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ORIGINAL ARTICLE

# Age of onset in obsessive–compulsive disorder: admixture analysis with a large sample

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**Background.** Research into age of onset in obsessive–compulsive disorder (OCD) has indicated significant differences between patients with early and late onset of the disorder. However, multiple criteria have been used arbitrarily for differentiating between early- and late-onset OCD, rendering inconsistent results that are difficult to interpret.

**Method.** In the current study, admixture analysis was conducted in a sample of 377 OC patients to determine the number of underlying populations of age of onset and associated demographic and clinical characteristics. Various measures of anxiety, depression, co-morbidity, autism, OCD, tics and attention deficit hyperactivity disorder (ADHD) symptoms were administered.

**Results.** A bimodal age of onset was established and the best-fitting cut-off score between early and late age of onset was 20 years (early age of onset $\leqslant$19 years). Patients with early age of onset were more likely to be single. Early age of onset patients demonstrated higher levels of OCD severity and increased symptoms on all OCD dimensions along with increased ADHD symptoms and higher rates of bipolar disorder.

**Conclusions.** It is suggested that 20 years is the recommended cut-off age for the determination of early *versus* late age of onset in OCD. Early age of onset is associated with a generally graver OCD clinical picture and increased ADHD symptoms and bipolar disorder rates, which may be related to greater functional implications of the disorder. We propose that age of onset could be an important marker for the subtyping of OCD.

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**Key words:** Admixture analysis, age of onset, obsessive–compulsive disorder.

## Introduction

Obsessive–compulsive disorder (OCD) is a prevalent and highly debilitating disorder that the World Health Organization (WHO) has listed among the 10 disorders with the highest economic burden (Murray *et al.* 2004). Despite the existence of effective psychological and pharmacological treatments (Rosa-Alcázar *et al.* 2008), many patients do not respond or only partially respond to treatment (Fisher & Wells, 2005). Because OCD is a heterogeneous disorder with possible phenotypical differences, there has been increased interest in identifying more homogeneous subtypes with distinct patterns of co-morbidities and outcomes (Leckman *et al.* 2010). Attention has also been directed towards age of onset as an important way of subtyping patients (Janowitz *et al.* 2009). OCD has a bimodal distribution of age of onset with a peak of incidence in childhood and another in mid-adulthood (Swedo *et al.* 1989). The bimodal age of onset of OCD suggests different etiological factors, and patients with early age of onset are likely to have a stronger genetic or biological component than patients with late onset (Bolton *et al.* 2007).

Age of onset may be clinically relevant because early age of onset was found to be associated with a more severe form of OCD. Earlier research demonstrated that patients with early age of onset exhibited higher OC symptom severity scores, poorer prognosis for

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pharmacological treatment, higher co-morbidity (Rosario-Campos *et al*. 2001) and more tics and compulsions in comparison with patients with late age of onset OCD (Chabane *et al.* 2005). Patients with early age of onset were found to be predominantly male (Noshirvani *et al.* 1991), and neuroimaging studies indicate different patterns of brain activation in OCD patients with early and late age of onset (Busatto *et al.* 2001). In addition, patients with early age of onset report more hoarding obsessions, repeating compulsions and sensory phenomena preceding their repetitive behaviors (Rosario-Campos *et al*. 2001). However, results pertaining to differences between early and late age of onset have been inconsistent. For example, Ferrao *et al.* (2006) found no differences in age of onset between responders and non-responders to pharmacological treatment for OCD. Some researchers (Douglass *et al.* 1995) have reported no elevation in tic rates in early age of onset patients and others have found no gender differences between early and late age of onset patients (Delorme *et al.* 2005; Janowitz *et al.* 2009). These conflicting results have contributed to the decision not to recommend age of onset as an OCD subtype in DSM-5 (Leckman *et al.* 2010).

One factor that may account for the inconsistencies found in the literature is the variable definitions for age of onset. Although most studies have used the definition of OCD onset (Taylor, 2011), some have used onset of first OC symptoms as the criterion for determining age of onset (e.g. de Mathis *et al.* 2009; Butwicka & Gmitrowicz, 2010) and others have used an in-between definition of onset of distressing OC symptoms (e.g. Tükel *et al.* 2005; Maina *et al.* 2008). However, the main reason for inconsistencies in age of onset of OCD research is probably the use of multiple cut-off scores to determine early *versus* late age of onset. Suggested cut-off points have been extremely diverse, ranging from 7 (Swedo *et al.* 1989) to 10 (Janowitz *et al.* 2009), 14 (Bellodi *et al.* 1992), 16 (Chabane *et al.* 2005), 18 (Pauls *et al.* 1995) and 30 (Grant *et al.* 2007). Some researchers have excluded patients in the middle age range in which overlap might exist between early and late age of onset patients or have created a third, intermediate age of onset group (Noshirvani *et al.* 1991; de Mathis *et al.* 2009). The approach of determining age of onset has often been tautological in the sense that an effort was made to find the cut-off score creating the largest differences in co-morbidity patterns (e.g. Janowitz *et al.* 2009; de Mathis *et al.* 2009).

A different approach that is gaining importance in determining age of onset of various psychiatric conditions, based on age distribution alone, is admixture analysis. It has been used with various psychiatric conditions such as social phobia, bipolar disorder, schizophrenia and age of first suicide attempt (Bellivier *et al.* 2003; Tozzi *et al.* 2011; Aderka *et al.* 2012). To date, only one study has used admixture analysis of age of onset in a sample of 161 OCD patients (Delorme *et al.* 2005). The results indicated that the best cut-off point between early and late age of onset is 21 years (i.e. the age of patients in the early age of onset group $\leqslant$20 years). In that study, early age of onset patients exhibited increased frequency of Tourette's syndrome and increased familial aggregation of OCD whereas late age of onset patients showed elevated prevalence of general anxiety disorder and depression. However, the results have not spurred use of the suggested cut-off scores, putatively due to a lack of replication of the data (Delorme *et al.* 2005).

