International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

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ARTICLE TITLE	OBSESSIVE COMPULSIVE DISORDER - A REVIEW OF TREATMENT METHODS
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3714
RECEIVED	02 August 2025
ACCEPTED	14 September 2025
PUBLISHED	16 September 2025
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OBSESSIVE COMPULSIVE DISORDER - A REVIEW OF TREATMENT METHODS

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ABSTRACT

Obsessive Compulsive Disorder (OCD) is a neuropsychiatric disorder characterized by the presence of recurring intrusive thoughts (obsessions) and compulsive actions (compulsions).
In the United States of America the prevalence of lifetime OCD in adult patients is estimated to be around 2,3% of the population, while 12-month OCD cases stand at 1,2%. Diagnostic criteria include:
- Presence of obsessions, compulsions or both
- Obsessions or compulsions are time-consuming or cause a lot of distress, or impair other aspects of life
- The symptoms are not caused by substance abuse or another medical condition
- The disorder is not better explained by symptoms of another mental disorder

Zohar-Fineberg Obsessive Compulsive Screen is a questionnaire which helps with assessment of OCD. Main lines of treatment consist of pharmacotherapy and psychotherapy. Pharmacotherapy relies primarily on selective serotonin reuptake inhibitors, while other medications include serotonin-noradrenaline reuptake inhibitors, clomipramine, neuroleptics and glutamate modifiers. Psychosurgery and neurostimulation both invasive and non-invasive, is reserved for treatment-resistant cases of OCD.

KEYWORDS

Obsessive-Compulsive Disorder, Selective Serotonin Reuptake Inhibitor, Cognitive Behavioral Therapy, Exposure and Response Prevention Therapy

CITATION

Michał Zdybel, Bartłomiej Józef Rdzanek, Weronika Skrzypek. (2025) Obsessive Compulsive Disorder - A Review of Treatment Methods. *International Journal of Innovative Technologies in Social Science*. 3(47). doi: 10.31435/ijitss.3(47).2025.3714

1. Introduction and purpose

Recurring intrusive thoughts (obsessions) and compulsive actions (compulsions) are characteristic symptoms of Obsessive-Compulsive Disorder that can occur separately or simultaneously. This disorder can often cause impairment in patients' everyday life. The main course of treatment consists of psychological therapy, pharmaceuticals, or surgery [1,2]. It is believed that compulsions are actions taken in response to obsessive thoughts [3]. This work is aimed at a review of available treatment methods. The work has been constructed by a review of articles available at PubMed database regarding the Obsessive Compulsive Disorder and its treatment.

2. State of Knowledge

2.1. Diagnosis

The tools used for screening of OCD are Zohar-Fineberg Obsessive Compulsive Screen (ZF-OCS) consisting of 5 questions related to OCD symptoms [1,4] and Obsessive-Compulsive Inventory which consists of 42 items with 7 subscales regarding: washing, checking, doubting, ordering, obsessing, hoarding and mental neutralizing, each rated on a scale from 0 to 4 [1]. The Obsessive-Compulsive Inventory-Revised (OCI-R) contains 18 items and 6 subscales. It contains less questions than OCI, making it easier to use repeatedly [1]. Pampaloni et al suggests that OCI and OCI-R are better screening tools when OCD is already suspected than ZF-OCS due to the previous also scoring the severity of the symptoms [1].

Obsessive Compulsive Disorder used to be categorised as an anxiety disorder under the DSM-4 however in DSM-5 it has been moved into the “Obsessive-Compulsive and Related Disorders” [1]. The diagnostic Criteria consists of:

A. Presence of obsessions, compulsions or both

B. Obsessions or compulsions are time-consuming or cause a lot of distress, or impair other aspects of life

C. The symptoms are not caused by substance abuse or another medical condition

D. The disorder is not better explained by symptoms of another mental disorder [3].

The Yale-Brown Obsessive Compulsive Scale is used to measure severity of OCD symptoms without specifying the type of obsession or compulsion. [5]

Patients with OCD feel shame related to their symptoms, especially obsessions related to sexuality, violence and religion [6], which can cause troubles with disclosing them to a physician [1,6].

