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Obsessive–Compulsive Disorder

Familial–Developmental History, Symptomatology, Comorbidity and Course with Special Reference to Gender-Related Differences

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Background. Demographic data, family history, psychopathological features, comorbidity and course of obsessive–compulsive disorder (OCD) are investigated and data generated to support the possible existence of two subgroups with gender-related differences of a broader nature.

Method. Two hundred and sixty-three OCD patients, consecutive admissions to the Institute of Psychiatry, University of Pisa over a period of 5 years, not excluding those with comorbid Axis I and Axis II conditions, were studied. Patients were evaluated with a specifically designed semi-structured OCD interview.

Results. We found a significantly greater history of perinatal trauma in men who also had an earlier onset, greater likelihood of never having been married and a higher frequency of such symptoms as sexual, exactness and symmetry obsessions and odd rituals; by contrast, women suffered a later onset of the disorder, were more likely to be married, had higher rates of associated panic attacks after the onset of OCD and a higher frequency of aggressive obsessions at the onset of their illness, and were less frequently associated with bipolar disorders.

Conclusions. Pathophysiological mechanisms in OCD seem to differ by gender. Perinatal trauma might predispose to earlier onset in men, whereas in women there is a close association between OCD and panic disorder.

Obsessive–compulsive disorder (OCD) has been shown to have a gender ratio of about 1 : 1 (Karno *et al*, 1991); nevertheless the impact of gender on demographic and clinical characteristics of OCD has been reported. Early onset is more common in male patients (Flament & Rapoport, 1984) and women have been found to have a later onset of OCD, often associated with eating disorders (Fahy *et al*, 1993) and depression (Noshirvani *et al*, 1991); Rasmussen & Tsuang (1986) hypothesised the existence of two subgroups of OCD, one with early onset and another with late onset; however, such a classification has not been confirmed by other studies (Leonard *et al*, 1989). Furthermore higher frequency of cleaning rituals, fear of contamination and avoidant behaviour has been found in women (Marks, 1987), whereas primary obsessive slowness, sexual obsessions (Roy, 1979), and social phobia (Marks, 1987) were prevalent in men.

Although interest in the aetiological understanding of OCD has increased during the last few years, much remains to be learned about its developmental background, comorbidity and pathophysiology; in this respect gender-related or gender-specific factors might influence the clinical expression of OCD phenomena. This clinical study on the manifestations and course of the disorder – deriving from a large collaborative study between the University of Pisa, Italy and the University of California, San Diego – will further explore the hypothesis that gender may influence the early expression of a more severe "organic" type of disorder in males (Capstick & Seldrup, 1977) and a later-onset disorder with depression comorbidity in females (Noshirvani *et al*, 1991).

Method

Two hundred and sixty-three patients who met DSM–III–R (American Psychiatric Association, 1987) diagnostic criteria for OCD were obtained from consecutive cases admitted to the Institute of Psychiatry, University of Pisa over a period of five years. We included comorbid axis II conditions and those with other axis I anxiety, major depressive, bipolar, Tourette and organic mental disorders,

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provided that obsessive–compulsive phenomena dominated the clinical presentation at index evaluation; only schizophrenia or schizophreniform or other psychotic disorders (Insel & Akiskal, 1986) served as exclusion criteria. We thereby suspended hierarchical diagnostic rules in order to better define those natural groupings in OCD which are known to have a high degree of comorbidity (Maser & Cloninger, 1990). This strategy thus permitted the examination of all the listed borders of OCD except with psychosis.

OCD questionnaire

Patients were evaluated with a specially constructed OCD questionnaire (OCD–Q), which is a semi-structured in-depth interview which collates relevant demographic data, family history, psychopathological features and course of illness. It lasts 90–120 minutes. The OCD–Q is divided into five sections, each of which covers specific aspects of OCD.

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, axis II personality disorders, psychiatric history and hospitalisations, 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 Centre 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, its age at onset; type of onset (acute or insidious); life events (based on Paykel *et al*, 1969) prior to onset; time interval between the event and onset; previous treatments and complications; type of course divided into episodic (full symptomatic remissions for months at a time), chronic (stable or fluctuating symptomatology) and deteriorative (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 states, if any, observed at index evaluation.

