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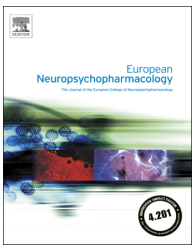

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Trajectory in obsessive-compulsive disorder comorbidities

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Abstract
The main goal of this study is to contribute to the understanding of the trajectory of comorbid disorders associated with obsessive-compulsive disorder (OCD) according to the first manifested psychiatric disorder and its impact in the clinical course of OCD and subsequent psychiatric comorbidities. One thousand and one OCD patients were evaluated at a single time point. Standardized instruments were used to determine the current and lifetime psychiatric diagnoses (Structured Clinical Interview for DSM-IV Axis I and for impulse-control disorders) as well as to establish current obsessive-compulsive, depressive and anxiety symptom severity (Yale-Brown Obsessive-Compulsive Scale; Dimensional Yale-Brown Obsessive-Compulsive Scale, Beck Depression and Anxiety Inventories and the OCD Natural History Questionnaire). To analyze the distribution of comorbidities according to age at onset Bayesian approach was used. Five hundred eight patients had the first OC symptom onset till the age of 10 years old. The first comorbidity to appear in the majority of the sample was separation anxiety disorder (17.5%, n=175), followed by ADHD (5.0%, n=50) and tic disorders (4.4%, n=44). OCD patients that presented with separation anxiety disorder as first diagnosis had higher lifetime frequency of post-traumatic stress disorder (p=0.003), higher scores in the Sexual/Religious dimension (p=0.04), Beck Anxiety ($p<0.001$) and Depression (p=0.005) Inventories. OCD patients that initially presented with ADHD had higher lifetime frequencies of substance abuse and dependence ($p<0.001$) and worsening OCD course (p=0.03). OCD patients that presented with tic disorders as first diagnosis had higher lifetime frequencies of OC spectrum disorders

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(p=0.03). OCD is a heterogeneous disorder and that the presence of specific comorbid diagnoses that predate the onset of OCD may influence its clinical presentation and course over the lifetime.

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic disorder (American Psychiatric Association, 1994) with a lifetime prevalence of 1–3% in the general population (Torres and Lima, 2005; Ruscio et al., 2010). OCD rarely improves without treatment and is frequently associated with significant impairment of quality of life and social and familial relationships (Steketee, 1997). Its chronic course and associated burden renders OCD one of the most impairing psychiatric conditions according to World Health Organization (http://www.who.int). Moreover, currently available treatments fail to provide satisfactory improvement for a substantial number of affected individuals (Greist et al., 1995; Pallanti and Quercioli, 2006).

Obsessive-compulsive (OC) symptoms may begin at any point of the life span. Most often, they start in childhood (Walitza et al., 2010), with symptoms reported in some rare cases as early as 3 years of age (Koran, 1999). Indeed, age at onset was shown to be associated with several clinical correlates in OCD. Early onset (i.e., before 10 years of age) has been associated with a specific profile regarding concurrent psychiatric conditions including tic disorders, trichotillomania and body dysmorphic disorder (Hemmings et al., 2004; De Mathis et al., 2009).

Besides its clinical correlates, prepubertal onset of OC symptoms may also impact on the further development of psychopathology. Supporting this hypothesis it has been found that early onset of OCD is related to a higher familial loading (Rosario-Campos et al., 2005). Likewise, a longer duration of illness is associated with presence of comorbid depressive mood disorders and social phobia (Diniz et al., 2004). Yaryura-Tobias (2000) reported that there is a preferential temporal order of comorbid conditions in OCD across the lifespan. According to those authors an anxiety disorder, a mood disorder, an eating disorder, or a tic disorder is likely to occur first in patients who go on to develop subsequent comorbid diagnosis. In addition to the presence of a comorbid disorders, the presence and severity of additional symptoms may interfere with the patient's global functioning (Sukhodolsky et al., 2005). Furthermore, the periods which these symptoms started may have an impact on the clinical profile and future development of each disorder. Despite the clinical relevance of this topic, very few studies have taken into account a developmental perspective and investigated the effect of the ages of onset of comorbid disorders on the course and severity of OCD.