It is proposed that different subtypes of OCD require different therapeutic approaches. Pampaloni et al. suggests that some types of OCD like ones with stronger presence of sexual or religious obsessions may benefit from early addition of weak antipsychotics and cognitive therapy in addition to the baseline Selective Serotonin Reuptake Inhibitor (SSRI) treatment, rather than Exposure and Response Prevention therapy or SSRI alone [1,7].

Assessment of the degree of insight has an impact on therapy and it may be done during clinical assessment or Cognitive Behavioral Therapy. Pampaloni et. al also presents scales for measurement of this variable such as an element of YBOCS [1,5] and Overvalued Ideas Scale [1,8] and Brown Assessment of Belief Scale [1,9]. Moreover in their work they propose performing home visits, as they may allow for a more thorough assessment of patients’ daily difficulties such as rituals and routines like cleaning or checking.

Aside from the patient, the disorder also affects their family and close relationships. Involvement of family can have an impact on the course of OCD and its treatment. It is proposed that therapies that also target the patient's family accommodation may improve the outcomes in pediatric OCD [1,10]. Lebowitz et al. propose that there is an association between family accommodation and psychopathological severity, and less satisfying clinical outcomes [10].

According to some studies, around half of the patients with OCD didn’t respond to first-line treatment with SSRI [11,12]. To assess future treatment, it might be helpful to evaluate past pharmacological history including dosage, duration of treatment and side effects [1].

Disorders that should be considered in differential diagnosis while assessing OCD are: anxiety disorders, major depressive disorder, other obsessive-compulsive and related disorders, eating disorders, tics, psychotic disorders [1].

2.2. Epidemiology

In the United States of America the prevalence of lifetime OCD in adult patients is estimated to be around 2,3% of the population, while 12-month OCD cases stand at 1,2% [13]. OCD develops before 10 years of age in a quarter of the males, while females are often affected during adolescence. OCD usually affects individuals from 18 to 29 years of age, some onsets happen in patients older than 30 years of age [3]. OCD

symptoms can last for decades, however many patients can achieve remission [3]. OCD often co-occurs with other disorders, most common of those are anxiety disorders, mood disorders, impulse-control disorders and substance use disorders. Other disorders that commonly coexist are tic disorders and obsessive compulsive and related disorders (OCRD) [3,13].

2.3. Etiology

Etiology of OCD consists of cognitive, genetic, molecular, environmental and neural variables [14]. Recent studies suggest that imbalance in the habit learning system and goal-directed system plays an important role in the pathophysiology of OCD. Cortico-striatal-thalamo-cortical circuitry loop is involved in habits. Hyperactivity in that region is associated with high levels of glutamate and GABAergic transmission dysregulation [15]. The loop is made of two pathways: direct and indirect. The direct pathway is responsible for behavior initiation while the indirect one inhibits or modulates it [14]. In OCD there has been detected hyperactivity in the direct pathway [14,16]. Other diseases that affect Cortico-striatal-thalamo-cortical can co-occur with OCD, such as Parkinson disease, Sydenham chorea, traumatic brain injury, Tourette syndrome, Huntington disease, and epilepsy [14,17,18].

The response to clomipramine (serotonin reuptake inhibitor) points to the importance of serotonin in pathogenesis of OCD. Some studies point at the dysfunction of the glutamatergic system in OCD, paving the way for testing of glutamate modulating substances [16]. There are also premises of dopamine's involvement in OCD, due to the efficacy of antipsychotic drugs [14].

There is also an autoimmune side to the etiology of OCD, specifically in the Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS). Patients with PANDAS are characterized with more rapid onset of symptoms, comorbid anxiety and emotional lability. The conditions mentioned above are mediated by autoimmune reactions in response to inflammation [14,19].

