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Unraveling the complexity of obsessive-compulsive disorder: A comprehensive review

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ABSTRACT

Repetitive, intrusive thoughts (called obsessions) and repetitive behaviors (called compulsions) are hallmarks of obsessive-compulsive disorder (OCD), a chronic and crippling mental health illness. The goal of this review is to give a thorough overview of OCD, covering its description, etiology, epidemiology, symptoms, diagnosis, available treatments, and management techniques. With a multiple etiology that includes genetic, neurological, cognitive, and environmental variables, OCD is a complicated condition. Cognitive-behavioral therapy (CBT), particularly exposure and response prevention (ERP), and drugs such selective serotonin reuptake inhibitors (SSRIs) are effective therapies for obsessive compulsive disorder. OCD is a severe mental illness that has to be identified and treated as soon as possible. Healthcare providers must have a thorough understanding of OCD in order to diagnose patients accurately and treat them effectively. This study offers a thorough analysis of OCD, emphasizing the need for more research, education, and awareness of this condition.

Keywords: Obsessive compulsive disorder, Anxiety disorder, Congestive behavior therapy, Exposure and Response prevention.

INTRODUCTION

People with obsessive-compulsive disorder (OCD) have recurrent, unwanted, and uncomfortable thoughts, ideas, urges, or illustrations. OCD sufferers feel compelled to take certain actions above and beyond again, which are recognized as addictions or customs, in an effort to lessen such thoughts. According to research, the lifetime prevalence of OCD in the general population is approximately 3.5%; the disorder typically manifests in childhood or adolescence and peaks at the age of fourteen. It is possible for cases to begin in adulthood between the ages of 18 and 25; this peak may include recently diagnosed cases that may have begun earlier in their course but were not yet identified [1,2]. According to studies, between 23 and 34 percent of OCD sufferers also fit the DSM-IV criteria for OCPD. According to the SCID, 20% of the 262 OCPD participants in the study also satisfied the DSM-IV criteria for OCD [3].

Clinical manifestations- Obsessions (repeated unwanted thoughts or urges), compulsions (repeated, ritualized behaviors or thoughts), and primarily avoidance behaviors are the hallmarks of OCD. There are four dimensions of symptoms: 1) hoarding, 2) symmetry and order, 3) cleanliness and washing, and 4) obsessions and checking. The length of routine activities was examined in a recent publication [4]. Compared to healthy controls, OCD patients who experienced OCS during a particular daily living activity reported taking longer to complete 10 out of the 13 activities that were questioned (such as grocery shopping). More severe OCS was generally associated with longer durations. For the OCRD spectrum, distinct chapters have been added to the current DSM-5 and ICD-11criteria. The classification of OCD with 1) primarily obsessive thoughts or ruminations, 2) primarily compulsive acts, and 3) mixed obsessive thoughts and acts is not included in the ICD-11 criteria, in contrast to the ICD-10 criteria. Only one OCD combined type can be coded in ICD-11 due to the mixed type's predominance. Additionally, the ICD-10's previous requirement of a minimum symptom duration of two weeks was eliminated. The OCS are presumed to be time-consuming (i.e., require more than one hour per day) in the ICD-11 criteria [5]. The study of OCD's epidemiology examines the disorder's prevalence, how it spreads, and the factors that affect how it manifests in various demographic groups. OCD prevalence at some point in their lives, 1.6% to 2.3% of the general population will suffer from OCD. OCD is thought to affect 0.5% to 1.0% of people in any given year [6]. The four domains of home, work, relationships, and social life were evaluated for OCD-related impairment using the Sheehan Disability Scale (SDS). SDS scores of 7–10 indicated severe impairment, 4–10 indicated severe or moderate impairment, and 1–10 indicated any impairment. Age at Onset OCD typically strikes between the ages of 19 and 20. Differences in Sex with a ratio that ranges from roughly 1.2:1 to 1.5:1, OCD is slightly more common in women than in men [7].

