIMH	National Institute of Mental Health
PANDAS	Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection
ERP	Exposure and Response Prevention
APA	American Psychiatric Association
AACAP	American Academy of Child and Adolescent Psychiatry
DBS	Deep Brain Stimulation
V\C	Ventral Capsule
V\S	Ventral Striatum
PET	Positron Emission Tomography
GAD	Generalized Anxiety Disorder
US	United States
OCPS	Obsessive Compulsive Personality Disorder
DSM	Diagnostic and Statistical Manual Of Mental Disorder .
PTCD	Post Traumatic Syndrome Disorder

Acknowledgment

We would like to express our gratitude to God for his infinite mercy. To our parents, our families and friends including ***Afia Abdlmola,*** *for all their support, love and encouragement. We would also like to thank* ***Dr. Narges Kablan*** *and* ***Dr. Salma Bukhatwa*** *for their guidance and support. We are thankful for all that we have learned and we will treasure our memories of this time forever.*

Chapter I

Introduction

Introduction

(OCD) is a serious anxiety-related condition where a person experiences frequent intrusive and unwelcomed obsessional thoughts, often followed by repetitive compulsions, impulses or urges.

The illness affects as many as 12 in every 1000 people (1.2% of the population) from young children to adults, regardless of gender or social or cultural background. In fact, it can be so debilitating and disabling that (WHO) has actually ranked OCD in the top ten of the most disabling illnesses of any kind, in terms of lost earnings and diminished quality of life.

Based on current estimates for the UK population, there are potentially around 741,504 people living with OCD at any one time. However it is worth noting that a disproportionately high number, 50% of all these cases, will fall into the severe category, with less than a quarter being classed as mild case.[(1)]

For someone with OCD, their logical mind always remains functioning, even if their OCD mind is spiraling out of control. Most people with OCD know that their thoughts and behavior are irrational and senseless, but feel completely incapable of stopping them, often from fear that not completing a particular behavior will cause harm to a loved one. No matter how small the risk, the person with OCD will always feel responsible for preventing that bad event from happening.

Left unchecked and untreated, OCD will mushroom and feed upon itself and can have the power to consume if left unchallenged. Receiving appropriate treatment, care and support and sticking to the treatment plan is the key to long term recovery.

OCD is indeed a chronic, but also a very treatable medical condition. Most people can learn to stop performing their compulsive rituals and to decrease the intensity of their obsessional thoughts through (CBT). In many cases, CBT alone is highly effective in treating OCD but for some people a combination of CBT and medications can be effective. Medications may reduce the anxiety enough for a person to start and eventually succeed in therapy.

Fortunately, the medical profession is slowly starting to understand and identify OCD symptoms much more effectively, resulting in an improvement in treatment However, it does still depend on which part of the country you may live in. We aim in this study to increase the awareness about such disorder and how it could negatively affect the life of an OCD patient if left unchecked and untreated.

Definition of OCD

(OCD) is a neuropsychiatric disorder characterized by intrusive, unwanted thoughts, fears and images (obsessions) on the one hand and/or repetitive ritualized behavior or mental acts (compulsions) performed to relieve anxiety or distress on the other hand.[2]

History of OCD

Time changes all concepts OCD is no exception. Long time ago, (14th to the 16th century) it was believed that a person who experienced sexual or other obsessive unwanted thoughts is possessed by the Devil and accordingly should be treated by exorcism to banish the Devil from the possessed person.[3]

Modern concepts of OCD began to evolve in the nineteenth century, when Faculty Psychology, phrenology and Mesmerism were popular theories and when "neurosis" implied a neuro pathological condition, Like ourselves, psychiatrists then struggling to understand the mentally ill were influenced by intellectual currents coursing through philosophy, physiology, physics, chemistry and political thoughts Obsessions, in which insight was preserved, were gradually distinguished from delusions in which it was not. Compulsions were distinguished from impulsions which included various forms of paroxysmal, stereotyped and irresistible behavior. Influential psychiatrists disagreed about whether the source of OCD lay in disorders of the will, the emotions or the intellect.[5]

In the last quarter of the nineteenth century, the diagnostic category, neurasthenia (inadequate "tonus" of the nervous system), engulfed OCD along with numerous other disorders. As the twentieth century opened, isolated OCD was isolated from neurasthenia. It was proposed that obsessions and compulsions arise in the third (deepest) stage of psych asthenic illness. Due to the fact that an individual lacks sufficient psychological tension (a form of nervous energy) to complete a higher level of mental activities (those of will and directed attention), nervous energy is diverted into +and activates more primitive psychological operations that include obsessions and compulsions.[5]

As the twenty-first century began, advances in pharmacology, neuro- anatomy, neurophysiology and learning theory have allowed therapists to reach a more therapeutically useful conceptualization of OCD. Although the causes of the disorder still elude scientists, the recent identification of children with OCD caused by an autoimmune response to group A beta-hemolytic streptococcal infection promises to bring increased understanding of the disorder's pathogenesis.[2]

Epidemiology of OCD

Once considered a rare condition; experts now believe that OCD was often misdiagnosed in the past, partly through lack of knowledge amongst the health profession, but also partly because of a sufferer's reluctance to talk about their symptoms through fear of embarrassment and shame. Therefore reported numbers did not reflect the true number of cases. More recent research and understanding of the illness offers a much clearer picture of the problem. Around the world there are literally millions of people affected by OCD and it is considered to be the fourth most common mental illness in many western countries that will affect men, women and children regardless of their race, religion, nationality or socio-economic group.[6]

In the US there are about 1 in 100 adults – or between 2 to 3 million adults currently have OCD. This is roughly the same number of people living in the city of Houston or Texas. There is also at least 1 in 200.000 about or 500,000 kids and teens that have OCD. This is about the same number of kids who have diabetes. [7]

OCD affects men, women and children of all races and backgrounds equally. OCD can start at any time from preschool to adulthood. Although OCD can occur at any age, there are generally two age ranges when OCD tends to first appears: Between the ages 8 and 12 between the late teen years and early adulthood. [7]

Which is why some estimates suggest that maybe 2-3% of all those visiting their GP will be doing so because of OCD. These estimates are still considered to be underestimated with many people affected by OCD still suffering in silence through embarrassment and fear of being labeled. Others are unaware that their suffering is a recognized medical condition, which is why charities like OCD-UK must continue to work hard to raise awareness and remove the stigma of Obsessive-Compulsive Disorder.[7]

Signs and symptoms of OCD

OCD can also be a chameleon. For some people the OCD symptoms will remain unchanged, but for others it is not unusual that over time there may be changes to the type of OCD that becomes bothersome. Equally, it is not unusual for symptoms to wax and wane over time if untreated and become a little like a rollercoaster, with the severity increasing during times of stress, perhaps at work, university or within relationships, for example OCD symptoms usually include both obsessions and compulsions. However also possible to have only obsession symptoms or only compulsion symptoms. About one-third of people with OCD also have a disorder that includes sudden, brief, intermittent movements or sounds (tics).[8]

Obsessions

OCD obsessions are repeated, persistent and unwanted urges, thoughts or images that cause distress or anxiety. A person with OCD might try to get rid of them by performing a compulsion or ritual. Obsessions could include one or more of the followings:

a. Fear of contamination or dirt.
b. Having things orderly and symmetrical.
c. Aggressive or horrific thoughts about harming yourself or others.
d. Unwanted thoughts, including aggression, or sexual or religious subjects.

Examples of obsession signs and symptoms include:

a. Fear of being contaminated by shaking hands or by touching objects others have touched.
b. Doubts that you've locked the door or turned off the stove.
c. Intense stress when objects aren't orderly or facing a certain way.
d. Images of hurting yourself or someone else.
e. Thoughts about shouting obscenities or acting inappropriately.
f. Avoidance of situations that can trigger obsessions, such as shaking hands.
g. Distress about unpleasant sexual images repeating in your mind.[9]

Compulsion

OCD compulsions are repetitive behaviors that a person feels driven to perform. These repetitive behaviors are meant to prevent or reduce anxiety related to obsessions or prevent something bad from happening. However, engaging in the compulsions brings no pleasure and may offer only a temporary relief from anxiety. These compulsions are often not rationally connected to preventing the feared event. As with obsessions, compulsions typically have themes, such as:

a. Washing and cleaning

b. Counting

c. Checking

d. Demanding reassurances

e. Following a strict routine

f. Orderliness

Examples of compulsion signs and symptoms include:

a. Hand-washing until your skin becomes raw.

b. Checking doors repeatedly to make sure they're locked.

c. Checking the stove repeatedly to make sure it's off.

d. Counting in certain patterns.

e. Silently repeating a prayer, word or phrase.

f. Arranging your canned goods to face the same way.[10]

