



A COMPREHENSIVE REVIEW ON OBSESSIVE-COMPULSIVE DISORDER: AN UPDATE

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ARTICLE INFO

Received:

22 December 2023

Received in revised form:

24 March 2024

Accepted:

25 March 2024

Available online:

28 April 2024

Keywords: Obsessive-compulsive disorder, Serotonin, Tricyclic antidepressants, Pharmacology, Psychotherapeutics

ABSTRACT

Obsessive-compulsive disorder (OCD) is a severe and intricate mental illness that profoundly impacts the lives of individuals affected by it. This comprehensive review aims to thoroughly explore all facets of OCD, encompassing its clinical presentations, prevalence as a common mental disorder, its neurological underpinnings, treatment modalities, and broader societal implications. The subsequent overview seeks to advance mental health awareness and foster empathy by integrating diverse perspectives and synthesizing existing research findings. Ongoing research endeavors are delving into the potential therapeutic uses of ketamine, known for its dissociative properties, as well as psychedelic substances in combination with psychotherapeutic interventions, as innovative approaches to treating OCD. Additionally, the utilization of mindfulness-based interventions, particularly mindfulness-based cognitive therapy (MBCT), is actively being investigated, along with the potential effectiveness of repetitive transcranial magnetic stimulation (rTMS) as an adjunct therapy for obsessive-compulsive disorders. The incidence of suicide attempts among individuals diagnosed with OCD varies widely, ranging from 6% to 51.7%, with an average occurrence of 14.2%. In this review, an updated elaboration of all aspects of the disorder has been given.

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To Cite This Article: Ujjwal P, Sanjita D, Kumar FN. A Comprehensive Review on Obsessive-Compulsive Disorder: An Update. *Pharmacophore*. 2024;15(2):54-62. <https://doi.org/10.51847/7Qc5Z7dkCo>

Introduction

Obsessive-Compulsive Disorder (OCD) profoundly impacts individuals with persistent distressing thoughts and repetitive behaviors. It's a chronic condition affecting diverse backgrounds and imposing a significant societal burden [1]. The onset of fixations frequently triggers a surge in stress and anguish, lightened by ensuing compulsions. Common fixations incorporate fears of defilement, concerns hurting oneself or others, the requirement for symmetry, devout or moralistic stresses, and meddling considerations [2]. OCD involves obsessions (unwanted thoughts) and compulsions (repeated behaviors). Common obsessions include fears of contamination, while common compulsions include cleaning and checking. OCD is categorized under obsessive-compulsive and related disorders in the DSM-5 [3-5] OCD affects 1-3% of the global population across all ages and has a lasting impact on relationships and work. Understanding genetic, neurobiological, and environmental factors is crucial for effective treatment [6]. Neurobiological studies of OCD implicate brain regions like the orbitofrontal cortex, caudate nucleus, and thalamus, elucidating neural circuit complexities. Genetic research underscores hereditary influences on susceptibility. Treatment modalities encompass Selective serotonin reuptake inhibitors (SSRIs) and Cognitive behavioral therapy (CBT), particularly Exposure and response prevention (ERP), showing promising outcomes when combined [7-9]. The present review gives a detailed account on OCD starting from its history to its treatment for the better understanding about the disease by the researchers and medical person.

Brief History

Historical records dating back centuries describe obsessions and compulsions, with accounts found in texts like the *Malleus maleficarum* from the 15th century. These phenomena were initially interpreted through religious lenses, as evidenced by accounts of exorcisms. However, by the 19th century, figures like Jean-Étienne Dominique Esquirol began to define obsessions

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and compulsions in psychiatric terms, linking them to conditions like melancholy. By the early 20th century, the understanding of OCD shifted towards psychological explanations [10, 11]. In the nineteenth century, the rise of faculty psychology, phrenology, and mesmerism influenced the understanding of neurosis as a neuropathological disorder, laying the groundwork for modern concepts of OCD. Philosophical, physiological, and political ideas shaped medical approaches to mental illness during this time. In the 1950s, learning theories extended from phobic disorders to OCD symptoms, leading to the development of behavioral therapy. While successful in reducing compulsive rituals, these theories proved insufficient to explain all OCD symptoms. By the 1980s, research focused on the relationship between OCD and neurological conditions such as epilepsy, Tourette's syndrome, and memory problems [12-14].

