Review

Recent Advances in the Treatment of OCD

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Recent Advances in the Treatment of OCD

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Abstract

This review synthesizes recent advances in the management of obsessive-compulsive disorder (OCD), a chronic and disabling psychiatric condition in which 40–60% of patients remain symptomatic despite first-line treatments such as selective serotonin reuptake inhibitors (SSRIs) and cognitive-behavioural therapy with exposure and response prevention (ERP). Innovations in psychotherapy include inhibitory learning–based ERP, the Bergen 4-Day Treatment, intensive inpatient CBT, digital and virtual reality–delivered ERP, AI-assisted interventions, and adjunctive modalities such as metacognitive therapy, acceptance and commitment therapy, and danger ideation reduction therapy. Pharmacological progress has been slower, though high-dose SSRIs, venlafaxine, antipsychotic augmentation, glutamatergic modulators, cannabinoids, ketamine, psychedelics, and other investigational agents show promise for treatment-resistant cases. Neuromodulation techniques—particularly deep transcranial magnetic stimulation, accelerated TMS protocols, transcranial direct and alternating current stimulation, and drug-assisted TMS—offer non-invasive augmentation options, while advances in psychosurgery, including refined gamma knife capsulotomy, deep brain stimulation, and emerging adaptive closed-loop DBS, provide hope for the most refractory patients. Future directions emphasize integrative, personalized, and technology-enhanced approaches, leveraging neuroimaging, computational psychiatry, and biomarker-driven treatment selection to improve outcomes in this complex disorder.

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Introduction

Obsessive-Compulsive Disorder (OCD) is a chronic and often debilitating psychiatric condition characterized by the presence of intrusive thoughts (obsessions) and repetitive behaviors (compulsions). It affects approximately 2–3% of the general population and is associated with significant distress, functional impairment, and a markedly reduced quality of life. According to the World Health Organization, OCD ranks among the top ten most disabling medical conditions worldwide (Stein et al., 2019).

Current evidence-based treatments for OCD including clinical practice guidelines primarily include cognitive-behavioural therapy (CBT), particularly Exposure and Response Prevention (ERP), and pharmacological interventions such as selective serotonin reuptake inhibitors (SRIs). While these first-line treatments provide meaningful relief for many individuals, an estimated 40–60% of patients do not achieve adequate symptom remission and may require augmentation strategies (Stein et al., 2019).

Augmentation options include antipsychotic medications, glutamatergic modulators, and emerging neuromodulation techniques such as Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS). Despite these options, a significant subset of individuals remains treatment-resistant or even treatment-refractory. For these individuals, more invasive approaches like psychosurgery—including gamma knife capsulotomy and Deep Brain Stimulation (DBS)—may be considered if the illness results in severe functional impairment. However, even in this highly treatment-refractory population, surgical interventions offer only

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modest remission rates (approximately 50–60%), often requiring 6–12 months post-procedure to observe meaningful improvement(Balachander, Arumugham, et al., 2019; Janardhan Reddy et al., 2017; Stein et al., 2019).

Given these limitations, a substantial proportion of patients with OCD continue to experience chronic impairment. This underscores the urgent need for novel treatment modalities and improved management strategies. In this context, the present review aims to explore and synthesize newer advances in the management of OCD, with a particular focus on developments from the past decade.

Recent Advances in Psychotherapeutic Modalities for OCD

Exposure and Response Prevention (ERP), a core component of Cognitive-Behavioral Therapy (CBT), remains the gold-standard non-pharmacological treatment for obsessive-compulsive disorder. ERP involves the systematic and repeated exposure to obsession-triggering stimuli (e.g., touching "contaminated" surfaces) while simultaneously preventing the associated compulsive behaviors (e.g., hand-washing). Typically delivered over 16 to 20 sessions, ERP has demonstrated 60–80% symptom reduction in clinical trials by facilitating habituation and causing extinction of feared response and disrupting the obsession–compulsion cycle (Foa, 2010).

The cognitive elements of CBT complement ERP by addressing maladaptive beliefs such as inflated responsibility, overestimation of threat, thought action fusion, the need for certainty etc.,(Salkovskis, 2007). Despite its strong evidence base, ERP poses several challenges in real-world practice. These include initial exacerbation of anxiety, difficulty achieving habituation in some cases, habituation not translating into real world improvement, high dropout rates, and poor adherence. Moreover, successful implementation often requires access to well-trained therapists, which may be limited in many settings.

While self-guided ERP protocols have shown promise, particularly for individuals with milder symptoms, a significant subset of patients continues to experience insufficient benefit. This highlights the need for novel psychotherapeutic modalities or innovative modifications in the delivery and structure of existing ERP/CBT approaches.