The aim of the current study was to replicate and extend findings of admixture analysis of age of onset in OCD, using multiple demographic and clinical variables in a much larger sample of patients. We expected our results to replicate earlier findings, thus substantiating an accepted cut-off age based on validated admixture analysis and demonstrating the clinical relevance of subtyping OCD according to age of onset (Delorme *et al.* 2005).

## Method

### *Subjects*

Data were drawn from the baseline measurements of the Netherlands Obsessive Compulsive Disorder Association (NOCDA) study. NOCDA is an ongoing multicenter 6-year naturalistic cohort study to examine the course of OCD. The respondents are patients with a lifetime diagnosis of OCD referred to one of the participating mental health care centers for evaluation and treatment. Written informed consent was obtained from all participants after the study aims had been fully explained. In total, 419 respondents were included in the NOCDA study. More details about the rationale, objectives and methods of NOCDA can be found elsewhere (Schuurmans *et al.* 2012). Of the 419 respondents, age of onset data of 42 respondents were missing, resulting in a sample size of 377 respondents.

OCD and other DSM-IV diagnoses were confirmed with the aid of the Structured Clinical Interview on DSM-IV Axis I disorders (SCID-I; First *et al.* 1995). Age of onset was determined during the SCID as the first point in which patients fulfilled criteria for a DSM-IV OCD diagnosis. This criterion for the definition of age of onset was selected because it is in accordance with most of the studies investigating age of onset in OCD (Taylor, 2011). Furthermore, other

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criteria such as onset of first OC symptoms may be less reliable because developing children engage in a significant amount of ritualistic, repetitive and compulsive-like activity (Leckman *et al.* 2009).

### Measures

#### *Measurement of tics*

Tic severity was measure by the Yale Global Tic Severity Scale (Y-GTSS; Leckman *et al.* 1989), a semi-structured interview providing information about the number, frequency, intensity, complexity and interference of motor and phonic symptoms, which are rated on a 0–50-point scale (0=none, 50=severe), and impairment of motor and vocal tics, also rated on a 0–50-point scale (0=none, 50=severe). The total score of the Y-GTSS is rated on a 0–100-point scale.

#### *Attention deficit hyperactivity disorder (ADHD) symptoms*

To measure ADHD symptoms, the ADHD interview (DuPaul *et al.* 1998) was used. This interview consists of separate items for symptoms in the past and present (yes=0; no=1), with nine items of inattention symptoms and nine items of hyperactivity–impulsivity symptoms. If at least six inattention symptoms were met, an inattention ADHD subtype was assigned (ADHD-I), when at least six hyperactivity–impulsivity symptoms were met, a hyperactivity–impulsivity subtype was assigned (ADHD-HI), and whenever both criteria were met, a combined ADHD subtype was assigned (ADHD-C).

#### *Anxiety symptoms*

To assess anxiety symptoms we used the Beck Anxiety Inventory (BAI; Beck *et al.* 1988*a*), a 21-item questionnaire measuring different symptoms of anxiety, experienced in the past week.

#### *Depression symptoms*

We used the Beck Depression Inventory (BDI; Beck *et al.* 1988*b*), a 21-item questionnaire measuring the presence and severity of depression symptoms.

#### *OC symptoms*

To assess OC symptom dimensions, we used an adapted 80-item self-report version of the Yale–Brown Obsessive–Compulsive Scale (YBOCS; Goodman *et al.* 1989). Item scores of the YBOCS symptom checklist were summarized into four symptom dimensions according to the four-factor structure found by Leckman *et al.* (1997) and replicated in large OCD samples. These symptom dimensions include: aggression/checking, symmetry/ordering, contamination/washing and hoarding. Furthermore, the interview version of the 10-item YBOCS severity scale (scoring range 0–40) was used. During the interview, symptoms that patients reported in the YBOCS self-report were discussed, and only items that were assessed as clinically reliable were retained.

#### *Autism symptoms*

Autism symptoms were rated by the Autism-Spectrum Quotient (AQ; Baron-Cohen *et al.* 2001). The AQ entails a 50-item self-administered instrument specifically developed for adults with normal intelligence with scores on each item between 1 ('I fully agree') and 4 ('I fully disagree'; range 50–200). The AQ consists of five subscales each containing 10 items.

### Analytic strategy

We used admixture analysis to determine whether our sample data were derived from one or more normally distributed populations of origin (Bellivier *et al.* 2003; Delorme *et al.* 2005; Tozzi *et al.* 2011; Aderka *et al.* 2012). Admixture analysis uses maximum likelihood estimation to estimate the probability that the observed (sample) data would be found when assuming $K$ original Gaussian distributions. To determine the most likely number of origin populations, we estimated the $\chi^2$ goodness of fit for a single population, two populations and three populations separately. We followed the guidelines of Kolenikov (2001) and chose the best-fitting model according to the highest probability value of the $\chi^2$ goodness-of-fit test. This is because a significant $\chi^2$ value (with a probability value <0.05) indicates a significant difference between the model and the data and a high probability value indicates a good match between the model and the data. After determining the number of populations, we calculated the probability of each individual belonging to a given population consistent with prior studies (Bellivier *et al.* 2003; Delorme *et al.* 2005). We used this probability to divide individuals into their respective populations of origin. Specifically, for each individual we calculated the probability of belonging to each population, and then assigned each individual to the most likely population (i.e. the population with the highest probability value for that individual). An advantage of using admixture analysis is that it can detect a population of origin even if only a small percentage of the sample belongs to it. For instance, in a previous admixture analysis, a population constituting 12.5% of the sample was detected in a sample of 161 individuals (Delorme *et al.* 2005). All admixture analyses were performed using the script denormix and the statistics program Stata 10

