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Comorbidities of obsessive and compulsive symptoms in Huntington disease

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Abstract

Although current reports document a high rate of obsessive and compulsive symptoms (O/Cs) in Huntington disease (HD), there have been no studies published that have made an attempt to identify comorbidities of O/Cs in HD. We examined O/Cs in 1,642 individuals with a diagnosis of HD. Of those endorsing significant O/Cs (27.2%), nearly one-quarter reported obtaining treatment for OCD. Individuals with HD and O/Cs were older, had poorer functioning, and a longer duration of illness than those without O/Cs. Individuals with HD and O/Cs endorsed significantly higher psychiatric comorbidities of depression, suicidal ideation, aggression, delusions and hallucinations. Participants with the most severe O/Cs had greater bradykinesia and worse performance on the Stroop task, a measure of executive function. Clinicians should be aware that patients with HD and O/Cs might have a somewhat different clinical picture from those without, and may require a specialized treatment plan.

Keywords

Huntington disease; obsessive compulsive symptoms; comorbidity; cognition; motor signs; psychopathology

INTRODUCTION

Obsessive and compulsive symptoms (O/Cs) are common in Huntington disease (HD) with 20 to 50 percent of HD patients reporting O/Cs (Anderson et al., 2001; Beglinger et al.,

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2007; Marder et al., 2000; Paulsen et al., 2001). These rates are greater than observed in the general population. For example, Degonda and colleagues (Degonda et al., 1993) reported a 5.5% weighted lifetime prevalence of O/Cs by age 30 in the general population (excluding those meeting criteria for obsessive compulsive disorder; OCD).

The higher rate of O/Cs in HD is not surprising, given that distinctive neuropathological changes seen in HD are similar to those hypothesized to be responsible for OCD, namely dysfunction of cortico-striatal connections (Hedreen et al., 1995; Nordahl et al., 1989; Salloway et al., 1994; Sawle et al., 1991). Magnetic resonance imaging studies in HD have shown quantifiable decline in caudate volume over time (Aylward et al., 2000; Aylward et al., 1997; Paulsen et al., 2008; Rosas et al., 2001). As the disease advances, widespread cerebral atrophy occurs including cortical regions (Hedreen et al., 1991; Rosas et al., 2002; Vonsattel et al., 1985).

Disruption of fronto-striatal connections has been observed in primary OCD. Dysfunction in the orbitofrontal cortex, which has extensive connections to the basal ganglia, has been reported in imaging studies of individuals with OCD (Nordahl et al., 1989; Sawle et al., 1991). Functional imaging studies have implicated both striatal and cortical abnormalities underlying O/Cs in patients with primary OCD. Results of resting PET studies indicate increased orbitofrontal activity (Nordahl et al., 1989; Sawle et al., 1991) and caudate metabolism (Baxter et al., 1992; Benkelfat et al., 1990) in OCD patients. Reports suggest that normalization of caudate (Baxter et al., 1992; Benkelfat et al., 1990) and orbitofrontal cortex activation (Benkelfat et al., 1990; Swedo et al., 1992) occurs following remission of OCD symptoms.

Because the neuropathology of HD involves neural areas implicated in primary OCD, these changes in brain circuitry may be responsible for O/C symptoms in HD. Thus we would expect to see increased frequency of O/Cs in a movement disorder such as HD, due to striatal pathology and disruption of fronto-striatal circuitry. Within the past decade several researchers have characterized the interplay of O/Cs in basal ganglia disorders (Cath et al., 2001; Laplane et al., 1989; Swedo et al., 1998). The purpose of the current study is to better characterize O/Cs in HD. Although current reports document a high rate of O/Cs in HD, to date there have been no studies published that have made an attempt to identify and understand the association of comorbidities with O/Cs in HD. It is possible that those patients who have pre-existing psychiatric conditions are the ones primarily predisposed to experience O/Cs. It is also possible that O/Cs increase in severity commensurate with other clinical symptoms of disease, such as motor and cognitive dysfunction. Exploration of comorbidities associated with O/Cs in HD may offer insight into underlying mechanisms in these disorders.