Inhibitory Learning Principles in OCD

Recent developments in behavioral theory have shifted the conceptual foundation of ERP from a classical habituation-based model to an inhibitory learning framework, aiming to enhance treatment effectiveness and long-term outcomes in obsessive-compulsive disorder OCD (Craske et al., 2014; Jacoby & Abramowitz, 2016).

Limitations of the Habituation Model

Traditionally, ERP has been grounded in the theory of habituation, where repeated exposure to feared stimuli leads to a gradual reduction in anxiety both within and across sessions. While this model has informed decades of clinical practice, it often fails to explain real-world clinical outcomes. Many patients report reductions in anxiety during exposure exercises yet show limited overall improvement in OCD symptoms. Moreover, individuals who initially respond well to ERP may relapse over time, suggesting that mere anxiety reduction during sessions does not ensure durable therapeutic gains (Craske et al., 2014; Jacoby & Abramowitz, 2016).

The Inhibitory Learning Approach

In contrast, the inhibitory learning model posits that ERP's primary function is not to reduce fear directly, but to help individuals form new, non-threatening associations that inhibit the expression of previously learned fear responses. The objective is to create and strengthen new safety memories (e.g., "door knobs are safe") that compete with and suppress older, fear-based associations (e.g., "door knobs are contaminated and dangerous") (Craske et al., 2014).

Key principles of this model include:

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- **Anxiety tolerance over reduction**: Emphasizing the ability to experience anxiety without avoidance, rather than focusing solely on its elimination.
- **Expectancy violation**: Designing exposures that **contradict feared outcomes**, e.g., "I didn't harm my baby even after spending two hours alone with them."
- **Variability in exposure**: Varying contexts and stimuli during exposure to promote **generalization of learning**.
- **Deepened extinction**: Combining multiple feared stimuli during exposure to enhance learning.
- **Occasional reinforced extinction**: Deliberately allowing feared outcomes (e.g., touching a mildly dirty object) to occur to challenge threat beliefs more robustly.

This approach redefines treatment success not as the absence of anxiety, but as the presence of new, flexible, and adaptive responses to previously feared stimuli. ERP is thus reframed as a process of learning safety that overrides but does not erase obsessional fear.

Empirical Support and Ongoing Research

Emerging evidence supports the efficacy of inhibitory learning–based ERP. For example, a pilot RCT by Samantaray et al. (2018) found that interventions explicitly designed around inhibitory learning principles were associated with greater reductions in fear renewal and more durable outcomes compared to traditional habituation-based ERP (Samantaray et al., 2018). A more recent study published in frontiers (Kühne et al., 2024) reported encouraging preliminary results when comparing inhibitory learning-informed ERP to traditional models in OCD, suggesting enhanced generalization and lower relapse rates .

While these findings are promising, larger-scale, head-to-head trials are underway to rigorously test the superiority of the inhibitory learning model in OCD treatment. Nonetheless, the shift toward strategic, expectancy-violating exposures and flexible anxiety engagement represents a significant advancement in behavioral therapies for OCD.

The Bergens 4 Day Treatment (B4DT): A Novel and Concentrated CBT Approach for OCD

Hansen and colleagues in Bergen, Norway, have pioneered an innovative model for treating OCD by delivering cognitive-behavioral therapy in a highly concentrated format, demonstrating that intensive ERP over a short period can result in significant clinical gains. This Bergen 4-Day Treatment (B4DT) model has shown outcomes that are often comparable to or even superior to traditional outpatient ERP delivered once or twice weekly. Importantly, this method enhances treatment efficiency, as the entire therapeutic protocol is completed within just four days, potentially increasing accessibility and adherence (Hansen et al., 2019).

Subsequent studies have validated these promising results. A large body of research—including multi-site implementations—has shown high remission and recovery rates, along with long-term maintenance of treatment gains (Hansen et al., 2019; Launes et al., 2019; Skjold et al., 2024). Several ongoing multicenter trials are currently evaluating the scalability and generalizability of B4DT across different countries and clinical settings.

The B4DT is typically conducted in an outpatient mental health setting, with a group of three to six patients. Each patient is assigned a dedicated therapist, ensuring a one-to-one therapist-to-patient ratio. The first day of the program is focused on psychoeducation, motivational enhancement, and personalized treatment planning. The second and third days consist of intensive therapist-assisted exposure and response prevention (ERP) exercises lasting approximately eight to ten hours per day. On the fourth and final day, the emphasis shifts toward consolidation of therapeutic gains, development of relapse prevention strategies, and planning for long-term maintenance. Follow-up assessments are conducted at three months, six months, and four years post-treatment to monitor long-term outcomes.

The results from studies evaluating B4DT have been compelling. In one of the foundational studies, mean Y-BOCS scores decreased from 25.9 at baseline to 10.0 immediately post-treatment and

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remained low at 9.9 even four years later. Remission rates were 73% at post-treatment, with 69% of participants still in recovery at four-year follow-up (Hansen et al., 2019; Launes et al., 2019).