The fourth section is based on Winokur's approach as incorporated into the Family History version of the Research Diagnostic Criteria (Andreasen *et al*, 1977). It collates 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 fifth section is devoted to a symptomatological scale which permits the precise recording of the phenomena of OCD, the main contents of the obsessions (e.g. contamination, aggression or sex) and the associated phobias (e.g. agoraphobia, thanatophobia or mysophobia), and assesses the type of ritual involved (e.g. cleaning, checking or counting); this is the only part of the OCD–Q which is used during a prospective follow-up.

Diagnostic evaluation

All evaluations and diagnoses were conducted by two psychiatrists (PL and SR), each with at least five years of post-graduate clinical experience. Relevant clinical data were eventually submi ted to the senior Italian psychiatrist (GBC) who, following an abbreviated face-to-face clinical interview, assigned consensus diagnoses. In the early phase of the study, inter-rater agreement on the diagnoses of comorbid mood and anxiety disorders as well as the classification regarding type of onset, course and demoralisation reactions were ascertained (Klein, 1974).

Statistical analysis

We divided OCD patients into two groups on the basis of gender: 112 males and 151 females, with index ages ranging from 11 to 71 years. Significant differences between the groups refer to *t*-test or χ^2, whichever was appropriate. A *P*-value of less than 0.05 was considered statistically significant; conservatively we used two-tailed tests.

Results

Age, age at onset, manner of onset and course

The mean age at the time of index evaluation (Table 1) was 33.1 years, but with males it was significantly younger (30.8 *v.* 34.7 years, $P<0.01$), as was also the mean age at onset (21.1 *v.* 24.3, $P<0.02$) (Table 2). The majority of our patients (64.2%) reported significant life events in relation to the onset of OCD (Table 2). Only in a small proportion of cases (15.0%), were these events 'entrances' or 'desirable events', such as childbirth, marriage, promotion at work; the more common antecedent events were

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Table 1
Index age, education, occupational and marital status in OCD divided by gender

	Male (n=112) %	Female (n=151) %
Index age	30.8±11.6*	34.7±13.2
Educational level		
university graduate	8.9	5.3
university studies (not completed)	14.3	9.3
high school	29.5	28.5
high school (not completed)	13.4	4.0
junior school	22.3	16.6
junior school (not completed)	4.5	4.0
primary school	7.1	29.8
primary school (not completed)	0.0	2.6
Socio-economic status		
manager	0.9	1.3
professional	4.5	0.0
professional (lower level)	17.9	9.9
technician	12.5	8.6
specialised worker	8.0	2.0
semi-skilled worker	2.7	0.0
unskilled worker	10.7	5.3
student	19.6	12.6
housewife	–	43.1
unemployed	19.6	15.9
pensioner	2.7	1.3
Marital status		
married	24.1	56.9**
married more than one time	0.0	2.6
divorced	4.5	2.6
widowed	0.0	0.7

All comparisons statistically not significant with the exception of *$P<0.01$ and **$P<0.001$.
–, No comparison made because this role is defined by gender.

"exits" or other "undesirable events" such as losing a loved one, a severe medical illness, or major financial difficulties. Such negative events as separation and mourning, before the onset of OCD (Table 2), were much more frequent in males than in females (20.9 *v.* 10.7%, $P<0.02$). As might be expected, given the foregoing data, the mean age at the first psychiatric consultation was significantly younger in male patients (23.1 *v.* 25.6 years, $P<0.05$). The average interval between the onset of the illness and the first psychiatric help was about two years. There was no significant difference between genders with respect to type of onset and course parameters.

Marital status

As shown in Table 1, nearly half of our patients were single and significantly fewer male patients than female were married (24.1% *v.* 56.9%). Only 2.6% of the women in our study had been married more than once and 0.7% were widowed; only a very small proportion of our patients had been divorced, with a slightly higher incidence in men (whose illness would have rendered them less likely to be sufficiently adaptive for marriage).