METHODS

Participants

Participants were individuals with a clinical diagnosis of HD seen at one of the 43 sites affiliated with the Huntington Study Group (HSG) during the period of January of 1994–September of 1999 for their first visit. A clinical diagnosis of HD is given when a movement disorder specialist is more than 98% confident that abnormal extrapyramidal motor signs suggest a diagnosis of HD. All data used was stripped of all participant, examiner, and site-specific identifiers (we preserved relative links within the data by creating new random identification variables). The deidentification and subsequent use of these data for HD research was approved by the institutional review board at the University of Iowa.

There are 2,785 individuals with a clinical diagnosis of HD in this dataset. The current study assesses the relation between O/Cs and other aspects of HD including functioning, cognitive, motor, and psychiatric symptoms of HD. A total of 1,642 individuals (59 percent of total dataset) had complete data with regard to variables of interest. Cognitive variables were the most commonly missing variable. Not surprisingly, individuals with missing data were significantly more impaired as measured by the TFC ($t = 19.55$, $df = 1997$, $p < .001$) and had a longer duration of illness ($t = -9.57$, $df = 1377$, $p < .001$).

Measures

Participants were evaluated for the presence of motor, cognitive, and psychiatric symptoms using the Unified Huntington's Disease Rating Scale (UHDRS) (The Huntington Study Group, 1996), administered by trained raters. A detailed description of the UHDRS and the methods used to create factor scores can be found in Marder's article (Marder et al., 2000). The motor section of the UHDRS consists of a standardized examination of neurological symptoms common to HD. There are 31 questions rating motor function, each on a 0–4 point scale with 0 indicative of normal motor function. Factor scores, based a previous factor analysis (Marder et al., 2000) were obtained for oculomotor function, bradykinesia/fine motor performance, rigidity, dystonia, and chorea. The brief neuropsychological battery included a verbal fluency test, the Stroop Interference Task, and the Symbol Digit Modalities Test (Benton et al., 1976; Smith, 1973; Stroop, 1935). The behavioral section of the UHDRS includes 28 items assessing the frequency (0=never, 4=always) and the severity (0=not severe, 4=most severe) of psychiatric symptoms, including depression, suicidality, aggression, obsessions and compulsions, delusions, and auditory, visual, tactile, gustatory, and olfactory hallucinations. Ratings were conducted by trained staff with input from the patient and the family. Composite scores were created by multiplying the frequency score by the severity score for each psychiatric symptom, including O/Cs. Functional capacity was assessed using the Total Functional Capacity scale (TFC) (The Huntington Study Group, 1996), a 0 to 13 point scale with higher scores indicative of better functional ability. Neither CAG-repeat data nor psychiatric diagnostic evaluations were obtained as part of the HSG dataset, limiting genetic confirmation of HD and restricting a diagnosis of OCD.

Statistical Analyses

Participants with HD and O/Cs were compared to individuals with HD without O/Cs to look at differences in functional capacity, cognition, motor and other psychiatric abnormalities. To maximize correct identification of all participants with O/Cs, presence was defined by a score of "1" or greater on either the obsession or compulsion questions on the UHDRS. We first utilized a t-test to determine if there was a relation between the presence of O/C symptoms and severity of disease. Similarly, Pearson chi-squared analyses were used to assess for any sex differences across groups. MANCOVA analyses were then completed to assess the relation between O/C symptoms and motor, cognitive, and psychiatric symptoms of HD after controlling for severity of HD. Next, relations between O/Cs and other symptoms were assessed only within the group of individuals with HD and O/Cs. Among individuals who endorsed O/Cs, individuals with severe O/C symptoms (top 25 percent) were compared to those with less severe O/C symptoms (lower 24 percent). Again, we initially assessed for a relationship between severity of disease or sex and severity of O/C symptoms. A MANCOVA was again completed to assess the relation between O/C severity and motor, cognitive and psychiatric symptoms after controlling for disease severity as measured by TFC. All statistical analyses were completed using SPSS.

