

Risperidone and the Treatment of Psychiatric, Motor, and Cognitive Symptoms in Huntington's Disease

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Background. Huntington's disease (HD) is a progressive, neuropsychiatric disorder, and limited reports indicate that risperidone might improve motor and psychiatric functioning for these patients.

Methods. In a retrospective, chart review study to evaluate the effectiveness of risperidone on motor, psychiatric, and cognitive functioning in HD, 17 patients taking risperidone in the course of clinical care and 12 patients not taking any antipsychotic medication were compared across a year.

Results. Patients taking risperidone demonstrated significantly improved psychiatric functioning and motor stabilization, whereas patients not taking risperidone were stable psychiatrically and worsened motorically.

Conclusions. Although controlled clinical trials are clearly needed, these preliminary results support the use of risperidone in patients with HD in treating their psychiatric and possibly motor symptoms.

Keywords Huntington's disease, Risperidone, Treatment, Psychiatric symptoms, Motor, Cognition

INTRODUCTION

Huntington's disease (HD) is a progressive, genetically dominant, neuropsychiatric disorder, which affects voluntary and involuntary motor control, psychiatric symptoms, and cognitive functioning. Since no cure exists for HD at this time, interventions have largely focused on improving motor functioning (1-4). The treatment of psychiatric symptoms, however, may be particularly important in HD due to their deleterious effects on everyday functioning and quality of life (5). Given its beneficial effects on agitation, aggression, and psychosis in other dementias (6, 7), risperidone, an atypical antipsychotic and 5-HT₂ and D₂ receptor antagonist, has also been tried in HD. Risperidone's effectiveness on HD symptoms has been

reported in only a few published studies, most of which are single case studies.

In three separate case studies, treatment with risperidone led to significant improvements in psychiatric symptoms and/or choreiform movements across several weeks (8-10). Similarly, in a series of five patients with HD, Dallochio et al. (11) reported improved motor and/or psychiatric symptoms across six months. The current study extends prior work (e.g., greater sample size, longer period of observation, assessment of cognition and functional capacity, comparison group) by examining the benefits of risperidone on all HD symptoms, with the largest effects expected for psychiatric symptoms and motor functioning.

METHODS

All procedures were approved by the local Institutional Review Board prior to data collection. Retrospective chart

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analysis identified 17 patients diagnosed with HD who were prescribed risperidone as part of routine clinical care and who had assessments pre- and post-drug initiation (10 males, 7 females; mean age = 48.9 (7.7) years; mean education = 13.3 (1.96) years) (i.e., “risperidone” group). The average dose of risperidone in this group was 2.5 (1.9) mg daily, with a range of 0.75–6.0 mg. We also identified 12 patients diagnosed with HD who were not taking risperidone or any other antipsychotic medication at the time of data collection (7 males, 5 females; mean age = 51.7 (7.9) years; mean education = 12.7 (1.2) years) (i.e., “comparison” group). The comparison group was matched to the risperidone group on age, education, and pre-test Total Motor score of the Unified Huntington’s Disease Rating Scale ’99 (UHDRS). All patients were followed in a Huntington’s Disease Society of America (HDSA) Center of Excellence, and all diagnoses were made by a board-certified neurologist with expertise in movement disorders. Risperidone was prescribed as part of routine clinical care by either our clinic psychiatrist or the patient’s primary health care provider. In the risperidone group, the pre-test data were the data collected at the clinic visit prior to risperidone initiation, and the post-test data were the data collected at the next clinic visit. In the comparison group, a similar period of time was identified for these individuals. The average time period from the pre-test to the post-test evaluation was 14.8 (8.2) months in the risperidone group and 11.0 (3.7) months in the comparison group.

All participants in the current study provided informed consent prior to data collection, giving permission for any of their clinical data to be used for research purposes. All patients were administered the UHDRS, which is a clinical research tool for examining motor, cognitive, psychiatric, and daily functioning in patients with HD. Several summary measures from the UHDRS were used as outcome variables: Total Motor score, Total Functional Capacity, Total Psychiatric score, and Total Cognitive score. Briefly, the Total Motor score is the sum of the ratings across 31 different motor items (e.g., ocular pursuit, finger taps, chorea), and ranges from 0 to 124, with higher scores indicating more impaired motor functioning. The Total Functional Capacity score (12) quantifies a patient’s ability to perform both basic and instrumental activities of daily living, which is derived from reports of the patient and his/her companion, and ranges from 0 to 13, with higher scores indicating more intact functioning. The Total Psychiatric score (13) is the