Clinical Implications

When compared to weekly or biweekly ERP sessions, B4DT demonstrated higher rates of remission and recovery, along with superior adherence and significantly reduced dropout. These findings suggest that the Bergen 4-Day Treatment represents a promising alternative model for the delivery of ERP, particularly in systems aiming to reduce treatment delays and maximize resource efficiency.

Intensive Inpatient CBT for Treatment Resistant OCD

For individuals with severe, treatment-resistant OCD who have not responded adequately to outpatient CBT or ERP, intensive inpatient CBT programs offer a critical next-line treatment before progressing to more invasive options like neurosurgery. These programs provide a structured, immersive environment that facilitates frequent, therapist-guided exposure sessions, free from external distractions and avoidance.

Recent evidence supports the utility of this approach even in those who failed outpatient ERP. In a study by Balachander et al. (2020), patients with chronic, refractory OCD showed significant and sustained reductions in symptom severity following intensive inpatient ERP, with improvements maintained at long-term follow-up (Balachander et al., 2020). Standard inpatient protocols typically involve 2–3 hours of exposure per day, 5–6 days per week, for 4–8 weeks or longer, allowing for deeper therapeutic engagement, better adherence, and more personalized intervention.

A recently published review on high-intensity regular ERP suggests that high-intensity ERP is beneficial for people who do not respond to traditional ERP and other treatments (Trent et al., 2025).

Given the promising outcomes and durability of response, a trial of intensive inpatient ERP should be considered before escalating to neurosurgical interventions, as it may still produce meaningful benefit in a population previously deemed treatment-resistant.

Online Video-Delivered CBT for OCD: A Promising Alternative

Recent randomized controlled trials have demonstrated that video-delivered CBT, particularly ERP, is non-inferior to traditional face-to-face therapy for OCD, offering a scalable and accessible alternative to in-person treatment. A multisite RCT by Lundström et al. (2022) showed that online ERP was equally effective in reducing OCD symptoms, with comparable patient satisfaction and adherence (Lundström et al., 2022). This format holds particular value in addressing barriers such as limited availability of trained therapists and geographic or logistical constraints.

Supporting this, a meta-analysis by Loerinc et al. (2023) confirmed that online therapist-guided CBT yields significant symptom reduction, similar to conventional outpatient models (Lisi et al., 2023). These findings highlight the growing potential of digital therapy platforms in delivering effective, evidence-based OCD treatment, especially for underserved populations. As telepsychiatry becomes more mainstream, online CBT emerges as a key tool for expanding access to care without compromising treatment quality.

Virtual Reality–Based ERP: A Technologically Augmented Exposure Approach

Virtual Reality–based Exposure and Response Prevention (VR-ERP) is an emerging innovation in the treatment of OCD, offering a digitally immersive alternative to traditional in vivo exposure. VR allows for graded, controlled, and repeatable exposure to feared stimuli within a safe therapeutic environment, potentially enhancing patient engagement and participation—especially in those hesitant to confront real-life triggers.

A randomized controlled trial by Javaherirenani et al. (2022) evaluated the efficacy of VR-assisted ERP in individuals with contamination-type OCD (Javaherirenani et al., 2022). The study

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demonstrated that VR-ERP produced significantly greater reductions in obsessive and compulsive symptoms, as measured by the Y-BOCS, compared to standard CBT. Improvements were also seen in dysfunctional beliefs and functional disability, suggesting that VR can successfully simulate anxiety-provoking contexts that facilitate inhibitory learning. Notably, most studies in this domain have focused on contamination/washing subtypes, where real-world exposure can be logistically difficult or socially sensitive (Miegel et al., 2025).

VR-ERP addresses several limitations of traditional ERP, including poor adherence and limited access to in vivo stimuli. It allows therapists to create customizable, interactive exposure hierarchies within a virtual setting, potentially increasing treatment accessibility and standardization. However, current limitations include the difficulty in personalizing VR content to match the nuanced fears of individual patients. While ongoing technological advancements may soon overcome these barriers, especially with the growing interest in metaverse-based clinical applications, VR-ERP remains a promising but still developing modality (Miegel et al., 2025).

As the technology matures and becomes more widely available, VR-based exposure may represent a powerful adjunct or alternative to standard ERP—particularly for patients who are reluctant to engage in real-life exposures or for whom such exposures are not feasible.

