Obsessive-Compulsive Disorder: Defining the Phenotype

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Characterizing the obsessive-compulsive disorder (OCD) phenotype is important for treatment and etiologic studies. This article describes a family-study approach for identifying the spectrum of conditions related to OCD and subtyping OCD cases into homogeneous subtypes.

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Accurate diagnosis of obsessive-compulsive disorder (OCD) is necessary for planning appropriate treatment strategies, prognostication, conducting research into the etiology of the disorder, and instituting preventive programs. The success of these endeavors relies greatly on the specificity of the clinical diagnostic definition, which is especially important given the absence of laboratory tests to aid in the diagnostic process. On the surface, it would appear that OCD has an advantage over other conditions. It is one of the few psychiatric disorders for which there are pathognomonic features. These features, obsessions and compulsions, are necessary for the diagnosis. For a diagnosis of OCD to be made, the current nomenclature requires only that these symptoms result in impairment for the individual.

Despite this apparent advantage, defining the OCD phenotype remains problematic. In both clinicians' offices and research studies, it is often difficult to confidently ascertain the presence of obsessions and compulsions. Patients and research subjects often are secretive about these symptoms and avoid reporting them or disguise them. Furthermore, the resemblance of these symptoms to many of the egosyntonic obsessive-compulsive personality traits may make it difficult to establish their presence. Additionally, OCD, like many other psychiatric conditions, has a broad range of psychiatric syndromes that appear related to the condition. Finally, there is growing evidence that OCD may be a heterogeneous disorder with several distinct etiologies.

ETIOLOGY

Ideally, in medicine, classification is based on etiology. The pathophysiologic process results in specific clinical syndromes. This process is illustrated by the case of tertiary syphilis. Infection with the spirochete results in typical cerebral pathology, which ultimately leads to the clinical syndrome of general paresis of the insane (GPI). However, prior to the recognition of this syndrome, cases of GPI were included with cases of other psychotic or dementing conditions, resulting in misclassification.

Etiologic heterogeneity is an important issue for the researcher. If subjects are not classified as cases, yet share the etiology with those that are, the power of the study will be substantially reduced. This is problematic given that recruiting sufficient cases in an etiologic study is difficult and costly. If, on the other hand, subjects are classified as cases, yet have a different etiology from other cases, the resultant misclassification will reduce the likelihood of detecting important relationships.

Given that there is no known etiology for most cases of OCD, the importance of defining distinct syndromes is paramount. As described in the classic article by Robins and Guze,[1] several clinical characteristics, preferably in combination, are useful for differentiating syndromes. These characteristics include response to treatment, course

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and outcome, and familial relatedness. We have employed a family-study approach to begin to identify syndromes that may be etiologically related to OCD.

FAMILY-STUDY APPROACH

From a family perspective, the phenotypic spectrum of a condition comprises those disorders that occur more commonly among the relatives of case probands. With respect to OCD, the first step is to determine whether OCD itself is more common in the relatives of case probands than those of control probands. In the Johns Hopkins OCD Family Study, [2] we found that 12% of case relatives exhibited OCD compared with 3% of control relatives ($p = .001$). This is consistent with findings from other family studies[3] and indicates that there is familial transmission of obsessive-compulsive disorder. However, familiality extends beyond OCD. In the anxiety disorder domain, generalized anxiety disorder, separation anxiety disorder, panic disorder, and agoraphobia were significantly more common in the relatives of case probands than those of control probands.[4] Specific and social phobias, however, were not significantly different between the 2 groups. Among the affective disorders, recurrent major depression was significantly more common in case relatives than control relatives.

Bienvenu et al.[5] investigated the so-called "OCD spectrum" disorders in the same family study. Body dysmorphic disorder was significantly more common in case than control relatives. Hypochondriasis was more common in case relatives, although this was not significant. The eating disorders—anorexia and bulimia nervosa—were not significantly more common in the case relative group in this study. Kleptomania, pathological gambling, and pyromania—the impulse-control disorders—were rare in this sample. The grooming disorders—nail biting, pathologic skin picking, and trichotillomania—individually, were not significantly more common in case than in control relatives, but, as a group, were significantly more common in case relatives.