The main goal of this study was to contribute to the understanding of the trajectory of comorbid disorders according to the first manifested psychiatric diagnosis and its impact in the clinical development of OCD and subsequent psychiatric comorbidities. Based on our previous study we speculated that OCD patients who have tic disorders as the first symptom will present lower frequencies of mood disorders and anxiety disorders (De Mathis et al., 2009). Understanding OCD within a developmental perspective is essential for establishing the prognosis and for developing new treatment approaches taking into consideration subsequent diagnoses in children with initial signs of psychopathology.

2. Experimental procedures

2.1. Participants

The sample was composed of 1001 OCD patients. Patients were recruited from seven university based outpatient facilities located in six different Brazilian cities between August 2003 and August 2009. This sample is part of the Brazilian Obsessive-Compulsive Consortium (C-TOC). A complete description of the methodology of the Consortium can be found elsewhere (Miguel et al., 2008).

Patients were required to have a primary diagnosis of OCD according to DSM-IV confirmed by the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) in order to be part of the study. Exclusion criteria included having comorbid schizophrenia, mental retardation or any other condition that would impair their understanding of the protocol. This study was approved by the medical ethics committees from each of the university hospitals. All patients signed a written informed consent after a thorough description of the study and the assurance that their decision to participate in the study would not interfere with their access to treatment. Subjects younger than 18 years old also signed an informed assent form.

2.2. Clinical assessment

Experienced clinical psychologists and psychiatrists interviewed all patients. The following standardized instruments were applied to assess current and lifetime psychiatric diagnoses: Structured Clinical Interview for DSM-IV Axis I (SCID-I; First et al., 1995) and for impulse-control disorders. The age of onset of each diagnosis was assessed during patient interview and is presented as means. Current symptom severities were assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS; Goodman et al., 1986); Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS; Rosario-Campos et al., 2006); and the Beck Depression and Anxiety Inventories (Beck et al., 1961, 1988). The OCD Natural History Questionnaire (Leckman, 2002) was also completed to evaluate OCD course.

2.3. Statistical analyses

Statistical analyses were performed using the Statistical Package for Social Science version 16.0 (SPSS Inc., USA) and R: A Language and Environment for Statistical Computing 2.4.0.

The sample description was done by descriptive analyses: frequencies and percentages for discrete variables and means and standard errors for continuous variables.

Chi-square test was used for categorical variables, and Kruskal-Wallis and ANOVA tests were used for continuous variables. For all the tests the significant level was considered $p<0.05$.

To analyze the distribution of comorbidities according to age at onset we used a Bayesian approach—uses the likelihood as the only source of information containing in the observations, together with a prior distribution representing the scientist knowledge. We first investigated the mean age at onset and frequency of Axis I comorbidity distribution in the 1001 OCD patients. The disorder with the earliest age at onset (in other words, the first disorder to appear in the timeline) was OCD for the majority of the sample (n=416), separation anxiety disorder (n=175), followed by ADHD (n=50) and tic disorders (n=44). Afterwards, we chose to describe how each one of these disorders would influence the course of clinical and comorbidity patterns along the life span if they were the first diagnosis manifested.

3. Results

3.1. Demographics and clinical characteristics

A thousand and one OCD patients were evaluated for this study. The mean age was 34.8 years old (SE=0.41) at the time of the interview. Five hundred eight patients had the first OC symptom onset till the age of 10 years old (including 10 years old). The majority were females (56.8%), singles (54.4%) and employed (43.3%) at the moment of the interview. The mean frequency of years of education was 14.5 years (SE=0.15).

The current mean scores found on the following instruments were: Y-BOCS 25.51 (SE=0.24); DY-BOCS 21.15 (SE=0.20); Beck Depression 16.50 (SE=0.36) and Beck Anxiety 16.02 (0.37). The mean score of each dimension on the DY-BOCS was: "aggression/violence" (6.73; SE=0.17); "sexual/religious" (4.30; SE=0.15); "symmetry/ordering" (7.52; SE=0.19); "cleaning/contamination" (6.22; SE=0.16); "hoarding" (3.15; SE=0.13), and "miscellaneous" (7.54; SE=0.15).