Factors of Etiology and Risk OCD has numerous underlying causes, including genetics, brain biology,

and environmental variables. Factors related to genetics: There may be a hereditary component to OCD since it appears to run in families. Numerous gene variants related to serotonin, dopamine, and glutamate control have been found by researchers to potentially contribute to OCD. – Glutamate neurotransmission is linked to the SLC1A1 gene, which has also been linked to OCD. The COMT gene has been connected to OCD and influences how dopamine is transported. Accordingly, the MAO A gene has been linked to OCD and plays a role in serotonin transmission [8]. According to research on twins, identical twins are more likely than fraternal twins to suffer from OCD. First-degree relatives are far more likely to have the illness, which indicates a strong genetic relationship. Research indicates that between 45% and 65% of OCD cases are heritable [9]. The most studied alterations in human epigenetics are microRNAs (miRNAs) and DNA methylation (DNAm). Epigenetic changes are positioned as potential biomarkers for gene–environment interactions in the pathophysiology of OCD because DNA patterns can be acquired or lost over the course of a person's lifetime and are sensitive to environmental influences. In a two-step EWAS, found 305 differentially methylated CpG sites in a sample of 185 OCD sufferers and 199 controls in Germany. According to this theory, insulin may be hampered by dysregulated striatal dopaminergic transmission. Genes linked to the neurobiological processes underlying OCD, including BTBD3, DLGAP2, DLG2, GABBR1, MOG, BDNF, SLC6A4, and LEPR, have also been shown to exhibit epigenetic regulation [10].

The neurobiological theory of OCD suggests that issues with brain structure and function, particularly in regions such as the orbitofrontal cortex, anterior cingulate cortex, and basal ganglia, are the cause of the disorder. The orbitofrontal cortex supports executive functioning, impulse control, and decision-making. OCD symptoms may arise from problems in this area. The anterior cingulate cortex plays a key role in motivation, conflict observation, and mistake recognition; anomalies in this area can lead to repetitive behaviors that are characteristic of OCD [11].

Compulsive behaviors can result from issues with the basal ganglia, which are crucial for habit formation and movement control. OCD is also linked to problems in the cortico-striato-thalamo-cortical (CSTC) circuit, which controls impulse control and the development of habits [12,13]. Neurotransmitter Imbalances: Selective serotonin reuptake inhibitors (SSRIs) are useful treatments for OCD, and they are linked to serotonin imbalance. An imbalance in glutamate may potentially play a role in obsessive behaviors, as may increase dopamine activity [14,15].

Environmental Factors: Abuse or neglect are examples of stressful or traumatic events that can increase the likelihood of developing OCD. Children with PANDAS (Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections) may experience OCD symptoms that appear suddenly. Low birth weight, inherited maternal illnesses, or pregnancy issues have also been associated with an increased risk of OCD. Both classical and operant conditioning have the potential to reinforce compulsive behaviors [16,17]. Even though the precise pathophysiology of OCD is unknown, there is growing evidence that one of the primary contributing factors is abnormalities in the cortico-striato-thalamo-cortical (CSTC) circuits [18]. Glutamate is the main neurotransmitter in the CSTC, and studies suggest that people with OCD may have abnormal glutamate metabolism. Hyperactivity in the anterior cingulate, ventromedial striatum, and orbitofrontal cortex has been connected to OCD behavior. Moreover, high glutamate levels result in oxidative stress and excitotoxicity. Lower glutamate concentrations in the anterior cingulate, however, were linked to more severe symptoms in a group of women with OCD. Evidence for glutamate's suggested role in the pathophysiology of OCD comes from its pro-oxidant properties and activity in the CSTC. Thus, glutamate-modulating medications are increasingly being used to treat OCRD and OCD. The glutamate-modulating drugs riluzole, NAC, memantine, topiramate, lamotrigine, and glycine have been investigated for OCD and OCRD; however, contradictory results have been reported [19].

Support Vector Machine [SVM] is frequently used to identify OCD and forecast treatment response. By transforming the input features into a higher-dimensional feature space, SVM can produce nonlinear discriminant functions. This can improve classification performance by obtaining more complex input features through the use of nonlinear kernel functions rather than nonlinear SVM functions. Aydin et al. identified OCD with 85% accuracy by using SVM as a classifier with a Gaussian kernel function. By estimating the EEG complexity in multiple brain areas using permutation entropy, they showed that the OCD group had lower prefrontal and fronto-temporal EEG complexity than healthy controls [20].