AI-Assisted ERP: The Future of Scalable, Automated Psychotherapy for OCD

In recent years, numerous self-help applications and web-based platforms have emerged to support individuals with OCD, primarily offering psychoeducational modules, cognitive strategies, and basic exposure planning. While these tools provide accessible and affordable resources for many, fully personalized, AI-driven exposure and response prevention (ERP) systems remain limited and largely under development. Nevertheless, the rapid surge in artificial intelligence technologies suggests that automated, intelligent delivery of ERP may soon become a viable option, capable of addressing key barriers in OCD treatment—including limited availability of trained professionals, high treatment costs, and geographic inaccessibility.

Currently, most available digital tools offer unguided or minimally guided CBT, often focusing on knowledge dissemination rather than real-time adaptive exposure tasks. A systematic review and meta-analysis by Imai et al. (2022) found that unguided, computer-assisted self-help interventions for OCD showed small-to-moderate improvements in symptom severity, especially in those with mild-to-moderate illness, though outcomes were notably better when some form of human support was included (Imai et al., 2022). This underscores both the potential and current limitations of fully automated digital ERP systems.

A recent study by Bernstein et al. (2025) explored the feasibility of an AI chatbot delivering ERP guidance and observed promising results, though personalization and contextual relevance of exposures remained challenging (Bernstein et al., 2025).

As artificial intelligence continues to advance in natural language processing, behavioral modeling, and adaptive learning, it is likely that AI-assisted ERP platforms will soon offer fully autonomous, context-sensitive therapeutic interventions. These systems could dynamically generate exposure hierarchies, deliver real-time prompts, monitor emotional responses, and adjust strategies accordingly—effectively replicating the structure and intent of therapist-guided ERP.

In conclusion, while AI-based ERP is still in its infancy, early findings are encouraging. With further refinement, such tools could revolutionize OCD treatment by delivering scalable, personalized, and cost-effective care, particularly in resource-limited settings or for individuals unable or unwilling to engage in traditional therapy formats.

Miscellaneous/ New-Wave Psychotherapeutic Approaches for OCD

While Exposure and Response Prevention (ERP) remains the gold standard for OCD treatment, several other psychotherapeutic modalities have been explored either as standalone treatments or adjuncts to ERP. One such approach is Cognitive Therapy (CT), which focuses solely on cognitive restructuring without incorporating actual exposure tasks. CT aims to challenge maladaptive

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beliefs—such as inflated responsibility, overestimation of threat, and thought–action fusion—through logic-based reasoning and behavioral experiments (Salkovskis, 2007). However, multiple recent meta-analyses have concluded that cognitive restructuring alone is inferior to ERP or full CBT(Ferrando & Selai, 2021; Reid et al., 2021; Wang et al., 2024), suggesting that exposure is likely a critical mechanism in facilitating therapeutic change through processes such as inhibitory learning and experiential disconfirmation.

Other evolving therapies such as Mindfulness-Based Cognitive Therapy (MBCT) and Acceptance and Commitment Therapy (ACT) have gained popularity in recent years. ACT aims to increase psychological flexibility by encouraging individuals to accept intrusive thoughts without judgment and to commit to value-based actions despite ongoing anxiety or obsessions. MBCT incorporates mindfulness principles to help patients disengage from obsessive thoughts, reducing their emotional reactivity and intensity. Both approaches focus less on changing the content of thoughts and more on changing the relationship to those thoughts (Manjula & Sudhir, 2019). Although the evidence base is still emerging, these therapies have shown promise as augmentative strategies for patients with high experiential avoidance, or for those unwilling or unable to engage in traditional ERP.

Danger Ideation Reduction Therapy (DIRT) is a cognitive-behavioral intervention, for particularly contamination and checking subtypes. It targets the maladaptive beliefs that adverse events (e.g., illness, harm, or loss) will occur if compulsions such as washing or checking are not performed. By providing factual corrective information and structured cognitive tasks, DIRT aims to reduce these irrational danger ideations and thereby minimize avoidance behavior and compulsive rituals. The therapy includes components such as attentional focusing, cognitive restructuring, microbiological experiments, educational interviews, and probability tasks. DIRT is especially useful for patients who are unwilling or unable to engage in conventional ERP, or those with poor insight. Multiple case studies and trials have shown that DIRT can lead to significant reductions in OCD severity, even in treatment-refractory individuals, with durable effects over follow-up. A randomized controlled trial also found DIRT to be as effective as ERP, with potentially better long-term recovery rates. But number of studies are still very less (Manjula & Sudhir, 2019).

That said, head-to-head trials comparing these miscellaneous approaches to ERP are limited, and existing studies often suffer from small sample sizes or lack of long-term follow-up. While a few studies suggest non-inferiority of ACT or MBCT to ERP, these findings are considered preliminary due to their underpowered nature, and ERP continues to be regarded as the first-line psychotherapeutic intervention for OCD.