Another aspect of OCD etiology lies in behavioral learning-based models. Obsessive thoughts and coexisting fear develops through the pairing of a neutral stimulus with a distressing event. Later such stimulus becomes conditioned and triggers a conditioned response such as fear or obsessive thoughts. Later the patient learns that performing repetitive actions and rituals cause the obsessions to tone down, thus causing negative reinforcement by distress reduction. Due to this phenomenon, an Exposure and Response Prevention (ERP) therapy has been developed, which relies on exposure to situations that cause anxiety and prevention of ritualistic safety responses [20].

Cognitive errors and incorrect beliefs cause obsessional anxiety Such abnormalities include:

- heightened responsibility
- overemphasis on thought
- controlling thoughts
- overestimation of threat
- perfectionism
- intolerance of uncertainty

Cognitive therapy was created to combat these faulty beliefs. It usually relies on educating the patient about the implausibility and making them aware of the effect of those cognitions in influencing their thought processes [20].

2.4. Treatment

There are a variety of treatment options including psychotherapy, pharmacotherapy, neuromodulation and surgery [14,21].

2.4.1. Psychotherapy

In psychotherapy the cognitive-behavioral therapy (CBT) is one form of intervention used in treatment of OCD [14,21]. CBT relies on education, relaxation techniques, coping skills training, managing stress and training of assertiveness [22]. Exposure and response prevention (ERP) is considered to be the most effective form of psychotherapy [14,21]. ERP depends on provoking patients with stimuli to induce anxiety and inhibiting them from compulsive behaviors [14]. It has proven effective in OCD treatment both in individual and group settings, and both in-person and via internet sessions [14]. Some meta-analyses suggest that CBT is more effective than pharmacotherapy for the treatment of OCD, however such studies do not fully account for comorbidities, baseline severity of the disorder and other variables [3,14]. A study by Gerd Kvale et al.

provides promising data about intensive CBT sessions lasting four days in treatment of OCD [23]. Patients with cleaning and harm obsessions respond better to ERP and CBT than patients with compulsive hoarding. This weak response is explained by poor insight and coexisting personality disorders. Proposed modifications to therapy are among others motivational talks, focus training, time management training and longer treatment. Psychotherapy also provides a better response than Serotonin Reuptake Inhibitors in washing and cleaning compulsions. [21]

Obsession dominant patients (especially with sexual and religious obsessions) with relatively absent compulsions react worse to ERP and CBT. Until patients' beliefs about the nature of these obsessions are processed with cognitive methods, exposure techniques will be hard to implement due to patients' fear of their own thoughts [21].

Patients with contamination fear who refuse ERP therapy may answer well to danger ideation reduction therapy. This type of therapy doesn't contain ERP components, instead it focuses on reducing the expected danger of contamination [21].

Checking compulsions patients respond relatively well to ERP. Even better results are yielded when cognitive disorders such as increased responsibility for possible outcomes, exaggerated appraisal of harm, intolerance of uncertainty and memory distrust are corrected [21].

Psychotherapy and pharmacotherapy are often used together and this combination is especially beneficial in patients with more intense symptoms. In situations when SSRI therapy alone did not bring any improvement or brought minor improvement, CBT/ERP is a first-choice augmentation strategy [21,24].

2.4.2. Pharmacotherapy

Studies that compared different SSRIs did not conclude any of them being more advantageous than the rest. Choice of SSRI should be guided by differences in side effects and possible interactions with patient's medications. In OCD doses are higher than those used in treatment of depression, which introduces the risk of arrhythmia related to high doses of citalopram. If there is no response to SSRI, it is suggested to switch to another medication from this group. A recommended treatment strategy involves increasing the SSRI dose to its maximum across 4-6 week period and maintaining the dose for next 6-8 weeks for assessment of its efficacy. If the response is partial, then it is suggested to add booster medication such as second-generation antipsychotic instead of switching to another SSRI [21,22,25].