3.2. Comorbidity

Ninety two percent of the sample had at least one additional psychiatric diagnosis. Considering the high number of possible psychiatric diagnoses associated to OCD and aiming to facilitate further analyses, we combined *a priori* some disorders into distinct sub-groups (most in agreement with DSM-IV division, except the OC Spectrum Disorders). Specifically, *OC spectrum disorders* included trichotillomania, skin picking and body dysmorphic disorder; the *Anxiety disorders* included panic disorder, generalized anxiety disorder, simple phobia and social phobia; *Mood disorders* included unipolar depression; bipolar I and II disorders; *Impulse-control disorders* included compulsive buying, pathological gambling, pyromania, internet abuse, video game abuse, kleptomania, non-paraphilic sexual disorder; *Eating disorders* included anorexia nervosa, bulimia nervosa and binge eating; *Substance abuse and dependence disorders* included alcohol, cannabis, cocaine, stimulant, opium and hallucinogens abuse and dependence; *somatoform disorders* included somatization, pain disorder and hypochondriasis; Separation anxiety disorders, attention deficit hyperactivity disorder (ADHD), post-traumatic stress disorder (PTSD) and tic disorders were analyzed separately.

Table 1 and Figure 1 display the mean ages at onset and frequencies of Axis I comorbidity distribution in the 1001 OCD patients. The comorbid psychiatric diagnosis with the youngest mean age at onset was separation anxiety (5.9 SE=0.12), followed by ADHD (7.5 SE=0.27) and tic disorders (12.3 SE=0.43).

Table 1 Mean age at onset and frequency of Axis I comorbidities in 1,001 OCD patients.

	Age at onset		Frequency	
	Mean	SE	*N*	%
Separation anxiety	5.9	0.12	276	27.6
ADHD	7.5	0.27	127	12.7
Tic disorders	12.3	0.43	284	28.4
OCD	12.6	0.23	1001	100.0
Anxiety disorders	13.6	0.35	653	65.3
Ob. Spectrum disorders	15.8	0.47	275	27.5
PTSD	18.1	0.95	191	19.1
Impulse-control disorders	20.0	0.60	239	24.0
Eating disorders	21.7	0.81	114	11.4
Substance abuse disorders	22.5	0.93	102	10.2
Somatoform disorders	22.6	1.25	77	7.7
Mood disorders	24.3	0.45	704	70.3

SE=standard error; ADHD=attention deficit hyperactivity disorder; PTSD=post-traumatic stress disorder.

From the whole sample, we selected four groups according to the psychiatric diagnosis that was first recorded: one with OCD as the first diagnosis; separation anxiety disorder as the first diagnosis, ADHD as the first diagnosis and tic disorders as first diagnosis. As shown in Figure 1, those comorbidities had the mean age at onset prior to the OCD onset. The purpose of this division was to determine if these groups were different in terms of clinical characteristics and patterns of lifetime comorbidity (Figure 2).

In Table 2 the mean ages at onset of Axis I comorbidities and their frequencies according to the four groups are presented. The main findings were:

- OCD patients that presented with separation anxiety disorder as first diagnosis tended to present higher frequency of post-traumatic stress disorder (p=0.003).
- OCD patients that presented with ADHD as first diagnosis had higher frequencies of substance abuse and dependence ($p<0.001$) in the subsequent years.
- OCD patients that presented with tic disorders as first diagnosis had higher frequencies of OC spectrum disorders (p=0.03) along their life span.

Regarding other clinical variables (OCD course and family history), OCD patients with ADHD as first diagnosis presented a progressive and continuous worsening of the OC symptoms (p=0.03) compared to the others groups (data not shown).

Comparing the overall OCS current severity (according to the Y-BOCS and the DY-BOCS mean total scores) between the groups no significant differences were found. OCD patients with separation anxiety disorder as first diagnosis, however, presented higher scores specifically in the Sexual/Religious dimension (p=0.04), Beck Anxiety ($p<0.001$) and Beck Depression Inventories (p=0.005) (Table 3).

