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Stressful life events and obsessive-compulsive disorder: clinical features and symptom dimensions

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University of Turin's Institutional Research Information System and Open Access Institutional Repository

Title: Stressful life events and obsessive–compulsive disorder: clinical features and symptom dimensions

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Abstract

The potential role of stressful life events (SLEs) in the genesis of obsessive–compulsive disorder (OCD) has been suggested by several authors, but whether the number or the severity or the type of SLEs preceding the onset of OCD has a triggering effect is unclear. Further, sociodemographic and clinical features of OCD

preceded by SLEs, and the relationship between type of SLEs and type of obsessive–compulsive symptomatology remain mainly unexplored. The aims of this study were to compare the clinical features of OCD with and without SLEs preceding it and to examine the relationship between type of SLEs and OCD symptom dimensions.

The number and type of SLEs which occurred before the onset of OCD were determined in 329 patients: the raters had to decide whether an occurrence 12 months before the onset of OCD would fit any of the 61 items on Paykel's list, and each event reported was carefully investigated in order to determine the exact time of occurrence. At least one event preceded the onset of OCD in 200 patients (60.8%), and this was significantly associated with female gender, abrupt onset of the disorder and somatic obsessions. Moreover, Log- Reg Analysis identified three specific traumatic events (“hospitalization of a family member”, “major personal physical illness”, “loss of personally valuable object”) significantly associated with a symptom dimension (symmetry obsessions, repeating, ordering/arranging, counting, and checking compulsions). Additional evidence regarding the association among SLE-preceded OCD, female gender, somatic obsessions and symmetry/ordering symptoms should be obtained to advance the understanding of OCD.

Key Words: OCD, Obsessions, Compulsions, Stressful events, Onset

1. Introduction

Obsessive–compulsive disorder (OCD) is a neuropsychiatric condition classified as a severe mental illness by the National Advisory Mental Health Council (Manderscheid and Sonnenschein, 1996). OCD affects an estimated 1% to 3% of the population worldwide, and it is considered one of the most disabling of the anxiety disorders, leading to unemployment, need for disability or welfare assistance, and having important costs for society (DuPont et al., 1995; Stein et al., 1997; Kessler et al., 2005; Ruscio et al., 2010). Further, evidence of persistent impairment in family life and activities of daily living is reported, as well as extensive family involvement and accommodation of OCD symptoms with a burden that leads families to reduce their social activities and increase their isolation and distress (Lochner et al., 2003; Albert et al., 2007). Genetic epidemiology studies have let to the proposal for OCD of a multifactorial model of inheritance where multiple genetic and biological risk factors act together with environmental stressors causing the disease onset (Hettema et al., 2001; Grisham et al., 2008; Nicolini et al., 2009; Pauls, 2010). Although the possible role of stressful life events (SLEs) in the genesis of OCD has been suggested by several authors in children (Gothelf et al., 2004), conflicting results have been reported in adults: a significant excess of events over the year prior to onset of the disorder was reported by some studies (McKeon et al., 1984), but no difference was reported by other investigations (Khanna et al., 1988; Maina et al., 1999). Moreover, whether the number or the severity or the type of life events that occur before the onset of OCD has a triggering effect is unclear. The limited available data are generally based on case reports, case series, or on studies with methodological shortcomings such as the assessment of stressful events with self-report checklists or the unspecified premorbid study period (Rudin, 1953; Pollit, 1957; Ingram, 1961; Lo, 1967; Rasmussen and Tsuang, 1986; Neziroglu et al., 1992). With regard to sociodemographic and clinical features of OCD associated with stressful events, preliminary evidence suggested that women may have greater risk of initial onset of OCD after precipitant events (Bogetto et al., 1999). Beyond this finding, a recent article

supports the contention that when the onset of OCD is associated with stressful precipitants, the disorder presents a different clinical pattern (Real et al., 2011): later onset of the disorder, history of complicated birth, less family history of OCD and presence of contamination/cleaning symptoms. Nevertheless, this study did not take into account the administration of a standardized instrument for detecting the presence of life events at the onset of OCD. The association between type of triggering life events and type of obsessive–compulsive symptomatology remains mainly unexplored.

