Obsessive-Compulsive Disorder Among Schizophrenic Patients: An Exploratory Study Using Functional Magnetic Resonance Imaging Data

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Despite the growing research on the etiology of obsessive-compulsive disorder (OCD), and schizophrenia, the clinical distinction between the two disorders is not clearly understood. In the present investigation, we sought to better understand the relationship between OCD and psychotic disorders by examining functional magnetic resonance imaging (fMRI) data from a group of schizophrenic patients with varying degrees of OCD symptomatology, based on results of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the National Institute of Mental Health (NIMH) rating scales of OCD. While subjects performed a cognitive challenge paradigm that included a verbal fluency task, activation data from the left dorsolateral prefrontal cortex were collected and analyzed. We hypothesized that the fMRI signal patterns in schizophrenic patients with high levels of OCD symptomatology would differ from that of schizophrenic patients with a low level of OCD. For the group as a whole, no significant relationship was found for scores of either rating scale and fMRI signal change; however, a significant association was found for a subgroup of patients. For these schizophrenics, there was a negative relationship between OCD symptomatology and activation of the left dorsolateral prefrontal cortex. These results support the suggestion of several researchers that a relationship between OCD severity and neurophysiological activity exists in schizophrenia.

RECENT REPORTS suggest that the distinction between obsessive-compulsive disorder (OCD) and the psychotic disorders may not be as clear as previously thought. Eisen et al.[1] found that 7.8% of 77 patients with schizophrenia also met the DSM-III-R criteria for OCD. Berman et al.[2] found that 25% of 102 patients diagnosed according to the DSM-III-R criteria for schizophrenia had significant OCD symptoms. Lewis et al.[3] report on three pair of monozygotic twins who were concordant for both OCD and either a psychotic disorder or schizotypal disorder. Hwang and Opler[4 (p. 471)] indicate that "recent epidemiological and clinical studies increasingly support the presence of a subgroup of OCD schizophrenic patients with minimal to no insight into their symptoms," and suggest that this contradicts the traditional distinction between OCD and psychosis. Kozak and Foa[5 (p. 351)] conclude that "distinctions among obsessions, delusions, and overvalued ideas are not sufficiently clear to be of diagnostic utility."

Differential diagnosis has often proven difficult. For example, DSM-IV[6 (pp. 418-419)] describes OCD as a subset of anxiety disorders in which individuals have "at some point recognized that the obsessions or compulsions are excessive or unreasonable"; however, it offers the option of the specifier "with poor insight," in which "for most of the time during the current episode, the individual does not recognize that the obsessions or compulsions are excessive or unreasonable." Furthermore, DSM-IV allows for the dual diagnosis of delusional psychotic disorder or schizophrenic disorder in addition to OCD. Although traditionally OCD has been distinguished from psychotic disorders on the basis of the compulsions or obsessions "being recognized by the individual as foreign to his personality (and) of which he has insight,"[7 (p. 842)] there is a growing body of literature suggesting that at least some forms of OCD coexist with a psychotic disorder.

In the present investigation, we sought to better understand the relationship between OCD and the psychotic disorders by examining functional magnetic resonance imaging (fMRI) data from a group of schizophrenic patients with varying degrees of OCD symptomatology. We hypothesized that we would find fMRI signal differences when we compared schizophrenic patients who had high levels of OCD with schizophrenic patients who had low levels of OCD. We measured activation of the dorsolateral prefrontal cortex (Broadman's areas 46 and 10) using a word-fluency challenge test.[8] Although the dorsolateral prefrontal cortex has been largely associated with the psychopathology

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of schizophrenia, whereas the orbitofrontal cortex has been associated with the neurobiological basis of OCD,[9,10] several authors[11,12] have suggested that both dorsolateral prefrontal-basal ganglia and orbitofrontal-basal ganglia circuits are important in OCD. The current study was based on imaging data collected with a surface coil, and therefore, technical limitations prevented us from accurately measuring signal changes in the orbitofrontal cortex due to its more medial location. To the best of our knowledge, this study is one of the first to examine OCD among schizophrenic patients from a biological perspective. Thus, the current investigation was considered exploratory.

