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Is Compulsive Hoarding a Genetically and Neurobiologically Discrete Syndrome? Implications for Diagnostic Classification

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Although standard diagnostic classifications consider obsessive-compulsive disorder (OCD) to be a single diagnostic entity, it has become clear that it is a heterogeneous disorder, with great variability in clinical presentation. This heterogeneity has complicated the interpretation of clinical, neurobiological, and genetic studies in OCD. Therefore, researchers have sought to identify clinically meaningful phenotypes that might be more homogeneous and heritable to facilitate our understanding of the etiology and pathophysiology of OCD and ultimately lead to improved treatments (1). Factor analytic studies have consistently identified four principal OCD symptom dimensions: 1) harm-related, aggressive, sexual, and religious obsessions with checking compulsions; 2) symmetry obsessions with arranging and repeating compulsions; 3) contamination obsessions with cleaning compulsions; and 4) hoarding and saving symptoms (1, 2). These symptom factors are relatively stable over time and show different patterns of genetic inheritance, age at onset, comorbidity, and treatment response (see 1 for review). Cluster analyses, which seek to identify mutually exclusive, categorical subgroups, indicate that some of these symptom factors, such as hoarding, may constitute discrete subtypes of OCD (3, 4).

Hoarding is defined as the acquisition of and inability to discard items, even though they appear (to others) to have no value (5). Hoarding behavior has been observed in several neuropsychiatric disorders, including schizophrenia, dementia, eating disorders, autism, and mental retardation, as well as in non-clinical populations, but it is most commonly found in OCD (6). 30% to 40% of OCD patients report hoarding and saving symptoms (6–8), and about 10% to 15% have hoarding as their most prominent symptom factor (3, 6). Compulsive hoarding is most commonly driven by obsessional fears of losing important items that the patient believes will be needed later, distorted beliefs about the importance of possessions, excessive acquisition, and exaggerated emotional attachments to possessions (5). Compulsive hoarding and saving leads to clutter that can cover living and work spaces, rendering them unusable. Hoarding frequently causes significant impairment in social and occupational functioning. In severe cases, it can produce health risks from infestations, falls, fires, and inability to cook or eat in the home (6).

In this issue of the *Journal,* Jack Samuels, Ph.D., et al. report results from the OCD Collaborative Genetics Study, finding "suggestive" linkage of compulsive hoarding to a marker on chromosome 14 in families with OCD. The linkage became stronger when only families with two or more family members with compulsive hoarding were tested. Compulsive hoarding is well known to run in families. Hoarding behaviors are significantly more prevalent in the relatives of hoarding OCD patients than nonhoarding OCD patients (9). In the OCD Collaborative Genetics Study, hoarding was the most strongly familial of the OCD symptom factors, with robust correlations among sibling pairs (10). Only two previous genetic studies have examined the hoarding phenotype. Lochner et al. (8) found that the *met/met* (L/L) genotype of the catechol *O*-methyltransferase *val*158*met* polymorphism on chromosome 22q11 was significantly more prevalent in Afrikaner OCD patients with

hoarding symptoms than in Afrikaner nonhoarding OCD patients or comparison subjects. A genome scan conducted in sibling pairs with Tourette's syndrome found significant linkage of the hoarding phenotype with markers on chromosomes 4q34–35, 5q35.2–35.3, and 17q25 (11). Although Samuels et al. did not replicate these prior findings, they provide the first identification of a susceptibility locus for hoarding in families with OCD and add to the mounting evidence indicating that compulsive hoarding is an etiologically discrete phenotype.

Frost and Hartl (12) posited that hoarding and saving symptoms are part of a discrete clinical syndrome. The core symptoms are urges to save, difficulty discarding, and excessive acquisition, but the syndrome also includes indecisiveness, perfectionism, procrastination, difficulty organizing tasks, and avoidance. In addition, many compulsive hoarders are slow in completing tasks; frequently late for appointments; and display circumstantial, overinclusive language. Patients who have hoarding as their most prominent and distressing OCD symptom dimension and display these associated symptoms are considered to have the "compulsive hoarding syndrome" (6, 13).

Compulsive hoarders differ in many important ways from other OCD patients. Compared with nonhoarding OCD patients, OCD patients with hoarding symptoms have earlier age at onset of OCD symptoms; greater prevalence of symmetry, ordering, counting compulsions, and indecisiveness (9); older age when presenting for treatment; more severe family and social disability, anxiety, depression; lower insight; and lower global functioning (6, 8, 13). They also show a different pattern of comorbidity, with significantly greater prevalence of social phobia, generalized anxiety disorder, specific phobias, bipolar II disorder, dysthymia, personality disorders, and pathological grooming disorders (8, 9). Hoarders often have less insight into their symptoms than do nonhoarding OCD patients (6, 9), which may make them less likely to seek treatment.

Early studies investigating the influence of OCD symptom factors on treatment response found that hoarding symptoms were associated with poor response to serotonin reuptake inhibitors (SRIs). However, several subsequent studies did not confirm this association (14). In fact, the only prospective trial of standardized pharmacotherapy in compulsive hoarders to date found that they responded equally as well to the SRI paroxetine as nonhoarding OCD patients. Hoarding symptoms improved as much as other OCD symptoms, and no correlation was found between hoarding severity and treatment response (14). However, hoarding has consistently been associated with poor response to cognitive behavior therapy for OCD (15, 16). Taken together, these studies suggest that compulsive hoarding is a clinically distinct subtype of OCD.