Table 2
Main characteristics of OCD by gender

	No gender differences %	Male (n=112) %	Female (n=151) %
Age at onset		21.1±10.6	24.3±11.3*
Type of onset			
acute	28.0		
insidious	72.0		
Life events prior to onset			
entrance or desirable	15.0		
undesirable or exit		20.9	10.7*
Time interval (weeks)	17.8		
Previous treatments and sedat			
Tricyclics		53.6	70.2**
Benzodiazepines	71.6		
Neuroleptics	50.2		
Benzodiazepine misuse	8.8		
Alcohol misuse		8.1	2.6***
Type of course			
episodic	25.9		
chronic	63.9		
deteriorative	9.1		

*$P<0.02$; **$P<0.006$; ***$P<0.04$.

Prior treatment

Before coming to our attention, most OCD patients had had previous medical or mental health consultations (physicians, neurologists, psychologists or homeopaths). There were no gender differences in this respect (Table 2). However tricyclic antidepressants had been prescribed to a significantly higher degree for females than males (70.2% *v.* 53.6%, $P<0.006$). An equally high percentage of our patients had been treated with benzodiazepines (71.6%) or neuroleptics (50.2%), with no gender differences.

OCD patients tend not to abuse substances (Table 2) and only a small percentage (8.8%) of our patients had misused benzodiazepines, with no gender prevalence. However, alcohol misuse was significantly more frequent in male patients (8.1% *v.* 2.6%; $P=0.04$).

Personality antecedents

With respect of personality, we used DSM–III–R criteria for Axis II at the trait level (requiring one

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item less than the diagnosis of a disorder). Obsessive–compulsive traits were very common in our study population (Table 3), with no significant differences between genders (53.2% in men *v.* 49.3% in women); significant gender differences were found only with the avoidant trait (24.1% in men *v.* 13.2% in women, $P<0.02$).

Perinatal trauma

As shown in Table 3, a history of birth trauma (a dystocic delivery, involving the application of forceps, a breech presentation or prolonged hypoxia) was reported significantly more frequently in males than females (22.4% *v.* 12.9%, $P<0.04$).

Symptomatology

The most common obsessions at onset were doubting obsessions (53.0%) and fear of contamination (34.6%) (Table 4). Sexual, symmetry and exactness obsessions significantly prevailed in male patients, while aggressive obsessions were more frequent in female patients. Odd rituals and those relating to superstition were significantly more common in male patients. With a few exceptions (Table 4), differences between genders at the onset of the disorder remained essentially stable over much of the course of the illness. Thus, at index evaluation, sexual, symmetry and exactness obsessions and odd rituals still prevailed in male patients; cleaning rituals were more frequent in female patients, while differences in the percentages of male and female subjects with aggressive obsessions were no longer significant. On the whole, obsessions and compulsions tended to increase with time.

Comorbidity

Major depression was reported by 43.0% of the patients, with no differences between gender (Table 3). In only 14.1% did such depression precede OCD.

Among our OCD patients, the most common associated feature of OCD at the index evaluation was demoralisation (65.4%), as might be expected after a disabling illness. The association with frank bipolar disorder was negligible, with only four patients (1.5%) reporting full manic episodes; more often, OCD patients had developed hypomanic episodes (13.0%) and these were significantly more frequent in male subjects (17.1% *v.* 8.6%; $P<0.03$). Frank bipolar disorder in all instances had preceded the onset of OCD; on the other hand, most hypomanic episodes had occurred after treatment of the OCD with clomipramine.

Table 3
Aetiologically relevant items in OCD by gender

	No gender differences %	Male (n=112) %	Female (n=151) %
Perinatal trauma		22.4	12.9*
Birth order			
no siblings	23.7		
first-born	56.2		
Personality traits			
compulsive		53.2	49.3
avoidant		24.1	13.2**
dependent	8.4		
histrionic	4.4		
schizoptypal	3.6		
paranoid	4.4		
Hospitalisation	23.3		
Comorbidity			
suicide attempts	12.1		
major depression	43.0		
demoralisation	65.4		
manic episode	1.5		
hypomanic episode		17.1	8.6***
GAD	15.0		
Panic attacks			
prior to OCD onset	14.0		
after OCD onset		6.2	13.9*

*$P<0.04$; **$P<0.02$; ***$P<0.03$.

Generalised anxiety disorder (GAD), which preceded the onset of OCD in 15%, did not show any gender differences.

