Article

Adults With Early-Onset Obsessive-Compulsive Disorder

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Objective: Obsessive-compulsive disorder (OCD) is a clinically heterogeneous disorder with a bimodal age at onset and range of treatment outcomes. This study attempted to ascertain the importance of the age at OCD symptom onset for a better phenotypic precision. Therefore, the authors compared adult OCD patients with an early symptom onset to OCD patients with a later symptom onset.

Method: Forty-two adult outpatients with OCD were evaluated with semistructured interviews: 21 with symptom onset before the age of 10 (early-onset group) and 21 with symptom onset after the age of 17 (late-onset group).

Results: Early onset was associated with higher scores on the Yale-Brown Obsessive Compulsive Scale, higher frequencies of tic-like compulsions, higher frequency of sensory phenomena, and a higher rate of comorbid tic disorders. The early-onset group also responded less well to treatment with clomipramine and selective serotonin reuptake inhibitors.

Conclusions: The results indicate that age at onset may be an important factor in subtyping OCD and that the phenotypic differences found were not restricted to childhood.

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Obsessive-compulsive disorder (OCD) is a clinically heterogeneous disorder, with many possible subtypes (1, 2). Recent studies have suggested that age at onset may be an important distinguishing feature and that children with OCD, as well as OCD adults with an early onset of symptoms, may represent a distinct subgroup (3, 4). For instance, prepubertal onset of OCD has been associated with male preponderance (5), higher rate of comorbid tic disorders (6), higher frequency of compulsions not preceded by obsessions (3), and a greater familial loading for OCD (7).

Considering that obsessive-compulsive symptoms normally shift during the course of the disease (8), fundamental questions remain regarding the natural history of OCD. First, is the age at symptom onset an important factor for establishing more homogeneous subgroups of OCD patients? Second, do the clinical features associated with juvenile-onset OCD persist into adulthood? Finally, are childhood and adult OCD the same or different disorders? Unfortunately, longitudinal studies are scant, and studies with adult OCD patients have not ascertained age at onset in a systematic way.

The main goal of this study was to address the first question. In order to verify whether age at symptom onset is an important factor in subtyping OCD, we assessed a range of clinical characteristics in adult patients that could possibly differentiate between those with OCD symptom onset before age 10 and those whose symptom onset occurred after age 17.

Specifically, we hypothesized that the early-onset group would include more male subjects and that they would display a greater number of tic-like compulsions, a higher frequency of sensory phenomena preceding their symptoms, a higher rate of comorbid tic disorders, and a poorer treatment response to monotherapy with antiobsessional agents.

Method

Subjects

Fifty-seven consecutive outpatients who met DSM-IV criteria for OCD were ascertained from the OCD Spectrum Disorders Project, University of São Paulo Medical School, São Paulo, Brazil. Fifteen patients were excluded: 12 whose onset of symptoms occurred between the ages of 11 and 16 years and three who had a comorbid diagnosis of schizophrenia. The remaining 42 adult patients (23 men and 19 women; mean age=32.1 years, SD=9.1, range=18–59) were divided into two groups according to age at symptom onset: age 10 or earlier (early-onset group, N=21) or age 17 or later (late-onset group, N=21). After complete description of the study to the subjects, written informed consent was obtained.

Age-at-Onset Criteria

It is not clear whether age at onset should be determined according to the beginning of the obsessive-compulsive symptoms or when the level of clinical impairment warrants a diagnosis of OCD. In the present study, we defined "age at onset" as the age that the patient, or a family member, remembered as the beginning of the obsessive-compulsive symptoms. There is also no agreement in the literature about the age threshold for defining "early onset" in OCD patients. Some authors have considered the age of 17 as a threshold (9–11), whereas others have used a mean age of 14 (12) or 7 (13) to divide their samples. We selected age 10 as a threshold for early onset and age 17 for late-onset. These thresholds are consistent with the age advocated by Geller and colleagues (3) to ensure prepubertal onset and also are consistent with an OCD genetic family study (7). The latter study revealed a

higher morbidity risk to first-degree family members of early-onset (≤10 years) OCD probands, compared with the first-degree family members of probands with later onsets.

In addition to direct interviews with the probands, we were able to interview independently at least one other individual in 36 (86%) of the families in an effort to validate the historical information provided by the proband.

Clinical Assessments

The presence and severity of obsessive-compulsive symptoms and tics were determined by using the checklists and rating scales of the Yale-Brown Obsessive Compulsive Scale (14, 15) and the Yale Global Tic Severity Scale (16), respectively. Specific ages at onset for each of the symptoms related by the patients and relatives of the probands were obtained whenever possible.

