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Episodic course in obsessive-compulsive disorder

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Abstract The course of obsessive–compulsive disorder (OCD) is variable, ranging from episodic to chronic. We hypothesised that the former course is more likely to be related to bipolar mood disorders. With the use of a specially constructed OCD questionnaire, we studied 135 patients fulfilling DSM-III-R criteria for OCD with an illness duration of at least 10 years and divided by course: 27.4% were episodic and 72.6% chronic. We compared clinical and familial characteristics and comorbidity. Univariate analyses showed that episodic OCD had a significantly lower rate of checking rituals and a significantly higher rate of a positive family history for mood disorder. Multivariate stepwise discriminant analysis revealed a positive and significant relationship between episodic course, family history for mood disorders, lifetime comorbidity for panic and bipolar-II disorders, late age at onset and negative correlation with generalized anxiety disorder. These data suggest that the episodic course of OCD has important clinical correlates which are related to cyclic mood disorders. This correlation has implications for treatment and research strategies on the aetiology within a subpopulation of OCD.

Key words Obsessive–compulsive disorder · Bipolar disorder · Episodic course

Introduction

The course of obsessive–compulsive disorder (OCD) is remarkably variable. In their review of previous follow-up studies, Goodwin et al. (1969) found that the course of OCD could be divided into three categories: (a) unremitting or chronic; (b) phasic with periods of complete remission; and (c) episodic with incomplete remissions that permitted normal social functioning. According to these authors, although there was a considerable variation between studies as to the percentage of patients falling into each category, the majority of patients fell into the last group. Subsequently, Black (1974) reviewed three studies and found that 11–14% of 219 patients had phasic course, 24–33% had a fluctuating course and 54–61% had a static or worsening course. Insel and Murphy (1981) cited a rate of chronic course ranging from 50 to 85% of cases; a lower percentage of patients showed an episodic course with periods of complete remission of the obsessive–compulsive symptomatology. More recently, Rasmussen and Eisen (1989) reported that continuous or deteriorative course was the most prevalent, with less than 2% pursuing an episodic course.

Despite its prognostic and therapeutic importance, systematic data about subtype of OCD based on the clinical course are meager and comparative research on large case series has not been performed. Ravizza et al. (1991) proposed two subtypes of OCD with episodic (at least a symptom-free period of 1 month per 1 year of follow-up) or continuous course (with a mean length of illness of 5 years). The episodic group was characterized by late onset, usually after 25 years, gender distribution of 2 to 1 favouring females and tendency to show fewer compulsive symptoms. The chronic subtype was more prevalent in males (2 : 1), had an early onset (before 25 years), presented more compulsive symptoms and had a high rate of concomitant depressive symptomatology. However, in this research only patients with a short length of illness were included, which means that their chronic course could have become episodic with the evolution of the illness.

The aim of the present study was to assess the frequency of episodic course in a large case series of OCD with a 10-year history of illness. In addition, we compared clinical and familial characteristics of those with episodic

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vs continuous course. Based on classical European concepts (Mayer-Gross et al. 1969) and our clinical experience, we hypothesized that episodic OCD is closely linked to affective spectrum, and more specifically to soft bipolar disorder.

Subjects and methods

From 1985 to 1995 we evaluated a total of 345 outpatients with the diagnosis of OCD according to DSM-III-R criteria (1987), consecutively enrolled at the Section of Psychiatry of the Department of Psychiatry, Neurobiology, Pharmacology and Biotechnology, University of Pisa (Italy). All patients gave informed consent for their participation in this study.

Of these patients, 190 were females (54.9%) and 155 were males (45.1%); the mean age was 32.5 years (SD 12.5 years, range 18–74 years). Regarding marital status, 141 (40.9%) were married, 12 were (3.5%) divorced and 191 (55.4%) were not married; 19 (5.5%) were university educated, 152 (44.1%) had a high-school level of education and 166 (48.1%) had a lower level of education. Concerning work activities, 10 (2.9%) were managers, 74 (21.4%) were white-collar workers, 51 (14.8%) were blue-collar workers, 65 (18.8%) were students and 143 (41.4%) were unemployed.

Each patient was independently evaluated by two psychiatrists (P.L. and S.R.) with at least 3 years of clinical experience. All diagnostic information was submitted to the senior psychiatrist of our team (G.B.C.) who made consensus diagnoses. Lifetime or intraepisodic comorbidity with other anxiety, mood and personality disorders was not excluded. However, patients with organic mental disorder, schizophrenia, schizophreniform or other psychotic disorders were excluded.

