Obsessive-compulsive disorder: current management options

PAUL HARRIS, LYNNE DRUMMOND AND NAOMI FINEBERG

Obsessive-compulsive disorder is a disabling condition that can severely affect daily activities in both adults and children. This article discusses the psychological and drug treatments available, and highlights instances where referral for specialised treatment is appropriate.

In everyday speech, someone may be described as 'obsessive' about a subject that interests them deeply such as football or a particular pop band. This, however, is a far cry from the severely disabling and overwhelming experience of obsessive-compulsive disorder (OCD).

Both the International Classification of Diseases (ICD-11)[1] and Diagnostic and Statistical Manual of Mental Disorders (DSM-5)[2] define OCD as comprising either obsessions or compulsions, or both together. For the first time, both the DSM-5 and now the ICD-11 contain a separate chapter, distinct from anxiety disorders, solely devoted to Obsessive Compulsive Related Disorders (OCRDs).

Obsessions are unwanted thoughts, images or impulses that intrude on consciousness and cause anxiety or distress (see Table 1). They often involve harm-related themes. Intrusive obsessional thoughts differ from delusions in that they are egodystonic and are recognised by the individual as irrational.

Compulsions are ritualistic behaviours that are often developed in an attempt to reduce obsessional anxiety (see Table 2). They are either not really connected to the obsessive fear or are clearly excessive. For example, a woman with unwanted thoughts of having sex with strangers may develop a compulsion to wash her hands repeatedly, or a man with the obsession that his home may be burgled may check he has locked the front door 25 times. Compulsions may reduce anxiety or distress, but if so only by a small amount. Moreover, reassurance afforded by the compulsion is short lived. The temporary relief serves only to reinforce the compulsion and the act is repeated over and over.

Who suffers from OCD?

Epidemiological studies have shown that OCD affects males and females roughly equally throughout the world.[3] OCD is found in all cultures and social classes.

In a prospective study of 591 subjects aged between 20/21

- Fear of causing harm to oneself or someone else (through an act of omission or commission)
- Fear of contamination
- Fear of behaving unacceptably
- Fear of losing objects or inadvertent disclosure of information
- Blasphemous or religious obsessions
- Fear of making a mistake (perfectionism)
- Need for symmetry or exactness

Table 1. Common obsessions

and 49/50 years from the general population of Zurich, Switzerland, interviewed seven times over 30 years, the cumulative prevalence of OCD was 3.5%, the prevalence of a sub-threshold obsessive-compulsive syndrome associated with less disability was 9.7% and the prevalence of obsessive compulsive symptoms was 11.2 %.[4] There appear to be two peaks in the age of onset of OCD symptoms, the first in early adolescence and the second occurring in early adulthood.[5] A longitudinal community-based study found that approximately two-thirds of cases had emerged by the age of 22 years.[6]

Many children display obsessive and compulsive behaviours; for example, counting and repeating rhymes and games, or even excessive hand-washing following a school talk on microbes. Although most children will simply grow out of this phase, a small but significant group, usually with more severe problems, will go on to develop OCD.

Some cases of acute childhood-onset illness are thought to be associated with infection with group A beta-haemolytic streptococci, originally described under the acronym PANDAS (paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections) and subsequently renamed paediatric acute neuropsychiatric syndrome (PANS), since evidence highlighted the fact that several agents other than streptococcus might be involved.[7] These patients may also develop tics or choreiform movements as part of the disorder. The incidence of this disorder has not been established. However, most patients present with a history of mild non-clinical obsessions prior to the onset of handicapping OCD. No specific life event is associated with the onset of illness, but almost any kind of stress may exacerbate the condition.

Behaviours
- Handwashing
- Cleaning
- Ordering and arranging
- Checking
- Asking for reassurance
- Hoarding

Mental acts
- Repeating words silently
- Counting
- 'Reliving' actions mentally
- Repetitive 'praying'
- Repeating words or sequences as a form of 'undoing' the obsession

Table 2. Common compulsions

Genetic and environmental factors contribute to the development of OCD, with good evidence suggesting that the cortico-striato-thalamo-cortical (CSTC) circuit is implicated in the pathophysiology of the disorder.[8] It is important to emphasise that those who suffer with OCD can have a reduced quality of life that is similar to patients with a diagnosis of schizophrenia.[9]

Treatment

NICE guidance on the treatment of OCD and body dysmorphic disorder (BDD) in both adults and children was published in 2005.[10] NICE has marked this guideline for update, and at the time of writing, a consultation process is underway.