Symptoms usually begin gradually and tend to vary in severity throughout the OCD person life ,Symptoms generally worsen when a person with OCD experiencing more stress, OCD considered a lifelong disorder and can be so severe and time-consuming that it becomes disabling ,Most adults recognize that their obsessions and compulsions do not make sense, but that is not always the case. Children may not understand what is wrong.[11]

Symptoms difference in children, adolescents and adults

Symptoms or not differ among children, adolescents and adults. A study carried on 20 children, 44 adolescents and 193 adults found that adolescents were more likely than children to report aggressive obsessions but they did not differ significantly from adults. Adults were more likely than children or adolescents to report miscellaneous obsessions (lucky or unlucky numbers, fear of losing things but the reverse was true for "miscellaneous" compulsions. Mental rituals were less common in children than adolescents or adults. Tic-like compulsions like rituals involving touching, tapping, rubbing, blinking, or staring were similar across age groups Epidemiologic studies report equal gender distributions in adolescent and adult samples. Clinical samples tend to show an equal gender distribution in adults and elevated proportions of males to females (61% to 69% male) in juvenile samples. Regarding gender differences in age at onset, some retrospective studies of adults have found that males report an earlier age at onset than females but others studies have failed to replicate this finding.[12]

Associated conditions related to OCD:

Dimorphic disorder is where the individual is preoccupied with one or more perceived flaws or defects in physical appearance that are not observable or minimal in others. Hoarding disorder is persistent difficulty with discarding possessions regardless of actual value. This results in accumulations of materials or items to the degree that it clutters active living areas and impairs [13]

functioning. Trichotillomania (hair-pulling disorder) is manifested by recurrent pulling out of one's hair, producing hair loss. Excoriation (skin-picking disorder) is recurrent skin picking resulting in skin lesions. [14]

Substance/medication-induced obsessive–compulsive and related disorder is where obsessions, compulsions, hair- pulling, skin-picking, or other body-focused repetitive behaviors result from a medication or drug abuse. Amphetamines and cocaine are known to produce obsessive–compulsive symptoms. Also Methylphenidate has been reported to produce obsessive–compulsive symptoms. Atypical antipsychotics have also been reported to produce OCD symptoms. More over Dopamine agonists, especially agonists of the D3 receptor (eg, ropininole, pramipexole, and pergolide), have been reported to produce OCD-like behaviors.[15]

Obsessive–compulsive and related disorder due to another medical condition manifests with obsessions, compulsions, preoccupations with appearance, hoarding, skin-picking, hair-pulling, and other body-focused repetitive behaviors, which is the result of a general medical disorder. Examples of medical illness that may produce obsessive–compulsive symptoms include Sydenham's chorea and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections. Obsessive–compulsive symptoms that occur exclusively with delirium are not considered an obsessive–compulsive-related disorder due to another medical condition.(16)

Obsessive–compulsive personality disorder (OCPD) consists of a pervasive pattern of preoccupation with orderliness, perfectionism, and mental and interpersonal control to the degree that flexibility, openness, and efficiency are impaired. In OCPD, the individual is preoccupied with details, rules, order, lists, organization, or schedules to the extent that the major point of the activity is lost. Individuals with OCPD are overly rigid and stubborn. Unlike OCD, OCPD lacks true obsessions and compulsions. The manifestations of OCPD are egosyntonic, the affected individual finds the behavior suitable and correct. The manifestations of OCD are egodystonic, the affected individual finds the behavior inappropriate and stressful. Persons with OCPD usually obtain pleasure with organizing and controlling. (17)

Tic disorders and Tourette's syndrome are a frequent comorbidity with OCD. Tics are sudden, brief, intermittent, involuntary, or semi voluntary movements or vocal sounds. Types of t[ics include simple motor tics, simple vocal tics, complex motor tics, and complex vocal tics. Simple motor tics include eye blinking, nose twitching, and head jerking. In theory, any skeletal muscle in the body could produce a tic. Complex tics involve several muscles. Examples of complex motor tics include head shaking, hair brushing, touching rude gestures and imitating gestures. Complex motor tics are stereo- typed movements. Complex motor tics can be confused with compulsive behaviors. Vocal tics are also known as phonic tics. Examples of simple vocal tics include sniffing throat clearing, grunting, humming, screaming, coughing and blowing. In theory any nonword vocal sound can be a vocal tic.(18)

Normal childhood behavior often involves making various noises. The feature distinguishing tics from normal childhood behavior is the constancy, repetitive, and inappropriateness of the behavior. Complex vocal tics are linguistically meaningful utterances and verbalizations. Complex vocal tics include shorting of obscenities, profanity, reparation one's own word, or imitating others. A diagnosis of Tourette's disorder is based on the presence of multiple motor

tics and at least 1 vocal tic. Over 50% of the patients with Tourette's syndrome will have significant obsessive–compulsive symptoms and approximately 30% will have a diagnosis of OCD.[19]

Comorbidity of OCD with psychotic disorders including schizophrenia has been reported. OCD symptoms may occur in 8% to 26% of patients with schizophrenia. This comorbidity could represent a subtype of schizophrenia referred to as ''obsessive–compulsive schizophrenia. Repetitive behavior resulting from a paranoid delusion is not a compulsion. Other psychiatric disorders that can occur with OCD include posttraumatic stress disorder, generalized anxiety disorder, panic disorder, and social phobia. Neurological disorders that can occur with OCD include temporal lobe epilepsy, Huntington's disease, multiple sclerosis, and possibly Parkinson's disease. Strokes affecting the inferior parietal, basal ganglia, caudate, and/or posterior frontal lobe have been reported to produce OCD symptoms acutely.[20-21]

Complications of OCD

The time consuming and oddness of the compulsions regularly strain social relationships with friends and family members. Quality of life and functional impairment occur. OCD can result in unemployment. Physical injuries can occur from certain rituals such as dermatological conditions from excessive hand washing. Criminal justice issues can result from OCD.[22]

Causes of OCD and Triggering Factors:

In spite of a range of theories and considerable research, scientists so far have not been able to identify a definitive cause for a person developing OCD. However, whilst this may be the case, it is believed that OCD is likely to be the result of a combination of either neurobiological, behavioral, cognitive, environmental, infection or genetic factors that trigger the disorder in a specific individual at a particular point in time. Below is a summary of some of the suggested theories around the cause of OCD.[37]

Neurobiological factors:

Neurobiological factors relating to the possible causes of OCD are an area of considerable research and theory. However, despite the recognition that certain parts of the brain are different in OCD sufferers, when compared with non-sufferers, it is still not known how these differences relate to the precise mechanisms of OCD. In an effort to identify the specific biological factors that may be important in the onset or persistence of OCD, the National Institute of Mental Health (NIMH)-supported investigators have used a device called the positron emission tomography (PET) scanner to study the brains of patients with OCD. Several groups of investigators have obtained findings from PET scans suggesting that OCD patients have patterns of brain activity that differ from those of people without mental illness or with some other mental illness. Brain-imaging studies of OCD showing abnormal neurochemical activity in regions known to play a role in certain neurological disorders suggest that these areas may be crucial in the origins of OCD. There is also evidence that treatment with medications or behavior therapy induce changes in the brain coincident with clinical improvement.[38-39]

Recent preliminary studies of the brain using magnetic resonance imaging showed that the subjects with OCD had significantly less white matter than did normal control subjects, suggesting a widely distributed brain abnormality in OCD. Understanding the significance of this finding will be further explored by functional neuroimaging and neuropsychological studies.[37-38]

Neurobiological causes of OCD have focused on a circuit in the brain which regulates primitive aspects of our behavior such as aggression, sexuality, and bodily excretions. This circuit relays information from a part of the brain called the orbitofrontal cortex (front part of the brain), to another area the striatum, and the thalamus (deeper parts of the brain). It also includes other regions such as the caudate nucleus of the basal ganglia (as shown in figure:1) . When this circuit is activated, these impulses brought the attention and cause a person to perform a particular behavior that appropriately addresses the impulse. For example, after a visit to the bathroom, a person begins to wash his/her hands to remove any harmful germs he/she may have encountered. Once a person performed the appropriate behavior , in this case washing hands — the impulse from this brain circuit diminishes and their stops washing their hands and go about their day. It has been suggested that if a person has OCD, the brain has difficulty turning off or ignoring

impulses from this circuit. This, in turn means the obsessions and compulsions continue, leading the person to wash their hands again and again.[39]