The present report derives from the Pisa–San Diego collaborative clinical studies on mood and anxiety disorders. All patients were evaluated in a face-to-face interview with a specially constructed OCD questionnaire, which is a semi-structured in-depth interview divided into five sections to collect systematically relevant demographic data, family history, psychopathological features and course of illness. The first section concerns gender, index age, education, occupational status and marital status based on the Adult Demographic and Personal Inventory (ADPI). The second section explores aetiologically relevant items such as perinatal organic insults and psychological trauma during childhood and adolescence, psychiatric history and hospitalizations, major depressive episodes, number of suicide attempts and chronological relationships between OCD symptoms and comorbid non-OCD pathology based on DSM-III-R criteria; reliable assessment of developmental and psychopathological antecedents at the Pisa Center is considerably aided by the fact that access to past records is readily made available by patients and their physicians and, in particular, by the availability of numerous family members to corroborate anamnestic data obtained from patients. The third section concentrates on OCD itself, previous treatments and complications, age at onset, type of course divided into episodic (full symptomatic remissions for at least 6 months at a time) and continuous (chronic, with stable or fluctuating symptomatology, and deteriorative, with progressive worsening of the illness with a sufficiently serious social decline as to render the patient unable to lead an independent existence). In addition, this section assesses concomitant anxiety and mood disorders, if any, observed at index evaluation. The fourth section, essentially based on Winokur's approach as incorporated into the Family History version of the Research Diagnostic Criteria (Andreasen et al. 1977), collects information concerning the history of psychiatric disorders in first-degree family members with regard to major depressive and bipolar disorders, panic disorder, substance abuse and schizophrenia: the availability of these family histories at the Section of Psychiatry is facilitated by the ready availability of relatives, many of whom accompany the index patient to the clinic. The fifth and final section, a symptomatological scale, permits the precise recording of the phenomena of OCD, the main contents of the obsessions (e.g. contamination, aggression or sex) and the type of rituals involved (e.g. cleaning, checking or counting).

The interview lasted approximately 1 h at baseline, and half an hour at subsequent visits, and was done by psychiatrists in training (S.R., P.L., A.M., C.P., S.P. and A.G.) with at least 2 years of experience in the diagnosis and treatment of OCD. To address the limitation common to all retrospective studies, clinical data were reviewed by the interviewer team for the purposes of consensual agreement. When questions arose, patients were recontacted for further clarification. Patient medical records were reviewed and information was obtained from family members and prior physicians. Each interviewer underwent a training program in the use of the interview instruments, which included direct observation of experienced interviewers, direct supervision of interviews and interrater reliability. High reliability and diagnostic concordance (Kappa values ranging fom 0.73 to 0.99) have been documented in previous reports on this case series (Lensi et al. 1996; Perugi et al. 1997).

One of the major aims of our investigation was to develop clinically meaningful subtypes of OCD. In this paper we are testing the hypothesis that episodic OCD is related to mood disorder. For the present analyses, from the original cohort of 345 OCD we selected 135 patients in whom the length of illness was ≥ 10 years. This duration of illness was necessary to permit subdivision by course. Among these 135 patients, 74 were females (54.8%) and 61 were males (45.2%); the mean age was 38.4 years (SD 13.3 years, range 18–74 years). Regarding marital status, 64 (47.4%) were married, 9 (6.6%) were divorced and 62 (45.9%) were not married; 11 (8.3%) were university educated, 53 (40.2%) had a medium level of education and 68 (51.5%) had a minimum level of education. Concerning work activities, 6(4.4%) were managers, 32 (23.7%) were white-collar workers, 20(14.8%) were blue-collar workers, 10 (7.4%) were students and 67 (49.6%) were unemployed. This subsample was similar to the larger sample in all demographic and clinical variables with the exception of: higher age ($t = 7.21$, $p < 0.0001$), lower age at onset ($t = –5.48$, $p < 0.0001$), fewer students ($\chi^2 = 29.7$, $df = 5$, $p = 0.00002$), more married ($\chi^2 = 12.9$, $df = 2$, $p = 0.001$), lower rate of comorbidity with social phobia ($\chi^2 = 4.91$, $df = 2$, $p = 0.026$) and higher rate of positive family history for OCD ($\chi^2 = 4.32$, $df = 2$, $p = 0.037$). As expected, this selection of patients with 10 years of OCD led to differences which are largely correlates of older index age. It is important to note that the subsample under investigation did not differ from the larger sample in parameters related to affective disorder, which is the central hypothesis under investigation in this study.