EEG complexity has been used in a number of studies as a discriminative feature from EEG signals to identify mental illnesses and forecast the results of treatment. Since it gauges the level of complexity or randomness, entropy, a nonlinear attribute, is appropriate for time series that are nonlinear, complex, random, and non-stationary, like EEG signals. Additionally, another study that used fractal dimensions to measure the brain's complexity of information processing revealed that OCD patients had higher frontal fractal dimensions across all frequency bands [21]. The presence and intensity of obsessive-compulsive symptoms are evaluated using the FOCI self-report measure. Good divergent and convergent validity have been shown for the FOCI. The severity items in this sample had a good internal consistency (α=0.88) [22,23]. The three-item Sheehan Disability Scale (SDS) is a self-report tool used to evaluate how symptoms affect social, familial, and professional life. A visual analog scale, with 0 denoting not at all and 10 denoting extremely, is used to rate each item. Internal consistency in this sample was good (α=0.82) [24,25]. The 16-item Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF) is a self-report survey that evaluates the degree of satisfaction with different aspects of life during the previous week. The final two questions use the same 5-point Likert scale to measure overall satisfaction, while the first 14 questions list various areas of life and are scored from 1 = Very poor to 5 = Very good. The Yale-Brown Obsessive Compulsive Scale-II (interview and self-report) is a self-report or interview tool used to evaluate the existence and intensity of obsessive-compulsive symptoms. Ten severity items measuring the time, control, interference, and distress related to obsessions and compulsions are included in these measures, along with 67 checklist items listing potential obsessions and compulsions. Furthermore, there are two severity items that are unique to either obsessions (obsession-free interval) or compulsions (resistance). A 6-point Likert scale, ranging from 0 to 5, is used to rate each severity item; higher scores indicate a higher presentation of severity. The Y-BOCS-II interview has shown good validity and reliability, as previously mentioned [26,27].

Pharmacotherapy

First-line treatments for OCD are SSRIs (escitalopram, fluoxetine, sertraline paroxetine, and fluvoxamine) because of their demonstrated efficacy, safety, tolerability, and lack of abuse potential (Figure 1). Given that there are no discernible variations in the effectiveness of different SSRIs [28], the side effects of SSRIs may be a major factor in selecting a particular SSRI. When compared to other anxiety or depression disorders, OCD is generally treated with the highest dose of SSRIs that can be tolerated. To ascertain responsiveness to a specific medication, at least 8 to 12 weeks of treatment are frequently required. It is better to switch to another SSRI rather than using the augmentation strategy if treatment with an SSRI doesn't work. It is advised to move to clomipramine or augmentation techniques, such as clomipramine or atypical antipsychotics, if the response is insufficient after switching SSRIs. The first drug to effectively treat OCD was clomipramine, a serotonin-selective TCA. SSRIs have a more favorable side-effect profile than clomipramine, which has long been the gold standard for pharmacological treatment. Clomipramine has

therefore been proposed as a second-line treatment for individuals who do not respond to SSRIs.

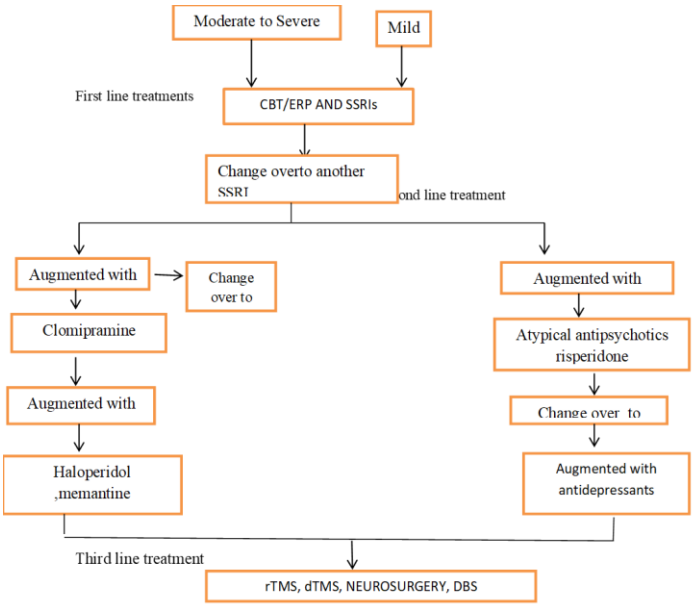

Figure 1: First line treatments of OCD

Glutamatergic drugs are used to treat obsessive-compulsive disorder. They can function chemically as ion channel modulators, glutamate co-agonists, receptor antagonists, and reuptake inhibitors to alter glutamate transmission. These drugs are generally well tolerated. Some of the agents have, however, been linked to particular adverse effects. The different drugs used, their suggested ideal dosages, and particular side effects are compiled in Table 1 [29].