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**Table 1.** *Admixture results for age of onset*

| | Estimate (S.E.) | 95% CI | Log likelihood | $\chi^2$ | $p$ |
|---|---|---|---|---|---|
| Single population | | | –1376.18 | 26.09 | <0.001 |
| Mean | 18.33 (0.48) | 17.38–19.28 | | | |
| S.D. | 9.40 (0.16) | 9.09–9.71 | | | |
| Two populations | | | –1348.98 | 4.52 | 0.21[a] |
| Early onset | | | | | |
| Mean | 12.82 (0.84) | 11.18–14.46 | | | |
| S.D. | 4.90 (0.38) | 4.15–5.65 | | | |
| Late onset | | | | | |
| Mean | 24.90 (1.84) | 21.30–28.50 | | | |
| S.D. | 9.27 (0.33) | 8.63–9.91 | | | |
| Three populations | | | –1337.28 | 7.11 | <0.05 |
| Early onset | | | | | |
| Mean | 13.26 (0.59) | 12.10–14.42 | | | |
| S.D. | 4.97 (0.26) | 4.46–5.47 | | | |
| Intermediate onset | | | | | |
| Mean | 25.45 (0.73) | 24.03–26.88 | | | |
| S.D. | 3.07 (0.54) | 2.01–4.13 | | | |
| Late onset | | | | | |
| Mean | 38.89 (1.28) | 36.38–41.41 | | | |
| S.D. | 4.48 (0.62) | 3.26–5.69 | | | |

S.E., Standard error; S.D., standard deviation; CI, confidence interval.
[a] The highest $\chi^2$ probability value indicates the best-fitting model.

(Kolenikov & Denormix, 2001). We examined differences between the groups using ANOVA and $\chi^2$ tests.

## Results

### *Sample characteristics*

The study sample consisted of 377 OCD patients, with an average age of 36.3 (S.D.=11.2) years. Of these patients, 57% were female; the average duration of education was of 11.7 (S.D.=4.5) years; 63% of the participants had a lifetime mood disorder; and 46% had a lifetime anxiety disorder other than OCD. Marital status of the participants included 59.7% single, 33.7% married, 6.1% divorced and 0.5% widowed. The mean duration of OCD symptoms was 17.9 (S.D.=12.3) years.

### *Admixture*

We computed the estimated $\chi^2$ goodness of fit for one, two and three populations. Table 1 summarizes the admixture results. The highest $\chi^2$ probability value belonged to the model with two populations. Thus, our sample was most probably derived from a mixture of two underlying populations. The early-onset population had a mean age of onset of 12.8 (S.D.=4.9) years whereas the late-onset population had a mean age of onset of 24.9 (S.D.=9.3) years. Of the total sample, 230 individuals (61.0%) belonged to the early-onset population and 147 individuals (39.0%) to the late-onset population. The cut-off between the populations was the age of 20 years: individuals younger than 20 belonged to the early-onset population whereas individuals aged $\geqslant$20 years belonged to the late-onset population. Figure 1 presents the age of onset frequencies and Fig. 2 presents the two populations of origin. One outlier with an age of onset of 59 years was excluded from analyses.

### *Differences between groups*

First, we assessed whether early- and late-onset OCD patients differed with respect to past or current treatments for OCD. No significant differences in past psychotherapeutic treatments ($\chi^2_1$=3.28, $p$=0.07) or in past pharmacological treatments ($\chi^2_1$=0.79, $p$=0.38) were found between individuals from the early- and late-onset groups. Furthermore, no significant differences in present use of anxiolytic medications ($\chi^2_1$=1.84, $p$=0.318) or in present use of antidepressant medications ($\chi^2_1$=2.77, $p$=0.10) were found between early- and late-onset OCD patients. Subsequently, we compared the early-onset population with the late-onset population on all demographic and clinical

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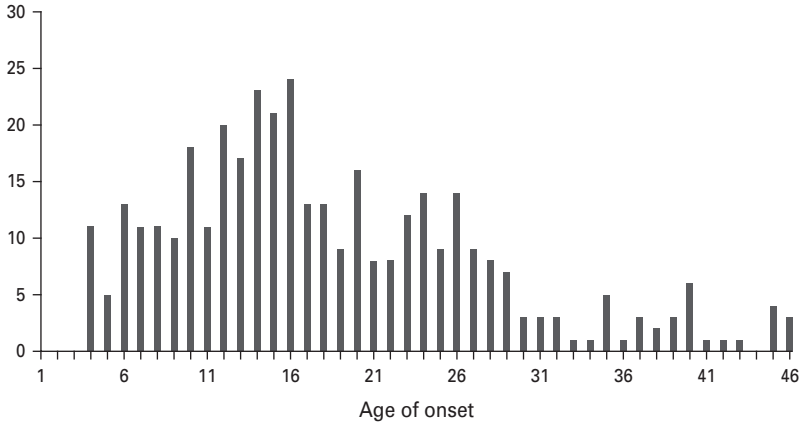


**Fig. 1.** Frequencies of age of onset ($n$=377).


**Fig. 2.** Estimated populations of origin.

measures. The results are presented in Table 2. Individuals from the early-onset group were significantly younger, more likely to live alone, and had fewer years of education compared to individuals from the late-onset group (nearly significant). In addition, individuals from the early-onset group had significantly more ADHD symptoms (both past and current), more compulsions, and overall more OCD symptoms compared to individuals from the late-onset group (Table 2).