In the Yale-Brown Obsessive Compulsive Scale checklist, there are two items under "miscellaneous" compulsions that describe the "need to touch, tap, or rub" and "rituals involving blinking or staring." In this study, we broadened the term "tic-like compulsions" to include either of these symptoms or at least one tic from the tic inventory section of the Yale Global Tic Severity Scale performed in order to relieve the distress caused by an obsession. The presence of tic-like compulsions was not included in the Yale Global Tic Severity Scale scores.

In addition, the USP-Harvard Repetitive Behavior Interview was used to assess the subjective experiences associated with repetitive behaviors (compulsions or tics). This interview was specifically designed to investigate phenomenological features and consists of questions assessing cognitive processes (thoughts, ideas, images, fears, and worries), autonomic anxiety, and sensory phenomena preceding or accompanying the repetitive behaviors (for details on the interview and definitions of sensory phenomena, see Miguel and colleagues [17–19]). Briefly, in an attempt to reconcile the various descriptions of sensory phenomena, Miguel and colleagues (19) proposed to divide them into bodily and mental sensations. Bodily sensations include focal or generalized body sensations (usually tactile, muscular-skeletal/visceral, or both) occurring either before or while the patient performs the compulsions or tics. Mental sensations include "urge only," "energy release" (mental energy that builds up and needs to be discharged), feelings of "incompleteness," and "just-right perceptions" (20, 21).

The Beck Depression Inventory (22) and the Beck Anxiety Inventory (23) were administered to all patients.

Psychiatric axis I comorbidity was further assessed by using the Structured Clinical Interview for DSM-IV (24) supplemented with additional modules designed by the authors for the DSM-IV diagnoses of Tourette's disorder, chronic tics, trichotillomania, kleptomania, compulsive gambling, and pyromania (available upon request from M.C.R.-C.). Attention deficit hyperactivity disorder was investigated through a module of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (25).

Treatment Response

Short-term treatment response was assessed in 32 (76%) of these 42 patients. Patients were considered to have responded if they reported at least a 40% decrease in total score on the Yale-Brown Obsessive Compulsive Scale over a 12-week period of active monotherapy with the following drugs: clomipramine (given to nine early-onset and 11 late-onset subjects; maximum dose=250 mg/day), fluoxetine (given to three early-onset and three late-onset subjects; maximum dose=80 mg/day), sertraline (given to three early-onset and two late-onset subjects; maximum dose=200 mg/day), and paroxetine (given to one early-onset patient; maximum dose=60 mg/day). Patients were not concurrently receiving any other forms of treatment.

It was not possible to assess the treatment response from the other 10 patients (24%). Four refused to receive any kind of medication, and six abandoned treatment before the end of 12 weeks.

Statistical Analysis

Statistical analyses were performed by using SPSS version 10.0 (SPSS, Chicago). Initial analyses that used standard statistical approaches were done to determine whether any demographic or clinical variables were associated with differences between the two groups.

In order to test the null hypotheses that the early- and late-onset groups would not differ with regard to gender, current tic-like compulsions, sensory phenomena preceding their symptoms, comorbid tic disorders, and treatment response, we performed Fisher's exact tests. A p value of 0.05, two tailed, was used to determine statistical significance when rejecting null hypotheses. However, since five tests of association were performed, a p value of 0.01 was required after Bonferroni correction to reject the null hypotheses.

Some clinical features, such as earlier age at onset (26, 27), longer illness duration (26), comorbid tic disorders (28), and presence of hoarding (29, 30), have previously been associated with poor treatment response to clomipramine and selective serotonin reuptake inhibitors (SSRIs). In order to simultaneously evaluate these clinical features, we entered treatment response (positive or negative) as the dependent binary outcome in a logistic regression analysis.

Results

Demographic and Clinical Features

There were no statistically significant differences between the two groups with regard to gender (early-onset group: 11 men and 10 women; late-onset group: 12 men and nine women). The early- and late-onset groups also did not significantly differ in terms of current age (mean=31.4 years [SD=7.7] and 32.9 years [SD=10.4], respectively; t=–0.52, df=40, p=0.60), years of education (mean=13.6 [SD=4.4] and 13.3 [SD=4.2]; t=0.21, df=40, p=0.80), or socioeconomic status scale score (mean=76.3 [SD=34.0] and 62.6 [SD=27.1]; t=1.4, df=40, p=0.10).

For subjects in the early-onset group, the age at onset of compulsions (mean=7.8 years, SD=1.6) was earlier than the age at onset of obsessions (mean=9.3 years, SD=3.6). For subjects in the late-onset group, obsessions and compulsions began at almost the same age (mean=23.9 years [SD=8.2] and 24.0 years [SD=8.2], respectively). These between-group differences were significant when compared by using a repeated-measures analysis (F=4.35, df=1, 40, p=0.04).