The current guideline states that adults with OCD should be treated according to a model of stepped-care ranging from public awareness and information through to specialised inpatient treatment for the most severely handicapped, treatment-resistant individuals (see Figure 1).[10] Figure 2 illustrates steps 3–5 of the NICE-recommended care pathway for adults with OCD.[10]

NICE guidance for children and adolescents is similar to that for adults, although the prescription of SSRIs for this group needs special care (see Figure 3).[10] Although SSRIs are efficacious in OCD in children and adolescents, their use has been associated with the development of harm-related events in the short term. For example, a meta-analysis including 27 randomised controlled trials of SSRI use in children and adolescents showed a small increase in suicidal thoughts and self-harm with SSRIs compared to placebo, although no completed suicides.[11] NICE states that an SSRI should not be prescribed to a child or adolescent without an assessment and diagnosis by a child and adolescent psychiatrist. Only fluvoxamine and sertraline are currently licensed for use in children and adolescents with OCD.

Psychological approaches

Exposure principles

Exposure works on the observation that someone with OCD who has an intense fear of a situation, when confronted with the situation, will either attempt to escape or perform activities (compulsions or rituals) to reduce or prevent the harm they fear will result. High anxiety is extremely unpleasant and, because escape and compulsive behaviours reduce the anxiety, the escape behaviours are reinforced by the reduction of the anxiety. Consequently, the symptoms are worsened by each episode of brief exposure and escape.

In exposure treatment, *a form of cognitive behavioural therapy,* ***(Author: this text added; is this OK?)*** the aim is to produce prolonged periods of contact with the feared situation until the anxiety reduces naturally (habituation). Although compulsions reduce anxiety and reinforce further compulsive behaviours and rituals, the reduction in anxiety produced by a compulsive ritual tends to be small and the effect temporary. In effect, rituals prevent or interrupt therapeutic exposure and instead increase

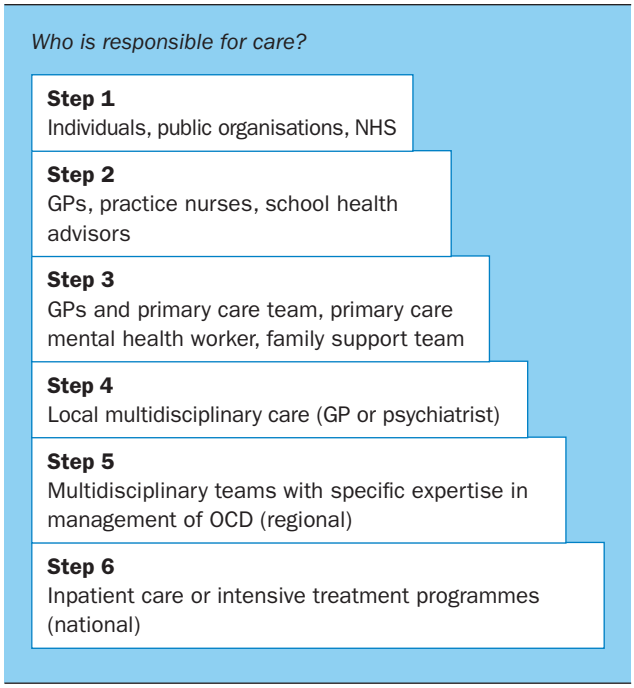

Figure 1. NICE-recommended stepped care model for the management of obsessive-compulsive disorder (OCD)[10]

the tendency to ritualise further.

With treatment, the patient is asked to expose themselves to the fear-provoking situation and remain in that situation until the anxiety has naturally reduced substantially. This usually takes between 60 and 90 minutes. For patients with obsessions and overt compulsions, the treatment involves a prolonged course of graded exposure in real life to the feared situation or situations, together with self-imposed response prevention.

Although this is a simple technique in theory, the skill lies in the therapist accurately assessing the correct fear-provoking cues, educating the patient about the therapy and helping him or her to agree on a level of exposure that will cause a degree of anxiety that can be tolerated.

Although exposure is the cornerstone of treatment of OCD, it needs to be combined with response prevention, *ie* encouragement not to perform compulsions, which can be either physical or mental. This can usually be achieved by demonstrating to the patient how they interfere with exposure. The combined therapy is known as exposure and response prevention (ERP).

