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LONG-TERM OUTCOME IN ADULTS WITH OBSESSIVE-COMPULSIVE DISORDER

Michael H. Bloch, M.D., M.S.^{1,2,*}, Christy Green^{1,2}, Stephen A. Kichuk, B.A.², Philip A. Dombrowski, B.A.¹, Suzanne Wasyluk, R.N.², Eileen Billingslea, M.A.², Angeli Landeros-Weisenberger, M.D.¹, Benjamin Kelmendi, M.D.², Wayne K. Goodman, M.D.³, James F. Leckman, M.D.^{1,2,4}, Vladimir Coric, M.D.^{2,5}, and Christopher Pittenger, M.D., Ph.D.^{1,2,6}

¹Child Study Center, Yale University, New Haven, Connecticut

²Department of Psychiatry, Yale University, New Haven, Connecticut

³Department of Psychiatry, Mount Sinai School of Medicine, New York, New York

⁴Department of Pediatrics, Yale University, New Haven, Connecticut

⁵Bristol Myers-Squibb, Neuroscience Global Clinical Research, Wallingford, Connecticut

⁶Department of Psychology, Yale University, New Haven, Connecticut

Abstract

Background—Obsessive-compulsive disorder (OCD) is a chronic condition that often produces lifelong morbidity, but few studies have examined long-term outcome (greater than 5 years) in adult patients. Available studies suggest that 32–74% of adult OCD patients will experience clinical improvement over the long term. However, these studies were conducted before validated OCD rating scales were established and the development of evidence-based treatments for OCD.

Methods—We investigated the 10–20 year outcome of 83 of 165 eligible subjects previously enrolled after participation in placebo-controlled trials of serotonin reuptake inhibitor (SRI) medications for OCD. We examined the association between clinical characteristics at initial assessment and OCD symptom severity at follow-up. We hypothesized that primary OCD symptom dimension and initial response to pharmacotherapy with serotonin reuptake inhibitors would be associated with later symptom severity.

Results—Only 20% (17 of 83) of subjects had experienced a remission of their OCD symptoms at follow-up (Y-BOCS = 8). Forty-nine percent (41 of 83) of subjects were still experiencing clinically significant OCD symptoms. Response to initial SRI pharmacotherapy was significantly associated with long-term outcome: 31% (13 of 42) of subjects who responded (CGI < 3) to initial SRI pharmacotherapy were remitted at follow-up, compared to 12% (3 of 25) of partial responders and none of the 16 subjects who had no response to initial SRI pharmacotherapy. We did not find a significant association between long-term clinical outcome and any of the OCD symptom dimensions.

Conclusion—Despite the introduction and dissemination of several evidence-based treatments for OCD, most adult OCD patients do not achieve remission. Initial response to pharmacotherapy was strongly associated with long-term outcome.

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*Correspondence to: Michael H. Bloch, M.D., M.S., Child Study Center, Yale University School of Medicine, PO Box 2070900, New Haven, CT 06520. michael.bloch@yale.edu.

Current address: Vladimir Coric, Child Study Center, Yale University, School of Medicine, PO Box 2070900, New Haven, CT 06520.

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Keywords

OCD/obsessive compulsive disorder; pharmacotherapy; anxiety/anxiety disorders; treatment; treatment resistance

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a chronic neuropsychiatric disorder characterized by obsessions (recurrent or persistent unwanted thoughts, images, or impulses) and/or compulsions (repetitive behaviors or mental acts), which are often performed to relieve anxiety associated with underlying obsessions. Once believed to be rare, OCD is now considered one of the most common psychiatric illness, affecting 1.8–2.5% of the general population.^[1–5] Patients with OCD experience an overall lower quality of life as evidenced by significantly poorer academic functioning, increased occupational problems, and interpersonal issues.^[6]