RESULTS

Participants were 1,642 individuals with a clinical diagnosis of HD. Approximately half of all participants were (50.4%) female with an average of one year of post-high school education (13.2 years, $SD=12.2$). Participants were an average of 7.0 ($SD=5.0$) years post-diagnosis of HD. Participants reported a significant history of treatment for psychiatric difficulties including depression (48.8 percent) obsessive compulsive disorder (8.6 percent), and psychosis (5.1 percent). Finally, 9.7 percent of all participants reported a history of at least one suicide attempt.

Overall, 27.2% ($n=446$) of participants reported presence of O/Cs; 24.0% reported obsessive symptoms, and 13.9% reported compulsive symptoms. Of individuals endorsing O/Cs, 48.7 percent reported only obsessive symptoms, 39.6 percent reported experiencing both obsessive and compulsive symptoms, and 11.7 percent reported experiencing compulsions only. Most participants reported mild O/Cs; the mean score for participants with O/Cs was 7.8 ($SD = 6.7$) on a 32-point scale. Among participants who endorsed current O/Cs, 21.6 percent reported obtaining treatment for OCD although type of treatment was not specified.

Participants with O/Cs had significantly poorer functioning, as measured by total functional capacity (TFC) and had a longer duration of disease compared to those without O/Cs (see Table 1 for specific details).

There were no significant sex differences between those with and without O/Cs ($\chi = 0.28$, $df = 1$ $p=.60$). Because participants with O/Cs experienced significantly more advanced disease, all future comparisons were made controlling for TFC total score.

After controlling for TFC, the overall MANCOVA model was significant ($F=16.02$, $df=15$, 1624 $p<0.001$). Participants with O/Cs exhibited significantly greater psychiatric symptoms including: depressed mood, suicidal ideation, aggression, delusions, and audiovisual hallucinations ($p<0.001$, see Table 2 for details). There were no significant relations between motor or cognitive symptoms and the presence or absence of O/Cs.

Next, the relations between O/C symptom severity and other symptoms of HD were assessed using only those individuals who reported O/Cs. Two groups were identified those with less severe O/C symptoms (the lowest 25th percent of the group, $n=116$) and those with more severe O/C symptoms (the highest 25th percent of the group, $n=121$). Again, there were no significant relation between sex and O/C symptom severity ($\chi = 1.23$, $df = 1$ $p=0.27$). Patients with more severe O/Cs experienced more severe functional impairment as assessed by TFC total scores than those with less severe O/Cs ($t=5.0$, $df=235$, $p<0.001$). There were no significant differences with regard to age or duration of illness between these two groups (see Table 3).

After controlling for TFC, the overall model was significant ($F=3.10$, $df=15$, 220 , $p<0.001$). Participants with more severe O/Cs had significantly more severe symptoms of depression, aggression, and delusions ($p<0.001$ see Table 4). Finally, there is a trend for individuals with more severe O/C symptoms to perform more poorly on the Stroop Color Word Interference task ($F = 5.57$, $df = 1$, $p=0.02$).

DISCUSSION

Obsessive and/or compulsive symptoms were reported in over 27 percent of this very large sample ($n = 1,642$) of individuals with a clinical diagnosis of HD. This proportion is much higher than the general population but consistent with previous HD reports (Anderson et al., 2001; Marder et al., 2000). Findings from this study extend our understanding of O/Cs in

HD. First, when compared to individuals with HD who do not endorse O/Cs, individuals with HD and O/Cs had significantly greater functional impairment and longer duration of disease. In addition, after controlling for illness severity, as measured by the TFC, those with O/Cs had greater severity of psychiatric symptoms. Among HD individuals with O/Cs, those with more severe O/Cs again reported higher rates of psychiatric symptoms, most notably depression, aggression, and delusions. In addition, individuals with more severe O/Cs exhibited a trend towards more impaired performance on a cognitive task (Stroop color word interference).