Prevalence and Demographics

In the US, approximately 2.3% of individuals experience OCD at some point in their lives, with prevalence rates ranging from 1% to 2.3% among children and teenagers under 18. OCD typically begins early, with an average onset age of 19.5 years [4, 15, 16]. Determining the age of onset and duration is critical in evaluating OCD, but definitions of childhood-onset versus adult-onset vary. Childhood-onset OCD may differ from adult-onset cases in characteristics and risk factors, with a higher frequency in males. The incidence of OCD has a bimodal distribution, with peaks in early childhood and early adulthood, exhibiting distinct gender distributions [17-19]. Recent research shows gender differences in OCD symptom onset: females typically experience symptoms after age 10, peaking during adolescence, while around 25% of males experience symptoms before age 10 [20].

Etiology of OCD

A complex interplay of genetic, neurological, cognitive, and environmental factors contributes to the development of OCD. Exploring these domains is crucial to understanding the diverse origins and maintenance of this mental condition

- *Genetic Factors* significantly contribute to OCD, with studies indicating a hereditary component. Individuals with a family history of OCD have a higher likelihood of developing the disorder themselves, highlighting the importance of genetic variables in OCD vulnerability [21].
- *Neurological Factors:* Neuroimaging shows brain irregularities in OCD-related areas like the orbitofrontal cortex and caudate nucleus. CSTC circuit dysfunction is significant. OCD involves neurotransmitter dysregulation, especially serotonin, dopamine, and glutamate [22].
- *Cognitive Factors:* OCD symptoms stem from distorted thought patterns like exaggerated responsibility and catastrophic thinking, driving compulsive rituals [23].
- *Environmental Factors:* Stressful events, trauma, and adverse childhood experiences can worsen OCD symptoms, interacting with genetic factors [24].
- *Immunological Factors:* Immune system dysregulation may contribute to OCD, with autoimmune disorders or infections possibly triggering or worsening symptoms [25].
- *Prenatal and Perinatal Factors:* Complications, infections, or substance exposure during pregnancy or birth are studied for their potential influence on OCD onset [26].
- *Epigenetic Factors:* Factors during prenatal or birthing phases, like complications or substance exposure, are examined for their role in OCD development [27].

Types of OCD

- *Contamination OCD*, involves obsessive fears of contamination, leading to compulsive cleaning or avoidance behaviors. Individuals feel dirty or impure even without direct contact with contaminants, experiencing discomfort and anxiety from unpleasant thoughts. They may wash excessively, use neutralizing strategies, or avoid triggering situations to cope with these feelings [28, 29].
- *Checking OCD*, affecting up to 80% of individuals with OCD, involves repetitive checking of external items like stoves and locks. This behavior aims to prevent harm, reduce uncertainty, or alleviate discomfort from perceived imperfections [4, 30].
- *Symmetry and Ordering OCD* focuses on a desire for perfection and symmetry, leading to compulsive behaviors like arranging and organizing items. Individuals with this type of OCD often feel a strong need for things to be precisely aligned or symmetrical, resulting in repetitive actions such as touching or tapping objects [31-33].
- *Hoarding OCD* is characterized by a persistent difficulty in discarding possessions, which leads to the gradual accumulation of items and the creation of cluttered and disorganized living spaces [34]. Compulsive hoarding involves excessive acquisition and difficulty discarding items, leading to clutter and distress. Approximately 15% to 40% of individuals diagnosed with OCD experience compulsions related to hoarding and saving behaviors [35].
- *Pure-O OCD*, or Purely Obsessional OCD, involves obsessions with mental compulsions rather than outward rituals. It's characterized by intrusive thoughts and internal cognitive processes used to manage them, lacking a distinct classification in the DSM-5 [36, 37].

Pharmacological Interventions

Treatment for obsessive-compulsive disorder (OCD) often involves pharmacological interventions focused on influencing neurotransmitter systems, particularly serotonin modulation. Medications prescribed for OCD aim to address the complex interplay of neurotransmitters, notably serotonin, to reduce symptoms and improve treatment outcomes.

- *Selective Serotonin Reuptake Inhibitors (SSRIs)*, such as fluoxetine (Prozac), fluvoxamine (Luvox), sertraline (Zoloft), paroxetine (Paxil), and escitalopram (Lexapro), are the primary pharmacological treatment for OCD. These medications work by increasing serotonin levels in the brain, which helps alleviate OCD symptoms [38].