Although it has not been the subject of intense inquiry, there has been some speculation about the relationship between postpartum OCD and aggressive obsessions: intrusive thoughts of harming the newborn have been noted by some authors (Maina et al., 1999; Uguz et al., 2007), but the evidence has not been confirmed by all studies (Forray et al., 2010; Labad et al., 2010). To our knowledge, no studies have been performed to investigate the association between type of preceding stressful life events and specific obsessive symptoms clusters or dimensions.

The primary goal of the present study was to examine whether there is any difference between clinical features of OCD with and without SLEs preceding it evaluated through a standardized method. In addition, we sought to examine the relationship between the type of events and OCD symptom dimensions. Particularly, we hypothesized that when OCD is preceded by severe stressful life events it would be more associated with some symptom dimensions. We refer to the multidimensional model of OCD suggested by Mataix-Cols et al. (Mataix-Cols et al., 2005; Bloch et al., 2008), which consistently identifies four symptom dimensions (symmetry/ordering, hoarding, contamination/cleaning, and obsession/checking) that have been associated with distinct patterns of comorbidity, genetic transmission, neural substrates, and treatment response. Although the dimensional structure of obsessive–compulsive symptoms is imperfect, this quantitative approach to phenotypic traits has the potential to advance the understanding of OCD and may aid in the identification of more robust endophenotypes.

2. Methods

2.1. Participants

Subjects for this study were recruited from all patients with a principal diagnosis of OCD consecutively referred to the Mood and Anxiety Disorders Unit, Department of Neurosciences, University of Turin (Italy), over a period of 9 years (January 2000– December 2008). This is a tertiary referral center mainly for patients from the Piedmont and Aosta Valley regions of Italy, located within the University General Hospital. Patients are referred by general practitioners or psychiatrists, although a few are self-referred.

Inclusion criteria were the following: principal diagnosis of OCD according to DSM-IV-TR (APA, 2000), minimum total score of 16 on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al., 1989a, 1989b), at least 18 years of age, and willingness to voluntarily participate in the study.

Exclusion criteria were: current psychoactive substance and drug abuse, current or previous diagnosis of organic mental disorder and/or schizophrenia.

The study design was reviewed by the local ethics committee. Written informed consent was obtained from patients after the procedure had been fully explained.

2.2. Procedures

Data were obtained through the administration of a semi-structured interview that we developed and used in previous studies (Bogetto et al., 1999; Maina et al., 1999; Albert et al., 2002; D'Ambrosio et al., 2010), with a format that covered the following areas:

(a) demographic data: age, sex, marital status (single, married, divorced, widowed), education level

and work status;

(b) diagnostic evaluation: Axis I and Axis II comorbidities were recorded by means of the Structured Clinical Interview for DSM-IV Axis I and Axis II Disorders (SCID-I and II) (First et al., 1997a, 1997b);

(c) obsessive–compulsive symptomatology: up to three primary obsessions and compulsions were listed for each subject using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Symptom Checklist (Goodman et al., 1989a, 1989b);

(d) onset and course of OCD: onset of symptoms was defined as the age at which the first obsessive and/or compulsive symptoms were noticed by the subject. OCD onset was dated within a 1-month period as the first occurrence of obsessive and compulsive symptoms that caused marked distress, were time consuming (more than 1 h a day) or interfered with the person's normal daily functioning (normal routine, occupational and social activities). Whenever possible, external corroboration for age of onset was obtained by directly interviewing, with patient's consent, a first-degree family member or other significant individual. For the purposes of the present study, we included only subjects for which it was possible to date onset of symptoms and disorder with an agreement between patients and their relatives. An attempt was made to date onset of OCD and onset of symptoms in a 4-week period; if there was uncertainty, a range was plotted and its mid-point was used in the analysis.