We also examined whether individuals with early onset differed from individuals with late onset on rates of co-morbid disorders. No group differences between early- and late-onset OCD patients was found in current or lifetime diagnoses of: major depressive disorder, dysthymic disorder, bipolar disorder, social anxiety disorder, panic disorder with or without agoraphobia, pure agoraphobia, generalized anxiety disorder, post-traumatic stress disorder, specific phobia, schizophrenia, substance-related disorders, somatoform disorders, and eating disorders. Significant differences were found on lifetime bipolar disorder ($\chi^2_1$=8.6, $p$<0.01) and on current ADHD-C subtype diagnoses ($n$=14, 6.1% in the early-onset group; $n$=2, 1.4% in the late-onset group; $\chi^2_1$=4.86, $p$<0.05). More individuals with early onset received a lifetime diagnosis of bipolar disorder and a current diagnosis of ADHD-C compared to individuals with late onset.

We also compared between individuals with early and late ages of onset on the types of obsessions and compulsions experienced. The results are summarized in Table 3. In all cases of significant differences, individuals with early onset reported more symptoms than individuals with late onset.

## Discussion

This study replicated and extended previous findings regarding age of onset in OCD and its clinical relevance in a large community sample. Our major findings were that age of onset in OCD is bimodal and that 20 years is the best cut-off age (early age of onset ⩽19 years and late age of onset >19 years). These results clearly confirm (20 *v.* 21 respectively) prior findings in admixture analysis of OCD patients (Delorme *et al.* 2005). Furthermore, the current study contains a much larger sample, with a sufficient number of patients throughout the age range (Delorme *et al.* 2005).

No significant differences in gender distribution were detected between early and late age of onset. This finding is compatible with earlier findings of admixture analysis in OCD (Delorme *et al.* 2005). Although most age of onset analyses of OCD patients detected a higher rate of males in early *versus* late age of onset patients, others have not found such gender differences between early and late age of onset OCD patients (e.g. Sobin *et al.* 2000; Grant *et al.* 2007; Janowitz *et al.* 2009). In a recent review of age of onset in OCD, Taylor (2011) detected significantly

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**Table 2.** *Demographic and clinical measures*

| Measure | Total ($n$=377) | Early onset ($n$=230) | Late onset ($n$=147) | Statistics | $p$ |
|---|---|---|---|---|---|
| Gender, $n$ (%) | | | | $\chi^2_1$=1.2 | 0.28 |
| Male | 164 (43.5) | 95 (41.3) | 69 (46.9) | | |
| Female | 213 (56.5) | 135 (58.7) | 78 (53.1) | | |
| Age (years), mean (S.D.) | 36.3 (11.2) | 34.1 (11.2) | 39.8 (10.3) | $F_{1,375}$=24.3 | <0.001 |
| Living situation, $n$ (%) | | | | $\chi^2_1$=10.5 | <0.01 |
| Living alone | 250 (56.3) | 167 (72.6) | 83 (56.5) | | |
| Living together | 127 (33.7) | 63 (27.4) | 64 (43.5) | | |
| Years of education, mean (S.D.) | 12.5 (3.3) | 12.2 (3.1) | 12.9 (3.5) | $F_{1,355}$=3.60 | 0.06 |
| YBOCS Obsessions, mean (S.D.) | 9.8 (4.4) | 10.1 (4.1) | 9.3 (4.7) | $F_{1,375}$=3.24 | 0.07 |
| YBOCS Compulsions, mean (S.D.) | 9.9 (4.8) | 10.3 (4.5) | 9.3 (5.3) | $F_{1,375}$=4.22 | <0.05 |
| YBOCS Total, mean (S.D.) | 19.7 (8.1) | 20.5 (7.7) | 18.6 (8.7) | $F_{1,375}$=4.81 | <0.05 |
| Y-GTSS, mean (S.D.) | 3.53 (10.99) | 4.19 (12.36) | 2.49 (8.36) | $t_{373.8}$=1.59[a] | 0.11 |
| Mood disorder current, $n$ (%) | 86 (22.8) | 54 (23.5) | 32 (21.8) | $\chi^2_1$=0.15 | 0.70 |
| Mood disorder lifetime, $n$ (%) | 238 (63.1) | 150 (65.2) | 88 (59.9) | $\chi^2_1$=1.10 | 0.29 |
| Number of mood disorders current, mean (S.D.) | 0.23 (0.42) | 0.23 (0.43) | 0.22 (0.41) | $F_{1,375}$=0.15 | 0.70 |
| Number of mood disorders lifetime, mean (S.D.) | 0.65 (0.51) | 0.67 (0.50) | 0.62 (0.53) | $F_{1,375}$=0.73 | 0.39 |
| Anxiety disorder current, $n$ (%) | 133 (35.3) | 76 (33.0) | 57 (38.8) | $\chi^2_1$=1.29 | 0.26 |
| Anxiety disorder lifetime, $n$ (%) | 175 (46.4) | 102 (44.3) | 73 (49.7) | $\chi^2_1$=1.02 | 0.31 |
| Number of anxiety disorders current, mean (S.D.) | 0.48 (0.76) | 0.44 (0.73) | 0.54 (0.80) | $F_{1,375}$=1.59 | 0.21 |
| Number of anxiety disorders lifetime, mean (S.D.) | 0.70 (0.91) | 0.69 (0.93) | 0.73 (0.89) | $F_{1,375}$=0.18 | 0.67 |
| Psychotic disorder current, $n$ (%) | 9 (2.4) | 5 (2.2) | 4 (2.7) | $\chi^2_1$=0.12 | 0.73 |
| Psychotic disorder lifetime, $n$ (%) | 15 (4.0) | 10 (4.3) | 5 (3.4) | $\chi^2_1$=0.21 | 0.65 |
| Substance dependence current, $n$ (%) | 14 (3.7) | 10 (4.3) | 4 (2.7) | $\chi^2_1$=0.66 | 0.42 |
| Substance dependent lifetime, $n$ (%) | 36 (9.5) | 26 (11.3) | 10 (6.8) | $\chi^2_1$=2.10 | 0.15 |
| Substance abuse current, $n$ (%) | 2 (0.5) | 1 (0.4) | 1 (0.7) | $\chi^2_1$=0.10 | 0.75 |
| Substance abuse lifetime, $n$ (%) | 12 (3.2) | 8 (3.5) | 4 (2.7) | $\chi^2_1$=0.17 | 0.68 |
| Somatoform disorders current, $n$ (%) | 21 (5.6) | 14 (6.1) | 7 (4.8) | $\chi^2_1$=0.30 | 0.58 |
| Somatoform disorders lifetime, $n$ (%) | 21 (5.6) | 14 (6.1) | 7 (4.8) | $\chi^2_1$=0.30 | 0.58 |
| Eating disorders current, $n$ (%) | 16 (4.2) | 12 (5.2) | 4 (2.7) | $\chi^2_1$=0.30 | 0.58 |
| Eating disorders lifetime, $n$ (%) | 39 (10.3) | 28 (12.2) | 11 (7.5) | $\chi^2_1$=2.13 | 0.15 |
| Number of current diagnoses, mean (S.D.) | 1.8 (1.2) | 1.8 (1.2) | 1.8 (1.1) | $F_{1,375}$=0.05 | 0.83 |
| Number of lifetime diagnoses, mean (S.D.) | 2.7 (1.4) | 2.7 (1.5) | 2.6 (1.3) | $F_{1,375}$=0.74 | 0.39 |
| Attention deficit symptoms past, mean (S.D.) | 2.4 (2.5) | 2.7 (2.6) | 1.9 (2.2) | $F_{1,375}$=9.72 | <0.01 |
| Attention deficit symptoms current, mean (S.D.) | 3.0 (2.4) | 3.3 (2.3) | 2.5 (2.4) | $F_{1,375}$=8.98 | <0.01 |
| Hyperactivity/impulsivity symptoms past, mean (S.D.) | 1.9 (2.3) | 2.1 (2.4) | 1.4 (2.0) | $F_{1,375}$=7.92 | < 0.01 |
| Hyperactivity/impulsivity symptoms current, mean (S.D.) | 2.2 (2.1) | 2.4 (2.2) | 1.8 (2.0) | $F_{1,375}$=8.43 | <0.01 |
| BAI, mean (S.D.) | 17.3 (12.0) | 17.9 (11.6) | 16.6 (12.7) | $F_{1,358}$=1.01 | 0.32 |
| BDI, mean (S.D.) | 15.2 (10.1) | 15.1 (9.8) | 15.3 (10.6) | $F_{1,357}$=0.05 | 0.83 |
| AQ, mean (S.D.) | 114.0 (16.1) | 114.7 (16.7) | 113.0 (15.2) | $F_{1,359}$=1.04 | 0.31 |