It has long been recognized that there is a familial relationship between OCD and tic disorders.[6] In the Johns Hopkins OCD Family Study, Grados et al.[7] found that tic disorders were more than twice as common among case relatives than control relatives.

Samuels et al.[8] reported that only obsessive-compulsive personality disorder, of all the DSM-IV personality disorders, was related to OCD. This personality disorder was significantly more common in case relatives than control relatives. Personality trait measures were also different between the 2 groups. The mean score of neuroticism was significantly greater in case relatives than control relatives (52.1 vs. 48.0; $p = .01$). Findings from the Johns Hopkins OCD Family Study and other OCD family studies, therefore, indicate a rather broad OCD-related phenotype.

These findings suggest 2 possibilities. First, the range and nature of syndromes related to OCD resemble Janet's broad, unitary construct of psychasthenia.[9] Second, the breadth of the psychopathology may indicate the presence of more homogeneous subgroups within the broad OCD spectrum. Support for familial heterogeneity is provided by segregation analysis conducted in the Johns Hopkins sample. We found a major gene effect in OCD, but there was evidence for heterogeneity based on the gender of the proband.[10] The heterogeneity of OCD based on other clinical features deserves further study.

OCD SUBTYPES

Several clinical characteristics useful for subtyping OCD have been suggested. These include age at onset of OCD and the presence of specific clusters of OCD symptoms, tic disorders, and comorbid psychiatric disorders. In this article, we will use age at onset and OCD symptomatology to illustrate possible subtypes.

Early age at onset has been related to increased familial loading in many medical conditions.[11] Pauls et al.[3] reported higher familial risk in OCD probands with an early age at onset. In the Johns Hopkins OCD Family Study, no case proband with an age at onset of OCD older than 17 years had a first-degree relative with OCD,[2] indicating that cases of OCD with earlier onset age are more likely to have a familial form of the condition. Hence, distinguishing early and late onset of OCD may prove useful for subgrouping cases.

There is long tradition of subgrouping OCD cases based on the specific obsessions and compulsions the patient exhibits. Subgrouping has been most usefully applied in clinical practice, where "checkers" and "cleaners" are distinguished for practical therapeutic purposes.[12] More recently, factor analytic studies of the specific obsessions and compulsions have been conducted using the Yale-Brown Obsessive Compulsive Scale Symptom Checklist.[13] These studies[14–17] have found factor solutions that have ranged from 3 to 5 factors. Despite the differences in the number of reported factors, the different studies report similar symptom constellations in their respective factors. This is all the more impressive given that the clinical methods used to record the symptoms, and the analytic methods to derive the factors, varied.

In addition to these tests of internal validity, other studies have examined the external validity of the derived factors. Rauch et al.[18] have shown differences in cerebral blood flow in specific anatomical regions based on symptom factor scores. The same group[17] has reported prognostic differences between these factors. Finally, Alsobrook et al.,[19] using segregation analyses, have shown differences in the patterns of inheritance for the different factors. Together, these studies suggest that distinguishing symptom-based subgroups may be a promising approach for the

identification of clinically and etiologically relevant, homogeneous classes within the OCD phenotype. Further research in this and other subtyping domains is important.

SUMMARY

Using a family-study approach, we have shown that the phenotypic spectrum of OCD is relatively broad and that promising leads for identifying homogeneous subgroups also exist within the OCD diagnosis. Further elucidation of the OCD phenotype is important for both clinical and research purposes. Studying additional clinical characteristics, such as treatment response and course and outcome, may identify distinct subgroups of OCD patients. Investigating potential endophenotypes, such as neuroanatomic and neuropsychological measures, may identify conditions with a common underlying pathophysiology.

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