Although panic attacks prior to the onset of OCD had had an average prevalence of 14% with no gender differences, such attacks were significantly more common in women after the onset of OCD (13.9% *v.* 6.2%; $P<0.04$).

Family history

Most of our patients reported a family history of one or more psychiatric disorders (76.6%) and 35.4% had relatives with depressive disorders. Only a minority (7.6%) of our patients had first-degree relatives with OCD, but a greater proportion (14.1%) had obsessional traits. Lifetime familial prevalence of classical anxiety disorder such as panic disorder was also quite high (19.4%) compared with population values (ECA). None of these familial rates favoured either gender.

Discussion

We found a significantly greater history of perinatal trauma among males who also had suffered from an earlier onset, were less likely ever to have been married, and were more likely to suffer from such

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symptoms as sexual, exactness and symmetry obsessions or odd rituals; by contrast women had suffered a later onset of the disorder, were more likely to be married, had higher rates of associated panic attacks after the onset of OCD and a higher frequency of aggressive obsessions at the onset of their illness, and were less frequently associated with bipolar disorders.

The question of 'organic' insult

The finding of birth trauma more frequently in males, which raises the possibility of perinatal 'organic' insults, is not specific to OCD and reflects a general trend in obstetric pathology, which involves a higher vulnerability in the male, presumably due to neurological, immunological and endocrinological factors. It has been proposed that males and females have different left–right cerebral hemisphere ratios (Swaab & Horman, 1984). As a consequence of such differences in structural and functional central nervous system (CNS) organisation, women have been hypothesised as being more vulnerable to life stressors. On this basis, they could be expected to break down with lesser environmental precipitants and a less severe personality pathology at a later age than males, as reflected in our data. Males, on the other hand, suffer a greater incidence of perinatal trauma and this could conceivably alter the serotonergic and dopaminergic systems believed to be involved in OCD (Rapoport & Wise, 1988) and thus induce an earlier onset of OCD. The foregoing considerations are generally in line with published literature. Capstick & Seldrup (1977), who investigated the association of OCD with neurological disorders and perinatal trauma, reported that a history of such trauma was strongly correlated with odd and magic rituals. In our series, odd rituals were more frequent in males, who also showed a higher incidence of birth trauma. Denckla (1988) found in 45 out of her 54 OCD patients (ages ranging from 6 to 20) positive neurological signs such as immaturity of the CNS and hemisyndrome and basal ganglia dysfunctions; the oldest patients lacked these features. However, the presence of these dysfunctions would not appear to be an adequate explanation of the subsequent onset of OCD and probably merely represents a risk factor in subjects predisposed to this disorder.

Table 4
Symptomatological features of OCD by gender

	Male (n=112) %	Female (n=151) %	P
(a) At onset			
sexual obsessions	27.0	12.7	0.003
aggressive obsessions	15.3	26.2	0.03
religious obsessions	10.8	10.1	ns
exactness and symmetry obsessions	28.6	8.0	0.001
financial obsessions	0.0	1.3	ns
contamination obsessions	30.6	37.6	ns
somatic obsessions	24.3	16.1	ns
doubting obsessions	58.9	49.0	ns
other obsessions	25.2	22.1	ns
checking rituals	54.9	51.7	ns
cleaning rituals	38.7	48.3	ns
order rituals	22.5	19.9	ns
counting rituals	29.1	19.9	ns
odd rituals	24.5	14.7	0.04
animal phobias	8.9	9.3	ns
mysophobia	23.4	29.8	ns
social phobia	17.3	11.3	ns
illness-phobia	24.3	23.2	ns
other phobias	15.2	17.3	ns
(b) At index evaluation			
sexual obsessions	33.0	16.7	0.002
aggressive obsessions	23.2	30.0	ns
religious obsessions	11.6	8.7	ns
exactness and symmetry obsessions	33.9	10.0	0.001
financial obsessions	3.6	2.0	ns
contamination obsessions	35.7	42.0	ns
somatic obsessions	31.2	22.5	ns
doubting obsessions	68.7	66.0	ns
other obsessions	31.2	27.3	ns
checking rituals	69.6	67.5	ns
cleaning rituals	43.7	59.6	0.01
order rituals	29.5	27.8	ns
counting rituals	34.8	25.2	ns
odd rituals	34.8	22.1	0.02
animal phobias	7.1	11.3	ns
mysophobia	24.1	33.1	ns
social phobia	12.5	13.3	ns
illness-phobia	30.4	22.5	ns
other phobias	17.9	18.1	ns

Gender-related symptomatological expressions

The higher frequency of sexual worries in males could derive from different social as well as ethological considerations, as could, similarly, the cleaning rituals which prevail in women (Khanna & Mukherjee, 1992).