OCD is often characterized by a fluctuating course but generally is unremitting with low remission rates. In a follow-up study of 144 patients treated for OCD in Sweden, only 20% experienced remission after 40 years.^[7] Although a substantial proportion (83%) experienced a decline in symptom severity from the point of their initial hospitalization, over half (52%) still had clinically significant OCD symptoms 40 years later. Other retrospective studies from the same time period followed-up with patients at time intervals of 5 years or longer and found that 32–74% of OCD patients demonstrated some improvement in symptoms.^[8–13]

While these studies added substantially to our understanding of the natural history of OCD, they had several methodological limitations: (1) the studies did not use standardized rating scales of OCD severity such as the Yale-Brown obsessive compulsive scale (Y-BOCS), which was introduced in 1989. Such scales allow for more objective measure of symptom improvement.^[14, 15] (2) There has been substantial diagnostic refinement since these initial studies were conducted. Most specifically, diagnostic clarification has resulted in the disentangling of OCD from obsessive-compulsive personality disorder. (3) Many of these studies relied exclusively on retrospective data collection. (4) When prospective studies were conducted, follow-up ratings were not conducted by individuals blinded to symptom severity at the time of initial evaluation, and thus any conclusions drawn concerning predictors of outcome are highly prone to bias.

Perhaps more importantly, improvements have been made in our understanding and treatment of OCD since these original studies were performed. The discovery and use of serotonin reuptake inhibitors (SRIs), especially the selective serotonin reuptake inhibitors (SSRIs), has dramatically improved patient outcome. Between 40–60% of OCD patients given an adequate trial of a SSRIs experience a response to treatment.^[16] Effective behavioral treatment involving cognitive-behavior therapy (CBT) with exposure and response prevention has become well established over the past two decades and further has improved outcomes, at least in the short term. Few studies have assessed long-term outcomes since the widespread adoption of evidence-based treatments.^[17] Therefore, most of the studies of the long-term natural history of OCD described above are outdated. The few studies specifically examining predictors of long-term treatment outcome in adults with OCD have failed to reach any consensus regarding predictors of poor outcome.^[7, 18]

We investigated predictors of clinical outcomes in a sample of OCD patients enrolled in pharmacotherapy trials at our site from 1986–1995 who received a follow-up interview to assess long-term outcome from July 2006–July 2007. We sought to determine whether the

following variables are related to long-term outcome: age of onset, symptom dimensions, presence of comorbid conditions, early response to SRI treatment, and duration of illness. We hypothesized that a nonresponse to initial SRI trial would be associated with reduced rates of long-term remission (Y-BOCS = 8). Previous meta-analysis has demonstrated an association between poor medication treatment response and long-term outcome in pediatric OCD.^[19] We also hypothesized that those with predominant symptoms in the aggressive symptom dimension would show higher rates of remission. Previous research had demonstrated an association between predominant OCD symptoms in the aggressive dimension and improved short-term pharmacological response in this same study population.^[20]

METHODS

SUBJECTS

One hundred and sixty-five subjects who were diagnosed with OCD and participated in a SRI clinical trial between 1986 and 1995 at the Yale OCD Research Clinic were eligible for this study. Each subject received a trial of at least one of three SRI medications (fluoxetine, fluvoxamine, clomipramine) for at least 8 weeks at the maximum tolerated dose as part of at least one of three randomized clinical trials (RCTs).^[21–23] Eligible subjects were recontacted 10–20 years after their trial participation (and 10–15 years after their last contact in our clinic) and asked to participate in a follow-up clinical interview to assess their current level of OCD symptom severity and of related conditions. Eighty-three (51%) of 165 subjects contacted agreed to participate in follow-up interviews. Table 1 depicts the characteristics of participants and nonparticipants in the follow-up study.