The comparison between episodic and chronic OCD on continuous variables was conducted using Student's *t*-test, and on categorial variables using χ^2 analysis. Fisher's Exact test was used when cell sizes were sparse and χ^2 analysis was unrealizable. Because we specifically hypothesized the link between episodic OCD and mood disorder, a *p*-value < 0.05 was considered statistically significant with two-tailed statistics; a *p*-value < 0.075 was described as a "trend". Multivariate statistics, conducted by means of discriminant analysis involving canonical discriminant functions, used 13 clinical variables to predict group membership (age, age at onset, lifetime comorbidity for major depression, generalized anxiety, social phobia, panic disorder, bipolar disorder types I and II, substance abuse, intraepisodic comorbidity for major depression, family history for anxiety disorders, obsessive–compulsive disorder, mood disorder).

Results

Thirty-seven (27.4%) patients showed an episodic course, characterised by complete remission of OCD symptoms for a period of at least 6 months, and 98 (72.6%) patients showed a continuous course.

Table 1 shows that patients with episodic and continuous course did not significantly differ in mean index age and mean age at onset of OCD. The gender ratio was approximately 1:1 in both groups. Concerning lifetime comorbidity, bipolar-II and panic disorder were more frequent in the group with episodic course, although in the direction of our hypothesis, this difference was not statistically significant at the 0.05 level. Greater support for our hypothesis is seen in the significantly higher rate of family history for mood disorders which did distinguish the episodic from the continuous course. Comparison of obsession and compulsion did not show any statistically significant difference between the two groups, with the exception of checking rituals, which were more frequently represented in patients with continuous course.

Substantial support for our hypothesis further came from stepwise discriminant analysis (Table 2) which showed a positive correlation between episodic course and family history for mood disorders, comorbidity for panic and bipolar-II disorders, higher age at onset and negative correlation with generalized anxiety disorder. However, the percentage of cases correctly classified at $p < 0.05$ level by the discriminant function was only 64.7%.

Discussion

Our study, being largely based on anamnestic information, was biased by the potential unreliability of patient retrospective recall. As we took care of these patients for a long period of time, we had the opportunity to at least partially correct any such biases by selective or partial re-interviews of patients and family members. We preferred a semi-structured interview performed by psychiatrists, rather than a structured interview by non-clinicians, because the investigation required expert phenomenological probing. The absence of independent raters may be a methodological limitation of our study. We contend, however, that such clinical investigation is not easily conducted in a "blind" manner. Given the systematic nature of our inquiry, we believe biases were minimized.

Table 1 Comparison of demographic and clinical features in OCD patiens with cyclic and continuous course

	Episodic (n = 37)[a]	Continuous (n = 98)[a]	t	p
Age (years), mean (SD)	36.8 (14.7)	39.0 (12.7)	–0.78	0.43
Age at onset (years), mean (SD)	17.3 (9.2)	19.2 (10.1)	1.06	0.29
Gender	N (%)	N (%)	χ^2 (df = 1)	p
Males	20 (54.1)	41 (41.8)	1.60	0.20
Obsessions				
Aggressive	14 (37.8)	44 (46.3)	0.77	0.37
Contamination	15 (40.5)	43 (44.8)	0.19	0.65
Sexual	12 (32.4)	25 (26.0)	0.54	0.46
Religious	6 (16.2)	9 (9.5)	1.20	0.27
Order	11 (29.7)	26 (27.4)	0.07	0.79
Somatic	12 (32.4)	25 (26.0)	0.54	0.46
Other	6 (16.2)	26 (27.4)	1.80	0.17
Compulsions				
Cleaning	15 (40.5)	54 (55.7)	2.45	0.11
Numerical	8 (21.6)	30 (31.3)	1.21	0.27
Checking	23 (62.2)	77 (79.4)	4.19	0.04
Order	13 (35.1)	30 (31.3)	0.18	0.66
Other	8 (22.2)	24 (25.3)	0.13	0.71
Comorbidity (lifetime)				
Major depression	13 (36.1)	42 (43.8)	0.62	0.42
Generalized anxiety	8 (22.2)	25 (25.8)	0.17	0.67
Panic disorder	11 (30.6)	10 (16.3)	3.31	0.06
Bipolar I	0 (0.0)	2 (2.0)	0.07	0.38[b]
Bipolar II	10 (27.8)	14 (14.4)	3.16	0.07
Social phobia	4 (10.8)	11 (11.5)	0.01	0.91
Comorbidity (intraepisode)				
Major depression	11 (29.7)	30 (30.6)	0.00	0.92
Substance abuse	12 (32.4)	27 (27.6)	0.31	0.57
Family history (first degree)				
Obsessive–compulsive	4 (10.8)	16 (16.3)	0.64	0.42
Mood disorders	20 (54.1)	34 (34.7)	4.19	0.04
Anxiety disorders	11 (25.7)	25 (25.5)	0.24	0.62

[a] The number of patients varied in the analyses because of missing data; percentages are based on the number of patients for whom data were available

[b] Fisher's exact test, n. s.