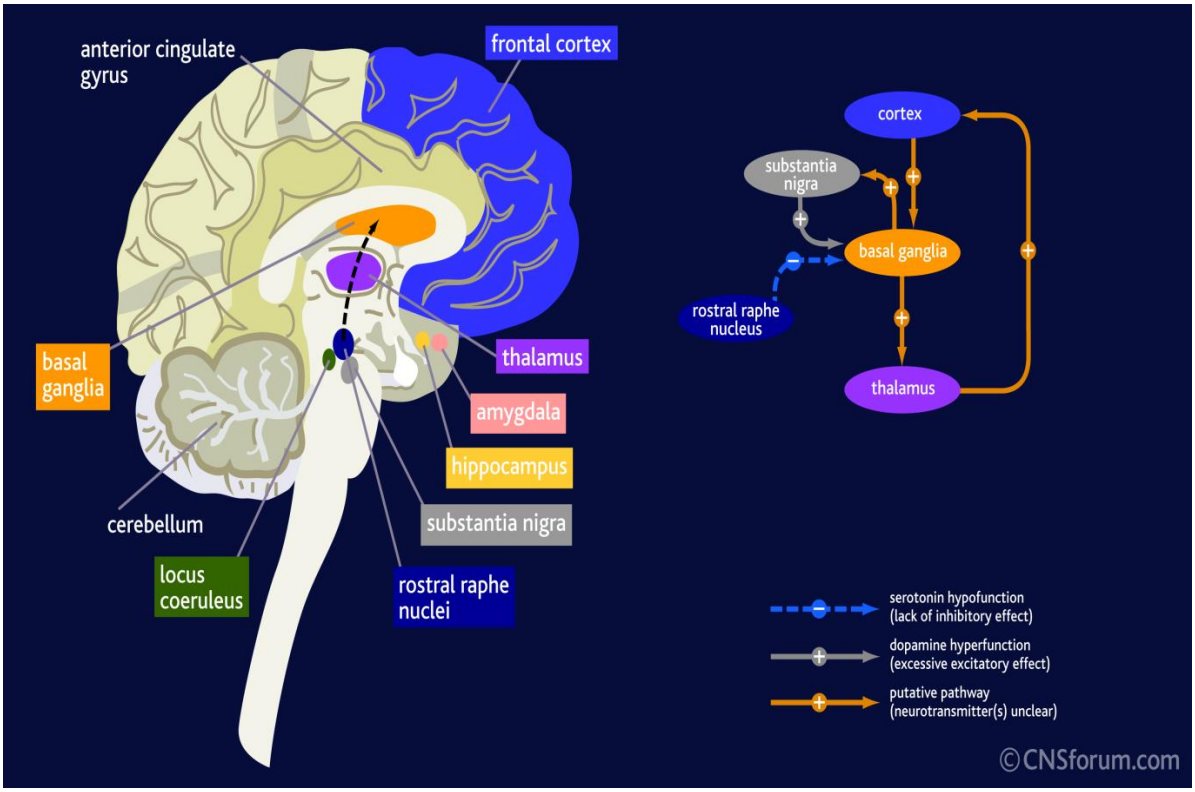

Figure1 : Areas of the brain implicated in the pathophysiology of OCD [36]

Serotonin abnormalities:

Abnormalities or an imbalance in the neurotransmitter, or brain chemical, serotonin, could also be the reason. Serotonin is the chemical in the brain that sends messages between brain cells and it is thought to be involved in regulating everything from anxiety(as shown in figure:2) to memory, to sleep. Medications known as Selective Serotonin Reuptake Inhibitors (SSRIs) are often used to treat OCD, although it is not fully known why the SSRI medications seem to help some people with OCD(as shown in figure:4)

Brain imaging studies have been used to show the differences between the brains of people with OCD and those without OCD(as shown in figure:3), but the scientific community is split over whether what researchers have found is a cause for, or a result of, having the disorder.[39-41]

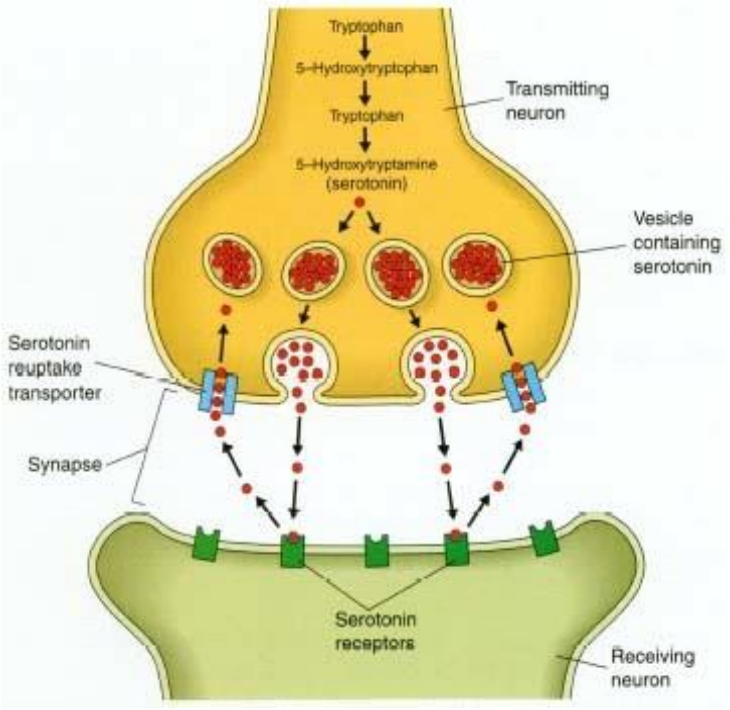

Figure 2 : Serotonin mode of action in the brain.[39]

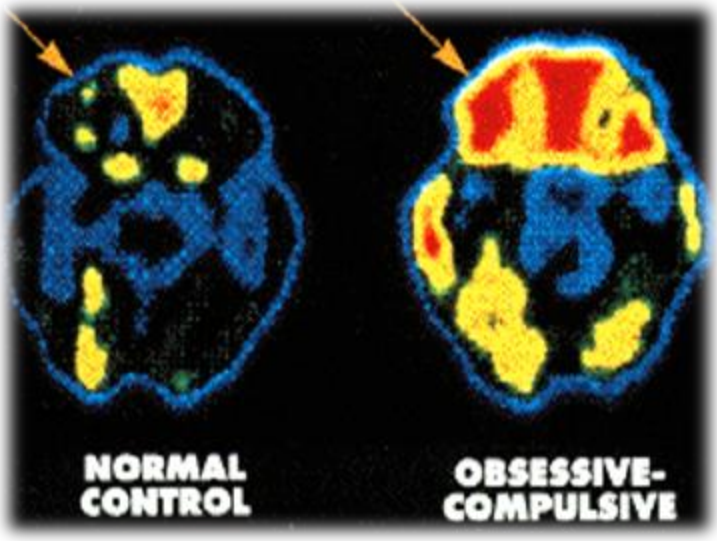

Figure 3 : PET scan a lower level of serotonin in OCD sufferers than normal one.[42]

Serotonin is a key chemical involved in OCD, And a key gene for this process is hSERT, hSERT has the instructions for making a serotonin transporter. The transporter's job is to mop up extra serotonin after a nerve splits it towards the next nerve cell in line. In some people with

OCD, hSERT works too fast, and may collect all the serotonin before the next cell has even heard the signal! Their nerves are whispering when they should be speaking out loud.[38-40]

One type of drug used to treat people with OCD slows down the collection of serotonin by transporters like hSERT. This means that serotonin stays in the space between the cells longer and increases the chances that the second cell will get the message which helps prevent some OCD symptoms.[39-40]

Research funded by the national institution of mental health (NIMH) , based in the US, examined DNA samples from patients with OCD and related illnesses, and the results suggest that OCD may be associated with a rare combination of two mutations within the human serotonin transporter gene (hSERT) (as shown in figure:2). Firstly, the hSERT gene codes for the human serotonin transporter and secondly the membrane protein responsible for the reuptake of serotonin from the synapse between two neurons. It is the transporter protein that is bound by serotonin reuptake inhibitors (SSRIs), resulting in blocking the transporter's function and leaving more serotonin available for neuronal communication within the synapse.[39-41]
The researchers discovered a mutation within the hSERT gene, which they labeled(I425V). The mutation appears to be associated with an increased expression of the hSERT gene, resulting in more transporter proteins appearing in the neuron's membrane. This results in increased reuptake of serotonin in those neuronal synapses, decreasing the amount of serotonin available in the synapse for signaling. The second mutation identified, a long allele of the promoter portion of the serotonin transporter gene (5-HTTLPR), results in similar cellular effects—an increase in transporter proteins leading to less serotonin being available for neuronal communication.

