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TRENDS AND PERSPECTIVES

From Treatment Response to Recovery: A Realistic Goal in OCD

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Abstract

Despite longitudinal studies reporting symptomatic remission rates ranging from 32% to 70%, Obsessive-Compulsive Disorder is considered a persistent and very disabling disorder. However, these studies suggest that recovery can be a realistic goal for a subgroup of the Obsessive-Compulsive Disorder population and that a clear definition of recovery is timely in Obsessive-Compulsive Disorder. The aim of this paper is to discuss the dimensions of and propose an operational definition of recovery in Obsessive-Compulsive Disorder. Considering the impact generated by the definition of recovery for other mental disorders, this article discusses how this concept may shape the future of research and clinical practice in Obsessive-Compulsive Disorder. Ultimately, the hope is that the management of Obsessive-Compulsive Disorder may parallel, and expand upon, some of the current approaches implemented in the care of schizophrenia, so that early diagnosis, stepped-care techniques, and a personalized approach can be used to create recovery-oriented treatment programs and influence policy making for Obsessive-Compulsive Disorder.

Keywords: recovery, remission, OCD, resistance, early diagnosis

Introduction

Obsessive Compulsive Disorder (OCD) is considered a persistent and highly disabling condition. More than 15 years ago, we examined the methodological issues related to refractoriness in OCD and suggested that the lack of consistent definitions was the main factor that prevented the development of a cumulative body of data on homogenous samples of "nonresponsive" patients and consequently the implementation of second-line treatments (Pallanti et al., 2002). At that time we proposed the use of operational definitions for the stages and levels of response based on the Clinical Global Impression Scale (CGI) (Guy 1976) and the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) (Goodman et al., 1989). These definitions were intended to enable data comparisons across studies and promote recategorization of patients in the clinical setting.

While the definition of such grades of nonresponse has helped in collecting data among different studies in this difficult to treat population, attention to the subpopulation of long-term responsive subjects is still neglected.

Effectively, resistance is often defined as the lack of response following the trial of just 1 selective serotonin reuptake inhibitor (SSRI) in research as well in clinical practice. This is critical in 2 ways: first, as it represents something of a tautology, defining OCD on the basis of the response to a specific treatment, and second, because it implies that SSRIs are all equivalent,

neglecting the fact that every so-called "SSRI" has its own specific mechanism and target of action, as clearly described by the Neuroscience Based Nomenclature of drugs. If responsiveness is defined as improvement from one SSRI, then it seems likely that there has been an overestimation of resistance based on this limited definition. Moreover, this view leads to the management of OCD as a homogeneous disorder, with the consequence that trials may fail to adequately account for the actual heterogeneity and high degree of comorbidity found in OCD.

The definition and characterization of "treatment-resistant OCD" remains a significant challenge for clinicians and is not adequately considered in the current guidelines (NICE 2006; APA 2007). This has helped in fostering studies and recommendations with several different algorithms for patients whose symptoms fail to respond adequately to first-line treatments (Pallanti et al., 2014; Van Ameringen et al., 2014; Grant et al., 2016; Menchón et al., 2016).

Traditionally in psychiatric disorders, response has been conceptualized as a short-term improvement in symptoms, while remission has been characterized by a significant reduction in symptoms, typically below the threshold utilized for the initial diagnosis.

In recent years, the concept of "recovery", broadly intended as sustained symptom remission along with return of function to premorbid levels (Andreasen et al., 2005), has gained increasing attention in psychiatry, directing research and clinical practice for disorders that are usually considered chronic and intractable. This is the case for schizophrenia, where the implementation of recovery-oriented programs has led to a great improvement in both symptomatic and functional outcomes (White et al., 2018).

However, the concept of recovery has not yet been applied to OCD, where generally "response" as opposed to "recovery" has been considered a reasonable outcome. Treatment response in OCD (typically a reduction of 25%–35% in the YBOCS) can convey a relative meaning in terms of clinical significance, and still correspond to high levels of disability (Farris et al., 2013; Macy et al., 2013). Moreover, the definition of treatment response in OCD is perhaps less compelling than that for anxiety disorders, where it is generally defined as at least a 50% reduction in the Hamilton Rating Scale for Anxiety (HAM-A) score from baseline (Sheehan, 2001; Bandelow, 2006).

The current low-outcome expectations in OCD and the apparent benefit conveyed by the introduction of the concept of recovery for other severe mental disorders prompted us to investigate this idea in OCD. Hence, our goal is to propose an operational definition of recovery that could be realistically applied in research and clinical practice.