The mean duration of illness for the total study group was 16.3 years (SD=10.1). The early-onset group had a mean duration of illness of 23.7 years (SD=7.9), whereas the mean duration of illness for the late-onset group was 8.9 years (SD=5.8).

Symptom Severity

The early-onset group had significantly higher total scores on the Yale-Brown Obsessive Compulsive Scale than did the late-onset group (mean=30.3 [SD=4.0] versus 26.6 [SD=5.4], respectively; F=6.14, df=1, 40, p=0.02). This

difference was due to significantly higher compulsion subscale scores in the early-onset group (mean=15.5, SD=2.2) than in the late-onset group (mean=13.0, SD=3.3) ($F=8.52$, df=1, 40, $p=0.006$). There were no significant differences between the early- and late-onset groups for scores on the obsessions subscale (mean=14.8 [SD=2.6] and 13.7 [SD=3.3], respectively) ($F=1.51$, df=1, 40, $p=0.22$).

There were no significant differences between the two groups in scores on the Yale Global Tic Severity Scale ($t=1.47$, df=10, $p=0.17$), the Beck Depression Inventory ($t=0.17$, df=39, $p=0.85$), or the Beck Anxiety Inventory ($t=0.27$, df=40, $p=0.78$).

Obsessive-Compulsive Symptoms

The early-onset group had a significantly higher number of subjects with tic-like compulsions (18 patients, compared to three patients from the late-onset group) ($p=0.00001$, Fisher's exact test). These compulsions were ascertained through items from the Yale-Brown Obsessive Compulsive Scale (15 patients from the early-onset group and three patients from the late-onset group) or the Yale Global Tic Severity Scale (three patients from the early-onset group).

Significantly more subjects in the early-onset group than in the late-onset group reported hoarding obsessions and compulsions (11 versus four patients, respectively; $p=0.05$, Fisher's exact test), repeating compulsions (17 versus 10 patients; $p=0.05$, Fisher's exact test) and miscellaneous compulsions (20 versus 14 patients; $p=0.04$, Fisher's exact test). There were no significant differences between the two groups for the other 11 categories of obsessions and compulsions as identified in the symptom checklist of the Yale-Brown Obsessive Compulsive Scale (data not shown).

Twenty-one patients (100%) from the early-onset group reported sensory phenomena preceding their repetitive behaviors, compared with 14 (67%) of the patients from the late-onset group ($p=0.008$, Fisher's exact test). When these subjective experiences were divided into bodily and mental sensations, it was found that relative to the late-onset group, the early-onset group experienced higher frequencies of both bodily ($p=0.04$, Fisher's exact test) and mental ($p=0.008$, Fisher's exact test) kinds of sensory phenomena.

Comorbidity

Thirty-five patients (83%) had at least one other lifetime DSM-IV axis I diagnosis. There were no significant differences between the two groups in lifetime axis I diagnoses, except for comorbid chronic tic disorders and Tourette's disorder, which were more frequent in the early-onset group ($p=0.01$, Fisher's exact test). A higher mean number of comorbid diagnoses was found in the early-onset group (mean=3.0, SD=1.7) than in the late-onset group (mean=1.8, SD=1.7) ($F=4.47$, df=1, 40, $p=0.04$).

Treatment Response

Only 31% (N=5 of 16) of the patients from the early-onset group responded to monotherapy with an antiobsessional agent (four patients treated with clomipramine and one patient receiving an SSRI) compared to 81% (N=13 of 16) of the late-onset group (nine patients treated with clomipramine and four patients receiving SSRIs) ($p=0.01$, Fisher's exact test).

The results of the logistic regression to predict treatment response in which age at onset, duration of illness, comorbid tic disorders, and the presence of hoarding obsessions or compulsions were simultaneously entered as independent variables indicated that only age at onset was significant (beta=–2.98, SE=1.49; Wald $\chi^2=4.01$, df=1, $p=0.04$). Duration of illness, comorbid tic disorders, and the presence of hoarding obsessions or compulsions did not independently contribute in this analysis.

Discussion

Studies of children and adolescents with OCD have reported both similarities and differences with the adult form of the disorder (3, 31). Although these studies have suggested that juvenile OCD may represent a distinct subgroup, it is still unclear whether the clinical manifestations persist into adulthood. Specifically, the effect of an early versus a later age at onset on the clinical phenotype, natural history, and treatment response has not been established.