The two mutations appearing together result in a significantly lower amount of serotonin available within the synapse than is seen with either one of the mutations alone, resulting in greater biochemical effects and more severe symptoms.[37-41]

Other neurotransmitters implicated such as dopamine, and glutamate. This is based on neuroimaging studies as well as pharmacological studies. The contrasting improvement in or aggravation of OCD symptoms from atypical antipsychotics suggests dopamine and/or serotonin contributes to OCD. Dopamine agonists and reuptake inhibitors can cause or worsen OCD symptoms. Serotonin is a modulator for dopamine. More recent research examined glutamate as a cause of OCD. Evidence supporting the role of glutamate in OCD include genetic studies,

neurochemical studies, animal models, pharmacological experiments, small clinical studies, and case reports with glutamate-altering drugs[40]

Behavioral and cognitive factors:

Research has revealed a great deal about the psychological factors that maintain OCD, which in turn has led to effective psychological treatment in the form of Cognitive Behavioral Therapy (CBT). For example, according to the Learning Theory, OCD symptoms are a result of a person developing learned negative thoughts and behavior patterns towards previously neutral situations which can result from life experiences.[39]

Many cognitive theorists believe that individuals with OCD have faulty beliefs and that it is their misinterpretation of intrusive thoughts that leads to OCD. According to the cognitive model of OCD, everyone experiences intrusive thoughts from time-to-time. However, people with OCD often have an inflated sense of responsibility and misinterpret these thoughts as being very important and significant which could lead to catastrophic consequences. The repeated misinterpretation of intrusive thoughts leads to the development of the obsessions and because the thoughts are so distressing, the individual engages in compulsive behavior to try to resist, block, or neutralize the obsessive thoughts.[37-40]

Some researchers believe that this theory questions the biological theory because people may be born with a biological predisposition to OCD but never develop the full disorder, while others are born with the same predisposition but, when subject to sufficient learning experiences, develop OCD.[40]

Environmental factors:

Stress and parenting styles are environmental factors that have been blamed for causing OCD, but no evidence is yet to show that stress, or the way a person interacted with their parents during childhood, causes OCD. Stress does not cause OCD, although a stressful event, like being involved in or witnessing a road traffic accident, may trigger its onset. If left untreated, everyday anxiety and stress in a person's life will worsen symptoms in OCD. Problems at school or work, university exam pressures and normal everyday problems that relationships can bring are all contributory factors to increasing the frequency and severity of a person's OCD.[41]

Infection factors:

Some children begin to exhibit symptoms of OCD after a severe infection such as strep throat. It is thought that the body's natural response to infection, the production of certain antibodies, when directed to parts of the brain might be linked in some way to **P**ediatric **A**utoimmune **N**europsychiatric **D**isorders **A**ssociated with **S**treptococcal Infection (PANDAS). Studies suggest the infection does not actually cause OCD, but triggers symptoms in children who are genetically predisposed to the disorder. It is thought that if OCD results from a strep throat infection the symptoms will start quickly, probably within one or two weeks.[37]

Genetic factors:

Another interesting line of research is in the area of genetics, and recent studies have indicated that there may be a considerable genetic basis for OCD. Some research points to the likelihood that OCD sufferers will have a family member with the OCD or with one of the other disorders in the OCD 'Spectrum'. However, the theory that OCD is inherited genetically is not conclusive - for example, identical twins will not necessarily both have OCD. So although the genetics may play a part, they aren't the whole story and learned or environment factors may play a part. It is unknown what other factors might be involved - perhaps an illness or even ordinary life stresses could induce the activity of genes associated with the symptoms of OCD. [39-40]

Commonly accepted in the past, but nowadays increasingly disregarded, the psychoanalytic theory wich suggests that OCD develops because of a person's fixation arising from unconscious conflicts or discomfort they experienced during infancy or childhood. This theory is now quite rightly disregarded due to the failure of psychoanalytic therapy to treat OCD.[38-40]

Major stresses or traumatic life events may precipitate the onset of OCD. However, these are not thought to cause the OCD, but rather trigger it in someone already predisposed to the disorder. Depression is also sometimes thought to cause OCD, although again opinion is split, with the majority of experts believing that depression is often a symptom of OCD rather than a cause.[39]

There is still a great deal of theoretical contention surrounding the definitive cause of OCD. However, all of the above theories offer compelling and highly informative insights, with the possibility that a combination of the theories may eventually be identified as the actual cause of OCD. Whilst the cause is currently still being debated, sometimes vigorously by the scientists, what is not in contention is the fact that OCD is indeed a chronic, but equally a very treatable medical condition.[40]

Diagnosis of OCD

Formal diagnosis may be performed by a psychologist, psychiatrist, clinical social worker, or other licensed mental health professional. The American Psychiatric Association published the Diagnostic and Statistical Manual of Mental Disorders (DSM). This manual is used by mental health professionals for the diagnose of OCD.[43]

General criteria required for a diagnosis of OCD include:

a. The patient must have either obsessions or compulsions or both.
b. The patient may or may not realize that their obsessions and compulsions are excessive or unreasonable.
c. Obsessions and compulsions are significantly time-consuming and interfere with the patient's daily routine and social or work functioning.

The obsessions must meet these criteria:

a. Recurrent, persistent and unwelcome thoughts, impulses or images are intrusive and cause distress.
b. The patient tries to ignore these thoughts, images or impulses or to suppress them with compulsive behaviors.[43]

Compulsions must meet these criteria:

a. Repetitive behavior that the patient feels driven to perform, such as hand-washing or repetitive mental acts, such as counting silently.
b. The patient tries to neutralize obsessions with another thought or action.
c. These behaviors or mental acts are meant to prevent or reduce distress, but they are excessive or not realistically related to the problem they're intended to fix.[43]

Diagnostic challenges

It's sometimes difficult to diagnose OCD because symptoms can be similar to those of OCPD disorder, anxiety disorders, depression, schizophrenia or other mental illnesses. Someone with true obsessions and compulsions has OCD, although it's possible to have both OCD and obsessive-compulsive personality disorder. [43]

Management of OCD

The most effective treatments for OCD are Cognitive Behavior Therapy (CBT) and/or medication. More specifically, the most effective treatments are a type of CBT called Exposure and Response Prevention (ERP), which has the strongest evidence supporting its use in the treatment of OCD, and/or a class of medications called serotonin reuptake inhibitors (SSRIs).[44]

Exposure and Response Prevention is typically done by a licensed mental health professional (such as a psychologist, social worker, or mental health counselor) in an outpatient setting. Medications can only be prescribed by a licensed medical professionals (such as a physician or a psychiatrist), who would ideally work together with a therapist of an OCD patient to develop a treatment plan. Taken together, ERP and medication are considered the "first-line" treatments for OCD. In other words, about 70% of people will benefit from ERP and/or medication for their OCD.[44]

Exposure and Response Prevention (ERP)

(CBT) refers to a group of similar types of therapies used by mental health therapists for treating psychological disorders, with the most important type of CBT for OCD being Exposure and Response Prevention (ERP).

The Exposure in ERP refers to exposing a person to the thoughts, images, objects and situations that make their anxious and/or start his/her obsessions. While the Response Prevention part of ERP, refers to making a choice not to do a compulsive behavior once the anxiety or obsessions have been "triggered." All of this is done under the guidance of a therapist at the beginning — eventually the patient will learn to do their own ERP exercises to help manage their symptoms. Add reference.[44-45]

Medications used for OCD

About 7 out of 10 people with OCD will benefit from either medication or ERP. For the people who benefit from medication, they usually see their OCD symptoms reduced by 40-60%.[45]

First-line treatments of OCD are the SSRIs and the TCA clomipramine. It is recommended to use the medium to upper dose range (as shown in table 1). OCD requires long-term treatment at an effective dose-level
(" The dose that makes you well, keeps you well "). If patients do not respond, consultation with a psychiatrist might be considered. [46-47]

Table 1: Displays the suggested starting doses, known effective doses, maximum recommended doses, and maximum doses occasionally prescribed for each SSRI and TCA clomipramine.[48-49]

SSRI & TCA	Start Dose and Incremental Dose (mg/day) a	Usual Target Dose (mg/day)	Usual Maximum Dose (mg/day)	Occasionally Prescribed Maximum Dose (mg/day) b
Citalopram	20	40- 60	80	120
Clomipramine	25	100- 250	250	C
Escitalopram	10	20	40	60
Fluoxetine	20	40-60	80	120
Fluoxetine	50	200	300	400
Paroxetine	20	40-60	60	100
Sertraline	50	200	200	400

Patients who are worried about side effects can be started at half these doses or less, Most patients will not experience substantial improvement earlier than 4 to 6 weeks after starting medication, and some who will ultimately respond will experience little improvement for as many as 10 to 12 weeks. Available trial data suggest that higher SSRI doses produce a somewhat higher response rate and somewhat greater magnitude of symptom relief ,These doses are sometimes used for

rapid metabolizers or for patients with no or mild side effects and inadequate therapeutic response after 8 weeks or more at the usual maximum dose. [48-49]