YBOCS, Yale–Brown Obsessive Compulsive Scale; Y-GTSS, Yale Global Tic Severity Scale; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; AQ, Autism-Spectrum Quotient.

[a] We used a $t$ test to correct degrees of freedom due to unequal variances. Levene's test of equality of variances was $F$=6.45, $p$=0.01, indicating that variances in the two groups were significantly different.

greater heterogeneity in studies investigating gender differences between early- and late-onset OCD patients than would be expected from random error. Taylor (2011) suggested this is due to moderator variables; however, various meta-analytic analyses could not detect a variable that might serve as such a variable and explain these conflicting findings.

Patients with early age of onset were more likely to live alone and tended to complete fewer years of education than patients with late age of onset. This finding is best understood in view of the clinical features characteristic of early age of onset patients that might be related to a general decrease in level of functioning relative to late age of onset patients (Eakin *et al.* 2004).

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**Table 3.** *Specific OC symptoms among individuals with early and late ages of onset*

| | Early onset ($n$=225[a]) | Late onset ($n$=145[b]) | Statistics | $p$ |
|---|---|---|---|---|
| YBOCS factors | | | | |
| Aggressive | 32.4 (7.3) | 29.3 (7.1) | $F_{1,362}$=15.5 | <0.001 |
| Symmetry | 17.6 (5.5) | 14.8 (5.2) | $F_{1,363}$=23.5 | <0.001 |
| Contamination | 14.5 (5.1) | 13.2 (4.7) | $F_{1,366}$=6.8 | <0.01 |
| Hoarding | 2.7 (1.3) | 2.5 (1.2) | $F_{1,368}$=3.4 | 0.07 |
| No. of OC symptom dimensions | 7.9 (3.5) | 5.8 (3.8) | $F_{1,368}$=28.05 | <0.001 |

OC, Obsessive–compulsive; YBOCS, Yale–Brown Obsessive Compulsive Scale.

Units of measurement for all results presented in the table are mean (S.D.)

[a] Data were not available for five individuals from the early-onset group and degrees of freedom vary as a result of missing data.

[b] Data were not available for two individuals from the late-onset group and degrees of freedom vary as a result of missing data.

