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Anxiety, Obsessive Compulsive, and Related Disorders (W Goodman and J Murrough, Section Editors)

Treatment of Obsessive-Compulsive and Related Disorders

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Opinion statement

Pharmacotherapy and cognitive-behavioural therapy (CBT) have been studied in many of the obsessive-compulsive and related disorders (OCRDs). Serotonin reuptake inhibitors (SRIs) and cognitive-behavioural therapies (CBT) are first-line considerations in many, but not all, of these conditions. There are fewer data available on the combination of these treatment modalities in OCRDs. In obsessive-compulsive disorder (OCD), the SRIs and CBT – which include exposure and response prevention (ERP) – are well-established safe and efficacious first-line treatments in adult and paediatric populations. While various pharmacotherapy augmentation strategies have been studied, the most evidence-based approach to date is augmentation with antipsychotic agents. There is also evidence of the value of CBT in the management of treatment-refractory patients. A number of SRIs, such as clomipramine and fluoxetine, have shown efficacy in randomized controlled trials of the pharmacotherapy of body dysmorphic disorder (BDD). There are relatively few data on pharmacotherapy augmentation approaches in BDD. CBT has also been found efficacious in a number of psychotherapy trials of BDD. Less is known about the optimal treatment of the other OCRDs, i.e., hoarding disorder (HD), trichotillomania (hair-pulling disorder, or HPD), and excoriation (skin-picking) disorder (SPD). While patients with HD may have been included in RCTs on OCD, no data from randomized controlled trials of pharmacotherapy specifically for HD have been reported. There is some support for the value of CBT in HD. In HPD, controlled trials of olanzapine, N-acetyl cysteine (NAC), and clomipramine (vs. desipramine) have provided evidence of efficacy. There also is evidence supporting the efficacy of behav-

iour therapy in reducing hair-pulling. Results from randomized controlled trials of SRIs in SPD have been mixed, with some agents such as fluoxetine and citalopram demonstrating improvement on certain measures of picking behaviour. Behaviour therapy also appears to be useful for SPD.

Introduction

The concept of a spectrum of obsessive-compulsive and related disorders dates back at least as far as proposals by Freud [1], suggesting that obsessive-compulsive personality, neurosis, and psychosis lie on a continuum [2]. In recent decades, data have accumulated on the diagnostic validity and clinical utility of the construct of obsessive-compulsive and related disorders (OCRDs).I In DSM-5 [3], for the first time, there is a separate chapter on these conditions. OCRDs in DSM-5 include obsessive-compulsive disorder (OCD), body dysmorphic disorder (BDD), hoarding disorder (HD), trichotillomania (hair-pulling disorder, or HPD), excoriation (skin-picking) disorder (SPD), substance/medication-induced OCRD, OCRD due to another medical condition, and other specified and unspecified OCRD (e.g., body-focused repetitive behaviour disorder).

Data supporting the diagnostic validity of this construct include genetic data demonstrating familial relationships and brain imaging data suggesting that the neurocircuitry implicated in these disorders differs from that involved in anxiety disorders. Given that these disorders are underdiagnosed and undertreated, it may be useful for clinicians to screen for the range of intrusive thoughts and repetitive rituals that are seen across this spectrum of disorders. Similar assessment tools are used to assess the severity of symptoms in various OCRDs. Given the high comorbidity of these disorders, if a patient presents with one OCRD, it is important to evaluate the presence and severity of other OCRDs.

DSM-5 diagnostic criteria include a number of other changes designed to improve treatment outcomes. First, diagnostic criteria have been updated on the basis of accumulating data. For example, the diagnostic criteria for HPD have been broadened so as not to unnecessarily exclude patients who do not meet the more stringent DSM-IV criteria, and diagnostic criteria for SPD have been added. Second, in order to ensure that patients with no insight are not misdiagnosed as having a delusional disorder and therefore inappropriately treated, DSM-5 allows patients with OCRDs and delusional levels of symptoms to be diagnosed as having an OCRD with no insight. Third, additional specifiers for OCRDs have been added, including tic-related in OCD and muscle dysmorphia in BDD, in order to assist in optimizing assessment and intervention.