Sertraline, for example, functions as a selective inhibitor of serotonin reuptake, prolonging serotonin transmission. Its long elimination half-life of approximately 26 hours allows for once-daily dosing, making it convenient for OCD treatment [39].

Sertraline strongly inhibits serotonin uptake, with minimal impact on dopamine and noradrenaline. It reduces serotonin turnover acutely and prevents depletion of central serotonin stores. It down-regulates central β -adrenoceptors and lacks significant affinity for muscarinic and histamine receptors. Sertraline is slowly absorbed orally, peaking 4 to 8 hours post a 100mg dose. It has linear pharmacokinetics within a 50 to 200mg dosage range, with increased bioavailability and peak plasma concentrations in the presence of food. It is extensively distributed in tissues, metabolized in the liver, and has a 26-hour elimination half-life, supporting once-daily dosing [39].

- *Tricyclic Antidepressants (TCAs)*: TCAs, like clomipramine, are effective for OCD due to their potent serotonin reuptake inhibition (**Figure 1**). However, they're less commonly prescribed than SSRIs due to their side effect profile [40].

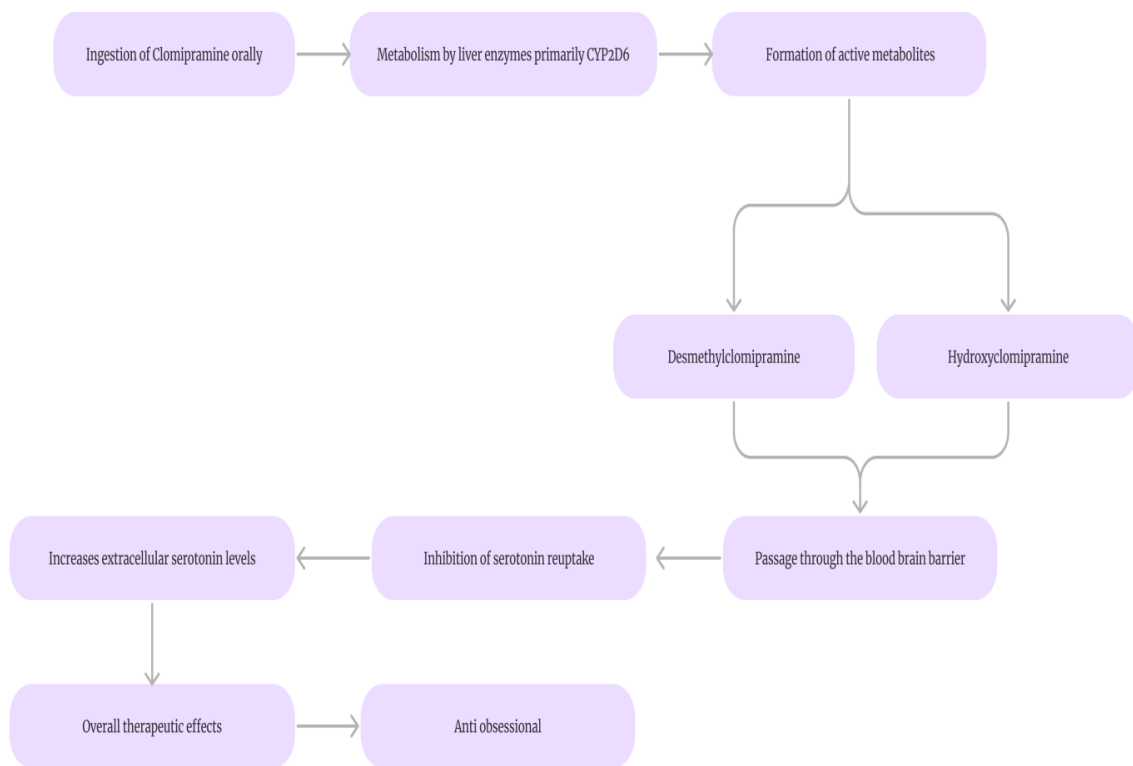


Figure 1. Mechanism of action of clomipramine

Clomipramine is a drug taken orally to treat OCD, and it is primarily metabolized by the liver through CYP2D6. Metabolites such as desmethylclomipramine and hydroxyclopmipramine raise serotonin levels outside cells by blocking reuptake, aiding in the effectiveness of treatment. These activities take place past the blood-brain barrier, boosting serotonin functions important for controlling symptoms of OCD.

