

**Obsessive Compulsive Foundation, Inc.****Compulsive Hoarding Website****The Neurobiology and Medication  
Treatment of Compulsive Hoarding**

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This is the third in a series of articles on compulsive hoarding presented in the OC Foundation newsletter.

Although standard psychiatric diagnostic classifications, such as, the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), consider obsessive compulsive disorder (OCD) to be a single entity, it has become clear that several different symptom dimensions of OCD exist. Large-scale studies of OCD symptoms have identified four principal symptom factors: 1) aggressive, sexual, and religious obsessions with checking compulsions; 2) symmetry obsessions with ordering, arranging, and repeating compulsions; 3) contamination obsessions with washing and cleaning compulsions; and 4) hoarding, saving, and collecting symptoms. These symptom dimensions appear to be relatively stable over time. Different symptom factors show different patterns of genetic inheritance and association with other psychiatric disorders. Perhaps most importantly, the symptom factors differ in their response to treatment. Thus, OCD appears to be a multidimensional and heterogeneous disorder. Despite this heterogeneity, virtually all prior neurobiological and treatment studies of OCD have grouped patients with diverse symptom patterns together.

Hoarding is defined as the acquisition of, and inability to discard worthless items even though they appear (to others) to have no value. Hoarding and saving behavior has been observed in several neuropsychiatric disorders, including schizophrenia, dementia, eating disorders, autism, mental retardation, as well as in non-clinical populations; but it is most commonly found in people with OCD. Between 18% to 42% of OCD patients have hoarding and saving compulsions; and about 10-20% of all OCD patients are thought to have compulsive hoarding as their most prominent and distressing type of OCD. This means there are between of 600,000 to 1.2 million people who hoard in the U.S. alone. Dr. Randy Frost and colleagues argue persuasively that hoarding and saving symptoms are part of a discrete clinical syndrome that also includes indecisiveness, perfectionism, procrastination, difficulty organizing tasks, and avoidance. OCD patients who have hoarding and saving as their most prominent and distressing type of OCD and show these other associated symptoms are considered to have the compulsive hoarding syndrome.

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, and excessive emotional attachments to possessions. Hoarders usually fear making "wrong decisions" about what to discard and what to keep, so they acquire and save items to prepare for every imaginable contingency. Two types of saving have been identified: instrumental saving, where possessions fulfill a specific desire or purpose, and sentimental saving, where possessions represent extensions of the self. Compulsive hoarding is further conceptualized as an avoidance behavior tied to indecisiveness and perfectionism. By saving possessions, the compulsive hoarder postpones making the decision to discard something; and therefore, avoids experiencing anxiety about making a mistake or being less than perfectly prepared. The most commonly saved items include newspapers, magazines, old clothing, bags, books, mail, notes, and lists. Living spaces become so cluttered that they cannot be used for the activities for which they were designed, causing significant impairment in social and/or occupational functioning.

#### Differences Between Compulsive Hoarding and Non-Hoarding OCD

Many clinicians and investigators believe that the compulsive hoarding syndrome is a distinct variant or subtype of OCD. Few studies have directly compared patients with the compulsive hoarding syndrome to non-hoarding OCD patients; but all of the studies that have made the comparison found greater functional disability and more severe psychiatric symptoms in hoarders than in non-hoarders. Compared to non-hoarding OCD patients, hoarders score higher on anxiety, depression, dependent and schizotypal personality disorder symptoms, and family and social disability. Our group found that compulsive hoarders had significantly higher anxiety and lower global

functioning than non-hoarders and did not respond as well to intensive, multi-modal treatment as non-hoarding OCD patients. Several studies have found that hoarders are less likely to be married than non-hoarders, indicating greater social dysfunction. A survey of elderly hoarders found that hoarding constituted a physical health threat in 81% of identified cases, including threat of fire hazard, falling, unsanitary conditions, and inability to prepare food. Hoarders often have less insight into their symptoms than non-hoarding OCD patients, making them less likely to seek treatment. Compulsive hoarders may have a different pattern of neurocognitive and information processing deficits than non-hoarding OCD patients. Taken together, these studies showed that patients with the compulsive hoarding syndrome have a unique, behavioral profile and a characteristic pattern of associated symptoms and functional disability.

Genetic and family studies suggest that compulsive hoarding may have a different pattern of genetic inheritance and comorbidity (coexisting illnesses) than other OCD symptom factors. The hoarding/saving symptom factor has a recessive inheritance pattern, whereas the aggressive/checking and symmetry/order symptom factors show a dominant pattern. A genome-wide scan conducted in sibling pairs with Tourette's Syndrome (in which there is a very high prevalence of OCD symptoms) found that the hoarding/saving symptom factor was significantly associated with genetic markers on chromosome 4, 5, and 17. One study found that 16 of 19 OCD patients with prominent compulsive hoarding (84%) reported a family history of hoarding behaviors in at least one first-degree relative, while only 37% reported a family history of DSM-IV OCD. A family study of OCD found that, compared with people with non-hoarding OCD, compulsive hoarders had a greater prevalence of social phobia, personality disorders, and pathological grooming disorders, such as, trichotillomania, skin-picking, and nail-biting, and higher rates of hoarding and tics in first-degree relatives. These studies indicate that the compulsive hoarding syndrome may represent a distinct subgroup or variant of OCD that may be caused by different genetic and familial factors than non-hoarding OCD.