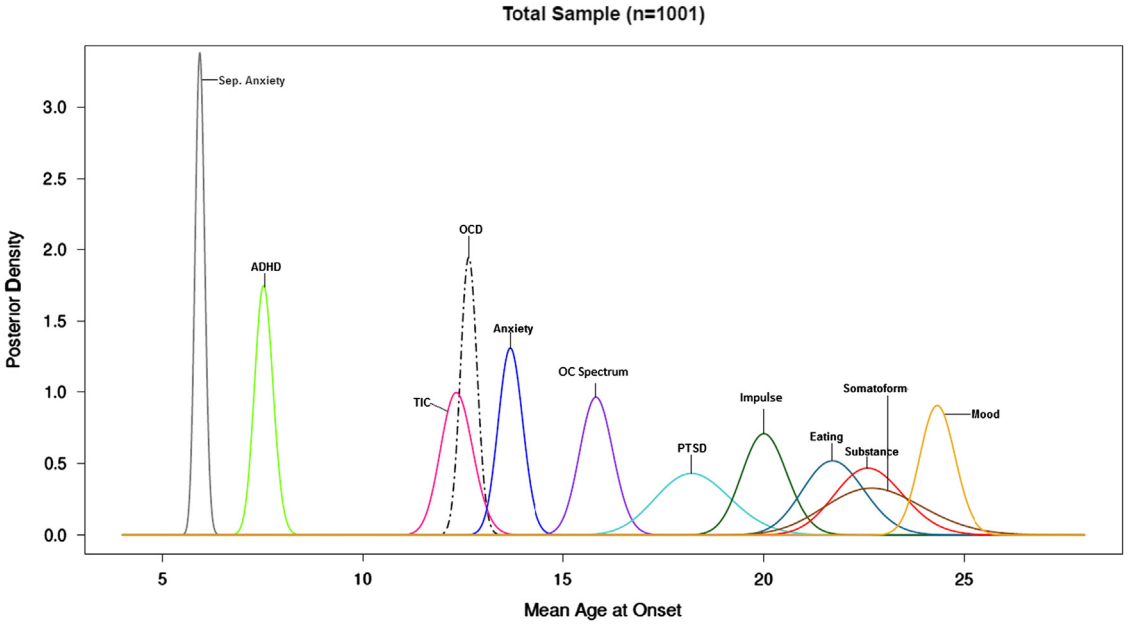

Figure 1 Mean age at onset and posterior distribution of Axis I comorbidities. In the graph above, we observed the curves of the *posteriori* density of the average of the age at onset for obsessive-compulsive disorder (OCD) and each comorbid diagnosis. These distributions are the normalized likelihood functions. In other words, for a specific comorbidity, the respective curve represents the density function of the age average for the comorbidity. The curve indicates that the true population average (parameter) is more likely to be at some point under the curve, with the highest probability near the peak. For instance, the average of age at onset of separation anxiety disorder (close to 6 years old) happens most likely before the onset of eating disorders (close to 22 years). The first is highly probable at 6 years with little chance of being far from this age. The second can occur at any point between 20 and 24 years, with the highest probability being near 22 years old. Sep. anxiety=separation anxiety disorders; ADHD=attention deficit hyperactivity disorder; TIC=tic disorders; and PTSD=posttraumatic stress disorder.