Clomipramine presents efficacy similar to or slightly higher than SSRIs. However due to the lower frequency and severity of side effects in SSRIs they are more favoured as first-choice medications compared to clomipramine [21,22].

Efficacy of SSRIs is high, however studies show that from 24 to 89% of patients showing positive results end up relapsing. In comparison ERP therapy has a 12% rate of relapse, which might point to higher efficiency, although it might stem from the fact that patients undergoing psychotherapy have more motivation to undergo treatment and have less anxiety making the exposure easier [21].

Children with OCD present weaker responses to SSRIs than adults. Poor insight, coexisting disorders, difficulty of family adjusting to illness of its member, cognitive deficits are reasons for worse response. Benefits of higher dosage of SSRIs have not been demonstrated in the pediatric population. While this group of pharmaceuticals has shown effectiveness in trials, there is concern regarding side effects in the pediatric patients population [21,25].

Pharmacological treatment is less efficient in treating obsessions without accompanying compulsions (especially of religious, somatic and sexual nature). Patients with somatic obsessions in particular present poor response to Serotonin Reuptake Inhibitors [21,26].

Serotonin Reuptake Inhibitors (SRI) should be given to patients who are considered for pharmacotherapy of OCD regardless of OCD subtype, as the characteristics of symptoms are not useful for planning of pharmacological treatment [21,26].

Other antidepressants like venlafaxine or mirtazapine show promising results in treating SRI resistant OCD and in case of poor or no improvement switching to venlafaxine is considered [3,21]. However, Pittenger et al. stated, that based on current state of knowledge serotonin-norepinephrine reuptake blockers cannot be recommended for monotherapy of OCD [25].

Another group of medications used in OCD treatment when SSRIs are insufficient are neuroleptics. Current standards state that when response to an SSRI drug is insufficient, another SSRI should be used. If the third attempt of treatment with SSRI doesn't bring expected results neuroleptics are used as augmentation of pharmacotherapy. If SSRI proves partially effective, neuroleptics can also be used earlier [3,21]. Neuroleptics

as an addition to SRI treatment can be useful when there are elements that increase the chances of success of pharmacotherapy, like severe obsessions, poor insight, and accompanying schizotypal personality disorder or tic presence. However use of second-generation antipsychotics can induce or increase severity of OCD/ORCD symptoms, as observed in patients treated for schizophrenia. Another issue with the use of neuroleptics are their adverse effects like metabolic problems, which is why it's important to consider the benefits and risks of such therapy in OCD patients. Atypical antipsychotics - aripiprazole and risperidone have the strongest proof of efficacy in augmentation of pharmacotherapy-resistant OCD [21,25].

The glutamate modulator has been tested in treatment of OCD, due to the suspected role of glutamatergic system dysfunction in the disorder's pathogenesis. Among the tested drugs that have shown reduction of OCD symptoms were riluzole used mainly to treat amyotrophic lateral sclerosis, memantine used in Alzheimer's disease treatment, N-acetylocysteine or lamotrigine [21,25,27]. However, there have been reports of lamotrigine inducing OCD symptoms while used in treatment of bipolar disorder [21].

5-HT-3 receptor antagonists such as ondasetron or granisetron, mainly used as antiemetics, have been reported effective, however due to poor methodology of available trials, they are recommended after the glutamate modulators have been tried [21,25].

In childhood, sometimes OCD is caused by a streptococcal infection resulting in autoimmune inflammation of the basal ganglia. Such cases are identified as PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections). Such subtypes of OCD may effectively be treated with antibiotics if the treatment is implemented early enough. It is important to remember that infection-related OCD constitutes merely a few percent of early-onset cases [21]. Regarding discontinuation of the treatment, it is suggested that once satisfying symptom control has been achieved, continuation of treatment is advised, if no contradictions are present [25].