### Medication Treatment for Compulsive Hoarding

There are two types of treatment that have been proven to be effective for OCD and are considered standard, front-line treatments: pharmacotherapy (treatment with medications) and cognitive-behavioral therapy (CBT), using the technique of exposure and response prevention (E&RP). Effective medication treatments for OCD include the serotonin reuptake inhibitor (SRI) medications, such as, citalopram (Celexa), escitalopram (Lexapro), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), and sertraline (Zoloft), and the tricyclic antidepressant clomipramine (Anafranil), which also strongly inhibits the reuptake of serotonin. The compulsive hoarding syndrome, however, has often proven refractory to treatment with these standard medications. In several studies of OCD treatment, hoarding and saving compulsions have been strongly associated with poor response to SRIs. A small study using open treatment with paroxetine or CBT for OCD patients found that nonresponders were significantly more likely to have hoarding/saving symptoms than responders. Hoarding and saving symptoms were a significant predictor of non-response. Another case series described treatment response in 18 compulsive hoarders treated openly with a variety of SRIs. Only one of the 18 had a marked response; nine had partial responses; and nine had minimal or no response. In an analysis of large-scale, multi-center, controlled trials of SRI treatment for patients with OCD, higher scores on the hoarding symptom dimension predicted poorer response to SRI treatment, after controlling for baseline severity. Thus, compulsive hoarding is a clear predictor of poor response to standard anti-obsessional medications. Despite this fact, no prior medication treatment study has specifically targeted the compulsive hoarding syndrome.

Thus far, the only type of treatment that has been found to be broadly effective for the compulsive hoarding syndrome is CBT that is specifically tailored to its symptoms and associated features. CBT for compulsive hoarding has been well described in the first two articles in this series by Drs. Randy Frost and Gail Steketee, and Karron Maidment, respectively. However, that does not mean that medications do not have a role in treating this syndrome; they are often necessary. Currently, the usual approach to treating compulsive hoarding with medications is still to start with SRIs. This is done for several reasons. Firstly, even though hoarding/saving symptoms are statistical predictors of poor response, there are still some compulsive hoarders that do respond to SRIs. Secondly, most hoarders also have other OCD symptoms that may respond to SRIs. Thirdly, compulsive hoarders frequently have coexisting illness, such as, depression and other anxiety disorders, that may respond well to SRI treatment. Mood stabilizers, such as, lithium, valproic acid (Depakote), and lamotrigine (Lamictal) are often added for patients with coexisting Bipolar Disorder (Manic-Depression). Anti-anxiety drugs, such as, buspirone (Buspar) and the benzodiazepenes, clonazepam (Klonopin), lorazepam (Ativan), and others, are sometimes added for patients with other coexisting anxiety disorders. Stimulant medications such as methylphenidate (Ritalin and others) and dextroamphetamine (Dexedrine, Adderall, and others), are often added for coexisting attention-deficit/hyperactivity disorder (ADHD). Antipsychotic drugs are used for patients with coexisting psychotic disorders, such as, schizophrenia and schizoaffective disorder. Because these coexisting disorders can interfere with CBT, they must

often be stabilized first before CBT can begin to be effective.

If adequate trials of SRIs (at the high doses needed for optimal anti-obsessional effect, for at least 12 weeks) fail to improve a patient's hoarding/saving symptoms, secondary (adjunctive) medications are often added on to the SRI. There are several medications that have been found to be at least partially effective for OCD symptoms that did not respond adequately to SRIs, including the atypical antipsychotic medications, risperidone (Risperdal), olanzapine (Zyprexa), and quetiapine (Seroquel). Older, typical antipsychotic medications, such as, haloperidol (Haldol) and fluphenazine (Prolixin), are also effective adjuncts to SRIs, particularly for patients with coexisting tic disorders, such as, Tourette's Syndrome, coexisting psychotic disorders, or schizotypal personality disorder. However, it is not known whether any of these medications are effective for the compulsive hoarding syndrome, since no medication study has ever specifically measured the response of hoarding/saving symptoms to medication treatment. Moreover, there has been very little investigation of the neurobiology of compulsive hoarding in humans. A better understanding of the neurobiology of compulsive hoarding is needed to develop more effective medication treatments for this syndrome.

### Neurobiology of Compulsive Hoarding

There is growing evidence of neurobiological heterogeneity within the diagnosis of OCD. Differences in brain structure and function may underlie differences in symptoms, comorbidity, and treatment response between the various symptom factors. Identifying neurobiological differences between OCD subtypes may allow for prediction of differential treatment response and the development of more syndrome-specific treatments. Recent data regarding the functional neuroanatomy of obsessive-compulsive hoarding has shed light on both the clinical presentation and poor treatment response of this syndrome.