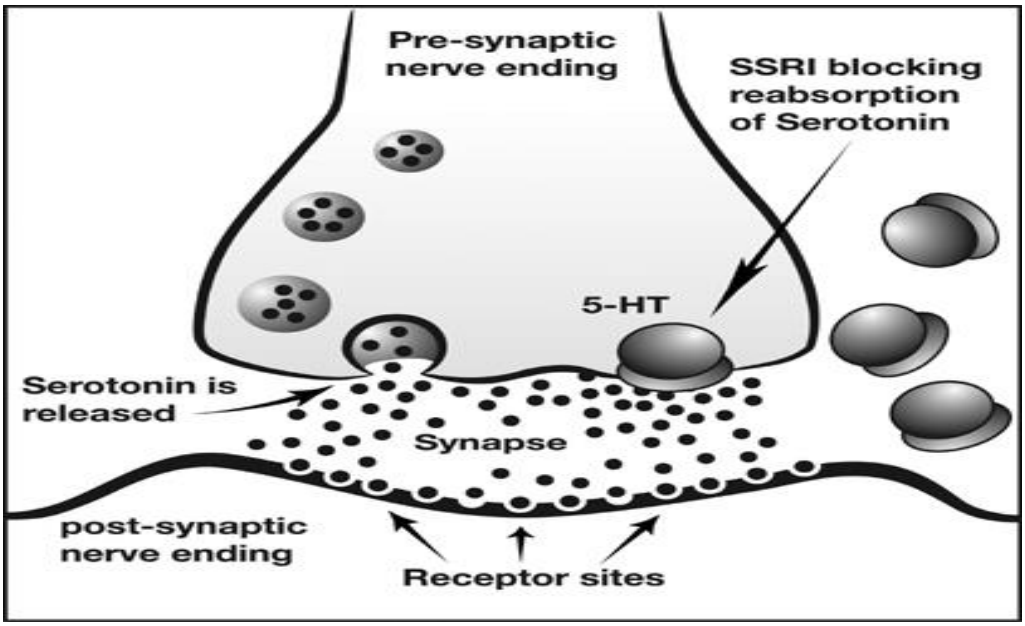

Figure 4 : Mechanism of action of SSRI (50)

Effectiveness

Regarding the effectiveness of the above mentioned drugs, there seems to be no significant difference in how well they work. However, for any given patient, one drug may be very effective, and the others may not. The only way to tell which drug will be the most helpful with the least side effects is to try each drug for about 3 months.

It remains unclear as to how these particular drugs help OCD, each of these medications affect serotonin. Adding these medications to the body can help boost serotonin and get the brain back on track.

After medications are stopped, symptoms do not return immediately; they may start to return within a few weeks to a few months. If OCD symptoms return after a medication is stopped, most patients will have a good response if the medication is restarted.[51-52]

Pregnant women with OCD

Women who are pregnant or are breastfeeding should weigh the decision to take these drugs with their doctor. If severe OCD cannot be controlled any other way, research has indicated that these medications seem to be safe. Many pregnant women have taken them without difficulty.
Some OCD patients choose to use exposure and response prevention (ERP) to minimize medication use during the first or last trimester of pregnancy.[51-52]

Side effect

The most common side effects of the SSRIs include gastrointestinal distress (especially in the first weeks of treatment), agitation, insomnia or somnolence, increased tendency to sweat, if mild queasiness or nausea occurs, it will usually disappear within 1 to 2 weeks at constant dose. Insomnia may necessitate addition of a sleep-promoting agent. [53]
Unlike the SSRIs, clomipramine is more likely to induce anticholinergic effects such as dry mouth, constipation, and blurred vision, although these typically diminish over time. Clomipramine is also more likely to induce delayed urination or, uncommonly, urinary retention. Histaminic blockade is associated with weight gain and sedation. Adrenergic blockade may lead to orthostatic hypotension and postural dizziness. Sodium channel blockade can induce seizures.[52]

Tricyclic antidepressant and Atypical antipsychotics

Clomipramine was the first pharmacotherapeutic agent found to have efficacy in OCD. The drug shares the pharmacological properties of the tricyclic group of antidepressants from which it is derived, but can be distinguished from other tricyclics by its potent effects at inhibiting the synaptic reuptake of the neurotransmitter serotonin (as shown in figure:5). However, its effects are not selectively mediated by serotonin mechanisms. As a tricyclic, clomipramine is associated with the adverse effects and toxicity in overdose that typifies this group of drugs. For this reason it is usually considered second-line after SSRIs for patients whose symptoms have failed to respond to SSRIs or who are unable to tolerate them.[65]

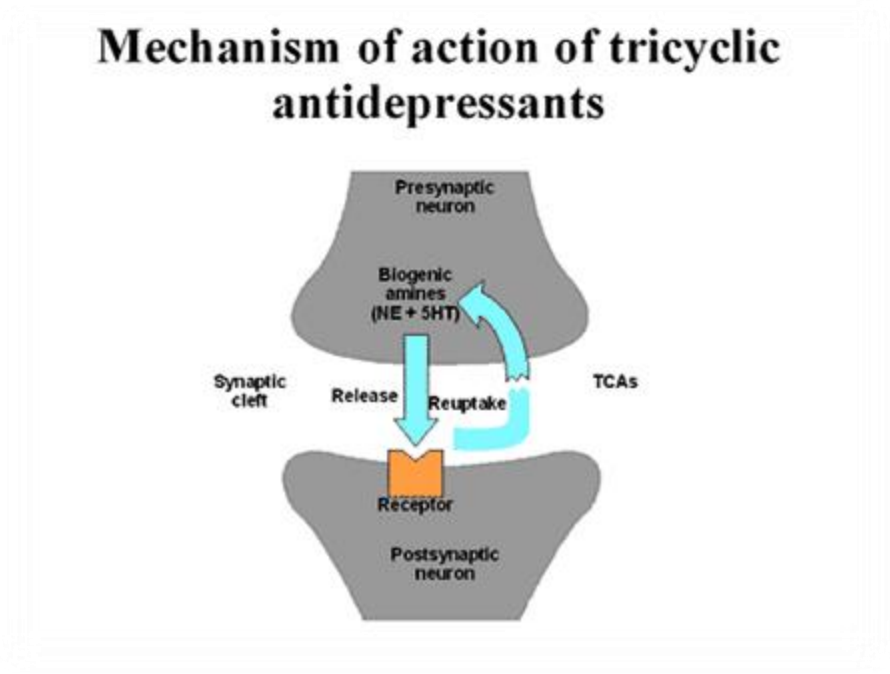

Figure 5 : Mechanism of action of tricycle antidepressants [66]

In a number of studies, atypical antipsychotics such as (Quetiapine) have been used as mono therapy in generalized anxiety disorder (GAD) or as add-on treatment for non-responsive cases of anxiety disorders, OCD and PTSD (post traumatic syndrome disorder), Side effects of atypical antipsychotics include sedation, orthostatic hypotension, sexual dysfunctions, metabolic syndrome, extrapyramidal effects and others. However, in most countries atypical antipsychotics are not licensed for these disorders. Therefore, treatment with these medications should probably be reserved only to a specialist setting(figure:6). [53]

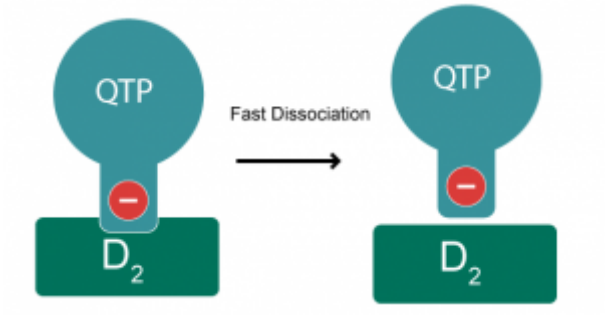

Figure 6 : Mechanism of action of atypical antipsychotic include rapid dissociation of D2 receptor(54)

Medication for Pediatric OCD

The best treatment for pediatric OCD includes both medication and exposure and response prevention (ERP) therapy. Medication should only be considered when there are moderate to severe OCD symptoms and ERP has not worked to treat symptoms.

Both ERP and medication effectively treat OCD in children and adolescents. Their use is supported by the treatment guidelines of the American Psychiatric Association (APA) and the American Academy of Child and Adolescent Psychiatry (AACAP).[55]

All OCD medications work slowly, It is important to not give up on a medication until it has been taken at the right dose for 10 to 12 weeks(Table:2), Studies have also shown that improvement of childhood OCD can continue for at least a year after starting medication.