- *Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)*: SNRIs, like venlafaxine and duloxetine, effectively inhibit the reuptake of norepinephrine and serotonin, showing promise in treating OCD symptoms. Controlled trials suggest they can alleviate symptoms, though outcomes vary across studies [41-43].
- *Benzodiazepines*, such as clonazepam and lorazepam, are sometimes used to alleviate anxiety symptoms in individuals with OCD (**Figure 2**). They may be considered when there's no history of dependency or tolerance to ensure safe use [44].

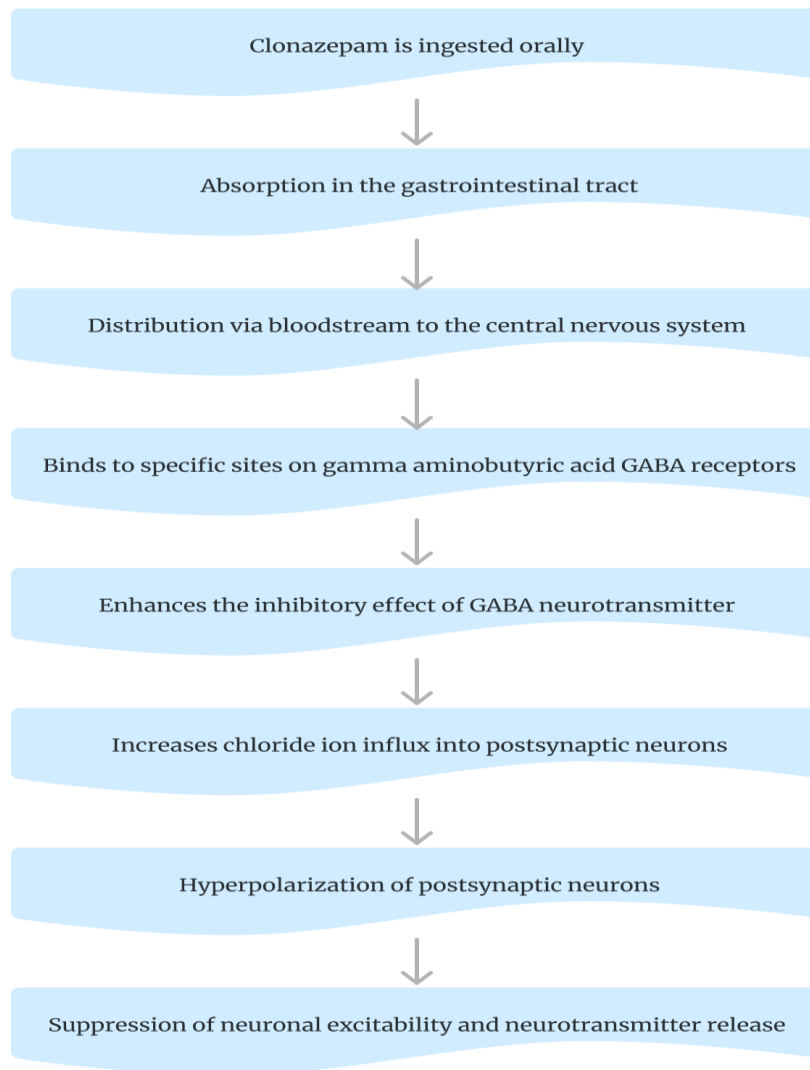


Figure 2. Mechanism of action of clonazepam

Clonazepam, taken orally, is absorbed through the gastrointestinal tract into the bloodstream, then transported to the central nervous system. There, it binds to GABA receptors, enhancing GABA's inhibitory effect. This increases chloride ion influx, hyperpolarizing neurons and suppressing excitability and neurotransmitter release.

- *Monoamine Oxidase Inhibitors (MAOIs)*: MAOIs, such as phenelzine and tranylcypromine, have shown effectiveness in treating OCD, especially when other antidepressants fail. They are considered as alternatives when standard interventions are inadequate for managing OCD symptoms, highlighting their potential usefulness in treating this condition [45].
- *Glutamate Modulators*: Glutamate Modulators, like N-acetylcysteine (NAC), show promise in alleviating OCD symptoms by modulating glutamate levels in the brain. Early research suggests NAC's effectiveness, but more comprehensive studies are needed to confirm its therapeutic efficacy for OCD [46].
- *Cannabinoid Receptor Modulators*: Research on cannabinoids, particularly cannabidiol (CBD), for OCD treatment is ongoing. CBD shows promise in reducing symptoms, but more research is needed to confirm its safety and effectiveness [47].