The same exposure tasks are then repeated by the patient at least daily (preferably three times a day) until there is little anxiety even at the commencement of the exposure. A more anxiety-provoking situation can then be tackled, and the process repeated until the patient has completed all the tasks on the individual anxiety hierarchy devised with the therapist.

The efficacy of self-exposure has led to the development of a number of self-help manuals. However, few patients can successfully complete a treatment programme without at least some professional guidance. The patient should ideally be seen initially for education about anxiety and its treatment and for help in devising treatment targets. Subsequent meetings are required to monitor progress, give encouragement and advise on any difficulties that may arise.

The most effective exposure has been shown to be:

- Prolonged rather than of short duration
- In real life rather than in fantasy
- Regularly practised with self-exposure homework tasks.

Outcome of psychological treatment

In controlled trials, the treatment of OCD using straightforward graduated exposure and self-imposed response prevention has been shown to be effective in the majority of patients that complete the treatment. A systematic review and meta-analysis of 37 randomised trials showed that cognitive behavioural therapies were superior in reducing symptoms compared to remaining on a waiting list or other psychological therapies acting as a control.[12]

Despite these good results, many patients fail to engage in exposure treatments while others relapse and require booster sessions. It is advisable to follow patients up for several months after the conclusion of therapy to ensure that their gains are maintained and that, if signs of relapse develop, they can be dealt with promptly before the patient has reverted to pretreatment levels of disability.

Despite its attractiveness in this disorder, there is little

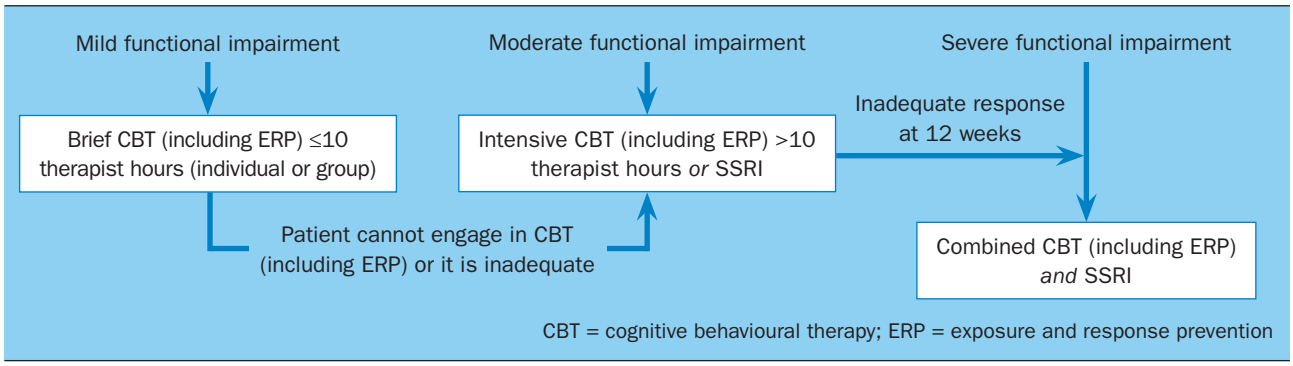

Figure 2. Treatment options for adults with obsessive-compulsive disorder (OCD) – steps 3–5 of the of the NICE-recommended care pathway[10]

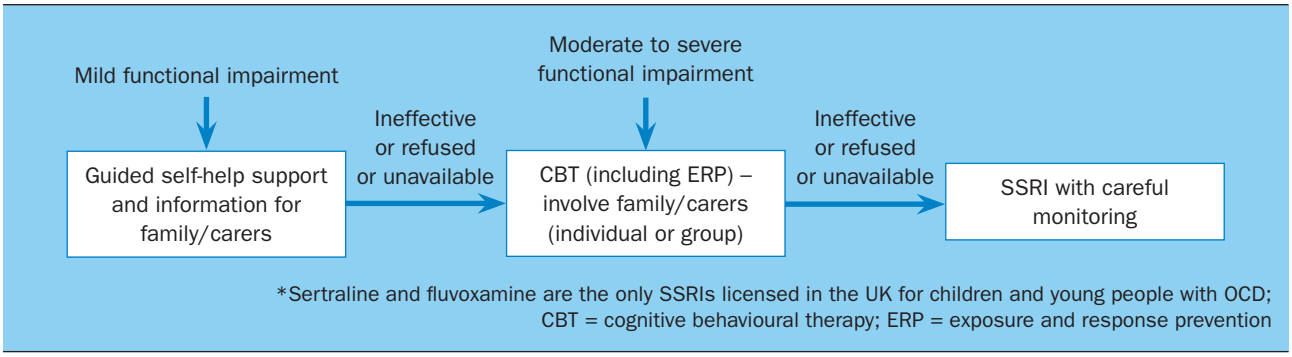

Figure 3. NICE-recommended treatment options for children with obsessive-compulsive disorder (OCD)[10]