Finally, Metacognitive Therapy (MCT) has emerged as a promising adjunctive or standalone modality. MCT targets dysfunctional metacognitive beliefs—such as beliefs about the importance of controlling thoughts or the danger of having certain thoughts—which are believed to underlie and maintain compulsive behavior (Manjula & Sudhir, 2019). A recent randomized controlled trial demonstrated that integrating MCT principles into ERP or CBT may lead to higher remission rates, suggesting that addressing both the content and the regulation of thinking can enhance outcomes. As a result, MCT is gaining popularity and may represent a valuable addition to the therapeutic toolkit for OCD (Exner et al., 2024).

Other therapies like Eye Movement Desensitization and Reprocessing (EMDR), Dialectical Behavioural Therapy (DBT) and certain psychodynamicaly oriented therapies are also tried in OCD with minimal benefit in recent years.

Recent Advances in Pharmacotherapy for OCD

Despite the chronic and disabling nature of OCD, progress in pharmacological treatment has significantly lagged behind that seen in other psychiatric conditions such as depression, bipolar disorder, schizophrenia, anxiety disorders, and substance use disorders. Over the past decade, several new pharmacological agents have been approved in those fields, while no new medications

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have received regulatory approval for OCD, highlighting a critical gap in innovation and therapeutic advancement.

The Clinical Practice Guidelines for OCD by the Indian Psychiatric Society (2017) provide a detailed synthesis of the current understanding of pharmacotherapy in OCD. According to these guidelines, monotherapy with a selective serotonin reuptake inhibitor (SSRI) remains the first-line pharmacological treatment, to be considered alone or in combination with cognitive-behavioral therapy (CBT), depending on factors such as illness severity, comorbidity, treatment history, side-effect profile, patient preference, and resource availability (Janardhan Reddy et al., 2017).

SSRIs—including fluoxetine, fluvoxamine, sertraline, paroxetine, citalopram, and escitalopram—are supported by robust evidence from randomized controlled trials and meta-analyses. However, OCD treatment typically requires higher doses and longer durations (up to 10–12 weeks or more) for a meaningful response compared to major depression. While earlier evidence suggested possible differences in efficacy among SSRIs, meta-analyses have found no significant differences, making the choice of SSRI largely dependent on clinical context and tolerability (Bloch et al., 2006; Fineberg et al., 2012).

Clomipramine, a tricyclic antidepressant with strong serotonergic properties, was historically considered superior to SSRIs. However, recent head-to-head trials and meta-analyses no longer support this claim, and its use is often limited by its adverse effect profile, including sedation, anticholinergic effects, and potential cardiac toxicity. Clomipramine is typically reserved for patients who do not respond to at least two adequate SSRI trials (Swierkosz-Lenart et al., 2023). Cross-titration with certain SSRIs like fluoxetine, fluvoxamine, and paroxetine must be done cautiously, as these drugs can raise clomipramine levels and increase the risk of side effects such as seizures.

There is also preliminary evidence supporting venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI), as non-inferior to SSRIs, although it is not yet widely adopted as first-line therapy (Balachander, Kodancha, et al., 2019). Use of high-dose SSRIs (e.g., fluoxetine >100 mg or sertraline >300 mg) has been reported in treatment-resistant OCD, but this remains experimental, and most guidelines caution against it due to risks such as serotonin syndrome and increased adverse effects (Janardhan Reddy et al., 2017).

For maintenance, SSRIs or clomipramine should be continued for 1–2 years after achieving sustained remission, with dose adjustments guided by tolerability and relapse risk. Most patients with moderate-to-severe OCD require long-term maintenance therapy to prevent recurrence, particularly in cases with chronic illness, residual symptoms, or prior relapse after discontinuation (Janardhan Reddy et al., 2017).

When patients fail to respond adequately to SSRIs, augmentation strategies are recommended. These include pharmacological, psychotherapeutic, and neuromodulatory interventions. CBT with ERP remains the most effective augmentation approach and should be prioritized when accessible. When CBT is not feasible, pharmacological augmentation is a valid alternative. Among pharmacological options, atypical antipsychotics, particularly risperidone and aripiprazole, have shown the most consistent evidence (Janardhan Reddy et al., 2017). Other agents such as glutamatergic modulators (e.g., memantine, N-acetylcysteine) and 5-HT3 antagonists like ondansetron have demonstrated preliminary benefits.

A recent network meta-analysis ranked ERP as the most effective augmentation strategy, for SRI resistant OCD, followed by deep Transcranial Magnetic Stimulation (dTMS), aripiprazole, and ondansetron, reflecting the growing interest in combining pharmacotherapy with neuromodulatory and behavioral techniques (Suhas et al., 2023).