Psychotherapies

- *Cognitive-Behavioral Therapy (CBT)*: Cognitive-Behavioral Therapy (CBT) is a highly effective treatment for OCD, focusing on understanding the connections between thoughts, emotions, and actions. It aims to identify and change harmful cognitive patterns and behaviors associated with OCD symptoms. Cognitive restructuring involves challenging and altering irrational thoughts, while behavioral strategies target maladaptive behaviors like compulsive rituals, using techniques to promote behavioral change [48, 49].

- *Exposure and Response Prevention (ERP)*, a variant of CBT, is highly effective for OCD. It involves exposing individuals to triggers while preventing compulsive responses, promoting therapeutic progress by confronting anxiety triggers, and abstaining from compulsions [23, 50].
- *Virtual Reality (VR)* is becoming more common in Exposure and Response Prevention (ERP) therapy. It offers a controlled, immersive environment for exposure exercises, known as Virtual Exposure. VR enhances realism and customization, optimizing therapeutic interventions by simulating scenarios that trigger obsessive responses [51, 52].

Emerging Treatments and Research in the Field

Deep Brain Stimulation (DBS) involves surgically implanting electrodes to regulate brain activity for severe, treatment-resistant OCD [53, 54]. Research is exploring the therapeutic potential of ketamine and psychedelics combined with therapy for OCD [55]. Transcranial Magnetic Stimulation (TMS) uses magnetic fields to modulate brain activity, being studied as a treatment for OCD [56, 57]. Pharmacological interventions targeting the glutamatergic system are under investigation for OCD treatment [58]. Mindfulness-Based Interventions like MBCT and MBSR are being studied to enhance OCD treatment by increasing self-awareness and reducing reactivity to obsessive thoughts [59, 60].

Assessment

- *Screening:* Using validated measures improves the systematic identification and rating of OCD symptoms. Self-report measures are cost-effective, easy to administer, and help reduce potential biases associated with interviews, making them optimal for initial symptom assessment [61].
- *Clinical Assessment:* OCD is now categorized under 'Obsessive-Compulsive and Related Disorders' in the DSM-5, having been reclassified from an anxiety disorder in the DSM-4. Diagnosis involves meeting criteria outlined in the DSM-5, which include experiencing obsessions or compulsions causing significant distress or impairment in functioning. Symptoms must not be attributed to substances, other medical conditions, or alternative mental disorders [18, 62]. The primary clinician-assessed metric for measuring OCD severity is the Yale-Brown Obsessive - Compulsions Scale (Y-BOCS). This tool includes a checklist of 69 items covering various obsessions and compulsion themes, allowing for comprehensive assessment. The severity scale consists of five questions, with scores ranging from 0 to 4. Scores categorize OCD severity as subclinical (0-7), mild (8-15), moderate (16-23), severe (24-31), or extreme (32-40) [63]. Obsessive-Compulsive Disorder (OCD) affects individuals and their families significantly. Assessments should include evaluating family accommodation for accurate diagnosis. Involving families in assessments helps gather relevant information and improves treatment adherence, ensuring a comprehensive approach to treatment planning [64-66].
- *Cognitive Behavioral Assessment of OCD:* A thorough evaluation of OCD with Cognitive Behavioral Therapy (CBT) is best done by a specialist in CBT, like a Cognitive Behavioral Therapist or Psychologist with CBT training. Individuals with OCD may feel ashamed, especially with sensitive obsessions. Using a CBT-based formulation can help understand the issue and plan treatment effectively. Salkovskis (1985) introduced a cognitive model for OCD therapy [67, 68].
- *Risk Assessment:* Risk to self: Historically, OCD has been linked with a lower suicide risk. However, individuals with OCD may still experience suicidal thoughts and attempts, with varying prevalence rates ranging from 6% to 51.7% for attempts and 26.3% to 73.5% for ideation [69, 70].
Risk to others: People with OCD often grapple with intrusive thoughts related to violence or aggression, leading to distress. This may result in inappropriate protective measures. Evaluating risks to others includes considering potential neglect of dependents, both physically and emotionally, as the demands of OCD can overshadow caregiving responsibilities [71, 72].
- *Neurocognitive Assessment:* Research suggests that individuals with OCD have cognitive-functional differences compared to healthy controls, including cognitive rigidity, poor executive functioning, processing speed, image recall, decision-making, and error monitoring deficits. They also exhibit impaired response inhibition and cognitive flexibility [73-75].
- *Immunological Assessment:* Research indicates that inflammation and immune alterations are prevalent in individuals with OCD, suggesting the importance of immunological assessments, particularly for patients resistant to standard treatments or experiencing acute symptoms. Streptococcal infections, characterized by antibodies cross-reacting with autoantigens, can contribute to behavioral and motor disorders. A comprehensive immunological evaluation for OCD patients should involve exploring personal and familial inflammation histories, observing inflammation symptoms, and conducting lab tests to measure inflammation levels [76].