evidence to suggest that cognitive therapy, *another form o* ***(Author: this text added; is this OK?),*** has any advantage exposure therapy in the treatment of OCD.[13] Cognitive therapy attempts to help the patient re-evaluate strongly held and distorted beliefs associated with their obsessional thoughts, and enable them to adopt a more accurate or realistic appraisal. Different techniques can be employed, but a common approach is to use 'behavioural experiments' to test the validity of the patient's beliefs about control and threat.[14]

However, accessing any form of ERP or CBT may be difficult for some individuals due to local service provision or patient factors. Therefore, treatment with remote access CBT, for example via an online platform, has been used in some circumstances. A meta-analysis showed similar results with remote CBT when compared to face-to-face CBT,[15] suggesting this technique may have some value.

Additionally, there are an increasing number of studies examining the possible use of so-called 'third-wave' therapies in OCD. These therapies are loosely based on the Buddhist ideas of mindfulness, and encourage the individual to be aware to what is happening in the present moment, rather than reacting automatically. This approach emphasises adopting a kind, compassionate, non-judgemental attitude to oneself. For example, rather than trying to neutralise internal experiences with compulsions, mindfulness teaches you to allow the moment to stay as it is.

Drug	Suggested dose range
Sertraline	50–200mg daily
Fluoxetine	20–60mg daily
Citalopram*	20–40mg daily
Paroxetine	20–60mg daily
Escitalopram	10–20mg daily
Clomipramine	100–250mg daily
*Not licensed for OCD in the UK	

Table 3. Suggested dose ranges of individual SSRIs and clomipramine for treating obsessive-compulsive disorder (OCD); the highest tolerated dose should be used. ***(Author: does this apply to just the SSRIs or to clomipramine as well?)***

So far, none of the third-wave therapies have been shown to be conclusively efficacious, although some authors have suggested that they may be useful in people with OCD refractory to ERP.[16]

Drug treatment

Multiple large multicentre trials have shown that both clomipramine and SSRIs are efficacious in OCD. This finding has been repeatedly confirmed, notably by a recent systematic review and network meta-analysis including 7643 patients from randomised trials.[17] This review also found that head-to-head comparisons between clomipramine and SSRIs, and also between individual SSRIs, have not displayed a distinct advantage of one medication over another. Therefore, in the face of potentially equivalent efficacy, the choice of drug depends to a large extent on the side-effect profile. Of the SSRIs, citalopram does not have marketing authorisation for OCD in the UK and would therefore be prescribed 'off label'.

SSRIs appear to be better tolerated than clomipramine[17] and are rarely fatal in overdose.[18] Clomipramine can produce unpleasant anticholinergic side-effects such as sedation, dry mouth, constipation, urinary delay, tremor and blurred vision; and occasionally, particularly at high dosages, convulsions and arrhythmia have been reported. Therefore, SSRIs should usually be used as the treatment of first choice, with clomipramine reserved for those who cannot tolerate SSRIs or who have failed to respond to them.

Choosing between SSRIs is difficult because their side-effect profiles are similar. Occasionally the possibility of a potential drug interaction directs the choice. In these circumstances, sertraline and citalopram may be preferred because they are relatively weak inhibitors of hepatic cytochrome P450-metabolising enzymes. Fluoxetine and its active metabolite have long half-lives, resulting in fewer withdrawal reactions and advantages for patients who frequently forget their medication.

Response to treatment in OCD is slow and gradual. Incremental improvement occurs over weeks and months and gains continue to be made for up to two years or for as long as treatment is continued. Patients may need to be persuaded to continue with treatment in the early stages if progress seems frustratingly slow.

What is the most effective dose?

There is good evidence that daily doses of SSRIs at the higher end of the dose range are more effective, but are associated with poorer tolerability.[19] However, given that improvements in OCD symptoms can take several weeks to establish, irrespective of the dose, it is advisable to start SSRIs at the lower end of their dose range. This will help minimise early side-effects. The dose can then be titrated upwards slowly while measuring clinical response.