ASSESSMENT

Baseline Assessment—At baseline, as part of their participation in an RCT of SRI pharmacotherapy for OCD, each subject had a clinical interview and was diagnosed with OCD by an expert clinician. Each subject was additionally asked to describe their major and minor OC symptoms based on the 15 categories of the Y-BOCS symptom checklist. Based on these answers, subjects were rated in the four previously described OC symptom dimensions^[24] as having either no symptoms present in a particular dimension (coded as a 0), any symptoms present in a particular dimension (coded as 1) or predominant symptoms in a particular dimension (the most impairing of the four dimensions, coded as 2). Medication response for all subjects was assessed using the clinical global improvement scale (CGI).^[25] Subjects were rated on response to the first SRI treatment they received at our research clinic. Subjects were asked about other clinical aspects of their OCD history such as age of onset, duration of illness and past treatment history. Comorbid conditions were determined based on the judgment of an MD-level clinician performing a clinical evaluation.

Follow-Up Assessment—Subjects who agreed to participate were brought back to the Yale OCD clinic or assessed by phone from July 2006–July 2007. Participants were interviewed by an experienced clinician about their current symptoms and previous treatments. Raters were blind to the specific answers and ratings conducted at baseline assessment and study hypotheses. The interviews took roughly 3 hr, and included both self-reports and evaluations done by the clinician. The interview asked questions about the current severity of the subject's OCD symptoms, measured by the Y-BOCS,^[14, 15] as well as other related anxiety conditions, measured by the HAM-A (Hamilton anxiety rating scale).^[26] The subject's depression ratings were taken using the HAM-D (Hamilton depression rating scale).^[27] Previous and current medications were recorded as well.

Data Analysis—All data analysis was performed in SPSS 19.0 for Windows. For a priori hypothesis testing, we used linear regression analysis. In linear regression models, OCD symptom severity at follow-up (Y-BOCS) was the dependent variable and gender, baseline age, and duration of follow-up were included as covariates. Variables of interest were added separately as independent variables to the model. Variables of interest included: Primary OCD symptom dimensions (forbidden thoughts [aggressive and sexual/religious separately], cleaning, symmetry, and hoarding), comorbid conditions (major depression, other anxiety disorders, substance abuse, eating disorders, and tic disorders), response to first SRI trial (responder (CGI = 2), partial responder (CGI = 3), or nonresponder (CGI = 4)), age of onset and duration of illness at baseline assessment. We had two a priori hypotheses that (1) nonresponse to initial SRI trial would be associated with reduced rates of long-term remission and that those with (2) predominant symptoms in the aggressive dimension would show higher rates of remission. We set the significance threshold for a priori hypothesis testing at $P < .025$ to account for our two hypotheses using a Bonferroni correction. By contrast, we set our threshold for statistical significance at $P < .05$ for all exploratory analyses. The variables examined in exploratory analysis were OCD symptom dimensions (other than aggressive dimension symptoms which was a primary hypothesis), comorbid conditions, age of OCD onset, and duration of illness at baseline assessment. Given our nine additional exploratory models, there was a significant likelihood of false-positive error in exploratory hypothesis testing, and thus all significant exploratory findings should be regarded as exploratory. Given our nine exploratory hypothesis tests, there was a 37% chance of finding at least one significant result at the $P < .05$ level. In order to express significant results in the most clinically salient terms, we also reported the likelihood of remission for subjects and proportion of individuals with clinically significant OCD symptoms. The threshold for OCD remission at follow-up was a Y-BOCS = 8 and the threshold for clinically significant symptoms at follow-up was a Y-BOCS = 16.

RESULTS

SUBJECTS

Eighty-three (51%) of 165 eligible subjects agreed to participate in follow-up interviews. There were no significant differences at baseline assessment between participants and nonparticipants (Table 1).

LONG-TERM OUTCOME

Seventeen (20%) of 83 subjects achieved OCD remission (Y-BOCS = 8) 11.7 ± 1.2 years after initial assessment. Forty-one (49%) of 83 subjects were still experiencing clinically significant OCD symptoms (Y-BOCS = 16) at follow-up. These individuals had severe enough OCD symptoms at follow-up that they could have qualified for another clinical trial for OCD.