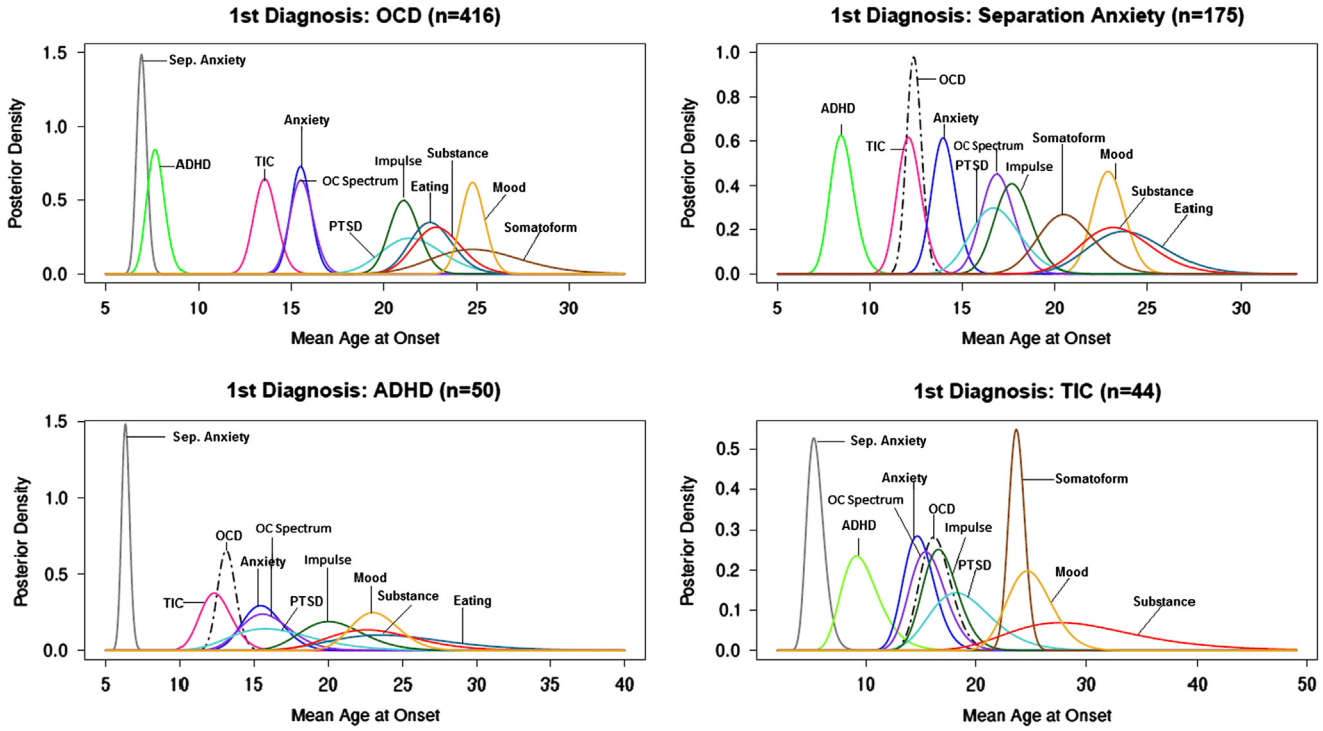

Figure 2 Mean age at onset and distribution of Axis I comorbidities when the first diagnosis was OCD (n=416); separation anxiety disorder (n=175); ADHD (n=50); and tic disorders (n=44) Sep. anxiety=separation anxiety disorders; ADHD=attention deficit hyperactivity disorder; TIC=tic disorders; and PTSD=posttraumatic stress disorder.

Table 2 Mean age at onset of Axis I comorbidities when the first diagnosis was OCD, separation anxiety disorder, ADHD, and tic disorders.

1° Disorder Comorbidity	OCD (*n*=416)				Separation anxiety (*n*=175)				ADHD (*n*=50)				Tic (*n*=44)				p-value
	Age at onset		Frequency		Age at onset		Frequency		Age at onset		Frequency		Age at onset		Frequency		
	Mean	SE	*N*	%	Mean	SE	*N*	%	Mean	SE	*n*	%	Mean	SE	*n*	%	
Sep. Anxiety	6.9	0.27	61	14.7	5.3	0.12	175	100.0	6.3	0.29	9	18.0	5.2	0.78	7	15.9	-
ADHD	7.6	0.59	33	7.9	8.4	0.75	21	12.0	6.4	0.26	50	100.0	9.1	1.74	6	13.6	-
Tic D.	13.5	0.70	111	26.7	12.0	0.70	56	32.0	12.2	1.04	11	22.0	6.8	0.67	44	100.0	-
OCD	10.1	0.32	416	100.0	12.3	0.45	175	100.0	13.0	0.63	50	100.0	16.1	1.68	44	100.0	-
Anxiety D.	15.6	0.61	282	67.8	13.9	0.77	137	78.3	15.1	1.55	35	70.0	14.2	1.85	34	77.3	0.058[a]
Spectrum D.	15.5	0.69	119	28.6	16.8	1.02	56	32.0	15.5	2.17	15	30.0	15.4	2.11	22	50.0	0.034
PTSD	21.4	1.15	74	17,8	16.6	1.46	53	30.3	15.7	3.02	9	18.0	18.2	2.70	6	13.6	0.003
Impulse-control	21.0	0.85	106	25.5	17.6	1.05	45	25.7	20.0	2.49	16	32.0	16.6	1.75	11	25.0	0.798
Eating D.	22.4	1.24	52	12.5	23.7	2.20	21	12.0	23.5	3.79	6	12.0	20.0	NE	2	4.5	0.490
Substance A. and Dep.	22.8	1.38	46	11.1	23.1	2.07	23	13.1	22.5	3.60	8	16.0	27.6	6.39	6	13.6	<0.001
Somatoform D.	24.7	2.44	29	7.0	20.4	1.64	23	13.1	27.5	12.50	2	4.0	23.6	0.88	4	9.1	0.055[a]
Mood D.	24.7	0.67	316	76.0	22.8	0.90	133	76.0	23.0	1.80	36	72.0	24.6	2.26	34	77.3	0.928

