

A case-control study of sex differences in strategic processing and episodic memory in obsessive-compulsive disorder

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Abstract

Although clinical and genetic data for obsessive-compulsive disorder (OCD) support the hypothesis of sexual dimorphism, the neuropsychological findings remain inconclusive. The aim of our study was to determine whether there are differences in cognitive performance between men and women with OCD as compared with healthy controls (HCs). A neuropsychological battery was administered to 50 patients with OCD (31 men and 19 women) and 50 HCs matched by sex, age, and educational level with patients. We evaluated intelligence, attention, episodic memory, and use of organizational strategies during encoding of verbal and nonverbal information. Male patients scored worse than controls did in measures of nonverbal memory tasks, whereas the cognitive performance of women with OCD was consistent with that of their HC counterparts. These results suggest a distinct pattern of cognitive dysfunction specific to the patients' sex. © 2010 Elsevier Inc. All rights reserved.

1. Introduction

Obsessive-compulsive disorder (OCD) is a heterogeneous disorder mediated by a range of different factors [1]. In recent years, significant advances have been made in characterizing the phenomenology and neurobiology of OCD [2,3]. A review of results from studies carried out in different areas of OCD suggested that sex is one of the elements involved in the heterogeneity of this disorder [4].

Men usually have an earlier onset of OCD than do women [5,6] and also show a higher prevalence of motor and vocal tics across their lifetime [7]. However, female patients with OCD present high comorbidity with major depressive disorder and eating disorders [5,8].

Sex hormones seem to influence the clinical expression of OCD. For example, estrogens have been linked to fluctuations in the severity of obsessive symptoms across the menstrual cycle, as well as with age at onset, because a proportion of women with OCD first develop the disorder at menarche [9] or during pregnancy [10]. Variations in the intensity of obsessive symptoms have also been observed in response to treatment with antiandrogens [11].

There are also sex differences at the phenomenological level, with a preponderance of sexual, symmetry, and ordering obsessions and odd rituals in men [6,7] and a higher frequency of contamination/washing and aggressive/checking symptoms in women [6,7,12]. Sex has also been associated with the response to pharmacological treatment, with men being more resistant to combined treatment with fluvoxamine and clomipramine [13].

Sex differences in patients with OCD have been found in some studies of functional neuroimaging, with correlations between symptom severity and brain levels of some metabolites at the anterior cingulate cortex in women [14] and higher levels of glucose metabolic rates on the right gyri in women and on the left gyri in men [15].

Genetic studies in obsessive patients have also reported sex differences and suggest that there is sexual dimorphism in OCD. Compared with male patients, obsessive women present a low activity-related allele of the monoamine oxidase A gene, whereas men present a low activity-related allele of the catechol-*O*-methyltransferase gene [16,17]. In this regard, a recent meta-analysis concluded that catechol-*O*-methyltransferase may play a role in the genetic etiology of OCD in men [18]. Furthermore, sex-based relationships have been reported between OCD and certain genetic polymorphisms; for example, the 5-HT-2A promoter and

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NTRK2 are associated only with female patients [19,20], whereas polymorphisms of the glutamate transporter gene SLC1A1 have been linked to obsessive men [21,22].