In addition to traditional and augmentation-based approaches, novel compounds are currently being investigated for treatment-resistant OCD. These include cannabinoids (e.g., cannabidiol) (Kayser et al., 2020), ketamine (Beaglehole et al., 2025), and psychedelics such as psilocybin (Pellegrini et al., 2025), being evaluated either as augmenting agents or monotherapies. Preliminary trials suggest potential benefits via mechanisms involving glutamate modulation, neuroplasticity enhancement, and altered emotional processing. However, these interventions are still experimental,

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and larger randomized controlled trials are underway to establish their safety and efficacy profiles. Their growing popularity reflects a shift toward neurobiologically-targeted, rapid-acting treatments, which may expand the pharmacological armamentarium in the future.

Newer drugs like Drugs being like tolcapone (COMT inhibitor), nabilone (CB1 receptor modulator), troriluzole (NMDA receptor modulator), celecoxib (COX-2 inhibitor), Nitrous oxide, Rituximab (immunomodulator), Naproxen (NSAID) Octagam 5% (immunoglobulin) etc., are being investigated for the treatment of OCD(Grassi et al., 2020).

Despite these advances, the overall progress in pharmacotherapy for OCD remains slow, and significant gaps exist in the development of new medications specifically approved for this condition.

Recent Advances in Neuromodulation in OCD

Neuromodulation has been explored for over two decades as a promising intervention in psychiatry, with its earliest applications dating back to the early 1990s. Its role has been extensively studied in various psychiatric disorders, including depression, schizophrenia, addictions, including OCD. In the context of OCD, neuromodulation offers a non-invasive, brain-targeted approach for patients who do not respond adequately to conventional pharmacotherapy and psychotherapy. While Electroconvulsive Therapy (ECT) has consistently been shown to have no significant role in the treatment of OCD, Transcranial Magnetic Stimulation (TMS) and transcranial Direct Current Stimulation (tDCS) have garnered increasing attention in recent years for their therapeutic potential (Janardhan Reddy et al., 2017).

Advances in TMS for OCD

Several rTMS protocols have been studied, targeting different regions implicated in the cortico-striato-thalamo-cortical (CSTC) circuitry dysfunction in OCD. Stimulation of the dorsolateral prefrontal cortex (DLPFC), dorsomedial prefrontal cortex (DMPFC), and supplementary motor area (SMA) has shown promise in reducing obsessive-compulsive symptoms. These regions can be targeted using different coil configurations: figure-of-eight coils can be used for DLPFC and SMA, while deep TMS coils are required for DMPFC and medial prefrontal regions. Stimulation of these areas is thought to downregulate hyperactive nodes in the CSTC loop, which contributes to the pathophysiology of OCD (Shivakumar et al., 2019). According to a network meta-analysis, deep TMS was ranked as the most effective intervention for SSRI-resistant OCD, with large effect sizes noted compared to other treatment strategies (Suhas et al., 2023).

One of the most notable developments in neuromodulation for OCD is the advent of deep TMS (dTMS). Unlike traditional TMS that stimulates superficial cortical regions, dTMS employs H-coils, particularly the H7 coil developed by BrainsWay, which allows stimulation of deeper brain structures implicated in OCD pathophysiology, such as the anterior cingulate cortex and medial prefrontal cortex. In 2018, the FDA approved the H7 coil for treatment-resistant OCD, marking a major milestone in device-based therapy. The commonly used clinical protocol involves high-frequency stimulation (typically 20 Hz) administered five days a week for 15–20 sessions(Roth et al., 2021).

More recently, there has been growing interest in intermittent theta burst stimulation (iTBS), a shorter-duration rTMS protocol that mimics natural theta rhythms believed to enhance neuroplasticity. iTBS is more time-efficient than traditional high- or low-frequency TMS and is hypothesized to offer superior efficacy in facilitating therapeutic learning during exposure therapy, although this remains under investigation. Current literature estimates that approximately 60% of patients respond to TMS (Shivakumar et al., 2019), but key questions remain—particularly regarding the optimal timing of initiation, long-term outcomes, and the role of booster sessions in maintaining gains.

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Accelerated TMS for OCD

There is growing interest in recent research on accelerated TMS protocols, where two or more sessions are delivered per day. This approach aims to reduce the overall treatment duration (in days) and is theoretically linked to enhanced neuroplasticity. A recent study on accelerated iTBS using deep TMS in OCD (2 sessions per day) has shown significant benefits (Mudunuru et al., 2024). Several RCTs are currently underway to evaluate the efficacy of accelerated versus standard protocols.

Advances in tDCS for OCD

Turning to transcranial Direct Current Stimulation (tDCS), interest in this modality is growing due to its low cost, portability, and ease of use. tDCS involves the application of a weak direct current to modulate cortical excitability: anodal stimulation increases excitability, while cathodal stimulation decreases it. Preliminary studies have shown encouraging results, particularly with anodal stimulation of the SMA or cerebellum, as well as cathodal stimulation of the SMA or orbitofrontal cortex (OFC) (Sreeraj et al., 2023). Although still investigational, tDCS holds promise as a cost-effective neuromodulatory adjunct, especially in resource-limited settings.