TREATMENT STATUS

Of the 83 participants completing the follow-up assessment, 59 (71%) were taking an SSRI or SNRI at follow-up (11 [65%] of the remitted cases; and 28 [68%] of the subjects with clinically significant symptoms at follow-up). Twenty-eight subjects (34%) reported receiving antipsychotic augmentation treatment for OCD and only 10 subjects (12%) were currently taking antipsychotic medications (1 [6%] of the remitted cases; and 6 [15%] of the subjects with clinically significant symptoms at follow-up). Forty-two participants (51%) reported previously receiving cognitive behavioral therapy for OCD involving exposure and response prevention. Only 7 subjects (8%) reported currently being enrolled in CBT for OCD (0 of the remitted cases; and 5 [12%] of the subjects with clinically significant symptoms at follow-up).

OCD SYMPTOM DIMENSION

There were no significant associations between primary OCD symptom dimension at baseline and severity of OCD at follow-up assessment as measured by YBOCS. Symptoms in the aggression dimension were associated with improved OCD symptoms at trend levels ($\beta = -0.35$, $t = -2.0$, $P = .055$) but not at the threshold for statistical significance in our study. Primary symptoms in the following symptom categories were not associated with OCD severity at follow-up assessment: cleaning ($\beta = -0.12$, $t = -0.7$, $P = .50$), sexual/religious ($\beta = -0.11$, $t = -0.6$, $P = .53$), symmetry ($\beta = 0.27$, $t = 1.5$, $P = .14$), and hoarding ($\beta = 0.16$, $t = 0.9$, $P = .38$). There was also no significant association with OCD severity at follow-up when sexual/religious and aggressive symptoms were combined into a single forbidden thoughts dimension ($\beta = -0.16$, $t = -1.4$, $P = .16$).

INITIAL RESPONSE TO PHARMACOTHERAPY WITH SEROTONIN REUPTAKE INHIBITORS

We found a significant association between improved initial response to SRI pharmacotherapy and severity of OCD at follow-up assessment. None of the 16 individuals who were rated as nonresponders to their initial SRI trial had OCD symptoms that remitted by follow-up assessment (Y-BOCS = 8). By contrast, 31% (13 of 42) of individuals who showed a full response to their first SRI trial were remitted at follow-up assessment. Twelve percent (3 of 25) of partial responders were remitted at follow-up. Figure 1 depicts the long-term outcome of subjects stratified by their initial response to SRI pharmacotherapy.

Similarly, the likelihood that an individual would still have OCD symptoms severe enough to qualify for another OCD treatment study at follow-up (Y-BOCS = 16) was significantly associated with initial SRI response. Seventy-five percent (12 of 16) of individuals who did not respond to their initial SRI had severe enough OCD symptoms to qualify for another OCD treatment study at follow-up. By contrast, 38% (16 of 42) of full responders and 52% (13 of 25) of partial responders to initial SRI pharmacotherapy had clinically significant OCD symptoms at follow-up.

COMORBID PSYCHIATRIC CONDITIONS

We found no association between comorbid conditions at baseline and follow-up OCD severity. No association was demonstrated for depression ($\beta = 1.78$, $t = 0.94$, $P = .35$), eating disorder ($\beta = -5.11$, $t = -1.16$, $P = 0.25$), substance abuse ($\beta = 0.26$, $t = 0.12$, $P = 0.90$), tic disorder ($\beta = -1.63$, $t = -0.41$, $P = .69$), or anxiety disorders ($\beta = -1.88$, $t = -0.65$, $P = .52$).

AGE OF ONSET AND DURATION OF ILLNESS

We demonstrated no significant association between age of OCD onset ($\beta = -0.20$, $t = 1.55$, $P = .12$) or duration of illness ($\beta = 0.92$, $t = 0.92$, $P = .36$) at baseline and follow-up OCD severity.