METHOD

We studied the left dorsolateral prefrontal cortical activation during a word-fluency verbal paradigm of 11 subjects (10 males, one female) meeting the DSM-IV criteria for schizophrenia. The subjects were those described previously in a study of word production applying fMRI methods. The previous study found that among schizophrenic patients and controls, the dorsolateral prefrontal cortex was differentially activated during the word-fluency task.[8] A more thorough description of the informed consent, subjects' intellectual levels, exclusion and inclusion criteria, and the details of the fMRI techniques used is found in the previous work. The patients were all outpatients receiving neuroleptic treatment, and were clinically stable for at least 1 year before the study. Each patient's chart was reviewed by a rater blind to the fMRI data (J.B.L.). The subjects were rated by chart review on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS)[13] and the National Institute of Mental Health's (NIMH) global OCD scale. Subsequently, a clinician familiar with the 11 patients (S.A.G.) reviewed the blinded clinician's scores. There was general agreement between the blind rater (J.B.L.) and the clinician (S.A.G.) familiar with these patients. Disagreements were discussed and a mutual consensus reached in these cases. A ranked order of OCD severity on each of the two OCD scales was assigned to each patient following this chart review and before examination of the fMRI data. This procedure was similar to that used in the Sweedo et al.[14] study of cerebral glucose metabolism in childhood-onset OCD. The subjects were also rated on anxiety with the NIMH global anxiety scale.

The dorsolateral prefrontal cortex was identified using T1-weighted saggital images in a plane parallel to and 7 mm below the anterior commissure-posterior commissure lines. Fifty sequential images of this region were obtained during the word-fluency task, each 3 seconds apart, using a gradient echo pulse sequence (TE = 40 ms, flip angle = 75 degrees). The word fluency task consisted of subjects being asked to generate as many words as possible beginning with the letters F, S, R, and T. Images were taken during alternation of one baseline 30-second period, two 30-second word fluency challenge periods, and two recovery 30-seconds periods. An image matrix of 64 × 128 was used with a 3-mm × 3-mm inplane resolution and a 7-mm slice thickness. Four pixels (6 mm × 6 mm) in the left dorsolateral prefrontal cortex (Broadman's areas 46 and 10) comprised the region of interest (ROI) that was used in the analyses.

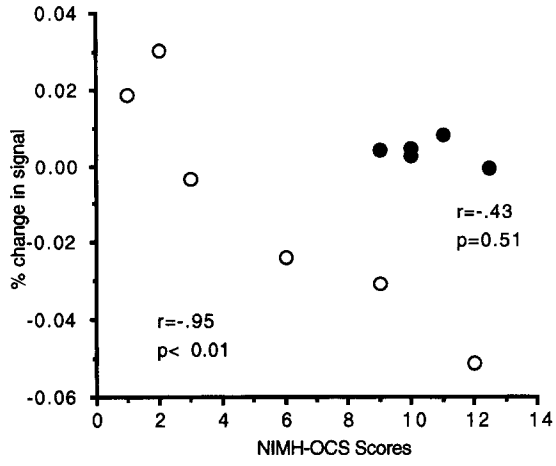

Fig 1. Correlation of frontal cortical activation with NIMH obsessive-compulsive scale. (○) Group I; (●) group II.

The relationship between the ratings of OCD among the 11 patients and the percent change in MRI signal in the dorsolateral prefrontal ROI during the word-fluency task was examined via nonparametric correlational coefficient (Spearman rank order).

RESULTS

There was no correlation between either the Y-BOCS or the NIMH scale ratings of OCD and the percent change in MRI signal. However, on visual inspection of the data, as shown in Figs 1 and 2, it appears that there are two clusters of schizophrenic patients with regard to the relationship between OCD ratings and MRI signal change. The first group (group I) exhibits a linear relationship between OCD scores and MRI signal change, whereas

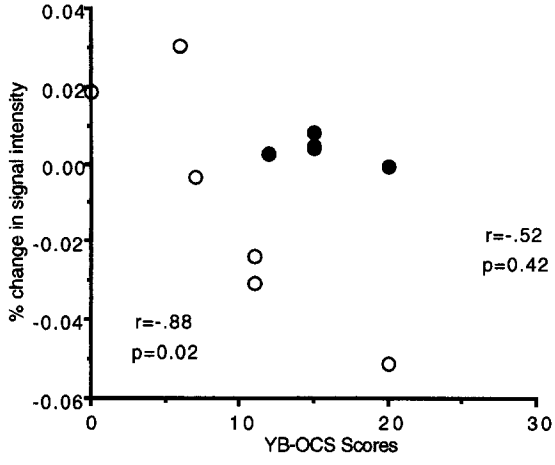

Fig 2. Correlation of frontal cortical activation with Yale-Brown obsessive-compulsive scale. (○) Group I; (●) group II.