Table 2: Displays the suggested effective dose for children .[55]

SSRI & TCA	**Brand name**	**Dose (mg/day)**
Fluvoxamine	(Luvox®)	50-300 mg/day
Fluoxetine	(Prozac®)	10-80 mg/day
Sertraline	(Zoloft®)	50-200 mg/day
Paroxetine	(Paxil®)	10-60 mg/day
Citalopram	(Celexa®)	10-40 mg/day*
Escitalopram	(Lexapro®)	10-20 mg/day
Clomipramine	(Anafranil®)	50-200 mg/day

Note : A child's response to each of the OCD medications varies. No two children respond in the same way. In general, clomipramine (Anafranil®) is not usually tried first because of its side effects [55]

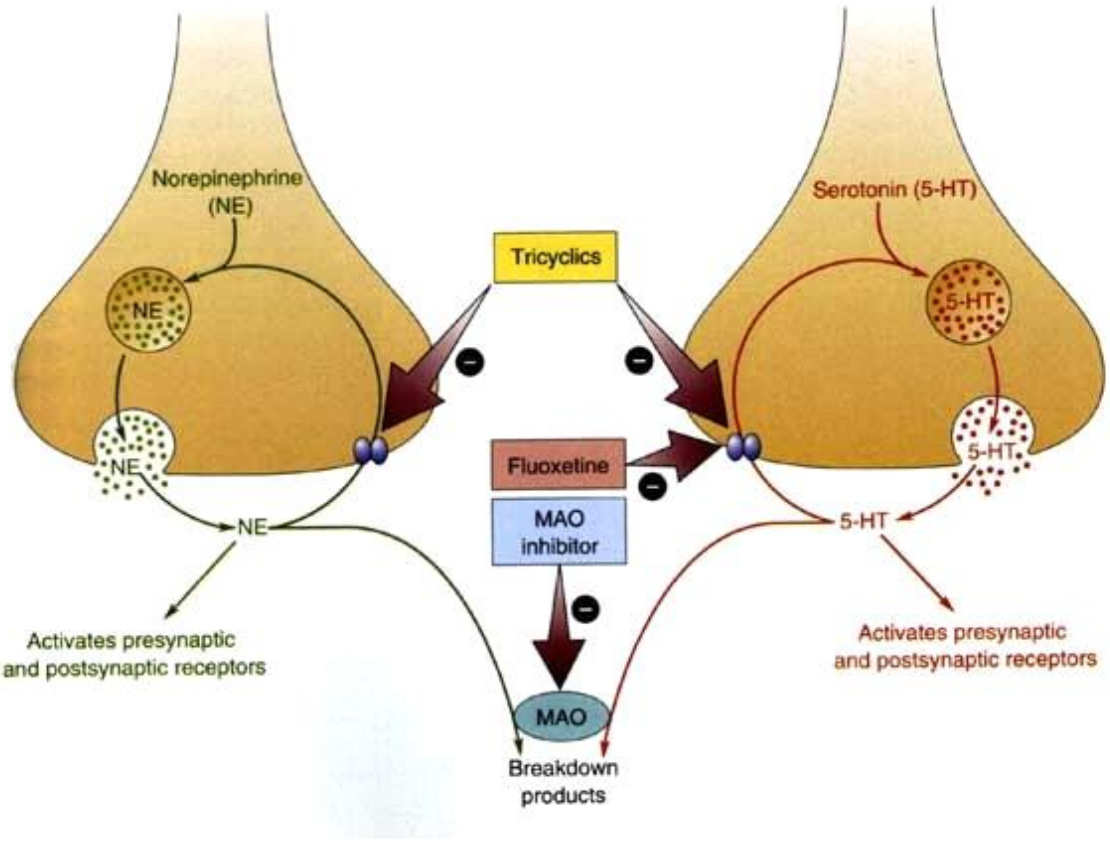

Figure 7 : fluoxetine mechanism of action [56]

More Intensive Options for OCD patients not responding to traditional therapy

Some OCD patients have tried traditional outpatient therapy and would like to try a more intensive level of care. The following lists therapy options from least intensive to most intensive:

a. Traditional Outpatient – Patients see a therapist for individual sessions as often as recommended by their therapist generally one or two times a week for 45-50 minutes.
b. Intensive Outpatient – Patients may attend groups and one individual session per day several days per week.
c. Day Program – Patients attend treatment during the day (typically group and individual therapy) at a mental health treatment center usually from 9am – 5pm up to five days a week.
d. Partial Hospitalization – Same as the Day Program but patients attend the treatment at a mental health hospital.

e. Residential – Patients are treated while living voluntarily in an unlocked mental health treatment center or hospital.

Inpatient -This is the highest level of care for a mental health condition. Treatment is provided on a locked unit in a mental health hospital on a voluntary or sometimes involuntary basis. Patients are admitted into this level of care if they are unable to care for themselves or are a danger to themselves or others. The goals of inpatient treatment are to stabilize the patient, which generally takes several days to a week, and then transition the patient to a lower level of care.[57-58]

Additional Treatment Options for OCD

When severe OCD proves resistant to treatment, there are more drastic options, including:

a. Brain Surgery
b. Gamma Knife
c. Deep Brain Stimulation (DBS)[59]

Brain Surgery for OCD

These interventions are only for individuals who do not respond well to cognitive behavior therapy or medications for OCD.[60]

Anterior cingulotomy (brain surgery)

This is a brain surgery that involves drilling through the skull and using a heated probe to burn an area within a part of the brain called the anterior cingulate cortex (the part of the brain highlighted on the right) (Figure:8) About 50% of those who did not respond to behavior therapy or medicines for OCD got some benefit from the procedure.[61]

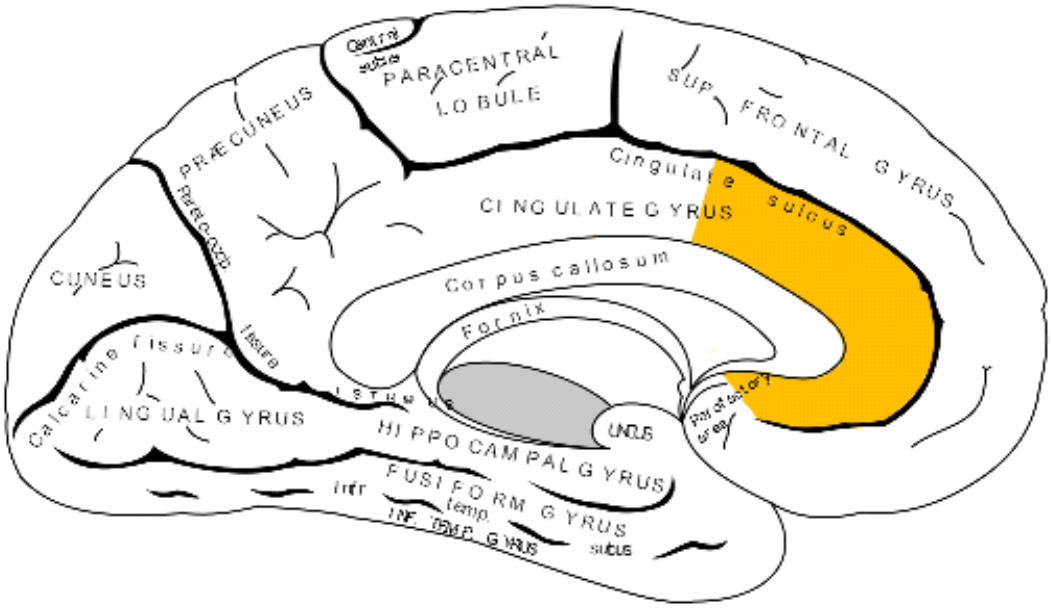

Figure 8 : Anterior Cingulate Cortex (highlighted in gold). [61]

Anterior capsulotomy (brain surgery)

This procedure is very similar to the surgery listed above. However, in this surgery doctors operate on a different part of the brain called the anterior limb of the internal capsule. About 50-60% of those who did not respond to behavior therapy or medicines for OCD got some benefit from the procedure.[61]

Gamma Knife Treatment for OCD

Gamma knife is a treatment for OCD that does not require opening the skull (figure:9). In gamma knife procedures, multiple gamma rays pass through the skull. On its own, a single gamma ray poses no danger to brain tissue. However, when gamma rays intersect, the energy level is high enough to destroy the targeted brain tissue (figure:9). The most recent version of this procedure is called gamma ventral capsulotomy. This is because the procedure is limited to the ventral (bottom) half of a brain area called the anterior capsule. About 60% of those who did not respond to behavior therapy or medicines for OCD got some benefit from the procedure.[62]

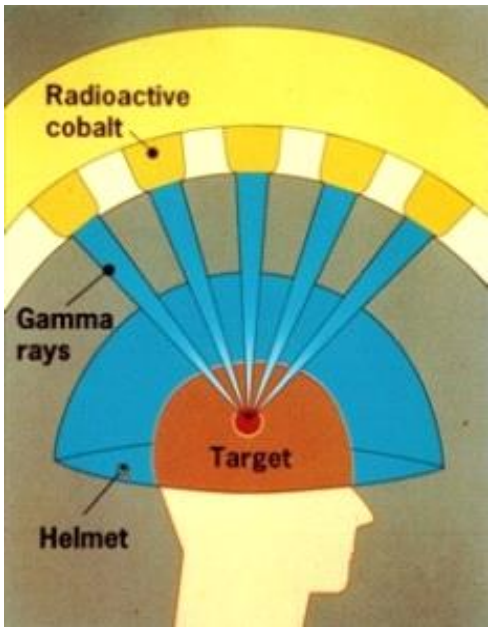

Figure 9 : Gamma knife process [62]

Deep Brain Stimulation (DBS)

This intervention is only for individuals who do not respond well to cognitive behavior therapy or medication.