DISCUSSION

This study examined long-term clinical outcomes in OCD patients since the introduction of modern pharmacological and psychotherapeutic interventions with demonstrated efficacy. Unfortunately, our results confirm that, despite the availability of such treatments, a very small proportion of adults with OCD achieve clinical remission over the long term. We found that initial response to SRI pharmacotherapy was strongly predictive of long-term outcome. Thirty-one percent of responders to their initial SRI trial achieved remission at follow-up (defined as Y-BOCS = 8), compared to 0% of nonresponders. These results are similar to the findings of a recent 2-year prospective longitudinal outcome study in adults with OCD.^[28] That study also reported a strong association between initial treatment

response and 2-year outcome.^[28] Our results expand upon finding and suggest that short-term treatment response is associated with more favorable long-term clinical outcomes a decade or longer after treatment. Although much of this association is likely do to efficacy of pharmacotherapy over the long term, it remains quite possible that other factors besides direct medication effects may account for this association. For instance, patients who experience a robust initial response to medication may also be more likely to engage in future treatment trials or ongoing clinical treatment for OCD than patients who do not respond to initial treatment. Ongoing clinical treatment and multiple therapies may be associated with improved likelihood of remission in OCD.

OCD symptoms in the aggression dimension were associated with decreased severity of OCD symptoms at follow-up at trend levels. However, this finding was likely the result of confounding because these symptoms were highly correlated with initial treatment response previously in this same sample.^[20] We found no correlation with other clinical factors such as OCD symptom dimensions, baseline levels of comorbid psychiatric illnesses, the age of onset, or the duration of illness.

Remission of symptoms leads to a better quality of life, improved social functioning and better patient satisfaction with treatment and life. Remission, not response, should be the goal for any psychiatric condition. This study highlights the need for more effective treatments in adults with OCD by suggesting that clinical remission is experienced by only a minority of patients seeking treatment for OCD.^[28] In this regard, a number of promising avenues are under investigation. Glutamate-modulating agents represent a promising new area for pharmacotherapy in refractory cases, although large, multi-center, double-blind, placebo-controlled studies are lacking.^[29–42] Neurosurgical techniques such as deep-brain stimulation or anterior capsulotomy remain a treatment option for the most severely impaired OCD patients.^[43]

Given the potential clinical relevance of our findings, it is important to highlight several study limitations. First, OCD severity and medication improvement at baseline was assessed using the CGI and the not current gold-standard measurement of OCD severity—the Y-BOCS. Y-BOCS ratings were not available on a large proportion of our sample at baseline (most specifically subjects who participated in the earlier trials) as they were not entered into electronic clinical databases and physical research charts had been destroyed. Therefore, the assessment of the subjects' severity of OCD at the follow-up assessment was measured differently than at the baseline assessment. Second, there was not a full participation rate in the follow-up study, leaving a smaller and potentially biased sample for the follow-up assessment. We did not find any significant differences between participants and nonparticipants in their baseline assessment; but this does not entirely exclude the possibility that the groups may have differed during the follow-up period. The modest sample size for this follow-up sample also limited our statistical power, especially with regards to the analysis of symptom dimension used to predict long-term outcome. These power issues were particularly apparent when examining hoarding symptoms as a predictor of long-term outcome as few subjects had primary hoarding symptoms.

Additionally, we could not control for treatments that subjects received during the follow-up interval. We did not have detailed prospective information on symptom severity before and after receiving individual treatments over this time period. If we had this detailed prospective information, we could have adjusted for treatment as a time-dependent covariate. However, we only had reliable information on current and past treatments received at baseline and follow-up, which is not appropriate for use as a covariate because the decision made by subjects to start or continue treatments (such as CBT or SRI pharmacotherapy) is not made at random and is influenced by both initial treatment efficacy

and residual OCD symptom severity. In our sample, subjects receiving SRI pharmacotherapy and/or CBT at follow-up had higher Y-BOCS scores than those not receiving treatment suggesting that subjects with greater residual OCD severity were self-selected to be more likely to engage in ongoing treatment. Specifically, the average Y-BOCS of 19.9 ± 6.2 in subjects receiving CBT at follow-up compared to Y-BOCS = 15.3 ± 8.5 in subjects not receiving CBT. The average Y-BOCS was 15.9 ± 8.3 in subjects taking an SRI at follow-up compared to 15.3 ± 8.8 in subjects who were not. The inability to adjust for treatments received during the follow-up interval remains a significant limitation of our study that cannot be reconciled through statistical analysis of the available data.

