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Huntington disease as a dual diagnosis disorder: Data from the national research roster for Huntington disease patients and families

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Abstract

Although an extensive literature characterizes a linkage between primary mental illnesses and substance use disorders, a paucity of research exists concerning dual diagnosis phenomena in Huntington disease (HD). Data from the National Research Roster on HD suggest that higher levels of alcohol and cigarette use are associated with greater ratings of psychiatric symptoms and a younger age of HD symptom onset, and that progressive alcohol use after HD symptom onset is linked with worsening psychiatric symptom progression. These findings suggest HD entails dual diagnosis phenomena similar to that identified in patients with primary psychiatric disorders.

Keywords

Huntington disease; Dual diagnosis; Alcohol; Nicotine; Psychiatric symptoms

1. Introduction

Huntington disease (HD) is an autosomal dominant neuropsychiatric disorder with onset ranging over the lifespan, and prevalence of 4–8 per 100,000 (Di Maio et al., 1993; Harper, 1992). Psychiatric manifestations occur more frequently in HD than other dementias and basal ganglia disorders, and often resemble schizophrenia, bipolar, and unipolar syndromes, obsessive–compulsive disorder, or their variants (Anderson et al., 2001; Folstein and Folstein, 1983; Mendez, 1994). HD causes progressive atrophy and neuronal loss in cortical-striatal

circuits corresponding to a progressive triad of motor, cognitive, and psychiatric symptoms (Cummings, 1993; Halliday et al., 1998; Joel, 2001; Litvan et al., 1998; Paulsen et al., 2001; Thieben et al., 2002; Vonsattel et al., 1985)].

Cortical-striatal circuits are also implicated in non-HD based psychiatric disorders including substance use disorders (SUDs), schizophrenia, bipolar and unipolar disorders (Chambers et al., 2001; Swerdlow and Koob, 1987). These disorders and SUDs are frequently comorbid (Kessler, 2004), possibly as a result of overlapping cortical-striatal circuit involvement mediating mental illness and SUDs (Chambers et al., 2001). Although these data and anecdotal reports suggest SUDs and HD could also be linked, studies exploring this association are scarce (Lopez and Jeste, 1997). Only one report directly examines alcohol SUDs in a clinical sample (King, 1985). To our knowledge, there are no studies examining smoking in HD.

The National Research Roster for Huntington Disease Patients and Families at Indiana University ranks among the largest data bases on HD. Here, we report the first examination of the roster for alcohol and cigarette use, psychiatric symptom severity, age at HD onset, and psychiatric symptom progression.

2. Methods

Since 1979, HD patients and families have voluntarily contacted the roster after becoming aware by brochures, the internet and other sources. Respondents sign informed consent, authorization to release information (approved by Indiana University IRB), and fill out a 13 page questionnaire gathering general information, and illness history. The questionnaire serves a broad array of potential research questions concerning HD natural course, associated factors, and impact, and was not programmed with respect to any particular hypothesis. Questionnaires are completed by first degree relatives (87%) and self report (4%).

The questionnaire states “The symptoms of HD and the age at which they appear differ greatly from individual to individual”. It then asks “At what age did the symptoms first appear?” Substance use and psychiatric symptom ratings before and after HD onset are then ascertained. Four forms of substance use are addressed: ‘alcohol’, ‘cigarettes’, ‘tranquilizers’, and ‘non-prescribed drugs’. Due to the ambiguity of the latter terms, only cigarette and alcohol use were examined. Responders rate subject’s alcohol and cigarette use: 1 (“not at all”); 2 (“light use”); 3 (“moderate use”); 4 (“heavy use”); 5 DK (“Don’t Know”). They also rate, from 1 (“doesn’t describe”) to 5 (“describes very well”), each of 10 negatively valenced affective characteristics (sad, nervous, worried, listless, depressed, angry, suspicious, irritable, moody, and quarrelsome) and each of three positively valenced characteristics (happy, calm, and energetic).

In examining substance use patterns, psychiatric symptom severity, and age of HD onset, cases were sub-grouped into four categories of substance use: (1) low alcohol/low cigarette use; (2) high alcohol/low cigarette use; (3) low alcohol/high cigarette use; and (4) high cigarette/high alcohol use. Reports of 1 (not at all) and 2 (light use) were ranked low use and reports of 3 (moderate use) or 4 (heavy use) were deemed high use. From among the 13 affective characteristics, the 10 negative affective ratings were summed to create a ‘pathological’ psychiatric rating (scores ranging 10–50), and the three positive ratings were summed to a ‘desirable’ psychiatric rating (ranging 3–15).