***p*-Value:** chi-square test for comorbidity proportion comparison in each group.

[a]Trend; SE=standard error; OCD=obsessive-compulsive disorder; ADHD=attention deficit hyperactivity disorder; PTSD=post-traumatic stress disorder; D=disorder; A=abuse, Dep.=dependence; NE=not evaluated.

Table 3 Comparison of severity of OC symptoms according to the first lifetime diagnosis (OCD, separation anxiety disorder, ADHD and tic disorders).

1st Comorbidity	OCD (*n*=416)		Separation anxiety (*n*=175)		ADHD (*n*=50)		Tic (*n*=44)		Total (*n*=1001)		*p*-value[1]	*p*-value[2]
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE		
Aggression[a]	5.57	0.244	6.45	0.395	6.37	0.694	5.05	0.767	5.82	0.193	0.143	0.141
Sexual, Religious[a]	4.22	0.240	5.43	0.387	5.04	0.741	4.48	0.747	4.61	0.191	0.053	0.042
Symmetry[a]	7.86	0.222	7.60	0.340	7.66	0.624	6.34	0.780	7.68	0.174	0.215	0.366
Contamination[a]	6.50	0.262	6.86	0.367	5.70	0.706	4.75	0.787	6.42	0.199	0.077	0.095
Hoarding[a]	3.53	0.212	3.08	0.295	3.98	0.570	2.73	0.601	3.40	0.160	0.317	0.330
Miscellaneous[a]	7.65	0.234	8.17	0.356	8.16	0.612	8.73	0.629	7.89	0.179	0.357	0.416
Global Impairment[a]	10.46	0.167	10.57	0.251	10.98	0.390	9.86	0.581	10.49	0.129	0.439	0.691
Total global[a]	21.61	0.297	21.79	0.455	22.98	0.631	21.09	1.056	21.72	0.229	0.417	0.699
Y-BOCS Obsessions	12.91	0.197	12.89	0.267	13.30	0.474	13.18	0.632	12.95	0.147	0.883	0.849
Y-BOCS Compulsions	13.20	0.203	13.02	0.310	13.30	0.515	12.75	0.718	13.13	0.158	0.875	0.946
Y-BOCS Total	26.11	0.372	25.91	0.541	26.60	0.951	25.93	1.237	26.08	0.285	0.950	0.954
Beck Depression	16.82	0.556	20.13	0.859	17.96	1.556	15.20	9.275	17.64	0.431	0.004	0.005
Beck Anxiety	15.59	0.538	20.49	0.929	18.30	1.631	16.30	10.333	17.09	0.439	<0.001	<0.001

[a]Derived from the Dimensional Yale-Brown Obsessive-Compulsive Scale; OCD=obsessive-compulsive disorder; ADHD=attention deficit hyperactivity disorder; ***p*-value[1]:** ANOVA; ***p*-value[2]:** Kruskal-Wallis non-parametric test; SE=standard error; D.=dimension; DY-BOCS=Dimensional Yale-Brown Obsessive-Compulsive Scale; Y-BOCS=Yale-Brown Obsessive-Compulsive Scale.

4. Discussion

The current results demonstrate, in a large multicenter sample, that the first psychopathological manifestation is associated with the development of distinctive lifetime trajectories of comorbid psychiatric disorders in OCD patients. These results suggest that from a developmental perspective OCD does not behave as a unitary disorder but rather as a group of symptoms that interact with additional psychopathology increasing the vulnerability for the development of subsequent specific disorders.