DBS has been used since the mid 1980's to treat the symptoms of movement disorders, such as Parkinson's disease (figure:10). DBS involves placing electrodes in targeted areas of the brain. Once the electrodes are in place, they are connected by wires under the skin to pulse generators under the skin (usually just below the collarbone).

The pulse generator, sometimes called an "implantable neurostimulator," contains a battery for power and a microchip to control the stimulation (figure:10). A doctor uses a hand-held wand and small computer to control the pulse generator through the skin. These pulse generators are similar to pacemakers. The biggest difference is that in DBS the electrodes are in the brain instead of in the heart.[63]

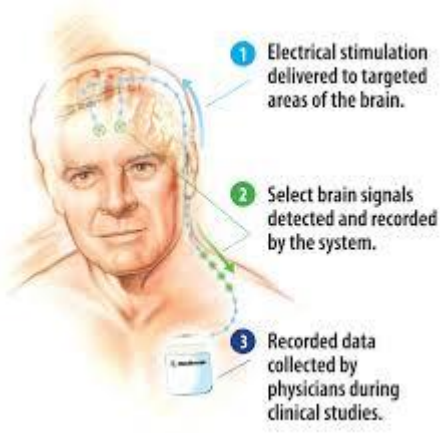

Figure 10 : The process of deep brain stimulation .(63)

In the late 1990's, based on positive research results in anterior capsulotomies, DBS researchers first implanted electrodes in the anterior capsule of treatment-resistant OCD patients. The early results were promising. Three of the first four patients experienced benefit (figure:10). Since then, larger trials have been done and the target area of the brain has moved slightly to an overlapping part of the brain called the ventral capsule/ventral striatum (VC/VS).(63) a worldwide study found that out of 26 patients with treatment-resistant OCD, 61.5% responded positively to DBS. This response rate is similar to the other surgeries described above. However, comparisons must be tentative since the number of patients treated with DBS is still relatively small. (63)

Benefits of DBS compared to other surgeries

DBS requires opening the skull, but it does not require destroying any brain tissue. In the other surgeries listed above, there is a fixed amount of brain tissue that is destroyed(figure:10). DBS allows for different amounts of electrical charge, giving the doctors a wider range of treatment.(63)

Famous people with OCD:

Michael Jackson - Michael Joseph Jackson (August 29, 1958 - June 25, 2009), seemed to have body dysmorphic disorder. He had over 30 cosmetic surgery operations and his ex-wife Lisa Presley has said he would never take off his make-up, even in bed. Body Dimorphic Disorder (BDD) is a negative preoccupation with physical appearance. Many who suffer from this disorder

are at a greater risk of becoming plastic surgery addicts. Individuals with BDD display symptoms similar to those who are diagnosed with OCD (Obsessive Compulsive Disorder).[64]

Leonardo DiCaprio - has revealed he suffers from Obsessive Compulsive Disorder. The 'Titanic' star says he has to force himself not to step on every chewing gum stain when walking along and fight urges to walk through a doorway several times, because he doesn't want his condition taking over his life.[64]

Howie Mandel - Howie Michael Mandel II (born November 29, 1955) is a Canadian comedian and actor, known for his roles on sitcoms and television including the popular TV show Deal or no Deal, Howie Mandel suffers from OCD and can't shake hands with anyone due to mysophobia. Basically being the fear of dirt and germs, for this reason Howie shaves his head because it helps him feel cleaner.[64]

Marc Summers - During an interview with Dr. Eric Hollander on Biggers & Summers, Summers revealed that he has obsessive compulsive disorder. Summers went public about his condition on various television shows, including The Oprah Winfrey Show and The Today Show. In 1999, Summers co-wrote a book with Hollander about his experience called Everything In Its Place: My Trials and Triumphs with Obsessive Compulsive Disorder.[64]

Albert Einstein - (March 14, 1879 - April 18, 1955) Being one of the most important great minds of his century Albert Einstein was then known to suffer from dyslexia mainly because of his bad memory and his constant failure to memorize the simplest of things. It is also thought that he had OCD. He would not remember the months in the year yet he would succeed in solving some of the most complicated mathematical formulas of the time without any trouble. He may have never learned how to properly tie his shoelaces but his scientific contributions and theories still have a major effect on all of today's current knowledge of science.[64]

Chapter II

Conclusion and Recommendations

Conclusion

OCD is an anxiety disorder featuring intrusive and troubling thoughts, which are perceived as the products of one's own mind unlike schizophrenia. The Patient affected by OCD feels compelled to carry out certain stereotyped behaviors, although he recognizes that his behavior is at times irrational. Entire brain functioning is disturbed in patients suffering from OCD, thereby producing devastating effects at the work-place as well as at homes of the patients. OCD is a complicated disorder. Selective serotonin reuptake inhibitors (SSRIs) and to some extent tricyclic antidepressants form the main stay in the symptomatic treatment of OCD. Most of the OCD cases are incurable. Therefore, there is a great challenge to discover new drug treatment for the management of OCD.

Recommendation

OCD is a chronic disease that requires long-term treatment with frequent follow up and a regular behavioral therapy. It is ranked by World Health Organization (WHO) in the top ten of the most disabling illnesses of any kind, in terms of lost earnings and diminished quality of life,[1] it is also considered to be the fourth most common mental illness in many western countries that will affect men, women and children regardless of their race, religion, nationality or socio-economic group.[6]

Accordingly we recommend the ministry of health and the health professionals to pay more attention for OCD and its treatment. OCD needs more attention and awareness in our community and in the Arab world.

Reference

1. Supporting children and adult affected by obsessive compulsive disorder http://www.ocduk.org/ocd. Retrieved at 18.6.2015 .

2. History of OCD, http://ocd.stanford.edu/treatment/history.html. Retrieved at (23.6.2015)

3. Aardema, F. & O'Connor. (2007). The menace within: obsessions and the self. International Journal of Cognitive Therapy, 21, 182–197. Retrieved at(25.7.2015)

4. M. A. Jenike; Baer, L & W. E. Minichiello. Obsessive Compulsive Disorders. Theory and Management. Littleton, MA: PSG Publishing, 1986.

5. Berrios G E (1989). "Obsessive Compulsive Disorder: Its conceptual history in France during the 19th Century". Comprehensive Psychiatry 30: 283–95.

6. Fontenelle LF, Mendlowicz MV, Versiani M (2006): The descriptive epidemiology of obsessive-compulsive disorder. Prog Neuropsychopharmacol Biol Psychiatry 30:327–337.

7. National Institute of Mental Health \l "Ruscio AM, Stein DJ, Chiu WT, Kessler RC. "The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication." Molecular Psychiatry. 2008 Aug 26. \l "March, J. & Benton, C. (2007). Talking Back to OCD. (pp.10-The Guilford Press.

8.Signs & symptoms of OCD http://www.mayoclinic.org/diseases-conditions/ocd/basics/ Retrieved at (6.7.2015)

9. Journal of the American Academy of Child & Adolescent Psychiatry

Volume 47, Issue 7, July 2008, Pages 773–778

10. Behaviour Research and TherapyVolume 39, Issue 7, July 2001, Pages 765–776

11. Journal of the American Academy of Child & Adolescent Psychiatry

Volume 35, Issue 7, July 1996, Pages 907–912.

12. Maria C. Mancebo, Ph.D.a,b, Abbe M. Garcia, Ph.D.b,c, Anthony Pinto, Ph.D.a,b, Jennifer B.Free man, Ph.D.b,c, Amy Przeworski, Ph.D.b,c, Robert Stout, Ph.D.b, Joshua S. Kane, M.D.b,Jane L. Eisen, M.D.b, and Steven A. Rasmussen, M.D.a,b. Juvenile-Onset OCD: Clinical Features in Children, Adolescents and Adults., Acta Psychiatr Scand. 2008 August ; 118(2): 149–159.

13.American Psychiatric Association. Obsessive-Compulsive and Related Disorders. Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Washington, DC: American Psychiatric Association; 2013; 235-264.

14.Kouris S. Methylphenidate-induced obsessive-compulsiveness. J Am Acad Child Adolesc Psychiatry. 1998;37(2):135.

