Obsessive-Compulsive Disorder

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Abstract

Introduction: Obsessive-Compulsive Disorder is a highly-disabling mental illness that results in the suffering of many individuals around the world. In this article, the disorder is fully looked into: how it occurs, its pathophysiology, its treatment, and the suggested future advances in the management and study of this disorder. **Research Methodology:** A number of search engines (Google Scholar, PubMed, google.com, etc.) were searched with the aforementioned keywords. This resulted in a plethora of results. These were, in turn, filtered through the known criteria regarding their eligibility for usage in review articles. Some sources were inaccessible and were, ergo, excluded from being used here. Moreover, other results were found to be published in predatory journals. Duplicate findings were, of course, eliminated. Following this, the results were filtered based on their relevance to the topic of the article. The data included here was revised and found to be eligible for use and then, and only then, were they included in this article.

Keywords: OCD; Obsessive-Compulsive Disorder; Neuropsychiatry;

Introduction

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) categorizes OCD (Obsessive-Compulsive Disorder) under 'Obsessive-Compulsive and Related Disorders' (ORCD) (1) and defines it as 'characterized by the presence of obsessions and/or compulsions' (1). ORCD is highly prevalent with 9.5% of the population suffering from it (2). Around 58% of those suffering from OCD will suffer from another one of the ORCDs (3). OCD is, by no means, a newly discovered illness, despite our understanding of it evolving. In fact, OCD has been discussed in religious texts dating at least as far back as the 17th century (4). It is, according to the World Health Organization (WHO), one of the most disabling disorders we know of (5). It is the 4th most common mental disorder, greatly disturbing patient's quality of life through disabling them from conducting their daily activities (6,7). CY-BOCS can be used to assess the severity of OCD (8–10). Considerable evidence exists supporting the hypothesis that anxiety and OCD share a dopaminergic mechanism of action; this possibly justifies why they present together in some instances (11–15). Despite this, the evidence for dopaminergic dysfunction in other disorders, such as tic disorders is far greater than that in OCD. However, given the high co-morbidity between the two, there is reason to believe that our understanding of the dopaminergic dysfunction in tic disorders may play a role in our understanding of OCD

(16).
Non-human primates have exhibited symptoms of OCD and, ergo, manifested themselves as an excellent system for study of the disorder and the its associated cognitive-motor dysfunctions (17–21). The close evolutionary adjacency to humans as well as their overall cognitive and emotional abilities aids greatly in translating findings to humans (22–25). It has been suggested that there exists a correlation between a history of OCD and a number of psychiatric disorders (26–34). Similarities encompassing impulse control disorders (ICDs) and OCD highly suggest the possibility of them being co-morbid (35). OCD is a medical disorder that, in addition to being highly debilitating, is of significant economic burden, as proven in 2023 study (36); further increasing the necessity of the publication of works such as this.

Research Methodology:

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Clinical presentation and diagnostic modalities:

An excellent summarization of OCD symptoms exists which states that OCD symptoms can be divided into 1) contamination fears and obsessive cleaning, 2) obsessive thoughts about causing harm and compulsive checking rituals, 3) obsessions with symmetry and compulsive ordering, and 4) obsessions relating to the unwarranted collection of objects and hoarding (37).
Many clinical presentations exist in regards to OCD and is, in a number of instances associated with other disorders, such as pathological gambling (PG). Many times, behavioral flexibility issues are noted during the examination. A possible account for these associations may be justified in the neural associations responsible for the reward-learning mechanism being faulty (38).
No laboratory investigations are diagnostic of OCD.
A study reported that as much as 69% of patients presenting with OCD presented with other psychiatric comorbidities, mood disorders and anxiety disorders were the most common at 48% and 32%, respectively (39). More data illustrated a lifetime comorbidity of major depressive disorder (MDD) in 50%, social phobia in 26%, specific phobia in 26%, generalized anxiety disorder (GAD) in 24%, dysthymia in 23%, and psychotic disorder in 4% (28). Another study reported findings that indicate higher rates of symptoms being in correlation with increase in depression severity (40).
Whether or not the associated comorbidities are to be considered primary or secondary to OCD is still a topic of controversy (41). A suggestion has been made to solve this conundrum; that is, to introduce comorbidity as a sub-classification of OCD (42). A Swedish study found that 'lifetime history of GAD, psychotic disorder, and sub- stance abuse were related to worse prognosis of OCD' (41); the same study also illustrated how an increase in comorbid conditions is inversely proportional to likelihood of recovery from OCD.
OCD can, as aforementioned, co-occur with a number of psychiatric illnesses. For example, Bipolar disorder (BD). When this happens, it has been found that the symptomatology of OCD does not differ as opposed to individuals suffering from OCD without BD (43). In fact, the comorbidity rate is between 11-21% (44).
Other instances in which OCD may present are during the perinatal period. Studies indicate between 2.2% and 16. 9% of women experience OCD in the post-partum (45,46) This period has been identified as one in which