For assessing substance use and psychiatric symptom progression, subjects were re-classified with respect to alcohol and cigarettes independently by whether use increased, was unchanged, or decreased after HD onset. These groups were then compared with respect to change in pathological and desirable psychiatric ratings after HD onset.

Consistent with prior studies using the roster (Kirkwood et al., 2001) juvenile onset HD cases (<20 years of age) were excluded reducing the data base from 2556 to 2303 cases. To work with the largest amount of data, further exclusions for missing data took place on an analysis by analysis basis.

Analysis of substance use groupings (independent factor) and psychiatric ratings, age of HD onset, and change in psychiatric ratings (dependent measures) entailed separate one-way analyses of variance (ANOVAs). Kurtosis and skewness ranged between $\{-1$ and $1.1\}$ for all subgroup distributions where ANOVAs were applied. Significance was identified at $p < 0.05$ and means are presented with standard deviations.

3. Results

The pool of 2303 cases included patients from all 50 states and the District of Columbia. Caucasians comprised 98% of this sample with 51.1% female and 48.9% male. Rigid and choreic forms of HD were reported in 3.7% and 69.2% while 27.1% answered “Don’t Know” or were missing. Average age at HD onset was 41.4 ± 10.8 , with mean birth year of 1923.7 ± 17.3 (16 of 2303 cases missing birth year).

From the sample of 2303 cases, 1976 answered questions needed for examining alcohol/cigarette use, psychiatric ratings, or age of HD onset. Table 1, upper panel, shows demographics of the four substance use groups categorized by degree of alcohol/cigarette use. 50.8% comprised the low alcohol/low cigarette use group; 9.1%, high alcohol/low cigarette; 20.6%, low alcohol/high cigarette; and 19.5%, high alcohol/high cigarette use.

Of the 1976 cases, 1060 responded to all pathological ratings after symptom onset, and 1381 responded to the three desirable ratings (Table 1, lower panel). The pathological ratings varied significantly between substance use groups ($F = 4.13$, d.f. = 3, 1059, $p < 0.01$), and generally increased in order of increasing alcohol/nicotine use. A separate ANOVA revealed no significant differences between substance use groups in terms of desirable ratings.

All 1976 subjects reported age at symptom onset which varied significantly between substance use groups ($F = 3.48$, d.f. = 3, 1975, $p < 0.05$). Here, the same substance use group ordering identified in the pathological ratings was ordered by decreasing age at HD onset.

From the sample of 2303 cases, 1851 responded sufficiently for detecting changes in alcohol use, and 2021 for cigarette use. Table 2, upper panel shows demographics of these groupings. For alcohol, 32% decreased, 59% unchanged, and 8.6% increased use; for cigarettes 1.2% decreased, 98% unchanged, and 0.6% increased use.

Of cases grouped by change in substance use, 954 from the alcohol and 988 from the cigarette grouping responded to all 10 pathological characteristics ratings before and after symptom onset (Table 2, lower panel). Groupings by changes in alcohol use varied significantly by changes in pathological ratings ($F = 7.76$, d.f. = 2, 953, $p < 0.001$); subjects with increased alcohol use had the largest increase in pathological ratings. Similar non-significant trends were observed in terms of cigarette use. Changes in patterns of alcohol or cigarette use had no impact on declining desirable ratings after HD onset.

4. Discussion

These findings suggest substance use and severity of psychiatric symptoms are associated in HD, whether in terms of combined alcohol and cigarette use, or progressive changes in alcohol use and psychiatric symptom course. Given that younger HD onset is associated with greater genetic and clinical liability to HD (Currier et al., 1982; Mahant et al., 2003; Marder et al.,

2000), greater substance use in HD patients with younger age of onset also supports this association. Taken together, these findings are consistent with the possibility of synergistic disease processes of HD and SUDs involving common cortical-striatal circuits.

Without matched control groups, the results cannot define increased risk of SUDs in HD. However, 40% and 29% of the sample were rated as high nicotine and/or high alcohol users respectively. By comparison, 26.5% of U.S. adults aged 18 or older in 1992 were smokers (CDC, 1994). For subjects in the HD roster reporting disease onset in 1992 or after, 41% were rated as moderate or high smokers. Greater frequencies of hospitalization for alcoholism (Jensen et al., 1993) and drunk driving offences (Jensen et al., 1998) have been observed in HD patients compared to at-risk controls, while another study found alcohol abuse/dependence in HD comparable to the general population at rates of 24% for males and 5.9% for females (King, 1985). The present study also identified higher levels of alcohol and/or cigarette use in male compared to female HD patients (Table 1), consistent with most studies on gender ratios of SUDs in the general population (Brady and Randall, 1999).