Outcomes in OCD: is Recovery a realistic goal? The Myth of the negative prognosis

To propose a definition of recovery in OCD that would be consistent with expectations for optimal outcome, it is important to evaluate existing studies reporting short- and long-term treatment outcomes.

Short-Term Clinical Trials on SSRIs and CBT

For the most part, randomized control trials investigating the efficacy of SSRIs and Cognitive Behavioral Therapy (CBT) in OCD have a mean duration of almost 12 weeks (Pizarro et al., 2014; Öst et al., 2015). These studies, designed to focus on short-term improvements, use response rather than recovery as the standard measure of treatment efficacy, usually operationalized as a reduction of at least 25% in the YBOCS or as a score of 1 (very much improved) or 2 (much improved) on the CGI-Improvement (CGI-I) scale. Meta-analyses of these studies demonstrated that these treatments conferred statistically significant changes in OCD (Soomro et al., 2008; Olatunji et al., 2013; Öst et al., 2015). Nonetheless, it is critical to consider that effect sizes do not necessarily correlate with clinically significant improvement. Few studies describe the clinical significance of response to treatment, using different cut-offs in severity scores ranging from 16 to 7 points at the YBOCS, to define the percentage of patients that rated in the subclinical range (Soomro et al., 2008; Olatunji et al., 2013; Öst et al., 2015). A recent meta-analysis (McGuire et al., 2015) examined diagnostic remission for youth with OCD receiving either CBT or serotonin reuptake inhibitors (SRIs) relative to the control conditions. Defining remission as reaching a CY-BOCS of 14 or as a reduction of 40% to 50% in CY-BOCS, that study remarkably found that the average remission rate across trials was 57% for CBT and 47% for SRIs.

Longitudinal Studies

Prospective studies conducted in the pre-SRIs/CBT treatment era found that spontaneous remission, with recovery defined as absence of clinically significant symptoms for 1 to 5 years, ranged between 20% and 30% (Goodwin, et al., 1969; Skoog and Skoog, 1999). A meta-analysis of long-term (≥1 year) studies in adult patients with OCD treated with SRIs or CBT found that more than one-half of the patients achieved remission, defined as a YBOCS rating <16 over 5 years of follow-up (Sharma et al., 2014). Remission rates reported in child or adolescent studies tend to be even higher (32%–70%) (Marcks et al., 2011). A very recent 3-year naturalistic outcome study conducted in 109 children and adolescents with OCD treated with CBT and augmented when indicated by SSRIs, and eventually a second-generation antipsychotic, studied response and remission (Melin et al., 2018). This study defined treatment response as a CY-BOCS total score ≤15 and remission as CY-BOCS total score ≤10. In this group, 66.1% participants were found to be in remission, while another 19.2% had responded to treatment at the 3-year follow-up. The results also indicate that improvement was found with regard to psycho-social functioning as measured by Children's OCD Impact Scale (COIS). Overall, longitudinal studies suggest that the prognosis in OCD is more favorable than is often believed (Sharma et al., 2014). Furthermore, the results show that full remission, defined as the absence of symptoms, minimizes the risk of relapse with a rate of recurrence 7% at year 1, 15% at year 3, and 25% at year 5 and beyond (Marcks et al., 2011; Eisen et al., 2013).

Summary

Short-term clinical trials are important in identifying therapeutic strategies and response rates; however, they may be limited in the ability to predict the potential for long-term remission of symptoms. Contrary to generally held beliefs and despite the differences in reported rates of remission, in part due to the heterogeneity of the disorder and different methods of defining remission, there is evidence from prospective studies that in the long term, a substantial proportion of patients with OCD (ranging from 32% to 70%) have a sustained remission of symptoms. Moreover, full remission has been associated with a lower risk of relapse.

