



Symptom dimensions are associated with age of onset and clinical course of obsessive–compulsive disorder

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ABSTRACT

Meta-analysis of the heterogeneous symptoms of obsessive–compulsive disorder (OCD) has found a four-factor structure of symptom dimensions consisting of cleaning, forbidden thoughts, symmetry, and hoarding. Research into age of onset of symptom dimensions has yielded inconsistent results, and it is unknown whether symptoms along these dimensions differ in their clinical course. We assessed age of onset and clinical course of different OCD symptom dimensions in a large cohort of adult patients. Nine-hundred fifty-five subjects were assessed using the Dimensional Yale–Brown Obsessive–Compulsive Scale. For age of onset analysis, we tested across three methods of classification: (1) primary (more severe) symptom dimension (2) clinically significant symptoms within a dimension or (3) any symptoms within a dimension. Age of onset was defined as the earliest age of onset reported for any individual item within a symptom dimension. For analysis of different types of clinical course, we used chi-square tests to assess for differences between primary symptom dimensions. OCD symptoms in the symmetry dimension had an earlier age of onset than other OCD symptom dimensions. These findings remained significant across all three methods of classification and controlling for gender and comorbid tics. No significant differences were found between the other dimensions. Subjects with primary OCD symptoms in the forbidden thoughts dimension were more likely to report a waxing-and-waning course, whereas symmetry symptoms were less likely to be associated with a waxing-and-waning course.

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1. Introduction

Obsessive–compulsive disorder (OCD) is a highly heterogeneous condition (Miguel et al., 2005). While current nosology (DSM-IV and ICD-10) considers OCD to be a unitary entity, there is great variability in symptomatic presentation (Lochner and Stein, 2003). Indeed, symptoms can present in such dramatically different ways that several individuals with equally severe OCD may have no specific symptoms in common (Bloch et al., 2008; Ferrao et al., 2006).

OCD symptom dimensions are a tool for capturing this heterogeneity. Factor analytic studies have yielded a fairly consistent four-factor structure of OCD symptom dimensions across the lifespan, consisting

of cleaning, forbidden (aggressive/sexual/religious) thoughts, symmetry (ordering/counting/repeating) and hoarding (Bloch et al., 2008). Recent studies suggest that these symptom dimensions differ in genetic association (Hasler et al., 2007; Samuels et al., 2007), neurocircuitry (Mataix-Cols et al., 2004; Rauch et al., 1998), and response to pharmacological (Landeros-Weisenberger et al., 2010; Mataix-Cols et al., 1999) and behavioral (Mataix-Cols et al., 2002) treatments.

It remains unclear whether symptoms along the different dimensions have a different natural history. Several studies have yielded conflicting results, with some indicating differences in age of onset (Honjo et al., 1989; Mataix-Cols et al., 1999; Minichiello et al., 1990) and others not finding any age-related patterns (Rettew et al., 1992). Interpretation of these conflicting results is further burdened by the limited sample sizes differing methodology; particularly problematic is their different methods of assessing and classifying symptom dimensions. For instance, several common OCD symptoms are often evaluated in a manner that leaves it unclear which dimension certain symptoms belong within (e.g. was “checking” due to harm-related obsessions, or due to obsessions that something was not done correctly). Additionally,

Abbreviations: OCD, Obsessive-Compulsive Disorder; ANOVA, Analysis of Variation; DY-BOCS, Dimensional Yale-Brown Obsessive Compulsive Scale; FT, Forbidden Thoughts; SYM, symmetry; CLEAN, Cleaning; HRD, Hoarding.

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participants generally only indicated whether or not particular classes of symptoms were present (and in some cases whether they were a major problem), meaning there was no distinction made between symptoms at varying levels of severity. This distinction is important, as without it, nascent and minor symptoms within a dimension might have been coded in the same manner as well-established and problematic symptoms. Distinct patterns of onset and natural history may be found at different severity thresholds — that is, if one considers all symptoms, or only clinically significant symptoms, or only primary symptoms. Further, identifying whether different symptoms are associated with distinct clinical course can potentially help clinicians to provide more accurate prognostic information and identify symptoms that demand treatment priority.

In an effort to enhance understanding of OCD symptom dimensions, we examined age of onset and clinical course of OCD symptomatology according to symptom dimension in a large cohort of OCD patients. We hypothesized that differences in age of onset would exist between dimensions, with the symmetry dimension having the earliest onset. Given that converging evidence (i.e. genetics, neuroimaging, clinical evaluation) suggests that OCD symptom dimensions may have distinct neurobiological underpinnings and differential response to treatment, we additionally hypothesized that OCD symptom dimensions would display differences in their clinical course.

2. Methods

2.1. Participants

A sample of 1001 OCD patients were recruited from 7 sites located across Brazil as part of the Brazilian Research Consortium on Obsessive-Compulsive Spectrum Disorders from 2005 to 2010. A full description of the recruitment and assessment procedure of this sample has been published elsewhere (Miguel et al., 2008). Due to the possibility of the clinical course not having fully emerged in adolescents, it was decided prior to data analysis that those under age 18 would be excluded; fifty-six subjects were excluded as a result. Nine-hundred fifty-five adults aged 18–65 were ultimately included in our analyses.