There is also significant overlap between anxiety disorders and some of the OCRDs (e.g., OCD, which was considered an anxiety disorder in DSM-IV [4]), and the order of these sections in DSM-5 (OCRDs follow anxiety disorders) reinforces the link in assessment and treatment among them. The conceptualization of anxiety disorders and OCRDs as lying on a broader spectrum of internalizing disorders may be useful. At the same time, anxiety disorders and OCRDs also have distinct psychobiological underpinnings and may require different treatment strategies [5]. There is evidence currently to suggest overlapping treatment guidelines for the various OCRDs. Serotonin reuptake inhibitors (SRIs) and cognitive-behavioural therapy (CBT) have been studied in many of these conditions. In this paper, we aim to provide readers an up-to-date review of evidence-based treatment options for the OCRDs now included in DSM-5.

Treatment

The aim of treatment in patients with OCRDs is to improve symptoms and to reduce the impact of these conditions on functioning and quality of life, with minimal adverse effects.

Pharmacotherapy

OCD

The findings of systematic literature reviews and meta-analyses of randomised double-blind placebo-controlled trials indicate that the tricyclic (TCI) antidepressant clomipramine and the selective serotonin reuptake inhibitors (SSRIs) (i.e., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) [6] are all effective in the treatment of OCD, specifically in reducing symptom severity and in decreasing impairment [7••], although SSRIs are better tolerated than clomipramine [8–11]. Similar considerations apply in paediatric OCD.

The findings of a meta-analysis of nine treatment studies involving SSRIs suggested greater efficacy (though poorer tolerability) with higher daily dosages [12], and increased daily dosage may be advised if there is insufficient response at a lower dosage. In addition, a longer-term course of SSRIs should be encouraged. The findings of acute treatment studies indicate that the number of responding patients increases steadily over time. For example, long-term (i.e., up to 12 months) double-blind randomised controlled studies have suggested an advantage for continuing with medication in patients who have responded to acute treatment [13–15]. The optimal duration of treatment however, is uncertain [16]. It is generally recommended that an effective SRI be continued for at least a year.

Forty to sixty percent of OCD patients do not respond adequately to pharmacotherapy trials with SSRIs [17]. Augmentation of SSRIs with antipsychotic medication is the most evidence-based option, and a number of randomised double-blind placebo-controlled augmentation studies has shown that the addition of antipsychotic agents such as aripiprazole, haloperidol, olanzapine, quetiapine, or risperidone is effective in treatment-resistant OCD patients [18••]. The use of other medications such as ondansetron [19] and granisetron in combination with SSRIs [20] may also be effective. In addition, three relatively small randomised placebo-controlled anticonvulsant augmentation studies demonstrated that the addition of topiramate [21, 22] or lamotrigine [23] to SSRIs reduced OCD severity. There are other glutamatergic agents that have shown potential in treatment-resistant OCD. These include riluzole, memantine, and other NMDA-receptor antagonists (such as amantadine and ketamine). With the exception of ketamine, no randomized controlled trial of these agents in OCD has yet been published. A single dose of ketamine was shown to reduce OCD in a recent randomized controlled crossover trial in treatment-free OCD patients [24, 25].

BDD

Clomipramine and SSRIs are currently considered the first-line pharmacological treatment for BDD. In particular, two blinded randomized controlled trials indicated that clomipramine [26] and fluoxetine [27] are efficacious in BDD. In a controlled and blinded crossover study, clomipramine was significantly more effective than the NRI desipramine, with improvements in obsessive characteristics, depression, insight, social performance, and illness severity [26]. Similarly, fluoxetine was shown to be significantly superior to placebo [27] in a double-blind parallel-group study. Four open-label studies

also suggested that fluvoxamine [28, 29], escitalopram [30], and citalopram [31] may decrease core BDD symptoms and improve associated features such as depression, anxiety, anger-hostility, psychosocial functioning, and quality of life. Results from two small open-label trials suggest that the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine [32] and the anti-convulsant levetiracetam [33] may be helpful for BDD, although these medications are not currently recommended as first-line treatment.