Recovery: Application of the concept to OCD

The concept of recovery in psychiatry has its roots in consumer advocacy. In the early 20th century, these groups claimed that people with severe mental illness could regain a complete state of health and function in society (Frese, 1998). With the development of psychopharmacotherapy and clinical trials, it became apparent that there was a need for consistency in defining criteria for both disease severity and response. At first, this process occurred for major depressive disorder, with the development of the HAM-D (Hamilton, 1960) that enabled clinical researchers to assess changes in symptoms over time and define response as a certain reduction in scores. However, the recurrence of episodes imposed the need to define concepts that incorporated criteria for both disease severity and duration of improvement. Consequently, remission and recovery were defined as maintenance of an endpoint score of <8 on the HAM-D for more than 2 and 6 months, respectively (Frank et al., 1991; Fava et al., 2007). Following this model, an expert working group proposed operational criteria for remission in schizophrenia (Andreasen et al., 2005). The main innovation was using a dimensional approach to describe the symptomatic domain. In addition, that working group concluded that subsequent definitions of recovery should also incorporate functional and cognitive outcomes. Although no clear consensus exists, the ultimate goal of recovery in schizophrenia includes sustained symptom resolution and return to full function (Liberman and Kopelowicz, 2005; Leucht, 2014).

Hence, as we have tried to illustrate, if the current data about outcomes in OCD justify better expectations for a disorder that is often considered severe and enduring, and the conceptualization and operational definitions of remission and recovery have led to important improvement in the standard of care of other mental disorders, then focusing on remission and recovery in OCD may be critical in optimizing the treatment.

There are several issues to consider in optimizing an operational definition of recovery in OCD.

Symptomatic Criteria

The first issue is whether one continuous measure such as the YBOCS is sufficient to assess the heterogeneity of symptoms in OCD. Factor analytic studies indicate that OCD encompasses 3 to 5 different obsessive-compulsive symptom dimensions that account for 70% of the variance (McKay et al., 2004; Mataix-Cols et al., 2005; Bloch et al., 2008). The YBOCS is not as sensitive in detecting avoidance and hoarding, and other scales have been proposed to overcome these limitations such as the Dimensional Yale-Brown obsessive-compulsive scale (Rosario-Campos et al., 2006).

The second issue is how to assess the clinical impact of a reduction in symptoms. A relative reduction in the YBOCS or attainment of an absolute cut-off are the most widely used measures of symptomatic response and remission in OCD, though neither is sufficient to capture the clinical significance. The combination of YBOCS and CGI-S scores has been reliably used to describe clinical severity in OCD, linking symptoms to clinical significance. Signal detection analysis used to compare judgments of remission at various discrimination thresholds on symptom measures using the YBOCS, showed that a posttreatment YBOCS score of ≤14 was the best predictor of symptom remission defined as having mild or no symptoms on the CGI-S, while a posttreatment YBOCS score of ≤12 was associated with a combination of minimal OCD severity and life satisfaction

and adaptive functioning in adults measured by the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) and the Social Adjustment Scale (Farris et al., 2013). A raw YBOCS total score of 11 was also found to be predictive of symptomatic remission in pediatric OCD patients (Skarphedinsson et al., 2017).

Durational Criteria

The criterion of duration has been less investigated and varies between disorders. One multi-round web-based survey conducted among experts in the field of OCD proposed using 1 week for remission and 1 year for recovery (Mataix-Cols et al., 2016). In the Longitudinal Interval Follow-Up Evaluation, 8 consecutive weeks of psychiatric status ratings of 2 or less was used to define recovery in anxiety disorders (Bruce et al., 2005). In schizophrenia, 3 to 6 months and 2 to 5 years have been proposed to define remission and recovery, respectively (Andreasen et al., 2005; Liberman and Kopelowicz, 2005; Jääskeläinen et al., 2013; Leucht, 2014). Given the severity of OCD, a conservative approach may be reasonable, and following the example of schizophrenia we may propose 12 weeks as a duration to define remission and 2 years to assess recovery.

Functional Criteria

Long-term symptomatic quiescence is a common but not absolute prerequisite for functional improvement (Iancu et al., 2014). Conversely, sometimes disability extinguishes even if symptoms remain present. Hence, it is important to assess objective and subjective functionality, independent of symptomatology, to derive a more complete measure of recovery.

The CGI-S is an important and reliable clinician-reported measure of functional changes. It is relatively coarse, however, and may fail to capture the subjective sense of self-improvement. There is the potential for significant functional improvement in various aspects of social and inter-personal function, for example, returning to school, obtaining employment, and sustaining personal relationships. Often these are the criteria by which patients judge whether a treatment is successful. Hence, a subjective evaluation of patients' assessment of their own functional improvement, which we may better define as quality of life, is likely to be a key ingredient in recovery. A useful tool to operationalize this experience may be the Work and Social Adjustment Scale (WSAS), a 5-item scale that investigates an individual's perception about the impact of the disorder on work, home management, social and private leisure activities, and close relationships. A total score <10 may be a good cut-off to indicate recovery (Mundt et al., 2002). A more detailed alternative may be the Q-LES-Q with a reliable cut-off score >70 (Farris et al., 2013). For children, the COIS children scale with a score <10 would be appropriate (Melin et al., 2018).