Odd rituals and exactness and symmetry obsessions are more frequent in males; as mentioned above, their presence would appear to be correlated with an early onset of the disorder and a history of birth trauma. Another significant difference between genders is the prevalence of aggressive obsessions in females. This fear of losing control may be due to an association with panic disorder, which is significantly more prevalent in women; it might also be related to motherhood and the fear of

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harming the newborn infant. The fact that, in our series, obsessions with harming the foetus or baby were more prevalent at onset than any index evaluation, would suggest that continuous exposure to these obsessions may eventually reduce their virulence. These considerations are generally consistent with other reports (Noshirvani *et al*, 1991).

Gender differences in comorbid anxiety and mood disorders

More than 50% of OCD patients receive concurrent diagnoses of other psychiatric disorders (Rasmussen & Eisen, 1994). Family data too, indicate an excess of anxiety disorders among the first degree relatives of OCD probands (McKeon & Murray, 1987; Black *et al*, 1993). Our data show that anxiety disorders are more frequent in female OCD patients. Some authors have hypothesised that anxious-sensitive traits and fluctuating anxiety are likely to be the first step in an evolution towards obsessive symptoms, conceived as an 'adaptive' reaction (Pollit, 1957). Indeed, our data do suggest that GAD is commonly associated with obsessive symptoms and that it is usually present before the onset of OCD. These considerations are generally consistent with the hypothesis that a special subgroup of GAD represents a *form fruste* of OCD (Akiskal, 1985); in fact, ruminative worrying and need to keep everything under direct control are shared features of the two disorders. Whether obsessive traits occur in excess in OCD patients and their relatives is an unresolved issue (Black *et al*, 1993).

Panic attacks seem to have a different relationship with obsessive symptoms, occurring both before and after the onset of OCD and being more common in women.

As for depression it may start before, during or after the onset of OCD; in some cases, the two disorders follow a parallel course, whereas in others their evolution appears independent of one another (Demal *et al*, 1993). Only one group of researchers (Noshirvani *et al*, 1991) has ever reported a gender (female) prevalence for depression in OCD; this was not observed in our sample. The type of mood disorder observed in excess in our case series was bipolar II (hypomania), which actually favoured males and tended to develop after pharmacologic treatment with antidepressants. Bipolar I (mania), which occurred rarely and without gender differences, typically preceded the OCD and took an independent course from it. Depression *per se*, which did not differ in the two sexes, in most cases complicated the course of OCD and tended to fluctuate between remissions and exacerbations. It is noteworthy that depressive symptoms were not always so pronounced as to meet the criteria for major depression; in some patients a marked degree of demoralisation may be secondary to the degree of suffering and incapacity caused by the illness. Overall, the findings of our investigations are only in part comparable with those of Noshirvani *et al* (1991) suggesting that OCD is a heterogeneous disorder in which the prevalence and intensity of symptoms depends upon a complex interaction between biological, personal and cultural factors, likely to differ from one study to another in different parts of the world.

Clinical implications

- A different pathophysiology of OCD in males and females is suggested.
- The suspension of hierarchical diagnostic rules permitted the exploration of the relationship of OCD with various anxiety and mood disorders.
- 'Organic' OCD males may have a worse prognosis and possibly poorer response to serotonergic antidepressants than OCD females with a later onset and more comorbid anxiety conditions.

Limitations

- Our case series is subject to the biases of referral patterns and selection criteria. The general psychiatric setting could partly explain the relatively large proportion of comorbid anxiety and mood disorders.
- Data on developmental and familial aspects were not obtained with blind methodology.
- No specific laboratory investigations of OCD patients with a history of birth trauma.

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