2.4.3. Psychosurgical treatment

Surgical therapy of OCD relies on severing of the pathways between structures affected by the disorder, like the pathway between the orbitofrontal cortex and the anterior cingulate cortex. Surgeries include anterior capsulotomy, anterior cingulotomy, subcaudate tractotomy and limbic leucotomy. Surgical treatment is reserved only for patients with very severe symptoms and who are resistant to pharmacotherapy and psychotherapy [14,21].

2.4.4. Neuromodulation

Neuromodulation in treatment of OCD consists of transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and deep brain stimulation (DBS) [28].

Transcranial magnetic stimulation outside of OCD is used in many neurologic and psychiatric conditions like neuropathic pain, depression, post-acute stage of stroke motor recovery. A strong, short-lasting magnetic field is created by passing electricity through a stimulation coil placed against the patient's head. It then passes through the skull and induces electric field in selected regions of the brain resulting in neuronal depolarization with the intention of altering the electrical activity in said region [28,29].

The targets for repetitive TMS are Dorsolateral Prefrontal Cortex, Supplementary Motor Area, Medial Prefrontal Cortex, Anterior Cingulate Cortex. [28,29]. The treatment guidelines suggest the possible efficacy of Low Frequency Repetitive TMS of the right Dorsolateral Prefrontal Cortex in OCD [29].

Different OCD symptoms activate different neural circuits in patients' brains. This finding created an approach, where brain regions for TMS are targeted based on symptom profile, neuroanatomy and/or circuit dysfunction [28,30].

TMS is paired with symptom-provocation prior to stimulation in order to activate brain regions responsible for OCD symptoms, which helps alleviate them [28].

Transcranial Direct Current Stimulation (tDCS) relies on conducting weak direct current through the brain between two electrodes. Cathodal stimulation seems to be inhibitory while anodal stimulation seems to cause excitations. Trials have shown the feasibility and efficacy of tDCS of targeting multiple brain regions [28].

Deep Brain Stimulation is a reversible and modifiable procedure utilizing pulsed electric signals at a specific pulse width, voltage and frequency in order to modulate activity of brain regions. It involves implantation of an electrode that can interact with neighbouring brain regions. The most common regions targeted in DBS are the anterior limb of the internal capsule, nucleus accumbens, bed nucleus of the stria terminalis, subthalamic nucleus, inferior thalamic peduncle, ventral capsule and ventral striatum [3,28].

In the guidelines released in 2014 by the American Society for Stereotactic and Function Neurosurgeons (ASSFN) [31] and 2021 update presents level I evidence for the use of bilateral subthalamic nucleus DBS in medically refractory OCD and level II evidence for targeting of nucleus accumbens in said therapy [32].

The World Society for Stereotactic and Functional Neurosurgery (WSSFN) in their guidelines acknowledges electrical stimulation by electrode implanted in the bed nucleus of the stria terminalis and/ or anterior limb of the internal capsule as an emerging therapy in OCD treatment [33].

3. Summary

Obsessive Compulsive Disorder with its many contributing factors remains a serious problem regarding psychological health and general wellbeing.

Psychotherapy and pharmacotherapy are fundamentals of OCD treatment.

The main course of psychotherapy is Cognitive Behavioral Therapy and Exposure and Prevention Therapy and are aimed at toning down the compulsions. Most commonly used pharmaceuticals are SSRI and clomipramine. Depending on the effectiveness of SSRI treatment, medication can be switched to another SSRI or other medications can be used as augmentation. They include narcoleptics, glutamate modulators, 5-HT-3 inhibitors. Psychotherapy and pharmacotherapy are often used together especially in patients with an intense course of OCD, to achieve the best reduction of symptoms.

Psychosurgical treatment relies on severing affected pathways like the pathway between the orbitofrontal cortex and the anterior cingulate cortex. This treatment is reserved only for patients with severe symptoms and resistance to pharmacotherapy and physiotherapy.

Neuromodulation relies on transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and deep brain stimulation (DBS). Neuromodulation is still a relatively underresearched field of treatment of OCD. More studies are needed in order to better target brain regions for more effective treatment.

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