Research assessing O/Cs in HD is limited; however the current results are in accordance with previous reports suggesting that O/Cs occur in 20 to 50 percent of individuals with HD. (Anderson et al., 2001; Marder et al., 2000; Paulsen et al., 2001) Early descriptions of the prodromal personality changes observed in HD included “obsessional features” (Dewhurst et al., 1969). Similarly, case reports have described instances of OCD (Cummings et al., 1992; De Marchi et al., 2001) and obsessive gambling in an HD pedigree (De Marchi et al., 1998). In contrast to the typical onset of O/C symptoms in the second decade of life in primary OCD, the onset of O/C symptoms in HD typically occurs in mid to late life commensurate with disease manifestation (Cummings et al., 1992; Scicutella, 2000). It is important to emphasize that the reported rate of O/Cs in HD for this and most other studies was obtained by a semi-structured interview using one question for each symptom. It is possible, if not likely, that obsessions and compulsions would be found with even higher frequency than seen in the current study if formalized assessment for them were performed.

Individuals with HD and O/Cs may have dysfunction in discrete circuits involving the frontal lobe. Cummings (Cummings et al., 1992) has described three distinct frontal-subcortical circuits that may modulate behavior. The orbitofrontal circuit, which projects from the anterior and lateral orbitofrontal cortex through the ventromedial caudate nucleus, to the ventral anterior and medial dorsal thalamic nuclei, is of particular interest. It has been suggested that dysfunction in this circuit may lead to the affective O/C symptoms observed in HD (Cummings et al., 1992; Paulsen et al., 2001). This hypothesis is in line with reports of dysfunction in the orbitofrontal cortex among individuals with OCD (Nordahl et al., 1989; Sawle et al., 1991). Future research of O/Cs in HD may benefit from functional imaging or other research initiatives to better elucidate the anatomical underpinnings of O/Cs in HD.

In the current study, individuals with HD and more severe O/Cs exhibited greater deficits on performance on the Stroop Interference Task, consistent with earlier work by Anderson and others (Anderson et al., 2001) in a small study of individuals with HD who received more formalized assessment for O/Cs. This suggests that O/C symptoms are associated with greater executive dysfunction and likely exhibit greater frontal dysfunction. Research suggests that individuals with OCD may have difficulty in changing strategies when the demands of a task change (Aronowitz et al., 1994; Schmidtke et al., 1998; Veale et al., 1996), although not all work concurs with this (Anderson et al., 2004).

In their discussion of why O/Cs were rarely reported in earlier work with individuals with HD, Cummings and Cunningham (Cummings et al., 1992) offer several factors, including lack of specific questioning, assignment of the symptoms to other categories of behavior (e.g. perseveration, psychosis), or the possibility that only a small number of persons with HD develop O/Cs. De Marchi and Mennella (De Marchi et al., 1998) suggest that it may be an embarrassing symptom for patients to discuss with health care providers, so they may not admit to these symptoms unless questioned specifically about them.

CONCLUSIONS

Clinicians should be aware to look for signs of additional psychiatric symptoms in patients with HD and O/Cs, including mood changes and problems with impulse control that can lead to aggression and suicide attempts. They should also be aware that patients with O/Cs may have more executive impairment than those without, which could lead to further behavioral difficulties. Bradykinesia may be more prominent in individuals with HD and O/Cs. The clinical picture of patients with more severe O/Cs may thus differ, featuring more bradykinesia and less dystonia and rigidity.

There are some limitations in the current study. First, O/Cs were assessed using a limited measure. It is unclear how many, if any, of the current participants would meet criteria for OCD. In addition, the cognitive battery was brief. Future studies would benefit from using more precise measures of obsessions and compulsions. In addition, a more comprehensive battery particularly focused on the assessment of executive functions would be extremely useful in helping to delineate the neuropathological changes underlying O/Cs. Finally, the current paper assessed O/C symptoms in a cross-sectional sample. Little is known about the development of O/Cs across the progression of HD; longitudinal study will be important.

Clinicians should be aware that patients with HD and O/Cs might have a somewhat different clinical picture from those without, and may require a specialized plan for treatment. Future work should focus on further defining whether there is a unique symptom profile in HD that is seen in patients with O/Cs. As more is learned about O/Cs in a basal ganglia disorder such as HD, it may enhance our understanding of primary OCD.

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Table 1

Demographic data for individuals with HD with and without O/Cs.