As an exploration using the HD roster, this study has considerable methodological limitations. The data represents a polling of family members, using non-validated, non-standardized research instruments subject to several potential response or selection biases and subjective weighting. Retrospective estimates of disease onset and illness course are difficult for professionals and lay-persons, and objective measures of HD disease provided by genetic or cognitive testing were unavailable. Nevertheless, this study suggests the need for greater attention to the prevalence, impact, and treatment of SUDs in HD. Given the similarity of these findings to studies on primary psychiatric syndromes where SUDs seem particularly associated with male gender, greater psychiatric morbidity, and earlier age of illness onset (Cantwell et al., 1999; Dixon, 1999; RachBeisel et al., 1999; Siegfried, 1998), further research on HD as a dual diagnosis condition with relatively well-defined genetic and neurobiological origins is warranted.

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Demographics (upper panel) of four substance use groupings, and analysis of HD psychiatric ratings and age of onset (lower panel)

Table 1

Group	Low alcohol/low cigarette, N (%)	High alcohol/low cigarette, N (%)	Low alcohol/high cigarette, N (%)	High alcohol/high cigarette, N (%)
Gender				
Male	359 (36)	111 (62)	235 (58)	275 (71)
Female	645 (64)	69 (38)	172 (42)	110 (29)
Marital status				
Married	773 (77)	124 (69)	288 (71)	251 (65)
Separated/divorced	178 (18)	38 (21)	99 (24)	103 (27)
Never married	48 (5)	17 (9)	18 (4)	30 (8)
Type of Huntington disease				
Choreic	722 (76)	131 (78)	285 (74)	274 (75)
Rigid	39 (4)	10 (6)	15 (4)	10 (3)
Don't Know	187 (20)	27 (16)	85 (22)	81 (22)
Psychiatric rating	Mean ± S.D. (N)			
Pathological	34.4 ± 10.8 (526)	34.9 ± 10.4 (104)	36.0 ± 9.9 (221)	37.3 ± 9.9 (209) *
Desirable	7.5 ± 3.2 (676)	7.3 ± 3.3 (137)	7.3 ± 3.3 (301)	7.4 ± 3.2 (272)
Age of HD onset	42.2 ± 11.2 (1004)	41.3 ± 11.1 (180)	40.7 ± 10.0 (407)	40.4 ± 9.5 (385) *

* Cases with missing data in lower panel are excluded, and bold cells with asterisk indicate significant ANOVA (*p* < 0.05).

Demographics (upper panel) of the groups by change in substance use after HD onset, and analysis of change in psychiatric ratings after HD onset (lower panel)

Table 2

Group	Alcohol decreased, N (%)	Alcohol unchanged, N (%)	Alcohol increased, N (%)	Cigarette decreased, N (%)	Cigarette unchanged, N (%)	Cigarette increased, N (%)
Gender						
Male	372 (63)	460 (42)	95 (59)	15 (60)	979 (49)	8 (62)
Female	222 (37)	637 (58)	65 (41)	10 (40)	1004 (51)	5 (38)
Marital status						
Married	422 (71)	828 (76)	103 (64)	20 (83)	1444 (73)	6 (46)
Separated/divorced	136 (23)	196 (18)	47 (29)	4 (16)	415 (21)	6 (46)
Never married	34 (6)	64 (6)	10 (6)	0 (0)	115 (6)	1 (8)
Type of Huntington disease						
Choreic	430 (78)	785 (75)	119 (77)	21 (84)	1404 (75)	12 (92)
Rigid	23 (4)	39 (4)	7 (5)	1 (4)	73 (4)	0 (0)
Don't Know	98 (18)	218 (21)	28 (18)	3 (12)	396 (21)	1 (8)
Change in psychiatric ratings	Mean ± S.D. (N)					
Pathological	13.9 ± 13.1 (313)	15.8 ± 11.7 (559)	19.5 ± 9.6 (84) *	15.8 ± 13.8 (16)	15.4 ± 12.0 (963)	21.4 ± 13.1 (9)
Desirable	-3.1 ± 4.7 (422)	-2.8 ± 4.8 (751)	-3.3 ± 5.1 (123)	-2.8 ± 4.1 (18)	-2.9 ± 4.9 (1327)	-5.3 ± 2.6 (10)

* Cases with missing data in lower panel are excluded, and bold cells with asterisk indicate significant ANOVA ($p < 0.05$).