Cognitive Criteria

It is reasonable to consider the necessity of assessing the cognitive functioning as part of the determination of recovery in OCD. Overall, results from neuropsychological studies in OCD do not support the presence of clinically meaningful neuropsychological impairments either in adults or youth with OCD (Shin et al., 2014; Abramovitch et al., 2015), suggesting that such criteria should not be included.

Other Considerations

It may be important to consider another subjective facet in the definition of recovery. Every mental disorder intrinsically entails a component of self-stigma, but this is particularly true for OCD, where diminished self-esteem is related to the perceived ego-dystonicity of the symptoms and the insight harbored by a high proportion of patients (Catapano et al., 2001; Murphy and Perera-Delcourt 2014). Moreover, it is questionable how a term that derives from the Inquisition Era, such as "obsessive-compulsive disorder" referring to a lucid demonic possession (Robbins 1959), is still included in the current nosography. Renaming the disorder may have potentially destigmatizing effects as happened for manic-depressive disorder, where renaming it as bipolar disorder has contributed to increase the search for treatments, and more recently there has been an open discussion regarding renaming schizophrenia (Ellison et al., 2015). Hence, it is reasonable to consider if a comprehensive definition of recovery should include the evaluation of self-stigma using one of the scales developed, such as the Internalized Stigma of Mental Illness scale (Boyd et al., 2014), where a total score <2 may be used to assess absence of internalized stigma (Lysaker et al., 2007).

Summary

Recovery in OCD may be operationally defined using a combination of symptomatic, durational, and functional (objective and subjective) criteria. According to current evidence, a YBOCS score of ≤12 may be a good cut-off to predict a clinical state where, if residual symptoms are present, they do not interfere with everyday life. A CGI-S score of 1 should also be satisfied in addition to self-reported functional measure such as the WSAS or the COIS. A duration of 2 years, following the example of schizophrenia, may be proposed as an appropriate duration (Table 1).

Recovery-Oriented Program in OCD: what we already have, what has to be done

The definition of recovery is critical, but by itself, is not sufficient. The broader goal is to implement recovery-oriented programs. Such programs should include approaches to improving early diagnosis, providing a stepped-care approach, and ultimately moving toward personalized treatments.

Early Diagnosis

Evidence shows that early diagnosis and treatment are positively related to outcome in OCD (Burchi and Pallanti, 2018). However, OCD has one of the longest durations of untreated

Table 1. Proposed Operational Definition of Recovery in OCD

Facets	Criteria
Symptomatic	YBOCS score ≤12
	CGI-S score of 1
Duration	2 years
Functional	Q-LES-Q >70 or
	WSAS <10
	COIS <10 (in children)

Abbreviations: CGI-S, Clinical Global Impression Scale; COIS, Children's OCD Impact Scale; Q-LES-Q, Quality of Life Enjoyment and Satisfaction Questionnaire; WSAS, Work and Social Adjustment Scale; YBOCS, Yale-Brown Obsessive-Compulsive Scale.

illness among psychiatric disorders with a delay between the onset of symptoms and the beginning of the first appropriate treatment in patients that eventually receive treatment that ranges from 7.75 (Italy) to 17 years (USA) (García-Soriano et al., 2014) In fact, OCD is often unrecognized and undertreated (Dell'Osso and Altamura, 2015). It has been estimated that between 38% and 89.90% of OCD sufferers neither ask for nor receive treatment (Goodwin et al., 2002; Mayerovitch et al., 2003; Subramaniam et al., 2012).

The belief that one can manage symptoms on his/her own, that OC symptoms are not associated with an illness, and the spontaneous fluctuation of symptoms were found to be the main reasons for delay in seeking treatment (Poyraz et al., 2015). Poor recognition of harm and taboo content were identified as reasons for underdiagnosis (García-Soriano et al., 2014). Moreover, the separation of OCD from the chapter of anxiety disorders in the DSM-5 may have decreased detection of these cases, especially in pediatric patients, who present prodromally with anxiety (Juckel et al., 2014; Burchi and Pallanti, 2018). This suggests the necessity of improving early detection of cases and sensitivity of assessment.