15.Serby M. Methylphenidate-induced obsessive-compulsive symp- toms in an elderly man. CNS Spectr. 2003;8(8):612-613.

16.Lemke NT, Bustillo JR. Clozapine-induced obsessive-compulsive symptoms in bipolar disorder. Am J Psychiatry. 2013;170(8):930

17.Desarkar P, Das A, Nizamie SH. Aripiprazole-induced obsessive- compulsive disorder: a report of 2 cases. J Clin Psychopharmacol . 2007;27(3):305-306.

18.American Psychiatric Association. Personality Disorders. Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Washington, DC: American Psychiatric Association; 2013; 645-684.

19.American Psychiatric Association. Neuro developmental disorders. Diagnostic and Statistical Manual of Mental Disorders, 5th edition. Washington, DC: American Psychiatric Association; 2013;31-86.

20.Jankovic J. Tourette's syndrome. N Engl J Med. 2001;345(16): 1184-1192.

21.Comings DE.Vocal Tics. Tourette Syndrome and Human Behavior. Duarte, CA: Hope Press; 1990;17-18.

22. Gyula Bokor, MD1, and Peter D. Anderson, PharmD, BCPP2

Journal of Pharmacy Practice 2014,Vol.27(2) 116130 .

23. Laven DL, Bednardczyk EM. CNS assessment using functional neuro-PET imaging. J Pharm Pract. 2001;14(4): 308-331.

24.Maia TV, Cooney RE, Peterson BS. The neural bases of obsessive-compulsive disorder in children and adults. Dev Psy- chopath. 2008;20(4):1251-1283.

25.Sbordone RJ, Saul RE. Neuroanatomy. Neuropsychology for Healthcare Professionals and Attorneys 2nd edition. New York: CRC Press; 2000:35-54.

26. Chacko RC, Corbin MA, Harper RG. Acquired obsessive- compulsive disorder associated with basal ganglia lesions. J Neuropsychiatry Clin Neurosci. 2000;12(2):269272.

27.Billett EA, Richter MA, King N, Heils A, Lesch KP, Kennedy JL. Obsessive-compulsive disorder, response to serotonin reuptake inhibitors and the serotonin transporter gene. Mole Psychiatry. 1997;2(5):403-406.

28.Nemoda Z, Szekely A, Sasvari-Szekely M. Psychopathological aspects of dopaminergic gene polymorphisms in adolescence and young adulthood. Neurosci Biobehav Rev. 2011;35(8): 1665-1686.

29..Hesse S, Muller U, Lincke T, et al. Serotonin and dopamine transporter imaging in patients with obsessive-compulsive disorder. Psychiatry Res. 2005;140(1):63-72.

30.Lemke NT, Bustillo JR. Clozapine-induced obsessive-compulsive symptoms in bipolar disorder. Am J Psychiatry. 2013;170(8):930.

31.Desarkar P, Das A, Nizamie SH. Aripiprazole-induced obsessive- compulsive disorder: a report of 2 cases. J Clin Psychopharmacol . 2007;27(3):305-306.

32 .Olijglagers JE, Werkman TR, Wadman WJ. Modulation of midbrain dopamine neurotransmission by serotonin, a versatile interaction between neurotransmitters and significant for anti- psychotic drug action. Curr Neuropharmacol. 2006;4(1):59-68.

33 Pittenger C, Bloch MH, Williams K. Glutamate abnormalities in obsessive compulsive disorder,: neurobiology, pathophysiology, and treatment. Pharmacol Ther. 2011;132(3):314-332.

34 .Marsh R, Maia TV, Peterson BS. Functional disturbances within frontostriatal circuits across multiple childhood psychopathologies. Am J Psychiatry. 2009;166(6):664-674.

35. Welch JM, Lu J, Rodriguiz RM, et al. Corticostriatal synaptic defects and OCD-like behaviors in SAPAP3 mutant mice. Nature. 2007;448(7156):894-900.

36. www.cnsforum.com Retrieved at 22Jul2015.

37. Supporting children and adult affected by obsessive compulsive disorder

Retrieved at 29Jul2015http://www.ocduk.org/what-causes-ocd

38.Obsessive-compulsive disorder **(**OCD**)** Tests and diagnosis http://www.mayoclinic.org/diseases-conditions/ocd/basics/tests-diagnosis/con-20027827 - 37k retrieved at 3.10.2015.

39.Causes of OCD http://www.camh.ca/en/hospital/health_information/a_z_mental_health_an_addiction_information/obsessive_compulsive_disorder/obsessive_compulsive_disorder_information_guide/Pages/ocd_causes.aspx#genetic. Retrieved at 3Aug2015.

40.National Institute of Mental Health \l "Ruscio AM, Stein DJ, Chiu WT, Kessler RC. "The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Retrieved at 10Aug2015

41." Molecular Psychiatry**.** 2008 Aug 26. \l "March, J. & Benton, C. **(2007).** Talking Back to OCD. (pp.10-11). The Guilford .

42. Image, PET scan a lower level of serotonin in OCD sufferers than normal one.

http://www.intechopen.com/books/obsessive-compulsive-disorder-the-old-and-the-new-problems/pathophysiology-of-obsessive-compulsive-disorder-affected-brain-regions-and-. Retrieved at 26Jul2015..challenge-towards-discov#article-front

43. Diagnosis Of OCD http ://www.mayoclinic.org/diseases-conditions/ocd/basics/. Retrieved at 15Aug2015

44. treatment of OCD https://iocdf.org/about-ocd/treatment/ Retrieved at 22Aug2015

45.Rauch SL, Jenike MA. Pharmacological treatment of obsessive-compulsive disorder. In: Nathan PE, Gorman JM, eds. Treatments that work. New York, NY: Oxford University Press,1998:359–376. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3285220/

46. Guidelines for the pharmacological treatment of anxiety disorders, obsessive– compulsive disorder and posttraumatic stress disorder in primary care (International Journal of Psychiatry in Clinical Practice, 2012; 16: 77–84) Retrieved at 4oct2015

47.Medication used for OCD Retrieved at 16sep2015 https://iocdf.org/about-ocd/treatment/

48. .Rauch SL, Jenike MA. Pharmacological treatment of obsessive-compulsive disorder. In: Nathan PE, Gorman JM, eds. Treatments that work. New York, NY: Oxford University Press,1998:359–376. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3285220/

49.International OCD Foundation's Scientific Advisory Board
Harvard Medical School https://iocdf.org/about-ocd/treatment/meds/ retrieved at 28.9.2015.

50.Journal of perinatology Image of SSRI http://www.natura.com\jp\journal\v25.
Retrieved at 7.9.2015.

51.instruction for patient who suffering from OCD
http://www.researchgate.net/publication/5990301_Practice_Guideline_for_the_Treatment_of_Patients_with_ObsessiveCompulsive_Disorder. Retrieved at 31Aug2015.

52. Comorbidity of obsessive-compulsive disorder and depression: prevalence, symptom severity, and treatment effect. (PMID:12523869) http://europepmc.org/abstract/med/12523869 Retrieved at 4 Sep2015 .

53. Guidelines for the pharmacological treatment of anxiety disorders, obsessive– compulsive disorder and posttraumatic stress disorder in primary care (International Journal of Psychiatry in Clinical Practice, 2012; 16: 77–84) .

54. Mechanism of action of atypical antipsychotic include rapid dissociation of D2 receptor
http://psychopharmacologyinstitute.com/antipsychotics/quetiapine/mechanism-of-action/
retrieved at 1.10 .2015 .

55. By Michael Jenike, MDChair, International OCD Foundation's Scientific Advisory Board
Harvard Medical School https://iocdf.org/about-ocd/treatment/ retrieved at 23.7.2015.

56. Figure of fluxtine mechanism of action http\\www.slideshare.com Retrieved at 2.10.2015.

57.By Michael Jenike, MDChair, International OCD Foundation's Scientific Advisory Board
Harvard Medical School https://iocdf.org/about-ocd/treatment Retrieved at 16sep2015.

58.More option for OCD patient https://iocdf.org/about-ocd/treatment/ Retrieved at 16sep2015

59. Additional treatment of OCD https://iocdf.org/about-ocd/treatment/ Retrieved at 16sep2015.

60. Brain Surgery for OCD https://iocdf.org/about-ocd/treatment/ Retrieved at 16sep2015.

61. Anterior cingulotomy https://iocdf.org/about-ocd/treatment/ Retrieved at 16sep2015.

62.Gama knife https://iocdf.org/about-ocd/treatme Retrieved at 16sep2015.

63.D.B.S https://iocdf.org/about-ocd/treatment/ Retrieved at 16sep2015.

64.Famous people with OCD http://www.disabled-world.com/artman/publish/famous-ocd.shtml Retrieved at 10Aug2015.