Table 2 Stepwise discriminant analysis between OCD patients with episodic (n = 36) and continuous (n = 9 4) course

Step	Variable	p	Discriminant function
1	Family history for mood disorders	0.06	0.62
2	Lifetime comorbidity for panic disorder	0.04	0.43
3	Age at onset (years)	0.03	0.46
4	Lifetime comorbidity for bipolar-II disorder	0.04	0.42
5	Lifetime comorbidity for generalized anxiety disorder	0.04	–0.37

Statistical analysis: Wilks lambda = 0.91, chi-square = 11.26, df = 1/5, p = 0.04; group centroids: episodic (n = 36) = –0.49, continuous (n = 94) = 0.19; 64.7% of cases were correctly classified

In our case series with a personal history of OCD during at least 10 years, 27.4% showed an episodic course with 6-month-intervals completely symptom free. This percentage is higher than that reported by other authors (Pollitt 1957; Black 1974; Rasmussen and Eisen 1989). This could be due to differences in inclusion criteria or, perhaps, to the possibility that rate of remission might vary in different centres. A major problem in this regard is the definition of episodic course. Periods of symptomatological remission in OCD may be spontaneous or related to favourable psychosocial factors. Similarly, successful treatment could explain a symptom-free interval and would not in this case justify speaking of an episodic course. However, in patients with a 10-year history of OCD, the natural history or course of the disorder entirely uninfluenced by therapeutic interventions is difficult to study, and few patients remain untreated for such a length of time. We therefore believe that symptom-free periods of 6 months appear as a reasonable operational criterion to distinguish patients who presented full remission from patients who did not.

Most of the patients had a positive family history for mood disorders and, as expected, this was more frequent in OCD patients with an episodic course. As for concomitant mood and anxiety disorders, episodic OCD patients had a higher lifetime comorbidity for panic disorder and bipolar-II disorder. Several studies have indicated a high prevalence of major depression in patients with OCD (Goodwin et al. 1969; Rachman and Hodgson 1980; Rasmussen and Tsuang 1986). Less attention has been paid to the relationships between OCD and bipolar disorders. Several clinical reports describe the concomitance of OCD and bipolar disorder (Baer et al. 1985; Gordon and Rasmussen 1988). In an epidemiological investigation, Boyd et al. (1984) reported that the presence of either mania or depression increased the probability of the presence of OCD. Recently, Kruger et al. (1995) observed that OCD occurs with equal frequency in a large sample of bipolar and unipolar depressives. Moreover, numerous case reports describe the development of mania or hypomania in OCD patients treated with serotonergic agents (Turner et al. 1985; Jefferson et al. 1991; Vieta et al. 1992; Steiner 1992).

Taking into consideration that obsessive-compulsive symptoms are relatively frequent in mood disorders, symptom-free periods in our patients with episodic OCD might be interpreted in connection with the remission of the affective disease. However, from our data it is evident (Table 2) that there are patients with continuous OCD and lifetime personal history of mania (n = 2; 2%) or hypomania (n = 14; 14.4%); therefore, the presence of different phases in mood disorders are not invariably related to change or remission of OCD.

Comorbidity for bipolar-II and panic disorders is frequently associated with a later age at onset and higher rate of family history for mood disorders only in a subpopulation of our OCD sample with episodic course, as suggested by the reclassification power of the discriminant function. This finding supports previous observations by our group (Savino et al. 1993) on 140 panic disorder patients, in whom we found that the presence of bipolar spectrum disorders increased the chance of concomitant OCD.

The foregoing considerations underscore the need to study the concomitance of panic disorder and bipolar disorder in episodic OCD. The occurrence of this comorbidity encourages particular caution in employing high dosages of serotonergic agents in the treatment of OCD symptoms. In these patients, it would be appropriate to evaluate the efficacy of lithium salts, other mood regulators and monoamine oxidase inhibitors.

The frequent co-occurrence of episodic OCD with bipolar-II disorder, and the presence of a positive family history for mood disorders, suggests the existence of common pathogenetic mechanisms between mood disorders and a subtype of OCD. Evidence based on a single family pedigree (Dilsaver and White 1986) suggests a genetic linkage between OCD and bipolar disorder, whereas other studies indicate increased prevalence of OCD in bipolar probands (Kruger et al. 1995) and high rates of obsessional traits in the offspring of bipolar probands (Klein et al. 1985). Coryell (1981) reported an equal incidence (2.3%) of mania in families of probands with OCD and in families with a bipolar-disorder member. In a more theoretical context, we suggest that, in a substantial minority of cases, phasic OCD symptoms may be the phenotypic expression of an underlying affective genotype (Mayer-Gross et al. 1969). Further investigations should focus on the prospective assessment of patients with comorbid OCD, bipolar-II disorder and panic disorder.

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