Conclusion

Obsessive-Compulsive Disorder (OCD) impacts between 1% and 3% of humanity and has a big impact on people, families, and society. The disorder manifests in diverse ways, from fears of contamination to hoarding behaviors, highlighting its intricate nature. Factors contributing to OCD include genetic predisposition, environmental influences, neurotransmitter imbalances, and cognitive distortions. Furthermore, OCD often co-occurs with conditions like depression, anxiety, and eating disorders, adding complexity to diagnosis and treatment. The societal impact of OCD encompasses reduced productivity, strained relationships, and stigma, which can impede access to support services. Addressing OCD effectively requires

comprehensive approaches that promote awareness, education, early intervention, and equitable access to evidence-based treatments, aiming to mitigate its effects and foster a more understanding and supportive environment for those affected. Pharmacological interventions, primarily SSRIs, and psychotherapy, particularly CBT with ERP, offer hope for individuals grappling with OCD. SSRIs aim to restore neurotransmitter balance, while CBT with ERP challenges distorted thinking and helps confront fears without compulsions, enabling individuals to regain control and lead fulfilling lives.

The future of treating obsessive-compulsive disorder (OCD) appears bright as advancements in therapeutic techniques continue to evolve. One such promising modality is Deep Brain Stimulation (DBS), which shows potential in addressing severe cases of OCD that have proven resistant to conventional treatments. Additionally, there is growing interest in psychedelic-assisted therapies, which offer novel approaches to alleviating OCD symptoms by exploring the therapeutic benefits of substances like psilocybin or MDMA under controlled settings. Furthermore, the advent of personalized medicine heralds a new era in OCD treatment, wherein interventions can be customized according to individual needs and genetic predispositions. This tailored approach holds the promise of enhancing treatment efficacy by addressing the specific biological and psychological factors contributing to each patient's condition.

The horizon of obsessive-compulsive disorder (OCD) treatment shines brightly as innovative modalities continue to emerge, offering renewed hope for individuals grappling with this challenging condition. Among these modalities, Deep Brain Stimulation (DBS) stands out as a beacon of promise, particularly for those afflicted with severe cases of OCD that have proven resistant to traditional treatment approaches. DBS can bring much-needed relief where previous therapies have failed by carefully regulating neural activity and implanting electrodes in certain brain areas. Apart from DBS, there's an increasing interest in investigating the potential therapeutic advantages of psychedelic-assisted treatments for OCD. These unconventional treatments involve the controlled administration of substances such as psilocybin or MDMA, often in conjunction with psychotherapy sessions conducted within carefully controlled settings. This innovative approach presents a fresh perspective on symptom alleviation, potentially disrupting entrenched patterns of OCD behavior and cognition and opening up new avenues for long-term healing and recovery. Furthermore, the advent of personalized medicine represents a significant leap forward in the realm of OCD treatment. By tailoring treatment strategies to the unique needs and genetic profiles of each patient, personalized medicine offers the potential for more precise and effective interventions.

In essence, the convergence of these innovative modalities—DBS, psychedelic-assisted therapies, and personalized medicine—heralds a new era in OCD treatment. With continued research, exploration, and refinement of these approaches, we stand poised to unlock transformative breakthroughs that have the potential to transform the landscape of OCD treatment, offering new hope and possibilities for individuals living with this challenging condition.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

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