Treatment for up to 12 weeks at the highest tolerated dose may be required to establish if there is an adequate treatment response, although the highest incremental benefits may often be seen earlier on in treatment.[20] Suggested dose ranges for individual SSRIs and also clomipramine are shown in Table 3.

OCD is a chronic illness, so it is important that treatment continues to be effective over the longer term. However, the optimal duration of treatment is currently uncertain. Continued treatment with SSRIs appears to sustain benefit and protect against relapse.[21]

Treating refractory OCD

Unfortunately, approximately one-third of OCD patients seem not to respond to these initial treatment options.[22] In this situation, a sensible first step would be to review the patient's diagnosis. If confidence is high that the correct diagnosis has been made, the steps outlined below can be considered.

Psychological approaches

If a patient does not respond to initial psychological treatment, it is worthwhile reviewing the treatment and analysing possible reasons for failure. The main reasons for treatment failure and the suggested actions to take are shown in Table 4.

Pharmacological approaches

Figure 4 examines possible treatment approaches for patients who have not responded to SSRI or clomipramine. Prescribers should ensure that an adequate trial of an SSRI or clomipramine (at least 12 weeks at the maximum tolerated dosage) has been attempted. An initial failure of either one of these drugs may be followed up by switching to an alternative SSRI or, if not yet prescribed, clomipramine. Again, the new drug should be trialled at maximum tolerated dosage for at least 12 weeks.

If there is still no satisfactory response, the dose of SSRI (not clomipramine) may be extended beyond the normal licensed (*BNF*)[23] daily dose limits. This can sometimes be beneficial.[24,25] As this involves prescribing outside the drug's labelled indications, fully informed consent should be obtained and documented. In the case of citalopram and escitalopram, higher dosing schedules should be accompanied by regular ECG monitoring to check for signs of QTc prolongation. In the case of all SSRIs, careful assessment and monitoring for adverse effects is advisable.

It should also be noted that some patients who have not responded to medication may still benefit from adjunctive CBT at this stage, if it had not yet been attempted.[26]

Possible explanation of previous failure	Action
Difficulty initiating or adhering to ERP	Consider cognitive therapy, motivational interviewing or family therapy Educate patient about the problem and discharge (can be re-referred if motivation changes)
Inadequate application of ERP	Ensure new course of therapy is fully aligned with the principles of ERP for OCD
Treatment in hospital/clinic has not generalised to home	Home-based treatment or treatment in hospital with weekend leave and domiciliary treatment
Cognitive (mental) rituals are prominent	Education plus either: Audiotape of anxiogenic thoughts *or* High-intensity ERP
Presence of co-morbid depression	Antidepressant drug followed by ERP Cognitive therapy for depression as necessary
Overvalued ideation that obsessions are realistic (poor insight OCD)	High-intensity ERP *or* Cognitive restructuring followed by exposure and response prevention *or* Psychoeducational approaches such as danger ideation reduction therapy (DIRT)
Failure to habituate without major depression or overvalued ideation	Cognitive therapy *or* Medication enhancement plus ERP *or* Neurosurgery/deep brain stimulation (when all of the above have failed)
ERP = exposure and response prevention	

Table 4. Common reasons for failure of psychological treatments for obsessive-compulsive disorder (OCD) and suggested actions

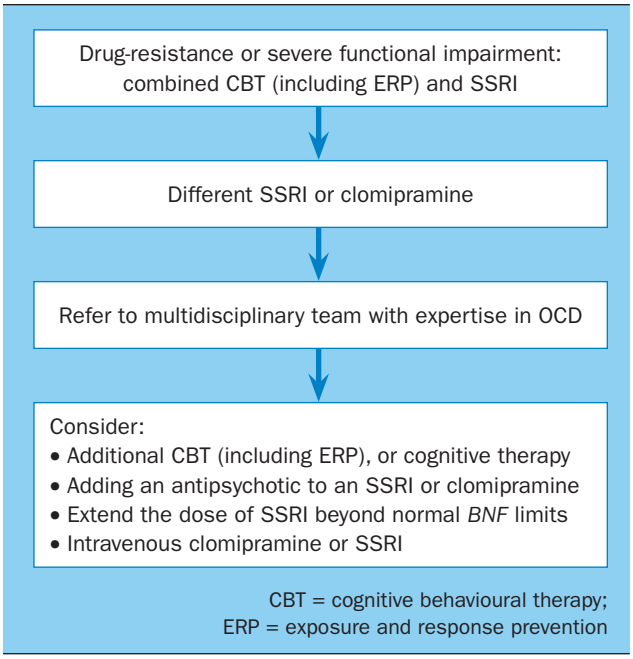

Figure 4. Possible approaches for patients with obsessive-compulsive disorder (OCD) resistant to drug treatment – steps 4–6 of the of the NICE-recommended care pathway[10]