Those OCD patients who reported antecedent symptoms of separation anxiety were shown to further develop additional anxiety and somatoform disorders and greater severity of the sexual/religious dimension, as well as more severe current depressive and anxiety symptoms. Moreover, this group of patients was more prone to develop PTSD when exposed to a traumatic event. Therefore, this group could be regarded as highly vulnerable for multiple anxiety disorders.

Previous studies have shown separation anxiety disorder as a predictor of several other disorders in adulthood. Manicavasagar et al. (2000) investigated through a retrospective assessment of childhood separation anxiety diagnosis whether there were continuities between juvenile and adult forms of anxiety. They found that symptoms of separation anxiety appeared to predate the onset of the other anxiety disorders and suggested that early onset separation anxiety disorder may persist into adulthood with a different set of complaints. In a recent study Mroczkowski et al. (2011) also found that childhood separation anxiety disorder was associated with anxiety disorders and dependent personality disorder traits in adult individuals with OCD. Adding to our findings, these previous studies point to the importance of separation anxiety as a marker of anxiety later in life. These results also reinforce the need for developing prevention programs regarding anxiety disorders.

OCD patients with ADHD as the first diagnosis presented higher frequencies of substance abuse and presented a progressive worsening OCD course. The association of ADHD and substance abuse has been reported before (Jacob et al., 2007). Some studies show the significance of behavioral symptoms of ADHD; inattentiveness, hyperactivity and impulsivity among children and subsequent substance abuse disorder (Sihvola et al., 2011). Impulsive behavior may subject boys to experimenting with psychoactive substances in general and promote continued substance use (Leeuwen et al., 2010). Of note, for the majority of patients with ADHD in our sample, the onset of a substance related disorder was predated by the onset of OCD, OCD spectrum disorders, PTSD, and other anxiety disorders. Perhaps in individuals with ADHD the development of an anxiety disorder might further increase the risk to develop a substance use disorder. This viewpoint is supported by earlier studies that indicate that anxiety symptoms and substance abuse and dependence are highly interconnected. For example, Terlecki et al. (in press) found that patients with higher social anxiety reported higher baseline alcohol consumption, providing with data supporting that greater anxiety may have a deleterious effect on alcohol consumption. In the same way, Mathew et al. (2011) found that participants who reported a history of panic attacks were significantly more likely to report current or lifetime daily cigarette smoking and significantly greater hazardous or harmful alcohol use than participants with no panic history. Another recent study (MacDonald et al., 2011) examined the longitudinal relationship between anxiety disorders in general, specific phobia in particular, and subsequent-onset alcohol use disorders in an adult population-based sample (n=587). The findings suggested a modest association between adult subclinical specific phobia and later onset of alcohol use disorders.

In a Brazilian sample of 630 OCD patients, male gender was consistently associated with alcohol use disorder and there was evidence that it independently predisposes to a more severe course of OCD (Neziroglu et al., 1994; Steketee, 1997). In accordance with our results, prevention programs for substance related disorders should aim the population with isolated ADHD or in addition to anxiety disorders.

OCD patients with tic disorders as the first manifested diagnosis presented with a higher frequency of OC spectrum disorders. This result supports the idea of the OCD, tics and other disorders being considered part of the OC spectrum (Cavallini et al., 2002; De Mathis et al., 2009). The concept of an obsessive-compulsive spectrum has been studied by many authors. These conditions are characterized as similar to OCD in terms of psychopathology, associated features (age of onset, clinical course, and comorbidity), presumed etiology, familial transmission, and/or response to treatments (Hollander, 1993). An important study conducted by Bienvenu et al. (2000) investigated comorbidity and family association relationships between OCD and obsessive-compulsive spectrum conditions (including somatoform and eating disorders, pathologic grooming conditions, and other impulse control disorders) using data from the Johns Hopkins OCD Family Study. They concluded that certain somatoform disorders, especially body dysmorphic disorder, and pathologic grooming behaviors are transmitted in families of patients with OCD and can be considered part of the OCD spectrum. In a very recent study, the same author et al. found that tic disorders and grooming disorders (nail biting, skin picking and trichotillomania) showed elevated comorbidity and familiarity with OCD (Bienvenu et al., 2011). Further support has been given to the idea of an OCD spectrum by Coffey et al. (1998). Those authors evaluated correlates of patients with Tourette's disorder (TD), OCD and TD+OCD and found that TD+OCD patients are more severe, and present higher rates of mood, anxiety, substance abuse and OCD spectrum disorders than patients with TD or OCD alone. In the light of those previous works, our results give further support for the idea of an OCD spectrum with different disorders appearing along the life cycle. This means that when viewed through a developmental perspective; symptoms belonging to different diagnostic constructs appear during relatively specific developmental phases and predispose to other symptoms in the following phases of life.