The onset was considered abrupt when the symptoms reached clinically significant intensity within 1 week of onset. All other types of onset were considered insidious. The course of the disorder was considered episodic when at least one circumscribed symptom-free interval (6 months) was present; all other types of course were considered chronic;

(e) life events: the raters had to decide whether an occurrence 12 months before the onset of OCD

would fit any of the 61 items on the list of Paykel et al. (1971). Each life event reported was carefully investigated in order to determine the exact time of occurrence. To facilitate accurate dating, a calendar for the investigated year was constructed, and the individuals were asked to show their geographical, work, and school positions throughout that year and to recall any circumstances that might serve as anchor points. A subject was considered to have experienced a severe event when any of the top 20 events on the list of Paykel et al. (1971) had occurred.

In addition, the following rating scales were included in the assessment: the Hamilton Anxiety Rating Scale (HAM-A), and the 17-item Hamilton Depression Rating Scale (HAM-D) (Hamilton, 1959; Hamilton, 1960).

2.3. Interviewers and raters

All semi-structured interviews were conducted in person by three investigators, each with at least 4 years of postgraduate clinical experience. Each patient was evaluated in two subsequent phases: (a) randomly by one of the three investigators, who used a semi-structured interview with a format that covered demographic data, diagnosis according to DSM-IV, and clinical features of OCD. The same interviewer assessed the patient with the rating scales; (b) randomly by one of the three investigators – with the exclusion of the interviewer who had examined the subject previously – and blindly with respect to the first examination, by a semi-structured interview to investigate the role of life events in the onset of the disorder. In conclusion, the same interviewer examined OCD status and demographic data and a different interviewer blindly examined life stress. Finally, data from the separate interviewers were reviewed with two senior psychiatrists and, if there were any events in proximity to symptom onset, a final check with the respondents on the time order was made.

2.4. Inter-rater reliability

Pearson's correlation coefficient between rater pairs and intraclass correlation coefficients demonstrated excellent agreement for the Y-BOCS total and individual items of 10 OCD patients assessed before the beginning of the study (Pb0.0001). In 10 depressed subjects, scores obtained by our raters of the HAM-D correlated above 0.90. The inter-rater reliability between rater pairs for the occurrence of events was over 0.80 (k coefficient).

2.5. Statistical analyses

For statistical purposes, the sample was divided into two subgroups according to the absence or presence of a stressful life event during the 12-month period prior to onset of OCD.

In order to analyze the differences in socio-demographic and clinical characteristics between the two groups, Student's t test and $\chi 2$ test for bivariate analyses were performed. Categorial variables were compared using Pearson's $\chi 2$ with Yates correction. Continuous variables were compared using the unpaired t-test for twoclass comparisons and Bonferroni correction. An α level of 0.05 (two-tails) was used for statistical tests.

A second analysis was performed dividing the sample into two subgroups: patients with at least one severe stressful life event (sSLE) during the 12-month period prior to onset of OCD and patients without any preceding stressful life events. To avoid confounding effects, we excluded from this analysis those patients with a non-severe stressful life event (n=121) prior to the onset of OCD.

Logistic regression (LogReg) was used to identify explanatory variables associated with the SLE-preceded OCD (or to the severe SLE-preceded OCD). Onset of OCD associated with SLE (or with severe SLE) was considered the dependent variable. Selection of significant variables was performed using a forward stepwise procedure. The probability of entering the equation was set at 0.05.

LogReg was also used to explore the relationship between sSLE-preceded OCD (independent

variable) and each of the four OCD symptomatology dimensions (dependent variables) obtained through the principal component analyses (PCAs) on obsession and compulsion symptoms employing the same method of previous studies (Leckman et al., 1997; Mataix-Cols et al., 2005). The principal component (factor) analysis was done in the total sample. As shown in detail in a recently published paper of our research group (Albert et al., 2010), symmetry obsessions plus repeating, ordering/arranging, counting, and checking compulsions loaded highly on the first factor (Factor 1); the second factor (Factor 2) included aggressive, religious, sexual, and somatic obsessions; contamination obsessions and cleaning compulsions loaded highly on the third factor (Factor 3); the fourth factor included hoarding obsessions and compulsions (Factor 4).

3. Results

There were 329 participants in the study with a main diagnosis of OCD. Descriptive information for the sample is presented in Table 1.