Table 1: Summary of glutamatergic medication used in OCD treatment

Drug	Dose/day	Adverse effects
Memantine	20 mg	Headache, drowsiness and lethargy
N-acetyl cysteine	2400 mg	Vomiting, flatus, gastroesophageal reflux
Lamotrigene	100 mg	Tremors, difficulty sleeping
Topiramate	<200 mg	Weight loss and paresthesia
Riluzole	100 mg	Hepatotoxicity, low white blood cell count, lung inflammation
glycine	60 mg	Unpleasant taste, sedation

As a noncompetitive NMDA receptor antagonist, memantine blocks ion channel pores, decreases calcium influx, and preferentially targets extra synaptic NMDA receptors. Studies indicate that it may decrease the activity of the CSTC direct pathway, alter the connectivity between ACC and OFC, and cause abnormal activity between the hippocampus and amygdala, all of which are linked to the pathophysiology of OCD [30]. The antiepileptic drug lamotrigine has also been used to stabilize mood. It decreases glutamate outflow by blocking presynaptic neurons' voltage-gated calcium channels. Patients with OCD and bipolar disorder and schizophrenia/schizoaffective disorder also reported these advantages. Lamotrigine augmentation's effectiveness in treating OCD has since been investigated in two DBRPCTs. It was demonstrated to improve affective symptoms and semantic fluency in the treatment group while also lowering YBOCS compulsion scores [31]. Ketamine acts on the NMDA receptor as an open-channel nonselective antagonist. Despite being a receptor antagonist, it uses intricate mechanisms to raise glutamatergic activity in the prefrontal cortex at low doses. Intravenous ketamine infusion has so far been shown to have anti-obsessional effects in a randomized cross-over trial and a few open-label trials [32]. The anti-obsessional effects of ketamine using various administration methods and multiple sessions require further well-controlled trials with larger clinical samples.

Paroxetine was shown to be equally effective when switched to serotonin–norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine; in refractory cases, paroxetine may be more effective than venlafaxine. As per the WFBSP guidelines, the lack of placebo-controlled trials led to the rating of venlafaxine, noradrenergic, and specific serotonergic antidepressant (NaSSA) mirtazapine at level of evidence B and recommendation level 2 [33]. Tolcapone is an inhibitor of the catechol-O-methyl-transferase (COMT) enzyme that improves dopamine transmission in the brain. A randomized, placebo-controlled crossover trial found it to be effective, but more research is required to determine whether it is a viable treatment option for OCD [34].

Psychotherapy

Psychoeducation is an educational approach designed to give psychiatric patients and their families the knowledge and skills they need. In order to establish a solid foundation for future treatment success, it is important to provide information about symptoms, prognosis, stigma, prejudice, and family accommodations. Family accommodation has been proposed as a key element of psychoeducation because recent research indicates that it is more successful in lowering OCD symptoms, especially in younger patients [35].

CBT is the most successful evidence-based treatment for OCD in psychotherapy, and all treatment guidelines recommend it as a first-line treatment approach. For OCD patients with mild to moderate symptoms, CBT/ERP monotherapy is advised. Meta-analyses of RCTs have consistently shown that CBT/ERP therapy significantly improves OCD symptoms [36], despite the limitation that the majority of psychotherapeutic trials included patients who were prescribed stable doses of SSRIs [37]. Cognitive reappraisal, behavioral intervention, and restructuring are some of the elements that make up CBT. The latter is the most commonly used psychological treatment of choice for OCD, usually in the form of ERP. ERP is a manualized, structured psychological intervention for OCD that consists of avoiding compulsive rituals and gradually and repeatedly confronting internal and external obsessional cues. With an emphasis on the inference process that results in obsessive beliefs and assumptions, IBT has been demonstrated to be a successful therapeutic approach for OCD. IBT is useful in lowering OCD symptoms, according to randomized controlled trials. By combining with CBT, it is currently developing into inference-based CBT [38].