Transcranial Alternating Current Stimulation (tACS) in OCD

A recent randomized, sham-controlled clinical trial by Perera et al. (2023) examined the effects of home-based individualized alpha transcranial alternating current stimulation (tACS) in individuals with OCD. The study found preliminary evidence that tACS significantly improves OCD symptoms**.** The intervention was non-invasive, personalized, and could be delivered at home, highlighting its potential for scalable treatment. These findings support further investigation of tACS as an adjunctive or standalone neuromodulatory therapy in OCD (Perera et al., 2023).

Drug Assisted TMS

Recent studies suggest that augmenting TMS with D-cycloserine, an NMDAR partial agonist that promotes synaptic plasticity, may significantly enhance treatment outcomes. In a randomized controlled trial by McGirr et al., iTBS combined with DCS led to a 39% improvement in OCD symptoms, outperforming both iTBS alone and sham (McGirr et al., 2025). Although promising, the study was prematurely terminated and lacked biomarker validation, making the results preliminary. Future research should clarify the role of symptom provocation, optimal TMS parameters, and alternative plasticity-enhancing agents. These findings highlight the potential for mechanistically informed pharmacological augmentation of TMS(Brown & Philip, 2025).

Neuromodulation and ERP

Another emerging avenue is the combination of TMS with ongoing CBT, particularly ERP-based tasks. Recent studies suggest that applying TMS during exposure exercises may enhance habituation and inhibitory learning through synergistic effects on neuroplasticity (Conelea et al., 2024). This approach is currently being explored in clinical trials and may represent a new frontier in augmentative treatment strategies, combining the psychological mechanisms of ERP with the neurobiological facilitation of TMS. Similar studies are being done with preliminary published data which is promising in tDCS augmentation while ERP (Gao et al., 2025).

Newer Advances in Psychosurgery in OCD

A significant proportion of individuals with OCD remain treatment-refractory, failing to respond even after multiple trials of SSRIs, augmentation strategies, and structured ERP. This subset of patients often experiences severe and persistent functional impairment, leading clinicians to consider psychosurgical interventions as a final recourse.

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Psychosurgery for psychiatric illness dates back to the 1880s, when Gottlieb Burckhardt performed early cortical resections on patients with psychosis. This was followed by the infamous leucotomy and lobotomy procedures developed by Egas Moniz in the 1930s, which were initially applied to chronically ill, unmanageable psychiatric patients. Over the decades, these crude approaches have evolved dramatically, particularly alongside advancements in stereotactic neurosurgery, neuroimaging, and functional brain mapping, with more precise and less invasive methods now being adopted—mirroring developments in other neurological disorders such as Parkinson's disease and other movement disorders (Lapidus et al., 2013).

Currently, two main psychosurgical procedures are accepted and commonly practiced for severe, treatment-resistant OCD: Gamma Knife capsulotomy (ablative surgery) and Deep Brain Stimulation (DBS). These interventions target critical nodes in the cortico-striato-thalamo-cortical (CSTC) circuitry, which has been implicated in the pathophysiology of OCD (Balachander, Arumugham, et al., 2019).

Eligibility Criteria for Psychosurgical Intervention

According to expert consensus and treatment guidelines (including the 2017 Indian Psychiatric Society guidelines), a patient must fulfill the following **criteria** before being considered for DBS or ablative surgery (Janardhan Reddy et al., 2017):

- **Severity**: Y-BOCS score >28 (severe OCD)
- **Chronicity**: Persistent, unremitting symptoms despite long-term treatment
- **Functional Impairment**: GAF ≤ 45
- **Failed Pharmacotherapy**: At least two adequate SSRI trials, a trial of clomipramine (unless poorly tolerated), and at least two augmentation strategies, including an atypical antipsychotic
- **Failed Psychotherapy**: Minimum of 20 ERP-based CBT sessions or inability to tolerate ERP due to severe anxiety
- **Adequate Trials**: No premature discontinuation due to mild side effects
- **Informed Consent**: Written consent from the patient
- **Commitment to Follow-Up**: Willingness to undergo pre- and post-operative assessments
- **Relative Contraindications**: Presence of comorbid intellectual disability, psychosis, severe personality disorder, or unstable neurological illness

As per the Mental Health Care Act 2017 (India), any surgical intervention for a psychiatric condition must be performed only after obtaining explicit informed consent and approval from the Mental Health Review Board.