External corroboration for age of onset was obtained in 195 patients (59.3%): all these subjects were included in the data analysis as it was possible to date onset of symptoms and disorder with an agreement between patients and their relatives. At least one stressful life event in the 12 months before the onset of the disorder was found in 200 patients (60.8%), and in 79 patients a severe stressful life event occurred (24.0%). In 129 patients (39.2%) no stressful life events occurred in the 12 months preceding the onset of the disorder.

3.1. Socio-demographic and clinical variables related to SLE preceding the onset of OCD

Socio-demographic and clinical features of the two subgroups (with SLE and without SLE) are summarized in Table 2.

Female patients experienced at least one SLE before onset of OCD more often than males (56.0%

vs. 44.0%; $\chi2$=11.084; d.f.=1; pb0.001). Moreover, patients with SLE-preceded OCD were more often characterized by an abrupt onset of the disorder (38.5% vs. 22.5%; $\chi2$=9.215; d.f.=1; p=0.003), and showed higher rates of current (61.5% vs. 47.3%; $\chi2$=6.427; d.f.=1; p=0.013) and lifetime mood disorders (70.5% vs. 57.4%; $\chi2$=5.976; d.f.=1; p=0.018). Finally, lifetime presence of somatic obsessions was found more frequently in patients with SLE-preceded OCD than in the other OCD patients (39.5% vs. 20,2%; $\chi2$=13.506; d.f.=1; p=b0.001). The results of the LogReg analysis of the relationship between the above-mentioned variables and the SLE-preceded OCD subtype are described in Table 3.

The following explanatory variables had been included in the analysis as independent variables: gender, type of onset, actual and lifetime mood disorders comorbidity, somatic obsessions.

The variable more significantly associated with the presence of SLE prior the onset of OCD is the lifetime history of somatic obsessions (OR: 2.586); the LogReg Analysis also confirmed the association of SLE-associated OCD with female gender and with abrupt onset of the disorder

3.2. Socio-demographic and clinical variables related to severe SLE preceding the onset of OCD

Considering the subgroup of patients with severe SLE-preceded OCD, the following significant differences were found in comparison with patients without any SLE preceding the disorder: more prevalent female gender (63.3%; $\chi2$=13.376; d.f.=1; pb0.001); higher rates of current (63.3% vs. 47.3%; $\chi2$=5.043; d.f.=1; p=0.036) and lifetime mood disorders (72.2% vs. 57.4%; $\chi2$=4.595; d.f.=1; p=0.046); more frequent somatic obsessions (39.2% vs. 20,2%; $\chi2$=8.971; d.f.=1; p=b0.005). LogReg Analysis used to identify explanatory variables (gender, actual and lifetime mood disorder comorbidity, somatic obsessions) confirmed the association of sSLE-preceded OCD with female gender (OR: 2.909) and with somatic obsessions (OR: 2.558).

Table 4 reports the list of severe stressful life events that have occurred in the 12 months prior to the

onset of OCD. The LogReg Analysis identified three of these traumatic events significantly associated with the factor 1 OCD symptom dimension (symmetry obsessions, repeating, ordering/arranging, counting, and checking compulsions).

4. Discussion

The primary goal of this study was to examine whether there is any difference between clinical features of OCD with and without preceding stressful life events. The total sample of patients screened for the investigation (n=329) appeared to be representative of a typical adult OCD population: the gender distribution, the age at onset, the clinical course, and the mean illness severity assessed with the Y-BOCS were consistent with the majority of clinical studies on OCD published in recent years. In addition, the prevalence of specific obsessive and compulsive symptoms were consistent with those assessed by other authors. In more than 60% of patients of our sample, at least one stressful life event occurred in the year before the onset of OCD and a severe event occurred in almost 25% of the sample. In some clinical aspects patients with SLE-associated OCD significantly differed from patients without SLE-precipitated OCD. All statistical analyses we performed showed that participants with SLE-triggered OCD (and also with severe SLE-triggered events) had a double rate of somatic obsessions (20.2% in OCD without SLE, 39.5% in OCD with SLE, 39.2% in OCD with sSLE). As this is the first study that systematically examined the clinical findings of OCD associated with SLE, the higher rate of somatic obsessions in these patients was an interesting finding that has never been reported or discussed in previous studies. The higher rate of somatic obsessions found may be simply related to the great frequency of stressful life events that concerned physical illnesses that we found in our sample: ‘hospitalization of family member’ and ‘major personal physical illness’ were both among the most represented severe SLEs of our sample. Future studies should explore this hypothesis. The findings of a greater risk for women to develop OCD after a stressful life event (OR: 2.148), and even greater after a severely stressful event (OR:

2.909) are consistent with data we preliminarily observed in another investigation (Bogetto et al., 1999) suggesting that environmental stressors play a more important role in female patients in causing the disease onset. Conversely, genetic and biological factors could be more determining in causing OCD in males that are characterized by an earlier onset of the disorder (Ruscio et al., 2010) with a higher familial loading (Pauls, 2010). It is possible, then, that gender might play a role in the recall of stressful life events as it has been shown that females tend to perceive some life events as more stressful than males do. As expected, acute onset was found to be highly represented among OCD patients with stressful life events preceding it. Comparing the type of onset of OCD, we can say that a stressful event significantly increases the probability of an abrupt onset. Although the statistical power of this data was not confirmed by the analyses performed on the population of patients with severe SLE, the statistical trend was confirmed. With regard to comorbidity, an association between SLEassociated OCD and higher prevalence of concurrent and lifetime mood disorders was found in the bivariate analyses, but the logistic regression did not confirm the data. The possible explanation is that the higher frequency of mood disorder comorbidities we found in patients with SLE-associated OCD (and with severe SLE-associated OCD) may simply reflect the gender differences of mood disorder prevalence. The second objective of our study was to examine the relationship between the type of events and the OCD symptom dimensions. Referring to the multidimensional model of OCD suggested by Mataix-Cols et al. (2005), we hypothesized that when OCD is associated with severe stressful life events, this type of OCD would be associated with specific OCD symptom dimensions. Our finding of a significant association between three different severe SLEs and prominent symmetry/ordering symptoms is of great interest: results from this investigation indicate that this symptom dimension is more associated with environmental factors. The reason why the regression analysis did not confirm the link between SLE-preceded events and somatic obsessions (that are actually included in factor 2 symptoms dimension) may be due to the fact that factor 2 included other types of obsessive symptoms (aggressive, religious, sexual). Taken together, our results suggest that, according to the multifactorial model of inheritance

for OCD, the impact of environmental stressors is greater for female patients. Moreover, the acute onset of OCD is more frequent when the disorder has been preceded by a stressful event. Finally, the clinical picture of OCD related to stressful events is more characterized by higher rates of somatic obsessions and by prominent factor 1 symptoms (according to the four symptoms dimension by Mataix-Cols). Our findings are not consistent with the recent paper by Real et al. which supports the contention that when the onset of OCD is associated with stressful precipitants, the disorder presents later onset of the disorder, history of complicated birth, less family history of OCD and presence of contamination/ cleaning symptoms (Real et al., 2011). As Real et al. did not take into account the administration of a standardized instrument for detecting the presence of life events at the onset of OCD, this could actually explain these different findings.

Our study has several strengths including a large, wellcharacterized clinical sample, standardized assessments and recruitment from several sites where OCD patients typically receive psychiatric treatment. This increases the generalizability of our findings to other clinical samples of OCD. However, results should be interpreted in the context of the study limitations. First, results cannot be generalized to individuals with OCD in the community. Second, although some efforts have been carried out to control the potential recall bias, the time elapsed between the onset of OCD and the study interviews could significantly influence the recall. Third, another limitation of our study is that we did not investigate treatment implications associated with SLE-associated OCD. Additional evidence regarding the association among stressful life events, female gender, somatic obsessions and symmetry/ordering symptoms in obsessive–compulsive disorder are necessary to advance the understanding of OCD and to aid in the identification of more robust endophenotypes of the disorders.

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