Combination strategies

If these strategies do not yield a favourable response, the addition of a dopamine antagonist (antipsychotic drug) can also be beneficial. Although no trials have shown their benefit as monotherapy, the effectiveness of the addition of a dopamine antagonist to either an SSRI or clomipramine is supported by several randomised controlled trials and meta-analyses.[27-29] According to these studies, the second-generation antipsychotics risperidone, quetiapine, olanzapine and aripiprazole and the first-generation antipsychotic haloperidol appear to be efficacious when used as adjunctive treatments. Because of their more favourable side-effect profiles, a second-generation antipsychotic should usually be trialled before haloperidol. Adjunctive dopamine antagonist medication may be particularly beneficial for patients with co-morbid tic disorders.[30]

There are currently no studies that have been designed to determine the optimal dosage of dopamine antagonists in OCD. Whereas the existing studies have found efficacy using moderate dosages (*eg* risperidone 500µg–6mg or aripiprazole 10–15mg daily) many clinicians have anecdotally found greatest benefit using low daily dosages (*eg* aripiprazole 2.5mg), as these may be better tolerated. Therefore, as a guide, it is recommended to initiate treatment with a low dose of adjunctive dopamine antagonist and titrate upwards slowly while carefully monitoring for side-effects such as sedation or extrapyramidal disorders. These medications can also potentially cause significant metabolic side-effects, so should be discontinued if no benefit is seen within 6–10 weeks.

Parenteral administration

Intravenous (IV) administration of an SSRI or clomipramine may also be considered if symptoms remain intractable. Although there are obviously practical considerations that might limit the usefulness of this approach, including the recommendation for continual ECG monitoring during and after the infusion, two double-blind trials have shown a benefit of IV clomipramine over the short term.[31,32] This approach may be best reserved for the treatment of inpatients in whom the risks to health or safety associated with their severe OCD are high (*eg* they are refusing to drink) and for whom a speedy resolution of symptoms is urgently required.

Novel pharmacological agents

At this point, if symptoms have still not responded satisfactorily, a specialist centre might consider using a novel pharmacological agent.

Although still a developing area of research, there is emerging evidence that abnormal glutamatergic transmission may play a role in the development of OCD. This has led to interest in the use of compounds acting on the glutamate system as treatments for OCD.[33] Adjunctive memantine has been trialled and has shown the most consistent promise when compared to similar agents,[34] but lamotrigine has also displayed some evidence of efficacy. Ketamine has attracted interest due to its rapid onset of action, although further research is needed in this area.

Neurosurgical and other somatic procedures

An extremely small number of individuals remain extremely incapacitated despite these interventions. In these patients, more invasive treatments such as neurosurgery may be considered. Two different approaches have been shown to help OCD sufferers.

One neurosurgical option involves a procedure that causes small areas of tissue damage in the brain circuits that are thought to function abnormally in OCD. A recent systematic review supported the efficacy of both dorsal anterior cingulotomy and anterior capsulotomy for highly treatment-refractory patients.[35] However, the observational nature of the available data limits the ability to directly compare these procedures.

The other neurosurgical approach is the use of electrical deep brain stimulation (DBS). This is a relatively new procedure that causes less irreversible tissue damage. A meta-analysis found that approximately 60% of patients undergoing DBS respond to this treatment.[36] A recent UK-based study involving six patients with highly refractory OCD has also demonstrated a good response to DBS.[37]

There are risks associated with both types of neurosurgical treatment and these need to be carefully weighed against the burden of chronic, severe OCD that has not responded to all other reasonable treatment approaches.

Alternative non-invasive approaches for targeted neurostimulation are actively under investigation as interventions for OCD. For example, transcranial magnetic stimulation has been studied in patients who have not responded adequately to SSRIs and has been found to be helpful, although further work

in this area is needed before recommendations can be confidently made.[38]

Conclusion

OCD is a condition that affects a sizeable proportion of the population. Most patients respond to psychological advice accompanied by ERP and/or psychopharmacological treatment.

