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Subtyping obsessive-compulsive disorder: Clinical and immunological findings in child and adult onset

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Abstract

It has been suggested that certain kinds of childhood OCD with specific clinical, biological and immunological characteristics may form a subgroup of OCD. We study the presence of these characteristics in child onset OCD and propose that the disorder be considered as a subtype of adult OCD. Forty adult patients with OCD were divided in two groups according to time of disease onset: 18 early onset and 21 late. Both sets were compared with a control group of 14 psychiatric patients. Child onset OCD was associated with higher mean ASLO titers, higher frequencies of history of tic disorders and tonsillitis in childhood and compulsive symptoms. No differences were found in D8/17 antibody titers or in other autoimmune parameters. The findings suggest that child onset OCD can be considered as a subgroup of adult OCD, although more specific biological markers are needed to identify it.

Keywords: Obsessive compulsive disorder; D8/17; ASLO; PANDAS; Tic disorders; Autoantibodies

1. Introduction

Obsessive Compulsive Disorder (OCD) is a common psychiatric illness that affects about 2% of the general population (Karno et al., 1988) but many of its ethiopathogenic mechanisms are still to be determined. OCD is also common among children and adolescents, with an estimated prevalence between 1% and 3.6% (Zohar et al., 1992). About one third of all adult cases of OCD have onset in childhood (Kolada et al., 1994). Child onset OCD presents specific clinical and biological characteristics that suggest that it may be a differentiated subtype. Clinical differences between types of OCD include sex distribution, family transmission, and prevalence of comorbid tics. Numerous studies demonstrate a high frequency of comorbid tic disorders, tic-like rituals when comorbid tics are absent, and Tourette syndrome in childhood onset OCD, with ranges between 20% and 59% – far higher than the general population, in which the presence of TS is estimated to be between 0.01% and 0.04% and that of tics 1% and 13%, or in adults with OCD, in which frequencies

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of these disorders are below 20% in all studies (Hanna, 1995; Leckman et al., 1997; Thomsen and Mikkelsen, 1995; Toro et al., 1992; Zohar et al., 1992). This relationship between child-onset OCD and tic disorders suggests that they are subtypes of the same underlying pathology.

In the pathogenesis of the disease a basal ganglia alteration may be involved (Rapoport, 1990), and the presence of OCD coincident with other disorders (chorea, dystonia, tics and Parkinson's) may be related to extrapyramidal movements. Neuroimaging techniques show greater dysfunction in the striatum (caudate and putamen) in child onset than in adult onset OCD (Luxenberg et al., 1988; Rosenberg et al., 1997).

In the search for an explanation for this striatal dysfunction, interest has increased in the possible link between streptococcal infections and the development of OCD and tic disorders in children (Garvey et al., 1998). It has been suggested that OCD in some susceptible individuals may be caused by an autoimmune response to streptococcal infections, a biological mechanism similar to that associated with Sydenham's chorea (SC), which is a manifestation of rheumatic fever following infection by group A β-hemolytic streptococci. In 1998, Swedo et al. described the diagnostic criteria for PANDAS (Pediatric Autoimmune Neuropsychiatric Diseases Associated to Streptococcal Infections) (Swedo et al., 1998). As in Sydenham's chorea, the PANDAS syndrome is believed to result from anti-streptococcal antibodies that cross-react with basal ganglia tissue. Consistent with this hypothesis, significantly elevated antineuronal antibodies were found in children with PANDAS (Swedo et al., 1991) and related neuropsychiatric disorders such as OCD and Tourette syndrome (Kiessling et al., 1993, 1994; Singer et al., 1998). The susceptibility marker D8/17 has been studied in SC and in rheumatic fever. This monoclonal antibody against B lymphocytes has expanded expression in rheumatic fever and in SC (Gibofsky et al., 1991; Khanna et al., 1989), and it has also been analysed in PANDAS patients. Some studies find a high positivity for this antibody in PANDAS patients compared with controls (Swedo et al., 1997), as have other studies with childhood-onset OCD or Tourette syndrome (Murphy et al., 1997; Chapman et al., 1998). Nevertheless, other studies find smaller differences in the percentages of positive patients, and others show negative results, especially those in adult populations (Bodner et al., 2001; Mathew, 2001; Eisen et al., 2001).

Some studies suggest that psychiatric conditions such as mood disorders and chronic stress states may favour the activity of autoimmune diseases and that these diseases have a correlation with the presence of autoantibodies. It is also known that depression often coexists with autoimmune subclinical thyroiditis, suggesting that depression may cause alterations in the immune system, or that in fact it is an autoimmune disorder itself (Elenkov and Chrousos, 2002). Moreover, some of the autoantibodies in human autoimmune diseases (such as rheumatoid arthritis or type I diabetes) are present in patients before the onset of disease (Scofield, 2004).

The main goal of this study is to determine whether an early age of onset of OCD is an important factor for subtyping adult OCD, and to find specific clinical and immunological characteristics in this group that would identify it as an autoimmune disease: sex, comorbidity with tics, history of recurrent tonsillitis, antistreptolisines, some autoantibodies (detected in organ-specific illnesses autoimmune and in systemic illnesses) and positivity of monoclonal antibody D8/17.

2. Materials and methods

2.1. Subjects

The OCD group comprised 40 patients with OCD, who fulfilled the DSM-IV diagnostic criteria for the disorder but had no other psychiatric comorbidity. The OCD group was divided into patients with child onset (onset before the age of 11, $n = 18$) and adult onset (onset after age of 11, $n = 22$).

The control group comprised 14 psychiatric patients who did not meet OCD criteria but met criteria for other psychiatric disorders (affective, adaptive, psychotic or anxiety disorders). Psychiatric patients with these diagnoses were taken as control group since in the literature it has not been found any positive association between them and immunological variables. All were seen at the Psychiatry Department at Hospital Clinic in Barcelona. The sample was recruited between 2000 and 2001; the procedures were approved by our institution's Ethics Committee and written informed consent was obtained from all subjects.

2.2. Measures

The Structured Clinical Interview for Diagnosis-IV (First et al., 1997) was administered to all patients. The Yale-Brown Obsessive-Compulsive scale was administered to assess the diagnosis (using the checklist items) and severity of OCD (Goodman et al., 1989). Comorbidity with tics was assessed by the Yale-Tic Inventory, the motor and vocal tics inventory of the Yale Global Tic Severity Scale (Leckman et al., 1989). A semi-structured questionnaire designed specially for the study was used to record age, sex, age of OCD onset, current medication, presence of a personal or family history of rheumatic fever, and history of tics and/or repeated tonsillitis in childhood. It contains detailed questions about difficult issues to establish such as age of OCD onset or history of repetitive tonsillitis. The medication taken by each patient was registered; this