4.1. Limitations

There are some limitations regarding this study that should be taken into account. This is a cross-sectional study and the best way to evaluate the trajectory and evolution of symptoms and comorbidities would be a longitudinal design

(Fullana et al., 2009; Eisen et al., 2010). The retrospective assessment of some variables (e.g., age-of-onset) is another limitation of our study, as there is the possibility of recall bias. In order to increase the reliability on the interview, a family member was also consulted whenever possible. However, the findings of this cross-sectional investigation are valuable as they represent the most complete information on the sequential presentation of comorbid psychiatric disorders in a group of clinically referred OCD patients.

A related issue is that we did not include OCD patients who naturally improved so that only persistent OCD cases were included. This may be particularly relevant for the early onset OCD cases and those with comorbid tic disorders (Bloch et al., 2006, 2009). For example, a meta-analysis of previous follow-up studies of pediatric-onset OCD suggested that as many as 40% to 59% of cases remit (Stewart et al., 2004). However when adult persistent cases are followed, the early-onset cases are at greater risk for a more severe course of illness (Eisen et al., 2010).

The artificial division of Axis I disorders into wider groups was a choice of the authors and necessary to facilitate the analysis. Despite the large sample, the relatively low number of individuals presenting some individual comorbidities made it necessary to create broader categories for analysis. Gathering diagnoses into different groups could lead to different results and this has not been tested. However, although the four groups used for the comparisons may seem apparently arbitrary, they reflect what is seen in the clinical practice. Another limitation was the not inclusion of schizophrenia in the sample. OCD occurs in up to 14.1% of patients with schizophrenia, which is greater than the estimated prevalence for the general population (~2–3%). On the other hand, the prevalence of schizophrenia in patients being treated for OCD is much smaller, reaching up to 1.7%. Moreover, the onset of schizophrenia following OCD is uncommon. After seven years follow-up of individuals at ultra-high risk for psychosis, Fontenelle et al. (2011) reported that for those whose OCD remitted no DSM-IV psychotic disorder was later diagnosed; whereas, for those with de novo onset of OCD symptoms, psychotic disorders eventually occurred but were mainly diagnosed as mood disorders with psychotic features or psychotic disorders not otherwise specified. In that ultra-high risk sample, two of six patients with chronic OCD symptoms were later diagnosed with schizophrenia (Fontenelle et al., 2011).

Finally the external validity of our findings cannot be guaranteed, since all patients were recruited at specialized OCD clinics, and therefore the results cannot be generalized to population-based samples (Fullana et al., 2009). Despite these limitations, the current study reinforces the idea that OCD is a heterogeneous disorder and that the presence of specific comorbid diagnoses that predate the onset of OCD may influence its clinical presentation. These results also reinforce the relevance of incorporating early interventions to prevent the development of additional psychopathology in children with early onset of psychiatric disorders. Furthermore, specific approaches may be tailored according to the first diagnosis in children with OCD. Special attention should be given to future anxiety and somatoform disorders for those with separation anxiety, to substance abuse for those with ADHD, and body dysmorphic disorder, trichotillomania and skin picking for those with tic disorders. Future interventional studies are still required to determine which types of early interventions are truly effective in the prevention of future psychopathology.

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Contributors

Authors Maria Alice de Mathis; Maria Conceição do Rosário; Juliana Belo Diniz and Euripedes Miguel designed the study. Authors Maria Alice de Mathis, Maria Conceição do Rosário, Juliana Belo Diniz, Ana Hounie and Ygor Ferrão managed the literature searches and analyses. Authors Victor Fossaluza and Carlos Alberto de B. Pereira undertook the statistical analysis. Authors Euripedes Miguel and James Leckman contributed with the development and the final revision. All authors contributed to and have approved the final manuscript.

Conflict of interest

Authors have no conflict of interest.

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