Based on the introduction of the attenuated psychotic syndrome, there may be an important opportunity to define subsyndromal OCD. The definition of such a condition may help identify people at risk of developing OCD and increasing early diagnosis (Wolitzky-Taylor et al., 2014). Education programs should be addressed to the general population with special emphasis on children, parents, and teachers but also to general practitioners (García-Soriano et al., 2014).

Further studies should be implemented to find external validators of the syndrome in the realms of brain connectivity, immunology, and inflammatory changes, eventually to be used as early biomarkers to identify prodromal OCD. An abundance of research has accumulated on potential biomarkers for OCD such as alterations in cortico-striatal thalamic circuits, alterations in plasma concentrations of hormones (i.e., cortisol), cytokines (i.e., IL1Beta, TNF-alfa), white blood cells (i.e., circulating natural killer cells and monocytes) and antibodies (i.e., antineural and D8/D17 antibody titers), alterations in electroencephalographic parameters (i.e., error related negativity amplitudes), and in genes involving serotonin and glutamate trafficking (Bandelow et al., 2017; Rodríguez et al., 2017). Currently, none of the putative biomarkers has sufficient specificity and sensitivity as a diagnostic tool, and increasing efforts may be needed to develop an assessment that integrates genetics with neuroimaging, neurophysiology, neurochemistry, and neuropsychology.

Stepped-Care Approach

In recent years, understanding of the heterogeneity of schizophrenia and the expectation for better outcomes has led to the implementation of recovery-oriented programs and new collaborative care models for affected patients (Davidson et al., 2005), with evidence of improvement in outcomes (Kidd et al., 2011; Röhricht et al., 2017). An analogous process would also be appropriate for OCD. The specific need for increasing efficiency of service provision in the care of OCD patients is recognized by guidelines that recommend management of these patients using a "stepped-care" approach (NICE, 2006). However, there is no clear guidance in the choice of treatments beyond the first line. The lack of a definition of a treatment algorithm and the inconclusive results on second-line strategies in OCD are in part explained by the lack of studies that stratify the heterogeneous OCD phenotype. These factors, along with the focus on

response to SSRIs, likely result in an overestimation of resistance of OCD and the lack of implementation of a stepped-care approach. There is still need for studies that stratify for ongoing medication (in type and dosage), for intrinsic characteristics of subjects (i.e., gender), and for characteristics of the disorder (type of onset, clinical staging, dimensions). There is also need for sequential treatment studies of adequate duration where patients enter the augmentation level only if they fail to adequately respond to the first defined intervention. The importance of integrated therapies in the care of OCD patients is well established by the fact that the best outcomes are enjoyed using combination therapies (Pallanti et al., 2002; Fineberg et al., 2013; Sharma et al., 2014). Models of an integrative approach that use combinations of pharmacotherapy with CBT, in a timely fashion, should be implemented. Given the unique nature of OCD and the involvement of family members with the symptomatology (Black et al., 1998), such an integrated approach should not neglect the intervention on families, especially in youth with OCD. The relationship between OCD severity and family accommodation (Wu et al., 2016) strongly supports the importance of a systematic and multidimensional treatment strategy employing structured programs.

Conclusion: Towards a personalized treatment

The definition of recovery is a realistic goal in OCD, especially in youth, and helps address the challenges present in the treatment of this difficult condition (Table 2). It suggests that there should be greater efforts toward early diagnosis, increased attention toward poorly recognized symptom dimensions, implementation of educational programs, and perhaps the definition of a subsyndromal condition that can detect prodromal signs of the disorder. It also calls for the implementation of stepped and stratified care programs redefining treatment expectations and providing a benchmark for longitudinal assessment of disease course.

The inclusion of recovery as one of the possible outcomes for OCD would attract more patients to treatment and reduce the duration of untreated illness, one of major cause of negative outcome. In addition, the prospect of recovery might impact policy-making and support funding for recovery-oriented programs, hopefully generating a virtuous circle.

We think that a recovery-oriented approach would eventually reshape the assessment of individual patients, foster a multidimensional assessment, and ultimately lead to a more personalized and likely much more successful treatment.

Table 2. Clinical Points

The importance of considering recovery in OCD

- Improve early diagnosis
- Give realistic hope to patients and advocacy groups
- Reduce stigma
- Increase effort and responsibility toward patients
- Increase treatment proactivity toward children and recent onset cases
- Prevent relapse and progression to chronicity and disability
- Inform new studies looking for definition of stepped/stratified care algorithm
- Orient the reimbursement to increase the investment for a treatable condition

Statement of Interest

None

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