Rigorous dose-finding studies, however, are lacking; however, as in OCD, effective SRI doses needed to successfully treat BDD often appear to be substantially higher than those typically needed to treat many other disorders, such as depression.

For patients who do not respond to SRI monotherapy, augmentation with buspirone, clomipramine, an atypical antipsychotic, bupropion, or venlafaxine may be helpful [34, 35]. In some patients, lithium and methylphenidate are also considered useful in SRI augmentation [34, 35], but there are currently no randomized controlled trial data to support the efficacy of these augmentation strategies.

HD

While patients with HD may have been included in RCTs on OCD, no data are currently available from randomized controlled trials of pharmacotherapy specifically for HD. An open-label study of paroxetine suggests that this agent may be useful in the treatment of HD.

HPD

Randomized controlled trials of SSRIs in HPD have failed to demonstrate efficacy [36]. However, it has been suggested that individuals with HPD respond more robustly to the serotonergic tricyclic antidepressant clomipramine than to the noradrenergic tricyclic desipramine [37].

While a controlled trial demonstrated evidence that olanzapine was effective in the treatment of HPD [38] the decision to use an antipsychotic drug in HPD must weigh potential advantages versus potential side effects. The partial glutamatergic agonist N-acetyl cysteine (NAC) [39] was shown to be effective in treating adults with HPD, and given its acceptable adverse event profile, it may be considered as a first-line intervention, pending further trials. NAC did not demonstrate efficacy, however, in a randomized controlled trial in children with HPD [40].

SPD

While clomipramine has been shown to be more effective than desipramine in OCD, BDD, and HPD – disorders with similarities to SPD – no controlled trials have compared clomipramine with desipramine in SPD. Nevertheless, a number of trials of SSRIs, using a range of different doses, have demonstrated improvement in some measures of skin-picking severity in patients with SPD [41•]. These include two trials of fluoxetine [42, 43] (both using a flexible dosing schedule up to either 60 mg/day [42] or 80 mg/day [43]) and citalopram (20 mg/day) [44]. An open-label study has provided evidence

that escitalopram (dosing schedule up to 30 mg/day) may also be effective in reducing pathological skin-picking [45].

Psychotherapy

Psychotherapeutic treatment of OCRDs consists of CBT, adjusted for each specific disorder. CBT includes cognitive interventions such as cognitive restructuring (i.e., focusing on misperceptions and replacing these with more realistic appraisals), behavioural interventions such as habit-reversal therapy (HRT) and exposure and response prevention (ERP) (i.e., exposure to feared-object situations, and resisting compulsive behaviours like reassurance-seeking, washing, checking, and mirror-checking), and acceptance-enhanced behaviour therapy.

OCD

Meta-analyses of controlled psychotherapy studies in OCD have provided evidence for the efficacy of behaviour therapy-based ERP alone, cognitive restructuring alone, and ERP plus cognitive restructuring [46]. As such, CBT can be considered a first-line intervention for OCD. CBT is also useful in paediatric OCD.

There is limited evidence that the combination of pharmacological and psychological treatment is superior to either of these modalities alone [47–49]. Notably, a series of small RCTs suggests that administration of D-cycloserine may hasten the response to CBT in OCD, although the studies provide no evidence that the overall effectiveness of CBT is enhanced [50–52]. This is clearly an area that deserves further exploration.

BDD

CBT is currently considered the psychotherapy of choice for BDD [53], with randomized controlled studies (one with waiting-list controls [54], the other with no treatment controls [55]) having provided evidence for its efficacy in BDD.

Although there are no RCTs examining the efficacy of combined SSRIs and CBT in BDD, it has been suggested that the combination may also be helpful for some patients with BDD [34].