there exists an increased vulnerability to onset or exacerbation of OCD (47), this was found to be more so in women (48). These usually have a theme of ensuring the infant's safety and/or preventing harm (47,49,50).
Obsessive symptoms of a sexual and/or violent/harmful nature seem to become manifest in OCD patients going through post-partum as opposed to during pregnancy or any other point in life (51). The characteristic OCD symptoms (those regarded with cleanliness) seem to occur less frequently during the post-partum period (47).
In so far as the co-occurrence between OCD and schizophrenia (in terms of onset) are concerned, 40% of patients reported the obsessive symptoms manifesting prior to psychosis, another 40% reported them occurring following them, and the remaining 20% reported them occurring concurrently (52). Moreover, 12-14% of schizophrenics meet the diagnostic criteria for OCD (52).

Genetic and Neurological Pathophysiology of OCD:

Work by Gasso and colleagues (53) revealed a total of 6 polymorphisms in pediatric individuals with OCD. These were SLC1A1 rs3087879, SLC6A3 rs4975646, CDH9 rs6885387, DRD3 rs3773679, NGFR rs734194, and rs2072446. There is significant evidence regarding the existence of a correlation between serotonergic imbalance and OCD, namely a polymorphism in 5-HTT (SLC6A4) has been connected to OCD patients (54,55).
Despite the serotonergic disruption seeming rather convincing, it is important to note that it is still based purely on empirical evidence and results that are, at best, controversial (56).
RNA sequencing is one of the more modern methodologies used to assess the roles neurons and astrocytes play in disorders pertaining to the brain (57).
In so far as pediatric patients are concerned, there is sufficient reason to believe that alterations to the corpus callosum, cingulum, arcuate fasciculus, uncinate fasciculus, inferior longitudinal fasciculus, superior longitudinal fasciculus, inferior fronto-occipital fasciculus, corticospinal tract, forceps minor and major, and the cerebellum are to be associated with signs and symptoms of obsessive-compulsive disorder (6). It seems highly plausible that these are structural phenotypes of the aforementioned genetic variant (6,53)
Furthermore, glutamate was found in high concentrations in OCD patient's Cerebro-Spinal Fluid (CSF) (58,59). This is of importance as a number of studies have found an association between polymorphisms in the genes SAPAP3 and SLC1A1 and OCD (60–62).
Researchers from China compared the gray and white matters of the brains of rhesus monkeys that exhibited sequential motor behaviors (SMBs) with monkeys that did not exhibit SMBs and found that the fractional anisotropy (FA) value of the corpus callosum (CC) was found to be lower in monkeys exhibiting SMBs (17).
Certain imaging modalities seem to possibly be of immense use in the near future when it comes to diagnosing OCD (63); namely, support-vector machine (SVM) model of combined functional Magnetic Resonance Imaging (fMRI) is promising as of this writing.
A recently conducted study found that alterations in the connections consisting the subcortical-cerebellum network as well as 'individualized structural covariance aberrance' being characteristic of OCD (64). These are significant findings as they immensely aid in increasing our understanding of the taxonomy of OCD.
In addition to the aforementioned, involvement of the cortico-striato-thalamo-cortical (CSTC) pathways, limbic regions as well as the reward circuit seem possible (65–69)
Imaging indicates the involvement of the cerebellum, parietal cortex and limbic cortex (35,70). Involvement in these areas can result in 'over-valuation of ideas with inhibited behavioral control' (35).
Another interesting finding in regards to imaging suggests that patients with poor insight into their OCD, when provoked, show changes in activation in circuits responsible for emotional and sensory processing as well as cognitive control (71).

Treatment Protocols:

In summary, treatment of OCD can be divided into: a) Psychotherapy, and b) Pharmacotherapy. Despite these being the guidelines in place, they prove ineffective in ~10% of cases (16).
The first-line psychotherapeutic method is Cognitive-Behavioral Therapy (CBT) including exposure and response prevention, which has been found to be effective in causing a decrease in OCD symptoms (21,72–76). Major issues regarding CBT completion such as is its limited accessibility, financial cost, and other factors should be placed into consideration (16,77).
Of the most effective pharmacotherapies is introduction of Selective-Serotonin Reuptake Inhibitors (SSRIs). In fact, they are the first-line pharmacological treatments (72). SSRI treatment (specifically fluoxetine) was found to significantly decrease the time of SMBs in rhesus monkeys (17). Further pharmacological interventions are listed to be introduced, when necessary (such as clomipramine (78) (which is no longer recommended as it may worsen OCD symptoms (16,79)), glutamatergic agents (16) and venlafaxine (80–82)).
In a study conducted on human participants, 40% of patients prescribed sertraline experienced remission (83). Published data indicates that 25-60% of individuals suffering from OCD continue to suffer from symptoms following the use of SSRIs and clomipramine (84,85).
As of this writing, a combination of low-dose aripiprazole and risperidone seems to be the most effective in controlling OCD symptoms (16,86–88).
Despite the cumulative efforts set forth, there still remains the issue of ~10% of patients still suffering from disability due to OCD despite correct treatment as per listed guidelines (89).
If the aforementioned treatment modalities fail to bring about desired results, data is suggestive of the use of Deep Brain Stimulation (DBS) as a final treatment modality (90). DBS is to be used on patients meeting certain criteria; these are (91):