ACT uses values-based approaches to promote behavioral commitment and psychological flexibility through the practice of acceptance and mindfulness. Despite obsessions, anxiety, and compulsions, ACT can support OCD patients in accepting their experiences and working toward meaningful aspects of their lives. ACT is useful for OCD, according to a recent meta-analysis that included a limited number of studies, but more thorough RCTs with larger sample sizes are required to confirm this [39]. ILT-based methods based on the theory of inhibitive learning. A new basis for comprehending how ERP can be optimized to overcome a significant portion of non-responders is offered by the inhibitory learning framework. The effectiveness of ERP, according to ILT, lies in its ability to support the creation of new safety-based learning that is powerful enough to thwart more traditional fear-based learning. At a longer follow-up, one controlled trial demonstrated that ILT-based ERP in combination with SSRI was more effective than SSRI alone [40].

Neuromodulation and neurosurgery

Approximately 20-25% of OCD patients do not respond to common psychological and pharmacological treatments. Typically, the main nodes in the cortico-striato-thalamo-cortical (CSTC) circuits linked to

OCD are the focus of neuromodulatory and neurosurgical therapies. Both noninvasive and invasive techniques, such as deep brain stimulation (DBS), repetitive transcranial magnetic stimulation (rTMS), and transcranial electric stimulation (tES), are included in neuromodulation.

Refractory OCD is treated with neuro-surgical techniques. Depending on the frequency of magnetic stimulation, rTMS modifies the excitability or inhibition of the major cortical nodes in the CSTC pathways by inducing noninvasive stimulation. With low-frequency stimulation, rTMS targets cortical areas such as the OFC and supplementary motor area (SMA) and has been shown to be effective in treating OCD [41]. Anterior cingulate cortex (ACC) and other deeper regions are more likely to be directly modulated by Deep TMS, a novel form of rTMS that uses distinct H-coils. In 2018, Deep TMS received FDA approval for treating OCD, and it was recently shown to have a long-lasting effect [42].

Transcranial direct current stimulation (tDCS)

A weak electrical current is applied to the scalp in tDCS, a type of tES, to cause focal and cortical modulation. Both small open-label and sham-controlled RCTs have provided encouraging evidence that tDCS has potential efficacy in treating OCD patients, despite inconsistent stimulation protocols. In order to determine the ideal stimulation parameters, future studies should involve larger representative samples of OCD [43].

Deep brain stimulation

An electrode that can produce electrical stimulation in particular subcortical areas of the neuronal circuitry is implanted neurosurgical as part of the potentially reversible and adjustable deep brain stimulation (DBS) procedure. Striatal regions, such as the thalamus/subthalamic nucleus or the anterior limb of the internal capsule/nucleus accumbens, are possible DBS targets for OCD [44].

Neurosurgery

In traditional neurosurgery, certain areas of the CSTC circuit that necessitate skull opening are subjected to irreversible focal tissue ablation. "Invasive" stereotactic surgery or "less-invasive" ablation using focused ultrasound or image-guided gamma radiation can both help precisely target the lesion. Although they are not common, adverse effects can vary depending on the surgical procedure and include headache, nausea, vomiting, weight gain or loss, personality changes, seizures, and decreased cognitive function. Magnetic resonance-guided focused ultrasound surgery (MRgFUS) and gamma knife radiosurgery are two more recent, less invasive techniques that do not require opening the skull. In recent open trials, the latter offers the possibility of safer and more economical surgical techniques, while the former may have negative effects related to radiation dose.

CONCLUSION

OCD is a complex mental health condition characterized by recurrent unwanted thoughts (called obsessions) and repetitive behaviors (called compulsions). OCD's precise causes are unclear, but research indicates that a number of factors, including genetics, brain function, cognitive patterns, and environmental influences, can contribute to the disorder. Fortunately, there are efficient interventions for OCD, such as selective serotonin reuptake inhibitors (SSRIs) and cognitive-behavioral therapy (CBT), particularly exposure and response prevention (ERP). CBT plus medicine may be the most beneficial combo for many people. Early detection and treatment of OCD is essential since delaying treatment raises the chance of developing other mental health conditions, worsens symptoms, and reduces quality of life. Thus, it's critical that medical professionals understand the symptoms of OCD and provide appropriate assistance. OCD is a difficult illness that has a significant negative impact on people's lives and society. For those impacted, improvements in brain research and treatment techniques have led to better results. In order to improve recovery rates and general quality of life, future research should focus on tailored medicines that pinpoint particular indicators of how well patients react to treatments and investigate novel targets.

Conflict of interest

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