Regarding clinical characteristics, early age of onset patients demonstrated no differences in anxiety and depression co-morbidity patterns compared to late age of onset patients. This finding diverges from earlier admixture findings in OCD where late age of onset patients presented with higher depression and generalized anxiety rates (Delorme *et al.* 2005). However, our current results are further strengthened by the dimensional measurements of anxiety and depression (by the BAI and the BDI) in which no significant differences were detected between early and late age of onset patients. In terms of specific symptom elevation, an interesting pattern of differences emerged. Early age of onset patients showed increased rates of ADHD (in past and also in present) symptoms. Palumbo *et al.* (1997) suggested that OCD, ADHD, Tourette's syndrome and autism share etiological overlap and constitute a group of developmental basal ganglia disorders. As early age of onset was often found to correspond with higher tic rates than late-onset OCD (e.g. Chabane *et al.* 2005), it was expected that rates of other disorders belonging to the suggested group of basal ganglia disorders would be elevated in early-onset OCD patients. We found only partial support for early age of onset relatedness to this cluster of disorders (as evidenced by the increase in past and present ADHD symptoms only). In contrast to these findings, earlier admixture analyses in OCD did not detect ADHD co-morbidity differences between early and late age of onset patients (Delorme *et al.* 2005). However, we have used a dimensional measure to assess increase in ADHD symptoms rather than a categorical division based on ADHD diagnosis alone. Therefore, our results might be more sensitive to detecting these differences. Indeed, when categorical definitions were used, only differences in ADHD of the combined type emerged between early- and late-onset patients. In addition, in the previous admixture research, patients were recruited in OCD university-based programs and the sample consisted of children and adults, whereas the current study concerns a study of adult OCD patients referred to mental health care centers.

Autism symptoms were not elevated in early *versus* late age of onset patients. This finding contradicts earlier findings in which OCD patients with ADHD demonstrated elevated rates of autism symptoms as well (Anholt *et al.* 2010). This difference might again be partially explained by the differences in the use of a categorical definition of ADHD (Anholt *et al.* 2010), for which few differences between early- and late-onset OCD patients were detected in the current study.

Early age of onset patients demonstrated higher overall OCD severity scores and higher obsession (nearly significant) and compulsion severity rates. In terms of symptom dimensions, early age of onset patients showed elevations on all OCD symptoms (with differences in hoarding symptoms being nearly significant). These results suggest that early age of onset is associated with a graver overall clinical picture of OCD. Patients with an early age of onset also exhibited higher rates of lifetime co-morbidity with bipolar disorder. This finding converges with results obtained with a large sample of bipolar disorder patients in which co-morbidity with OCD was related to a more severe symptom presentation in addition to significantly earlier age of onset (Goes *et al.* 2012). This clinical picture is in line with a cognitive-behavior treatment study in which OCD patients with early onset exhibited increased severity at post-treatment relative to late-onset OCD patients, a finding that was attributed to their higher severity before treatment

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rather than to their lack of response to treatment itself (Lomax *et al.* 2009). Possibly, these patients require a longer treatment aimed at optimal symptom reduction and at improving level of functioning. Taken together with demographic differences between early- and late-onset patients, these findings suggest that, in the treatment of patients with an early OCD onset, other issues beyond symptom reduction may require attention in treatment. These include interpersonal functioning (as suggested by Moritz *et al.* 2012) in addition to other academic and occupational functioning (as suggested by Mancebo *et al.* 2008).

These findings highlight the importance of age of onset as a marker of OCD well beyond the presence or absence of tics. Some researchers have questioned the use of age of onset as a marker because early-onset patients without tics might be similar to late-onset patients (Leckman *et al.* 2010). If this was the case, we would expect a more specific clinical presentation with symptom elevation in symmetry/ordering symptoms (Labad *et al.* 2008) but no symptom elevation in washing/contamination, which is infrequent in OCD with tic patients (Anholt *et al.* 2006).

Some methodological limitations in the current study should be mentioned. First, establishing age of onset was retrospective and subject to recall bias (Masia *et al.* 2003). Second, the present study was cross-sectional in nature and future studies should examine the relationships between ADHD, tics and OCD longitudinally to establish temporal relationships and inform developmental models. Third, it is possible that additional variables not included in the present analysis, such as personality characteristics, are responsible for the differences between early and late age of onset OCD. Future studies should take this into account to extend our understanding of these important subgroups. Fourth, impulse control disorders, presumably belonging to the OCD spectrum disorders (Hollander *et al.* 1996), are not assessed by the standard SCID used in the current study. Future research should examine differences in impulse control disorders between early- and late-onset OCD patients. Fifth, it is important to note that a controversy exists regarding whether the definition of age of onset relates to the beginning of symptoms, distress/impairment or fulfilling criteria for an OCD diagnosis (de Mathis *et al.* 2009). As most studies have used a definition of fulfilling criteria for an OCD diagnosis, this approach was used in the present investigation. It remains to be determined whether the use of another definition might produce different results.

In conclusion, early age of onset OCD is associated with generally high scores across all OCD symptom dimensions and severity. Although no increased co-morbidity patterns were detected in anxiety and depression diagnoses, increased ADHD symptoms and also a graver overall clinical OCD presentation may be related to a greater impact on functioning levels. Our results largely converge with earlier admixture analysis findings in OCD (Delorme *et al.* 2005), underscoring the validity and reliability of a cut-off point of age 20, which should be used in future research to further investigate age of onset characteristics, predictors and treatment outcome. Such use might decrease the inconsistencies characteristic of age of onset literature, and enable use of age of onset as an important marker of OCD. We also recommend that future research involves dimensional measurements of symptoms in addition to categorical co-morbidity rates, thereby achieving higher sensitivity to elevated scores in important symptom domains that do not necessarily meet criteria for full diagnoses.

## Declaration of Interest

None.

## References

**Aderka IM, Nickerson A, Hofmann SG** (2012). Admixture analysis of the diagnostic subtypes of social anxiety disorder: implications for the DSM-V. *Journal of Behavior Therapy and Experimental Psychiatry* **43**, 752–757.

**Anholt GE, Cath DC, Emmelkamp PM, van Oppen P, Smit JH, van Balkom AJ** (2006). Do obsessional beliefs discriminate OCD without tic patients from OCD with tic and Tourette's syndrome patients? *Behaviour Research and Therapy* **44**, 1537–1543.

**Anholt GE, Cath DC, van Oppen P, Eikelenboom M, Smit JH, van Megen H, van Balkom AJ** (2010). Autism and ADHD symptoms in patients with OCD: are they associated with specific OC symptom dimensions or OC symptom severity? *Journal of Autism and Developmental Disorders* **40**, 580–589.

**Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E** (2001). The Autism-Spectrum Quotient (AQ): evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders* **31**, 5–17.

**Beck AT, Epstein N, Brown G, Steer RA** (1988*a*). An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology* **56**, 893–897.

**Beck AT, Steer RA, Garbin MG** (1988*b*). Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clinical Psychology Review* **42**, 861–865.

**Bellivier F, Golmard JL, Rietschel M, Schulze TG, Malafosee A, Preisig M, Leboyer M** (2003). Age at onset in bipolar I affective disorder: further evidence for three subgroups. *American Journal of Psychiatry* **160**, 999–1001.

**Bellodi L, Sciuto G, Diaferia G, Ronchi P, Smeraldi E** (1992). Psychiatric disorders in the families of patients with

https://doi.org/10.1017/S0033291713000470 Published online by Cambridge University Press

obsessive-compulsive disorder. *Psychiatry Research* **42**, 111–120.

**Bolton D, Rijsdijk F, O'Connor TG, Perrin S, Eley TC** (2007). Obsessive-compulsive disorder, tics, and anxiety in 6-year-old twins. *Psychological Medicine* **37**, 39–48.

**Busatto GF, Buchpiguel CA, Zamignani DR, Garrido GE, Glabus MF, Rosario-Campos MC, Castro CC, Maia A, Rocha ET, McGuire PK, Miguel EC** (2001). Regional cerebral blood flow abnormalities in early-onset obsessive compulsive disorder: an exploratory SPECT study. *Journal of the American Academy of Child and Adolescent Psychiatry* **40**, 347–354.

**Butwicka A, Gmitrowicz A** (2010). Symptom clusters in obsessive-compulsive disorder (OCD): influence of age and age of onset. *European Child and Adolescent Psychiatry* **19**, 365–370.

**Chabane N, Delorme R, Millet B, Mouren MC, Leboyer M, Pauls D** (2005). Early-onset obsessive compulsive disorder: a subgroup with a specific clinical and familial pattern? *Journal of Child Psychology and Psychiatry* **46**, 881–887.

**Delorme R, Golmard JL, Chabane N, Millet B, Krebs MO, Mouren-Simeoni MC, Leboyer M** (2005). Admixture analysis of age at onset in obsessive-compulsive disorder. *Psychological Medicine* **35**, 237–243.

**de Mathis MA, Diniz JB, Shavitt RG, Torres AR, Ferrão YA, Fossaluza V, Pereira C, Miguel E, do Rosario MC** (2009). Early onset obsessive-compulsive disorder with and without tics. *CNS Spectrums* **14**, 362–370.

**Douglass HM, Moffitt TE, Dar R, McGeer R, Silva P** (1995). Obsessive-compulsive disorder in a birth cohort of 18-year-olds: prevalence and predictors. *Journal of the American Academy of Child and Adolescent Psychiatry* **34**, 1424–1431.

**DuPaul GJ, Power TJ, Anastopoulos AD, Reid R** (1998). *ADHD Rating Scale-IV. Checklists, Norms and Clinical Interpretation*. Guilford Press: New York.

**Eakin L, Minde K, Hechtman L, Ochs E, Krane E, Bouffard R, Greenfield B, Looper K** (2004). The marital and family functioning of adults with ADHD and their spouses. *Journal of Autism and Developmental Disorders* **8**, 1–10.

**Ferrao YA, Shavitt RG, Bedin NR, de Mathis ME, Carlos Lopes A, Fontenelle LF, Torres AR, Miguel EC** (2006). Clinical features associated to refractory obsessive compulsive disorder. *Journal of Affective Disorders* **94**, 199–209.

**First MB, Spitzer RL, Gibbon M, Williams JB** (1995). *Structured Clinical Interview for DSM-IV (SCID)*. Biometrics Research, New York State Psychiatric Institute: New York.

**Fisher PL, Wells A** (2005). How effective are cognitive and behavioral treatments for obsessive-compulsive disorder? A clinical significance analysis. *Behaviour Research and Therapy* **43**, 1543–1558.

**Goes FS, McCusker MG, Bienvenu OJ, MacKinnon DF, Mondimore FM, Schweizer B, DePaulo JR, Potash JB** (2012). Comorbid anxiety disorders in bipolar disorder and major depression: familial aggregation and clinical characteristics of comorbid panic disorder, social phobia, specific phobia and obsessive-compulsive disorder. *Psychological Medicine* **42**, 1449–1559.

**Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann R, Hill CL, Heninger GR, Charney DS** (1989). The Yale-Brown Obsessive-Compulsive Scale I: Development, use, and reliability. *Archives of General Psychiatry* **46**, 1006–1011.

**Grant GE, Mancebo MC, Pinto A, Williams KA, Eisen JL, Rasmussen SA** (2007). Late-onset obsessive compulsive disorder: clinical characteristics and psychiatric comorbidity. *Psychiatry Research* **152**, 21–27.

**Hollander E, Kwon JH, Stein DJ, Broatch J, Rowland CT, Himelein CA** (1996). Obsessive-compulsive and spectrum disorders: overview and quality of life issues. *Journal of Clinical Psychiatry* **57** (Suppl. 8), 3–6.

**Janowitz D, Grabe HJ, Ruhrmann S, Ettelt S, Buhtz F, Hochrein A, Schulze-Rauschenbach S, Meyer K, Kraft S, Ferber C, Pukrop R, Freyberger HJ, Klosterkotter J, Falkai P, John U, Maier W, Wagner M** (2009). Early onset of obsessive-compulsive disorder and associated comorbidity. *Depression and Anxiety* **26**, 1012–1017.

**Kolenikov S** (2001). Denormix: Stata module to perform decomposition of normal mixture (http://ideas.repec.org/c/boc/bocode/s416605.html). Accessed 24 July 2012.