Patients who do not respond to these measures may be helped by either more specialised or intensive psychological or pharmacological treatment. A small group of most severely disabled and treatment-resistant individuals may require referral for highly specialised treatment, either as an outpatient or inpatient, and some of these individuals may qualify for consideration of neurosurgical intervention.

Further reading

Drummond LM. *Obsessive-compulsive disorders: all you want to know about OCD for people living with OCD, carers and clinicians*. Cambridge: Cambridge University Press and Royal College of Psychiatrists, 2018.

Reghunandanan S, Fineberg NA, Stein DS (Eds). *Obsessive Compulsive Disorder (Second Edition)*. Oxford Psychiatry Library, Oxford University Press, UK, 2015.

References

1. World Health Organization. *International statistical classification of diseases and related health problems.* 11th revision (ICD-11). WHO, 2018.
2. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders* (*DSM-5).* APA, 2013.
3. Kessler RC, *et al*. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005;62:593–602.
4. Fineberg NA, *et al*. Lifetime comorbidity of obsessive-compulsive disorder and sub-threshold obsessive-compulsive symptomatology in the community: impact, prevalence, socio-demographic and clinical characteristics. *Int J Psychiatry Clin Pract.* 2013;17(3):188–96.
5. Anholt GE, *et al*. Age of onset in obsessive-compulsive disorder: admixture analysis with a large sample. *Psychol Med* 2013;21:1–10.
6. Fineberg NA, *et al*. A prospective population-based cohort study of the prevalence, incidence and impact of obsessive-compulsive symptomatology, *Int J Psychiatry Clin Pract* 2013;17(3):170–8.
7. Chiarello F, *et al*. An expert opinion on PANDAS/PANS: highlights and controversies. *Int J Psychiatry Clin Pract* 2017;21(2):91–8.
8. Milad MR, Rauch SL. Obsessive-compulsive disorder: beyond segregated cortico-striatal pathways. *Trends Cognitive Sci* 2012;16(1):43–51.
9. Subramaniam M, *et al*. Quality of life in obsessive-compulsive disorder: impact of the disorder and of treatment. *CNS Drugs* 2013;27(5):367–83.
10. National Institute for Health and Care Excellence. *Obsessive-compulsive disorder and body dysmorphic disorder: treatment.* CG31. 2005. Available from: https://www.nice.org.uk/Guidance/CG31
11. Bridge JA, *et al*. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. *JAMA* 2007;297:1683–96.
12. Öst LG, *et al*. Cognitive behavioral treatments of obsessive–compulsive disorder. A systematic review and meta-analysis of studies published 1993–2014. *Clin Psychology Rev* 2015. 40:156-69.
13. Ougrin D. Efficacy of exposure versus cognitive therapy in anxiety disorders: systematic review and meta-analysis. *BMC Psychiatry* 2011;11(1):200.
14. Reghunandanan S, *et al*. *Obsessive-compulsive and related disorders.* 2nd edn. Oxford University Press, 2015.
15. Wootton BM. Remote cognitive-behavior therapy for obsessive-compulsive symptoms: A meta-analysis. *Clin Psychol Rev* 2016;43:103–13.
16. Külz AK, *et al*. Mindfulness-based cognitive therapy (MBCT) in patients with obsessive–compulsive disorder (OCD) and residual symptoms after cognitive behavioral therapy (CBT): a randomized controlled trial. *Eur Arch Psychiatry Clin Neurosci* 2019;269(2):223–33.
17. Skapinakis P, *et al*. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis. *Lancet Psychiatry* 2016;3(8):730–9.
18. Isbister GK, *et al*. Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose. *J Toxicol: Clin Toxicol* 2004;42(3):277–85.
19. Bloch MH, *et al*. Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. *Mol Psychiatry* 2010;15(8):850–5.
20. Issaria Y, *et al*. Early onset of response with selective serotonin reuptake inhibitors in obsessive- compulsive disorder: a meta-analysis. *J Clin Psychiatry* 2016;77(5):605–11.
21. Fineberg NA, *et al*. Sustained response versus relapse: the pharmacotherapeutic goal for obsessive-compulsive disorder. *Int Clin Psychopharmacol* 2007 Nov;22(6):313-22.
22. Hirschtritt ME, *et al*. Obsessive-compulsive disorder: advances in diagnosis and treatment. *JAMA* 2017;317(13):1358–67.
23. Joint Formulary Committee. *BNF* 76. London: BMJ Group and Pharmaceutical Press, 2018.
24. Pampaloni I, *et al*. High-dose selective serotonin reuptake inhibitors in OCD: a systematic retrospective case notes survey. *J Psychopharmacol* 2010;24(10):1439–45.
25. Ninan PT, *et al*. High-Dose Sertraline Strategy for Nonresponders to Acute Treatment for Obsessive-Compulsive Disorder: A Multicenter Double-Blind Trial. *J Clin Psychiatry* 2006;67(1):15–22.
26. Simpson HB, *et al*. Cognitive-behavioral therapy vs risperidone for augmenting serotonin reuptake inhibitors in obsessive-compulsive disorder: a randomized clinical trial. *JAMA Psychiatry* 2013;70(11):1190–9.
27. Dold M, *et al*. Antipsychotic augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder: a meta-analysis of double-blind, randomized, placebo-controlled trials. *Int J Neuropsychopharmacol* 2013;16(3):557–74.
28. Veale D, *et al*. Atypical antipsychotic augmentation in SSRI treatment refractory obsessive-compulsive disorder: a systematic review and meta-analysis. *BMC Psychiatry* 2014;14:317.
29. Dold M, *et al*. Antipsychotic augmentation of serotonin reuptake inhibitors in treatment-resistant obsessive-compulsive disorder: an update meta-analysis of double-blind, randomized, placebo-controlled trials. *Int J Neuropsychopharmacol* 2015;18(9).
30. Bloch M, *et al*. A systematic review: antipsychotic augmentation with treatment refractory obsessive-compulsive disorder. *Mol Psychiatry* 2006;11(7):622–32.
31. Fallon BA, *et al*. Intravenous clomipramine for obsessive-compulsive disorder refractory to oral clomipramine: a placebo-controlled study. *Arch Gen Psychiatry* 1998;55(10):918–24.
32. Koran LM, *et al*. Rapid benefit of intravenous pulse loading of clomipramine in obsessive-compulsive disorder. *Am J Psychiatry*