Functional neuroimaging studies suggest that compulsive hoarding is also a neurobiologically distinct subtype or variant of OCD. Patients with the compulsive hoarding syndrome were found to have a different pattern of cerebral glucose metabolism than both healthy comparison subjects and nonhoarding OCD patients. Hoarders did not have the characteristic hypermetabolism in orbitofrontal cortex, caudate nuclei, and thalamus seen in nonhoarding patients. Instead, they showed significantly lower activity in the cingulate cortex (17). A symptom provocation study found that the pattern of brain activation associated with provocation of compulsive hoarding symptoms was different than that associated with provocation of other OCD symptom factors (18). Compulsive hoarders also appear to have a different pattern of neurocognitive deficits than nonhoarding OCD patients, reporting significantly more difficulty making decisions (6, 9) and showing impaired decision making performance, as well as different autonomic skin conductance responses (19).

The findings reviewed in this editorial raise questions about the nosology of compulsive hoarding and OCD. Currently, hoarding is listed in DSM-IV as a symptom of obsessive-compulsive personality disorder. However, the available evidence argues strongly against this classification. Hoarding severity does not correlate with the severity of obsessive-compulsive personality disorder symptoms (6). Of the eight diagnostic criteria for DSM-IV obsessive-compulsive personality disorder, hoarding was found to have the lowest specificity and predictive value (20). Compulsive hoarders have no more obsessive-compulsive personality disorder traits than comparison subjects (6), and only a small percentage of them meet criteria for obsessive-compulsive personality disorder (9). Therefore, hoarding should be removed from the diagnostic criteria for obsessive-compulsive personality disorder.

Phenomenological studies also suggest that compulsive hoarding is not simply one of the several component dimensions of OCD. While the harm/checking, contamination/cleaning, and symmetry/rituals symptom factors are strongly intercorrelated, hoarding does not correlate strongly with the other major factors, in either clinical and nonclinical cohorts (2, 6, 21). OCD patients do not report any more hoarding symptoms than healthy com-

parison subjects or patients with other disorders (21). Moreover, studies that have specifically recruited compulsive hoarders have found that many of them do not have other OCD symptoms (5, 6, 14, 21). Such patients would have been excluded by previous studies that used structured diagnostic interviews that did not include hoarding symptoms in their screening or diagnostic criteria for OCD.

Thus, compulsive hoarding syndrome appears to be a discrete entity, with a characteristic profile of core symptoms that are not strongly correlated with other OCD symptoms, distinct susceptibility genes, and unique neurobiological abnormalities that differ from those in nonhoarding OCD. These findings suggest that compulsive hoarding may be a separate but related OCD-spectrum disorder that is frequently comorbid with OCD, similar to the way body dysmorphic disorder and trichotillomania are now conceptualized (22).

The OCD Collaborative Genetics Study has conducted the largest genome-wide scan for OCD susceptibility genes to date and used rigorous diagnostic methods that included detailed questions about hoarding symptoms, which have often been neglected in previous studies of OCD. However, the linkage analysis by Samuels et al. has one important weakness. The phenotype examined was the presence of any hoarding symptoms, rather than clinically significant compulsive hoarding. Of the 235 OCD cases classified in this study as having compulsive hoarding, 36% had mild or no distress from their hoarding symptoms, and 53% spent less than 1 hour per day occupied with hoarding symptoms. Unless they had significant functional impairment resulting from their hoarding and clutter, these subjects would not have met the accepted criteria (12) for clinically significant compulsive hoarding: 1) the acquisition of and failure to discard a large number of possessions that appear (to others) to be useless or of limited value; 2) living or work spaces are sufficiently cluttered so as to preclude activities for which those spaces were designed; and 3) significant distress or impairment in functioning is caused by the hoarding behavior or clutter. Hence, the linkage findings may have been diluted by the inclusion of subjects who had only mild hoarding symptoms but not primary compulsive hoarding. Future studies should examine the more well-defined categorical phenotype of compulsive hoarding syndrome to improve their chances of identifying the specific genes involved in this condition.

Much more research is needed to delineate the epidemiology, etiology, genetics, pathophysiology, neurobiology, and treatment of compulsive hoarding. Unfortunately, no epidemiological study of compulsive hoarding has ever been conducted. Therefore, its prevalence must be determined in population-based studies, not just in clinical cohorts. We must determine how many compulsive hoarders meet DSM criteria for OCD and decide whether those criteria need to be changed to include compulsive hoarding symptoms. We must characterize compulsive hoarding in the elderly and determine whether late-onset compulsive hoarding is similar to early-onset hoarding. Studies of brain structure and function, neuropharmacology, neurochemistry, endocrine, and immune function must be done to determine the pathophysiology of compulsive hoarding and identify biological markers that might aid in diagnosis or provide targets of treatment. Finally, better treatments for compulsive hoarding must be discovered through clinical trials, particularly of non-SRI medications, such as stimulants, antiglutamatergic agents, and cognitive enhancers.

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