HD

Case studies [56, 57], uncontrolled clinical trials [58, 59], and a randomized waiting list-controlled trial [60] have demonstrated significant improvement in hoarding symptoms following treatment with CBT. Other (non-randomized controlled trial) studies have also suggested that multimodal approaches may be beneficial [59–61]. These include CBT either in individual or group format [59, 62•] as well as office and in-home visits emphasizing motivational interviewing, psychoeducation, decision-making training, exposure to situations of discarding items, cognitive restructuring, and response prevention (i.e., restricted acquisition of items) [56–58, 63].

It has been suggested that the combination of CBT and SRIs is useful in reducing hoarding symptoms and associated pathology [64••], although

no randomized controlled trials have been conducted to support this theory.

HPD

Cognitive-behavioral interventions have the largest supporting database for efficacy in HPD, in both adult and pediatric samples [65]. Randomized controlled trials and expert consensus guidelines support the use of CBT (HRT in particular), as first-line therapy for individuals with HPD [36, 65, 66]. HRT involves awareness training and self-monitoring, stimulus control to reduce the likelihood of initiating pulling, and competing response procedures in which other behaviours are substituted for hair-pulling (for example, squeezing a ball or knitting).

HRT has also been combined with acceptance and commitment therapy (ACT), an emerging cognitive-behavioral strategy that encourages acceptance of inevitable adverse experiences and promotes active commitment to adaptive strategies. In a randomized controlled trial of combined ACT/HRT, individuals in the treatment group demonstrated significant improvement in pulling and associated pathology compared to waiting-list controls [67].

Some studies have compared CBT and pharmacotherapy in the treatment of HPD. For example, CBT was shown to be more effective than clomipramine (250 mg/day) [68] and fluoxetine [69]. In addition, some data suggest that the combination of pharmacotherapy and psychotherapy may be useful. In a double-blind randomized medication augmentation study [70], individuals who had responded poorly to sertraline monotherapy were assigned add-on HRT, and those receiving sertraline and HRT showed significantly greater treatment gains than those treated with sertraline alone.

SPD

There is preliminary evidence for reduction in skin-picking with behavioural techniques such as HRT or acceptance-enhanced behaviour therapy (AEBT) [71]. For example, one controlled study suggested that, compared to waiting-list controls, individuals treated with HRT reported a greater reduction in skin-picking post-treatment and at follow-up [11]. Similarly, efficacy has been demonstrated for brief four-session CBT for SPD (consisting of psychoeducation, cognitive restructuring, emphasis on relapse prevention through enhancement of self-efficacy, and agreement on clearly defined measures to be applied in case of a lapse) in comparison with a waiting-list control, with treatment effects maintained at two-month follow-up [72•].

Other treatments

In research settings, there has been ongoing interest in targeting distinct brain circuits associated with OCRDs in treatment refractory patients. Repetitive transcranial magnetic stimulation (rTMS) has been studied in OCD, but is not considered a first-line approach [73]. Deep brain stimulation (DBS) and other neurosurgical approaches may be beneficial for some [74••, 75, 76].

Summary and recommendations

If left untreated, OCRDs may become chronic, resulting in substantial distress and psychosocial impairment. Treatment, on the other hand, may significantly contribute to alleviating symptoms and improving quality of life. Fortunately, both pharmacotherapeutic and psychotherapeutic interventions are now available for many of these conditions. As OCRDs remain underdiagnosed and undertreated, and as many misconceptions about these conditions persist, it is important to screen for these disorders and to provide psychoeducation to patients and communities. Advances in our understanding of the neurobiology of OCD may ultimately be useful in developing new targets for treatment.

Compliance with Ethics Guidelines

Conflict of Interest

Christine Lochner has received research support from the National Research Foundation of South Africa (NRF). Dan J. Stein has received research grants and/or consultancy honoraria from Abbott, AstraZeneca, Eli Lilly, GlaxoSmithKline, Jazz Pharmaceuticals, Johnson & Johnson, Lundbeck, Orion, Pfizer, Pharmacia, Roche, Servier, Solvay, Sumitomo, Takeda, Tikvah, and Wyeth. He also is a member of the Scientific Advisory Board of the Trichotillomania Learning Centre.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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