Additionally, we could not control for treatments that subjects received during the follow-up interval. We were unable to control for treatments being received at follow-up because we did not have detailed prospective information on symptom severity before and after receiving treatments. If we had this detailed prospective information, we could have adjusted for treatment as a time-dependent covariate. However, we only had reliable information on current and past treatments received at baseline and follow-up. The decision made by subjects to start or continue treatments (such as CBT or SRI pharmacotherapy) is not made at random and is influenced by both initial treatment efficacy and residual OCD symptom severity. Thus there is likely a self-selection bias toward more severely affected subjects receiving treatment at follow-up. This self-selection bias in treatment selection at follow-up is evidenced in our study by the worse OCD symptom severity experienced by subjects receiving SRI pharmacotherapy and/or CBT at follow-up than those subjects who were not. (Average Y-BOCS of 19.9 ± 6.2 in subjects receiving CBT at follow-up compared to Y-BOCS = 15.3 ± 8.5 in subjects not receiving CBT. The average Y-BOCS was 15.9 ± 8.3 in subjects taking an SRI at follow-up compared to 15.3 ± 8.8 in subjects who were not.) Adjusting for treatment at follow-up would have produced spurious analyses whereby known effective treatments for OCD (such as SRI pharmacotherapy or CBT) were being adjusted for as negative risk factors regarding outcome. The inability to adjust for treatments received during the follow-up interval remains a significant limitation of our study that cannot be reconciled through statistical analysis of the available data.

Our finding that OCD patients who do not respond to their first trial of SRI medications rarely achieve remission of symptoms over the longer term has important implications for both treatment and research. It would be of interest to investigate whether response to an initial round of CBT similarly predicts long-term outcome. Future investigations should focus on replication of our results using more nuanced baseline assessments involving the Y-BOCS but extended over longer durations than well-conducted previous longitudinal studies. It is also critical that we develop new treatments that help the large proportion of patients who do not experience adequate symptom relief from SRIs.

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Figure 1. Long-term outcome in adults with OCD stratified by initial response to SRI pharmacotherapy. Initial response to SRI pharmacotherapy was significantly associated with long-term outcome. Proportion of OCD patients remitted at follow-up is shaded in white, subjects with subclinical OCD symptoms are shaded in gray and those with clinically significant OCD symptoms at follow-up are shaded in black.

TABLE 1

Comparison of baseline characteristics between participants and nonparticipants in follow-up assessment

	Participants (N = 83)	Nonparticipants (N = 82)
Baseline age	42.0 ± 9.9 years	39.7 ± 12.1 years
Age of OCD onset	23.4 ± 7.9 years	24.8 ± 9.7 years
Duration of illness	15.9 ± 11.9 years	12.4 ± 11.2 years
GAF	55.6 ± 11.7	55.0 ± 12.5
Lifetime comorbid disorders		
MDD	45% (n = 37)	37% (n = 30)
Anxiety disorder	12% (n = 10)	20% (n = 16)
Tic disorder	6% (n = 5)	4% (n = 3)
Eating disorder	8% (n = 7)	7% (n = 6)
Substance abuse	31% (n = 26)	34% (n = 28)
Initial SRI response		
Full response	51% (n = 42)	49% (n = 40)
Partial response	30% (n = 25)	29% (n = 24)
Nonresponse	19% (n = 16)	22% (n = 18)