Table 1. Mean Score Data

Scale	Group I	Group II
NIMH OCS	5.5 ± 4.3	10.5 ± 1.3
Yale-Brown OCS	9.1 ± 6.6	15.4 ± 2.8
NIMH anxiety scale	6.6 ± 2.5	7.5 ± 2.5

Abbreviation: OCS, obsessive-compulsive scale.

group II displays no apparent relationship. In the group I schizophrenic patients (six subjects), the relationships between MRI signal change, and scores on the NIMH rating scale and the Y-BOCS are strong (.95 and .88, respectively). Among these subjects, greater OCD ratings are associated with less activation of the left dorsolateral prefrontal cortex. In contrast, group II is composed of schizophrenic patients (Figs 1 and 2) who do not show a relationship between OCD ratings and MRI signal change. Examinations of the scores on the NIMH scale of anxiety indicates no significant relationship among either group of subjects and MRI signal change. Group comparisons for symptom severity are shown in Table 1. Mean scores on the NIMH and Y-BOCS OCD scales differ between the two groups, although no difference is found for scores on the NIMH anxiety scale. As shown in Table 2, the two groups also differ on the mean number of hospitalizations, but not the age of onset or duration of illness.

DISCUSSION

In this preliminary and exploratory study of the neurobiological differences between schizophrenic patients with high and low levels of obsessive-compulsive symptomatology, we did not find a significant overall between-group difference in signal activation of the left dorsolateral prefrontal cortex. Given our small sample size, this may be due to limited statistical power. However, we did find a subgroup of schizophrenic patients in whom MRI activation of the left dorsolateral prefrontal cortex during a word-fluency challenge task was significantly associated with severity of OCD symptomatology. In this subgroup, we found that as OCD symptomatology increased, the activation of dorsolateral prefrontal cortex decreased. Since

Table 2. Demographic Data

Variable	Group I	Group II
Age of onset	21.6 ± 4.6	20.2 ± 5.7
No. of hospitalizations	3.7 ± 2.5	8.8 ± 6.3
Duration of illness	12.8 ± 7.6	14.6 ± 5.4

Yurgelun-Todd et al.[8] have demonstrated that left dorsolateral prefrontal activation during a word-fluency challenge is lower in schizophrenics than in controls, the activation pattern in this subgroup suggests that the continuum of OCD symptomatology follows a pattern of MRI activation that parallels the pattern seen in schizophrenic patients; specifically for group I patients, the relationship between OCD symptom ratings and MRI signal change is such that greater OCD symptom ratings are associated with a reduced MRI signal change. In the second group of subjects, no relation between OCD and MRI signal change appears to exist. However, this group presented with more severe symptomatology based on their greater number of hospitalizations and their significantly greater OCD ratings; therefore, it is possible that the relationship between OCD symptomatology and MRI activation is masked by the severity of illness in this group.

If there is a relationship between dorsolateral prefrontal cortical activation and OCD symptomatology in a group of schizophrenic subjects, does this elucidate anything with regard to the neurobiological substrate of OCD? A metabolic abnormality of the orbitofrontal cortex among OCD patients has been established by a number of authors.[3,15-17] However, little mention has been made of the relationship between the dorsolateral prefrontal cortex and OCD. There are at least two notable exceptions. Cummings[11] points out that a number of neurological diseases affecting the basal ganglia (Syndman's chorea, Huntington's disease, postencephalitic Parkinsonism, and strokes to the globus pallidus) have produced de novo OCD symptoms in patients suffering from these disorders. He goes on to suggest that two "parallel circuits," the orbitofrontal-basal ganglia circuit and the dorsolateral prefrontal-basal ganglia circuit, "are particularly important for our understanding of obsessive-compulsive disorder."[11 (p. 496)] Malloy[12] points out that the dorsolateral frontal cortex sends fibers to the orbitofrontal cortex and suggests that an abnormality in this connection contributes to OCD symptoms, possibly via "reduced modulation of limbic anxiety arousal due to interruption of descending DL (dorsolateral) inhibitory influences."[12 (p. 208)] Thus, there is limited literature suggesting that abnormalities of the dorsolateral prefrontal cortex may be associated with OCD symptoms, either as an anatomically and behavior-

ally relevant nearby frontal-basal ganglia circuit (Cummings' point), or through the direct effect of the two circuits on one another (Malloy's point). In support of the latter perspective, a recent review of the prefrontal cortex[18] concludes that "the dorsolateral prefrontal cortex is poised to serve as the principal organ for integrating information from the three (prefrontal-subcortical) circuits," one of these being the orbitofrontal-subcortical circuit.[18 (p. 5)]

Recognizing the limitations of a retrospective chart-review study and the fact that we divided our cohort of schizophrenic patients after examining the MRI-OCD rating scale relationships, we must regard this study as exploratory and preliminary. However, the findings of this study are consistent with the limited previous literature implicating the interplay of the dorsolateral prefrontal with the orbitofrontal cortices in OCD. In addition, the findings are suggestive of a relationship between OCD severity and neurophysiological activity that has been associated with schizophrenia.[8] Indirectly then, this seems to offer biological evidence in favor of the argument that in some cases, OCD symptomatology is not entirely independent from the psychotic disorders.[1-5] Further, the findings suggest a possible line of inquiry to further clarify the biological interface between OCD and schizophrenia.

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