In the field of neuropsychology, the sex differences observed in the cognitive functioning of obsessive patients are less obvious than those described in terms of epidemiology, clinical features, comorbidity, neuroimaging, response to treatment, and genetics. Meanwhile, sex differences in the cognitive functioning of the general population have been consistently found. These consist of better performance in tasks related to verbal skills and memory, in perceptual speed and accuracy, and in fine motor skills in women, whereas men tend to outperform women on tests of visual memory and on mathematical and spatial ability (see Sherwin [23], for a revision). To date, only 2 studies that analyze sex differences in neuropsychological performance among obsessive patients have been published, and they reach opposing conclusions. The study by Zohar et al [24] compared the cognitive performance of male and female medication-free patients with OCD, with no control group, on tasks that evaluate dorsolateral prefrontal cortex function using the Wisconsin Card Sorting Test and orbitofrontal cortex function using the Object Alternation Test. The authors found no neuropsychological differences with respect to sex, although they did report associations between the severity of obsessive symptoms and performance on certain orbitofrontal tasks according to the patients' sex. They argue that these results support the hypothesis of sexual dimorphism in OCD. In the other published study, by Mataix-Cols et al [25], sex differences in cognitive performance were evaluated in a group of obsessive patients compared with a control group. These authors report sex differences in the performance of some cognitive tasks (verbal fluency tasks and the Stroop test), although they observed no differences between men and women on most verbal memory, nonverbal memory, and executive function tasks. They did, however, find negative correlations between some tasks that evaluate executive function and the severity of obsessive symptoms, but only in women. In this case, the authors conclude that sex does not seem to be a major determinant of neuropsychological function in OCD.

Neuropsychological studies in OCD have reported poorer cognitive performance on tasks of verbal and nonverbal memory in patients as compared with healthy controls (HCs) [26,27]. Furthermore, most of these studies suggest that the changes in neuropsychological performance are mediated for both types of information by dysfunctions in the processing stages [26,28,29].

Analyses of sex differences in neuropsychological performance in OCD are useful to deepen our knowledge of the neurobiological bases and heterogeneity of OCD. Furthermore, these analyses could help to explain the clinical differences between male and female patients.

The main aim of our research was to explore the existence of sex differences in the execution of verbal and nonverbal memory tasks. We have focused on the use of organizational

strategies during information processing in both kinds of memory tasks, an area that has not been addressed in the previous studies. In addition, our sample was bigger and better matched with HCs than were the samples of previous studies.

2. Method

2.1. Subjects

The study comprised a total of 50 patients (31 men and 19 women) recruited from a series of consecutive admissions to the Obsessive-Compulsive Disorders Unit of Bellvitge University Hospital in Barcelona during 2004 and 2005. All those included met the criteria for OCD described in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* [30], and in each case, the diagnosis was confirmed by 2 experienced psychiatrists (P.A. and J.M.M.) through 2 separate interviews conducted 1 month apart and using the Structured Clinical Interview for *DSM-IV* Axis I Disorder [31]. The exclusion criteria were having a history of substance abuse and/or dependence, neurological disease (except tics), head injury with loss of consciousness, a history of bipolar disorder, and a history of psychotic episodes and having undergone electroconvulsive therapy and/or neurosurgery. Eight (16%) patients had tics, all of them motor tics. Fifty HCs covering both sex groups were included and carefully matched with the patients for age (± 2 years), hand dominance, sex, and educational level. The HC had no history of neuropsychiatric disorder and had never been prescribed psychoactive drugs.

Patients with OCD with comorbid psychiatric disorders were not excluded from the present study provided that OCD was both the dominant pathology and the reason for seeking treatment. The Structured Clinical Interview for *DSM-IV* Axis I Disorder-Clinician Version was used to assess the presence of axis I disorders, and the Structured Clinical Interview for *DSM-IV* Axis II Personality Disorders was used to assess the presence of personality disorders [31].

A total of 49 (98%) obsessive patients were receiving psychopharmacological treatment at the time of the neuropsychological assessment. Treatment with psychoactive drugs had remained stable and unchanged for a period of at least 12 weeks before the assessment. Among patients receiving such treatment, 33 (66%) were receiving monotherapy: 31 were taking serotonin reuptake inhibitors (SRIs) and 2 were taking monoamine oxidase inhibitors. Sixteen (32%) patients had a prior history of resistance to at least 2 treatments in monotherapy with SRIs. Of these, 14 received a combination of 2 SRIs, whereas the other 2 were treated with a combination of an SRI and an atypical antipsychotic.

The clinical data analyzed in the sample of obsessive patients included sociodemographic variables (sex, age, and educational level) and the age at onset of OCD, with these data being collected retrospectively through direct interview. In the patient group, the intensity of depressive symptoms was measured by the Hamilton Depression Rating Scale

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