Ablative Procedures

Two ablative techniques are most commonly used:

- **Anterior Capsulotomy**: This involves the stereotactic ablation of the **ventral anterior limb of the internal capsule (ALIC)** to disrupt hyperactive fronto-striatal circuits. Lesions can be created using **Gamma Knife radiosurgery**, **radiofrequency ablation**, or **MR-guided focused ultrasound**.
- **Anterior Cingulotomy**: Involves lesioning of the **anterior cingulate cortex and the cingulum bundle**, which are involved in emotional regulation and cognitive control.

These procedures are now performed with high precision, and serious complications such as cognitive deficits or personality changes are rare. Common side effects include transient headache, fatigue, and emotional blunting. Approximately 50–60% of patients respond to ablative surgery, typically showing improvement over 6 to 12 months. Importantly, these patients are expected to continue pharmacological and psychotherapeutic interventions post-surgery. These procedures are relatively cheap and non-invasive compared to DBS (Balachander, Arumugham, et al., 2019).

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Deep Brain Stimulation (DBS)

DBS represents a reversible, adjustable alternative to ablative psychosurgery. Electrodes are implanted bilaterally into targeted brain areas and connected to a subcutaneous pulse generator. Commonly targeted sites include the ventral capsule/ventral striatum (VC/VS), nucleus accumbens, subthalamic nucleus, and bed nucleus of the stria terminalis. DBS allows programming and titration of stimulation parameters, enabling clinicians to optimize response and minimize side effects (Balachander, Arumugham, et al., 2019).

Response rates with DBS are comparable to those of ablative surgery, with about 60% of patients showing ≥35% reduction in Y-BOCS scores. The response is gradual, with improvements emerging over several weeks to months. Side effects include surgical complications (e.g., infection, hemorrhage) and transient neuropsychiatric symptoms such as hypomania, anxiety, or mood changes. When conducted at experienced functional neurosurgery centers, DBS is considered a safe and effective option for selected patients (Balachander, Arumugham, et al., 2019).

Recent Developments and Future Directions in DBS

Recent advances in DBS research have focused on targeting new anatomical loci within the CSTC circuit, including the anterior-medial subthalamic nucleus (STN) and individualized connectivity-based targets identified via diffusion tensor imaging (DTI) or functional MRI (Chabardes et al., 2020). A first-in-human application of responsive deep brain stimulation (rDBS) targeting the ventral striatum in a treatment-refractory OCD patient demonstrated that electrophysiological signals correlated with obsessive and compulsive symptoms could be used to trigger stimulation in a closed-loop manner. This rDBS approach produced rapid, robust, and lasting symptom improvement**,** supporting its feasibility as a personalized, physiologically guided DBS strategy for OCD (Nho et al., 2024). These developments aim to enhance precision and improve response rates in treatment-refractory populations. Several other ongoing studies are exploring closed-loop (adaptive) DBS, real-time feedback-guided stimulation, and biomarker-informed targeting—highlighting the future potential of personalized neuromodulation in OCD (Widge, 2023).

Conclusion and Future Directions

Despite being one of the most chronic and disabling psychiatric disorders, OCD continues to lag behind other major psychiatric conditions in terms of therapeutic innovation. First-line treatments such as SSRIs and CBT with ERP remain the mainstay of management, but a substantial subset of patients remains treatment-resistant, necessitating augmentation strategies, neuromodulation, or even psychosurgical intervention. While advances in psychotherapy—such as inhibitory learning-based ERP, metacognitive therapy, and intensive formats like the Bergen 4-Day Treatment—are refining traditional CBT models, pharmacological progress has been limited, with no new drug approvals in the past decade. Neuromodulatory approaches such as TMS, and tDCS offer non-invasive adjunctive options, and psychosurgical procedures like DBS and gamma knife capsulotomy are increasingly refined for severe, refractory cases. Each modality brings incremental improvements, but the overall pace of advancement remains slower compared to disorders like depression or schizophrenia.

Looking forward, the future of OCD treatment lies in integrative, personalized, and technology-enhanced care. In psychotherapy, AI-assisted and VR-delivered ERP hold promise for expanding access, improving personalization, and reducing therapist burden. Further head-to-head trials are needed to establish the relative efficacy of newer cognitive and mindfulness-based therapies. In pharmacotherapy, the emergence of glutamatergic agents, psychedelics, and cannabinoids opens new avenues, though rigorous trials and regulatory clarity are essential. In neuromodulation, adaptive DBS, targeted circuit modulation using connectomic data, and home-based tDCS protocols may improve outcomes in resistant OCD. Finally, advances in genetics, neuroimaging, and computational psychiatry are beginning to elucidate individual-level mechanisms underlying OCD,

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offering hope for biomarker-driven treatment selection. While OCD has trailed behind in terms of therapeutic breakthroughs, the current trajectory of innovation in neuroscience, AI, and precision medicine gives reason for optimism that more effective, personalized, and scalable treatments will soon transform the management of this complex disorder.

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