1997;154(3):396–401.
33. Marinova Z, *et al*. Glutamate-modulating drugs as a potential therapeutic strategy in obsessive-compulsive disorder. *Current Neuropharmacol* 2017;15(7):977–95.
34. Kishi T, *et al*. Combination therapy of serotonin reuptake inhibitors and memantine for obsessive-compulsive disorder: a meta-analysis of double-blind, randomized, placebo-controlled trials. *J Alzheimer's Dis* 2018. 64(1): 43–8.
35. Brown LT, *et al*. Dorsal anterior cingulotomy and anterior capsulotomy for severe, refractory obsessive-compulsive disorder: a systematic review of observational studies. *J Neurosurg* 2016;124(1):77–89.
36. Alonso P, *et al*. Deep brain stimulation for obsessive-compulsive disorder: a meta-analysis of treatment outcome and predictors of response. *PloS One* 2015;10(7).
37. Tyagi H, *et al*. A randomised trial directly comparing ventral capsule and anteromedial subthalamic nucleus stimulation in obsessive compulsive disorder: clinical and imaging evidence for dissociable effects. *Biol Psychiatry* 2019;85(9):726–34.
38. Trevizol AP, *et al*. Transcranial magnetic stimulation for obsessive-compulsive disorder: an updated systematic review and meta-analysis. *J ECT* 2016;32(4):262–6.

Declaration of interests

Dr Paul Harris: none to declare
Dr Lynne Drummond has received grants from MRC and NIHR.
Prof Naomi Fineberg has received research grants, paid speaking engagements including travel and hospitality, honoraria for lectures or editorial duties, financial support to attend meetings or royalties from the following organisations; ECNP, UK NIHR, EU H2020, Abbott, Sun Pharma, Indian Association of Biological Psychiatry, BAP, RCPsych, CINP, Taylor and Francis, Elsevier, Oxford University Press, Wiley.

Dr Paul Harris is a Higher Trainee in General Adult Psychiatry at the South London and Maudsley NHS Foundation Trust, Dr Lynne Drummond is a Consultant Psychiatrist running a highly specialised inpatient and home-based service for severe, complex, resistant OCD at South West London and St George's Mental Health NHS Trust, and Professor Naomi Fineberg is Professor of Psychiatry at the University of Hertfordshire and Consultant Psychiatrist at the Hertfordshire Partnership University NHS Foundation Trust Highly Specialised OCD Service, Rosanne House, Welwyn Garden City