2.2. Procedure

Each site's ethics review boards reviewed and approved all methods. Experts in OCD trained to reliably use protocol instruments interviewed participants. Participants with primary OCD (per DSM-IV criteria) were included. An OCD diagnosis was established by administration of the Structured Clinical Interview for DSM-IV (First et al., 1995). OCD was considered the primary psychiatric condition when this was the disorder for which the patient sought treatment and the diagnosis was verified by an experienced clinician. This diagnostic evaluation was conducted at the same session or in close temporal proximity to when symptom ratings were conducted. Exclusions included comorbid schizophrenia or any condition that interfered with participants' ability to effectively take part in the protocol. Demographic and clinical data was obtained through use of a questionnaire produced by the Consortium.

OCD symptom severity within each symptom dimension was assessed with the Dimensional Yale–Brown Obsessive–Compulsive Scale (DY-BOCS) (Rosario-Campos et al., 2006). The time spent on symptoms, level of anxiety, and level of interference are each rated on a 0 (least severe) to 5 (most severe) scale, for a total score of 0–15, for each dimension at the current and worst-ever time period. For the age of onset analysis, OCD symptom dimensions of subjects were classified in three ways: (1) primary symptom dimension (2) clinically significant symptoms within a dimension or (3) any symptoms within a dimension. The DY-BOCS ratings of symptom dimensions were restructured into the four symptom dimensions identified by a large meta-analysis of previous studies in the area (Bloch et al., 2008). Severity in the forbidden thoughts dimension was defined for a subject as the higher of the severity scores in either the sexual/religious or aggressive DY-BOCS dimensions. As a

sensitivity analysis we also report results for sexual/religious and aggressive OCD symptoms separately. For analysis involving primary symptom dimension, subjects that scored highest on their worst-ever ratings in the miscellaneous dimension or had a tie between two or more symptom dimensions were excluded. Clinically significant symptoms within a dimension was defined by having a worst-ever DY-BOCS score in a dimension equal to or greater than 6, which roughly corresponds to a score on the more widely used Yale–Brown Obsessive Compulsive Scale (Y-BOCS) of 16, a standard threshold to identify clinically significant symptoms. Any symptom within a dimension was defined as having a worst-ever score greater than 0 in that dimension. Thus, a participant could (and often did) qualify for more than one dimension when symptom dimensions were defined by clinical significance or presence of symptoms but could only qualify for one primary dimension.

Age of onset for each symptom dimension was determined by the earliest age of onset reported for any individual item within a symptom dimension on the DY-BOCS checklist. This information was reported at the same time to when a clinical diagnosis was established. Clinical course of OCD was determined using a graphical-based question in which individuals were given six possible graphical options to describe their OCD course. These options are depicted in Fig. 1 and include (1) constant, (2) episodic, (3) waxing-and-waning, (4) deteriorating then constant, (5) progressively deteriorating and (6) other. Subjects who chose “other” were excluded from this analysis.

Analyses were conducted in SPSS 19.0. One-way omnibus analysis of variance (ANOVA) was used to test for overall significance in age of onset of DY-BOCS symptom dimensions. Analyses were conducted testing primary symptoms, clinically significant symptoms, and any symptoms. Post-hoc pairwise comparisons were then conducted to identify significant differences between OCD symptom dimensions when the overall test was significant. For analysis of the association between primary symptom dimension and type of clinical course, chi-square tests were utilized. When the overall chi-square test was significant, individual post-hoc tests were performed to determine which clinical course options were reported at significantly increased or decreased rates for each dimension.

For results related to the primary symptom dimension, we conducted additional analyses to determine the possible confounding effects of gender and comorbid tic disorders on our findings, as male gender and comorbid tic disorders have been associated with both an earlier age of onset (de Mathis et al., 2009) and increased likelihood of symptoms in particular OCD dimensions (Labad et al., 2008; Rosario-Campos et al., 2006). For the age of onset data, we added gender and tic disorder as additional covariates in a one-way ANOVA in SPSS.

The evidence concerning a relationship between gender, the presence of tic disorders, and longitudinal course of symptoms is considerably sparser, but there exists some evidence, at least in pediatric OCD, that gender and presence of a comorbid tic disorder is associated with adulthood outcome (Bloch et al., 2006, 2009). Therefore, we decided to examine possible confounders in this analysis as well. The Mantel–Haenszel chi-square test was used to assess confounding across gender and tic disorder strata.

3. Results

3.1. Participants

Demographics characteristics of subjects are depicted in Table 1.

3.2. Age of onset

We found a significant association between age of onset and primary dimension of OCD symptoms $F_{(3, 519)} = 5.43, p < 0.001$. Symptoms in the symmetry dimension (age of onset = 13.6 ± 8.6) were associated with an earlier age of onset than symptoms in the hoarding (age of onset = $18.3 \pm 11.3, p < .05$), cleaning (age of onset = $16.9 \pm 8.3, p < .01$), and

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