In this report, by assessing adult patients, our data indicate that the phenotypic differences found between the early- and late-onset groups are not secondary to a developmental phase or restricted to childhood. These findings also support the view that age at symptom onset is likely to be a clinically important factor in subgrouping patients with OCD.

As predicted, the early-onset group, when compared to the late-onset one, was characterized by significantly higher frequencies of tic-like compulsions, sensory phenomena preceding their repetitive behaviors, higher probability of comorbid tic disorders or Tourette's disorder, and a poorer short-term treatment response to antiobsessional agents. Contrary to our expectations, there were no gender differences between the two groups. Although without stochastic significance after Bonferroni correction, the early-onset group also had an earlier onset of compulsions compared to obsessions, a higher mean number of comorbid diagnoses, and higher frequencies of repeating compulsions and hoarding obsessions and compulsions. Taken all together, the early-onset group presented phenotypic characteristics reported in most studies of children and adolescents with OCD (3).

Of note is the fact that in the early-onset group, the mean age at onset of compulsions was 2 years earlier than the onset of obsessions and that this difference was significant when compared to data for the late-onset group. This se-

quence is in agreement with previous descriptions of children with OCD in which compulsions commonly preceded the onset of obsessions (3, 32) and differs from the usual pattern seen in individuals with an adult onset. The fact that the early-onset individuals had significantly higher scores on the compulsion subscale of the Yale-Brown

Obsessive Compulsive Scale reinforces the idea that early-onset individuals continue to be more vulnerable to a broad range of compulsions throughout the lifespan.

Consistent with the view that early-onset patients are more burdened by compulsions, we also found that they had significantly higher frequencies of sensory phenomena than did the late-onset group. The same tendency has been described among patients with OCD associated with Tourette's disorder relative to OCD patients without tics (17–19). It is important to mention that in these earlier studies the mean age at onset for the patients with "OCD associated with Tourette syndrome" was 7 years (SD=2.5). In addition, among the eight "OCD alone" patients who reported sensory phenomena preceding their compulsions, seven had had their symptom onset before the age of 10. These findings reinforce the idea that the presence of sensory phenomena is not restricted solely to Tourette's disorder patients. In some instances, these subjective phenomena are more troublesome than the obsessions and compulsions. Hence, there is a need for incorporating these concepts into the routine assessment of OCD patients.

The Yale-Brown Obsessive Compulsive Scale symptom checklist analysis revealed differences between the two groups for hoarding/collecting and repeating compulsions and a statistically significant difference for tic-like compulsions. Tic-like compulsions have been reported as occurring in up to 70%–80% of the OCD patients with comorbid tic disorders (1, 33–36). Taken all together, these findings suggest an important overlap between the early-onset group and the "tic-like" OCD subtype (4, 37).

Although presence of hoarding (29, 30), comorbid tic disorder diagnosis (28), and longer illness duration (26) have been associated with a poor treatment response to antiobsessional agents, the results from the logistic regression in our data suggest that age at onset is the most powerful variable associated with a poor treatment response to standard treatment with clomipramine or an SSRI. Although preliminary, this finding emphasizes the importance of including the assessment of age at onset in future clinical trials.

The limitations of the study include the small size, the retrospective reports of age at onset, and the fact that the consecutive patients were recruited from a specialty clinic and may overrepresent severely affected OCD patients. Also, the fact that we used Bonferroni correction only for the initial hypothesis testing means that the significant findings from the exploratory analysis should be viewed with caution.

These results need to be replicated in a larger study that includes patients of different ages and with similar illness duration. Since the study was not designed to allow for conclusions regarding underlying pathophysiology, future research in genetics, neuroimaging, and immunology will be necessary to determine if these early-onset patients have specific biological markers or neurobiological substrates influencing the expression of OCD. Future studies addressing the issue of how these substrates interact with environmental factors, such as exposure to streptococcal infections or pregnancy and delivery traumas, will be extremely important given recent evidence suggesting that such factors may influence the expression of OCD in some cases (38, 39).

In addition, the cross-sectional study design and the requirement that obsessive-compulsive symptoms persisted into adulthood may have been a source of ascertainment bias, e.g., any patients with early-onset OCD that recovered would have not been identified. On the other hand, studies of adult OCD patients who have been symptomatic since childhood can offer us important clues on the possible factors that contributed to the persistence of their symptoms. At the same time, it is clear that prospective longitudinal studies are needed to fully address the course of early-onset OCD.

Therefore, the findings of this study support the notion that age at symptom onset is a clinically important factor in subtyping OCD and that early-onset patients may represent a distinct and valid OCD subtype with regard to symptom profiles, natural history, and response to treatment with antiobsessional agents.

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