a) Non-response to SSRIs at maximum dosage for at least 12 weeks
b) A full course of clomipramine (maximum dose) for at least 12 weeks
c) Addition of an atypical antipsychotic for at least 8 weeks
d) A full course of CBT
e) Y-BOCS = at least 28 points
f) Global Assessment of Functioning (GAF) score of less than 45 points
g) OCD duration of 5 or more years

DBS has been found to be of immense impact on the quality of life of those who underwent it (92); these results are rather similar to those reported by individuals suffering from Parkinson's when administered the same treatment (93).
There are adverse effects that need be placed into considerations whenever DBS is being considered for treatment. These side effects include:

a) Hypomania (16)
b) Intracranial infection (16)
c) Intracranial bleeding (16)
d) Epileptic seizures (16)
e) Disturbed sleep (16)
f) Weight gain (16)
g) An increase in anxiety (16)
h) Increased risk of suicide (controversial) (94)

Another treatment proposed is trasncranial Direct Current Stimulation (tDCS) which showed that anodal pre-

SMA tDCS could possibly improve symptoms of OCD (95). Side effects reported included fatigue, tingling, itching, headache, nausea, and insomnia (96). tDCS has an excellent safety profile; however, 'the data on the potential efficacy of tDCS in OCD do not currently justify systematically proposing this therapy in resistant or refractory cases' (16).
Bilateral low-frequency repetitive trasncranial magnetic stimulation (rTMS) targeting the supplementary motor area (SMA) was found to reduce OCD symptoms (97).
During follow-up, relapses may, and do, occur. However, 90.3% of pediatric patients seem to improve at the end of 3-year long follow-up (98).
Anti-psychotics such as aripiprazole, risperidone, and haloperidol have all shown positive results when used as adjuvant therapies in the treatment of OCD (35,99). However, there have been cases in which aripiprazole seemed to induce OCD in patients, or at least exacerbate the disorder (100–104) Other antipsychotics such as quetiapine, olanzapine, and paliperidone did not yield such positive results (86,105–107). In fact, olanzapine and clozapine seem to induce OCD symptoms (108). Of course, OCD is, at many times, a comorbidity of conditions which require treatment with antipsychotics, ergo, it is important that iatrogenic causes are excluded (52).
Aripiprazole-induced OCD seems, as per reports, to manifest with hypersexuality, compulsive shopping, and hyperphagia (35).
Not much data exists in regards to the management of anti-psychotic-induced OCD. One study looking into the effects of clozapine-induced OCD reported that introduction of aripiprazole resulted in clinical improvement (109). Similar results were reported in regards to olanzapine-induced OCD being treated using aripiprazole (35).
Data indicated the addition of an SSRI to anti-psychotic treatment may be of benefit in regards to anti-psychotic-induced OCD (110).
In some instances, patients suffering from OCD will not respond to the aforementioned treatment modalities. When that is the case, the patient is deemed either resistant or refractory. A patient is deemed resistant if they have been placed on the highest tolerated dose of SSRIs/clomipramine for at least 12 weeks combined with, at least, 30 hours of Cognitive Behavioral Therapy (CBT) yet exhibited a reduction of under 25% on the Yale Brown Obsessive-Compulsive Scale (Y-BOCS) (16). On the other hand, a patient is deemed suffering from refractory OCD when placed on three antidepressants, with the inclusion of clomipramine, as well as two trials on atypical anti-psychotics (111). Some have proposed the refractory label be reserved to those who do not benefit at all (or even deteriorate) when treatment is administered (112).
As of this, evidence is strongly suggestive of the use of (DBS) in treatment of such patients (113). In fact, a study reported improvement in patient's YBOCS in the matter of 6-9 weeks following DBS, with an average improvement rate of 45% during the final follow-up session (114).
An experiment took place in which Rituximab was introduced to OCD patients but yielded no significant reduction in symptoms (115).

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