Our group recently conducted a positron emission tomography (PET) brain imaging study that measured cerebral glucose metabolism (a measure of brain activity) in patients with the compulsive hoarding syndrome, compared with non-hoarding OCD patients and controls without any psychiatric disorder. We found that compulsive hoarders had a unique pattern of brain activity that was distinct from that seen in either non-hoarding OCD patients or controls. Compulsive hoarders had significantly lower metabolism in the posterior cingulate gyrus and occipital cortex (a brain region involved in visual processing) compared to controls, whereas non-hoarding OCD patients had significantly higher glucose metabolism in bilateral thalamus and caudate, structures previously found to have elevated activity in OCD. Hoarders and non-hoarding OCD patients also differed from each other, with hoarders having significantly lower metabolism in the dorsal (superior) part of the anterior cingulate gyrus and thalamus than non-hoarding OCD patients. Across all OCD patients studied, hoarding severity was significantly correlated with lower activity throughout the dorsal anterior cingulate gyrus. Our findings suggest that the compulsive hoarding syndrome may be a neurobiologically distinct variant of OCD. In addition to the observed differences in cerebral glucose metabolism, our results raise the question of whether compulsive hoarders also have structural brain abnormalities and neurocognitive deficits that differ from those seen in non-hoarding OCD patients.

The symptoms of the compulsive hoarding syndrome may be mediated by diminished activity in several parts of the cingulate cortex, a structure on the midline surface of the brain. The cingulate cortex is connected with both the limbic system, the more primitive part of the brain that mediates emotional responses, and with the associative neocortex, which mediates higher-order cognition. Thus, the cingulate cortex is involved with both emotional and cognitive processing. Functions of the anterior cingulate cortex include focused attention, executive control, motivation, assigning emotional importance to stimuli, monitoring response conflict, emotional self-control, problem-solving, error detection, and response selection. The anterior cingulate also plays a key role in decision-making, especially in choosing between multiple conflicting options. The posterior cingulate cortex is involved in the monitoring of visual events, spatial orientation, memory, and processing of emotional stimuli. It modulates activity in several brain regions involved in the putative functional neurocircuitry of OCD, including the orbitofrontal cortex, anterior cingulate cortex, and caudate. Thus, lower activity in both the anterior and posterior parts of the cingulate gyrus may mediate the remarkable difficulty in making decisions, attentional problems, and other cognitive deficits seen in compulsive hoarders.

Diminished activity in the cingulate cortex may also contribute to the poor response of the compulsive hoarding syndrome to standard anti-obsessional treatments. Lower activity in the anterior cingulate gyrus has been strongly associated with poor response to antidepressant treatment, while lower posterior cingulate gyrus activity has been found to correlate with worse response to fluvoxamine and cingulotomy in patients with OCD. Thus, the finding of low cingulate gyrus activity in the compulsive hoarding syndrome is quite consistent with its poor response to standard treatments for OCD.

### Future Strategies for Treatment Development

Future medication treatment approaches should target brain dysfunctions specifically associated with compulsive hoarding, such as, the diminished activity in the Cingulate Cortex. Future treatment approaches should also target the information-processing deficits that appear to be present in patients with the compulsive hoarding syndrome, including faulty decision-making, deficits in organization/categorization, and problems with attention and memory. No study to date has measured neurocognitive functioning in compulsive hoarders, but if consistent cognitive deficits were found, specific treatment approaches could be developed to ameliorate those deficits, potentially resulting in improvement in the overall syndrome.

Possible strategies to improve underlying cognitive deficits in compulsive hoarders might include cognitive enhancers, such as donepezil (Aricept) or galantamine (Reminyl), which are used to treat Alzheimer's disease and other types of dementia. These medications improve memory, attention, and overall cognitive functioning in demented patients by increasing the availability of the neurotransmitter, acetylcholine, in the cerebral cortex. Acetylcholine is critically important for memory and cognitive functioning, and is severely diminished in the brains of patients with Alzheimer's disease (but not in OCD). It is unclear whether cognitive enhancers can improve cognitive function in non-demented patients, but preliminary studies suggest that they may improve attention and cognitive functioning in patients with ADHD. These drugs are now also being tried for some patients with Tourette's Syndrome but have not yet been tried in OCD. We plan to try them in patients with the compulsive hoarding syndrome, as adjuncts to standard medications. We hope that they will improve attention, organization/planning abilities, and decision-making in compulsive hoarders, thereby making it easier for patients to discard items and organize their time and living space.

Another class of medications that could potentially prove helpful for the compulsive hoarding syndrome includes the stimulants frequently used for patients with ADHD. These medications improve attention, alertness, and information processing speed by increasing the function of the neurotransmitters, dopamine and norepinephrine. Stimulant medications have been shown to increase the functioning of brain areas, such as, the cingulate cortex, involved in attention and executive functioning. Because people with the compulsive hoarding syndrome appear to have diminished activity in the Cingulate Cortex, we predict that they might benefit from treatment with stimulants. We are now testing stimulant medications as adjuncts to standard medications for the treatment of compulsive hoarding.