	No O/Cs (n=1196) Mean (SD)	O/Cs Present (n=446) Mean (SD)	t-statistic
Age	47.38 (12.29)	48.59 (12.09)	-1.79
TFC	8.41 (3.20)	7.80 (3.12)	3.47**
Duration of illness (years)	6.65 (4.83)	7.78 (5.31)	-3.69**

Note.

**
p≤0.001. TFC = Total Functional Capacity; lower scores reflect poorer functional capacity.

Table 2

Total Functional Capacity (TFC) corrected UHDRS Factor and Cognitive test scores by O/C status.

UHDRS Score	No O/Cs (n=1196) Mean (SE)	O/Cs Present (n=445) Mean (SE)	F-statistic
Oculomotor	8.65 (0.13)	8.60 (0.22)	0.04
Bradykinesia	15.34 (0.17)	15.01 (0.28)	0.99
Rigidity	1.44 (0.04)	1.44 (0.07)	0.00
Dystonia	3.17 (0.11)	3.47 (0.18)	2.18
Chorea	10.98 (0.15)	11.31 (0.25)	1.26
Depression	7.06 (0.27)	12.66 (0.44)	118.60**
Suicidal Ideation	0.56 (0.06)	1.23 (0.10)	35.10**
Aggression	3.86 (0.17)	7.77 (0.28)	141.16**
Delusions	0.13 (0.04)	0.72 (0.07)	52.19**
Hallucinations	0.04 (0.03)	0.22 (0.22)	13.60**
Verbal Fluency	18.02 (0.27)	18.10 (0.45)	0.02
Symbol Digit	22.45 (0.27)	22.88 (0.44)	0.72
Stroop Color	42.65 (0.40)	42.50 (0.66)	0.04
Stroop Word	56.75 (0.52)	57.19 (0.85)	0.19
Stroop Color Word	22.82 (0.28)	22.61 (0.46)	0.15

Note: df = 1, 1640.

**
p≤0.001. UHDRS = Unified Huntington's Disease Rating Scale. SE = Standard Error. All scores reflect raw scores.

Table 3

Demographic data for individuals with HD and Low or High O/C symptom severity.

	Low O/Cs (n=116) Mean (SD)	High O/Cs (n=121) Mean (SD)	t-statistic
Age	51.15 (13.42)	48.64 (11.44)	1.55
TFC	8.70 (2.79)	6.71 (3.31)	4.99**
Duration of Illness (years)	7.63 (4.80)	8.85 (5.92)	-1.65

Note.

**
p<.001. TFC = Total Functional Capacity, lower scores reflect poorer functional capacity.

Table 4

Total Functional Capacity (TFC) corrected UHDRS Factor and Cognitive test scores by O/C symptom severity Group

UHDRS Score	Low O/Cs (n=116) Mean (SE)	High O/Cs (n=121) Mean (SE)	F-statistic
Oculomotor	9.48 (0.44)	8.82 (0.43)	1.08
Bradykinesia	16.01 (0.60)	15.76 (0.58)	0.09
Rigidity	1.58 (0.14)	1.37 (0.14)	1.06
Dystonia	3.88 (0.39)	3.24 (0.38)	1.38
Chorea	11.43 (0.51)	11.40 (0.50)	0.01
Depression	10.16 (1.04)	16.43 (1.02)	17.56**
Suicidal Ideation	1.13 (0.25)	1.49 (0.26)	0.88
Aggression	5.92 (0.71)	9.81 (0.70)	14.61**
Delusions	0.29 (0.25)	1.50 (0.24)	11.94**
Hallucinations	0.15 (0.20)	0.53 (0.19)	1.75
Verbal Fluency	17.70 (0.86)	18.72 (0.84)	0.68
Symbol Digit	21.40 (0.85)	21.81 (0.83)	0.11
Stroop Color	38.65 (1.30)	42.37 (1.28)	3.94
Stroop Word	53.73 (1.75)	55.68 (1.71)	0.61
Stroop Color Word	20.36 (0.97)	23.63 (0.95)	5.57

Note: df = 1, 236,

* p<.05,

** p≤0.001. UHDRS = Unified Huntington's Disease Rating Scale. SE = Standard Error. All scores reflect raw scores.