**Labad J, Menchon JM, Alonso P, Segalas C, Jimenez S, Jaurrieta N, Leckman JF, Vallejo J** (2008). Gender differences in obsessive-compulsive symptom dimensions. *Depression and Anxiety* **25**, 832–838.

**Leckman JF, Bloch MH, King RA** (2009). Symptom dimensions and subtypes of obsessive-compulsive disorder: a developmental perspective. *Dialogues in Clinical Neuroscience* **11**, 21–33.

**Leckman JF, Denys D, Simpson HB, Mataix-Cols D, Hollander E, Saxena S, Miguel EC, Rauch SL, Goodman WK, Phillips KA, Stein DJ** (2010). Obsessive-compulsive disorder: a review of the diagnostic criteria and possible subtypes and dimensional specifiers for DSM-V. *Depression and Anxiety* **27**, 507–527.

**Leckman JF, Grice DE, Boardman J, Zhang H, Vitale A, Bondi C, Alsobrook J, Peterson BS, Cohen DJ, Rasmussen SA, Goodman WK, McDougle CJ, Pauls DL** (1997). Symptoms of obsessive-compulsive disorder. *Archives of General Psychiatry* **154**, 911–917.

**Leckman JF, Riddle MA, Hardin M, Ort SI, Swartz KL, Stevenson J, Cohen D** (1989). The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. *Journal of the American Academy of Child and Adolescent Psychiatry* **28**, 566–573.

**Lomax CL, Oldfield VB, Salkovskis PM** (2009). Clinical and treatment comparisons between adults with early- and late-onset obsessive-compulsive disorder. *Behaviour Research and Therapy* **47**, 99–104.

**Maina G, Albert U, Salvi V, Pessina E, Bogetto F** (2008). Early-onset obsessive-compulsive disorder and personality disorders in adulthood. *Psychiatry Research* **158**, 217–225.

**Mancebo MC, Greenberg B, Grant JE, Pinto A, Eisen JL, Dyck I, Rasmussen SA** (2008). Correlates of occupational

disability in a clinical sample of obsessive-compulsive disorder. *Comprehensive Psychiatry* **49**, 43–50.

**Masia CL, Storch EA, Dent HC, Adams P, Verdeli H, Davies M, Weissman MM** (2003). Recall of childhood psychopathology more than 10 years later. *Journal of the American Academy of Child and Adolescent Psychiatry* **42**, 6–12.

**Moritz S, Niemeyer H, Hottenrott B, Schilling L, Spitzer C** (2012). Interpersonal ambivalence in obsessive-compulsive disorder. *Behavioural and Cognitive Psychotherapy* **13**, 1–16.

**Murray CJ, Lopez AD, Wibulpolprasert S** (2004). Monitoring global health: time for new solutions. *British Medical Journal* **329**, 1096–1100.

**Noshirvani HF, Kasvikis Y, Marks IM, Tsakiris F, Monteiro WO** (1991). Gender-divergent aetiological factors in obsessive-compulsive disorder. *British Journal of Psychiatry* **158**, 260–263.

**Palumbo D, Maughan A, Kurlan R** (1997). Hypothesis III. Tourette syndrome is only one of several causes to a development basal ganglia syndromes. *Archives of Neurology* **54**, 475–481.

**Pauls DL, Alsobrook 2nd JP, Goodman W, Rasmussen S, Leckman JF** (1995). A family study of obsessive-compulsive disorder. *American Journal of Psychiatry* **152**, 76–84.

**Rosa-Alcázar AI, Sánchez-Meca J, Gómez-Conesa A, Marín-Martínez F** (2008). Psychological treatment of obsessive-compulsive disorder: a meta-analysis. *Clinical Psychology Review* **28**, 1310–1325.

**Rosario-Campos MC, Leckman JF, Mercadante MT, Shavitt RG, Prado HS, Sada P, Zamignani D, Miguel EC** (2001). Adults with early-onset obsessive-compulsive disorder. *American Journal of Psychiatry* **158**, 1899–1903.

**Schuurmans J, van Balkom AJ, van Megen HJ, Smit JH, Eikelenboom M, Cath DC, Kaarsemaker M, Oosterbaan D, Hendriks GJ, Schruers KR, van der Wee NJ, Glas G, van Oppen P** (2012). The Netherlands Obsessive Compulsive Disorder Association (NOCDA) study: design and rationale of a longitudinal naturalistic study on the course of OCD and clinical characteristics of the sample at baseline. *International Journal of Methods in Psychiatric Research* **21**, 273–285.

**Sobin C, Blundell ML, Karayiorgou M** (2000). Phenotypic differences in early- and late-onset obsessive-compulsive disorder. *Comprehensive Psychiatry* **41**, 373–379.

**Swedo SE, Rapoport JL, Leonard H, Lenane M, Cheslow D** (1989). Obsessive-compulsive disorder in children and adolescents. Clinical phenomenology of 70 consecutive cases. *Archives of General Psychiatry* **46**, 335–341.

**Taylor S** (2011). Early versus late onset obsessive-compulsive disorder: evidence for distinct subtypes. *Clinical Psychology Review* **31**, 1083–1100.

**Tozzi F, Manchia M, Galway NW, Severino G, Del Zompo M, Day R, Matthews K, Struass J, Kennedy JL, McGuffin P, Vincent JB, Farmer A, Muglia P** (2011). Admixture analysis of age at onset in bipolar disorder. *Psychiatry Research* **185**, 27–32.

**Tükel R, Ertekin E, Batmaz S, Alyanak F, Sozen A, Aslantas B, Atli H, Ozyildirim I** (2005). Influence of age of onset on clinical features in obsessive-compulsive disorder. *Depression and Anxiety* **21**, 112–117.