sum of the product of frequency and severity for 11 psychiatric symptoms (e.g., anxiety, hallucinations, depression), and ranges from 0–176, with higher scores indicating increased psychiatric symptoms. The Total Cognitive score is the sum of the age and education corrected T-scores ($M = 50$, $SD = 10$) for three cognitive tests (verbal fluency, symbol digit modalities, and Stroop interference), each of which independently taps working memory and executive functioning, with higher scores showing better cognitive abilities. Effects of risperidone on the different outcome measures were compared with dependent t-tests (pre- vs. post-tests) within each group, and the alpha level was set at $p < 0.05$. Effect sizes (Cohen’s d) were determined using dependent t-test descriptive statistics.

RESULTS

As seen in Table 1, the comparison group displayed a trend of worsening Total Motor scores across time ($p = 0.05$), whereas these motor scores did not change on follow-up in the risperidone group ($p = 0.58$). Conversely, the risperidone group’s Total Psychiatric score significantly improved on follow-up ($p = 0.03$, Cohen’s $d = .67$), whereas there was no significance change in the comparison group’s psychiatric functioning ($p = 0.54$, Cohen’s $d = .15$). Both comparison and risperidone groups displayed significant declines in functional capacity ($p = 0.04$ and 0.02 , respectively), and trends towards worsening cognitive functioning on follow-up ($p = 0.12$ and 0.09 , respectively), with effects sizes in the small to medium range.

CONCLUSIONS

In this sample, risperidone appeared to have a beneficial effect on psychiatric symptoms associated with HD, which is consistent with prior findings in HD (8–10) and other dementias (6, 7). There was also a trend in its ability to stabilize motor decline, as patients who were prescribed risperidone did not evidence additional motor impairments across fifteen months but patients not taking this medication did. Both groups, however, continued to show decline in general functional capacity and cognition.

Table 1 Pre- and Post-test Outcome Measures in Risperidone and Comparison Groups

	Risperidone					Comparison				
	Pre	Post	<i>t</i> , <i>df</i>	<i>p</i>	<i>d</i>	Pre	Post	<i>t</i> , <i>df</i>	<i>p</i>	<i>D</i>
Total Motor	38.6 (22.3)	40.3 (19.5)	−0.6, 12	.58	.08	39.5 (24.6)	45.6 (25.4)	−2.2, 10	.05	.24
Total Psychiatric	34.9 (30.2)	17.9 (19.5)	2.4, 15	.03	.67	23.2 (17.9)	20.1 (23.8)	0.6, 10	.54	.15
Total Functional	8.9 (3.9)	7.3 (3.8)	2.5, 15	.02	.41	9.6 (3.1)	8.8 (3.0)	2.3, 10	.04	.26
Total Cognitive	82.2 (34.6)	71.0 (23.8)	1.9, 12	.09	.38	81.3 (32.4)	76.1 (39.1)	1.7, 10	.12	.14

Note. Means and standard deviations are reported for pre- and post-test scores. T-values, degrees of freedom (*df*), and *p*-values are from dependent *t*-tests within each group, and Cohen’s *d* values were calculated from dependent *t*-tests.

Psychiatric manifestations of HD have been widely reported (5), and the usual course of this disease is associated with a worsening of these symptoms (13). Consistent with its effect in other psychiatric conditions (14), risperidone significantly reduced overall psychiatric symptomatology in our HD sample. Specific improvements were observed on psychiatric assessment items from the UHDRS that measure hallucinations ($p < .05$) and apathy ($p < .05$), with trends appearing on items tapping anxiety ($p = .09$) and low self-esteem ($p = .09$). Whereas most HD literature focuses upon risperidone's effects upon motor control, Dallochio et al. (11) reported that a 3 mg daily dose significantly improved one patient's social withdrawal, thought insertion, and hallucinations. It should be noted that although the risperidone group's psychiatric functioning was worse at pre-test, both groups were elevated, even at post-test, which suggests only partial remission of these symptoms.

As with psychiatric functioning, declining motor, cognition, and functional capacity is expected in HD (5). Whereas our comparison group displayed this expected decline in motor functioning, the risperidone group in this study displayed a stabilization of the Total Motor score across a 14.8 month period. Although these findings are encouraging when compared to other clinical trials in HD (1–4), they are somewhat inconsistent with existing literature that has reported risperidone-related *improvements* in motor functioning (8–11). This discrepancy with the literature may be due to the lower doses of risperidone prescribed in our study (e.g., mean dose = 2.5 mg vs. 6 mg in Dallochio et al. (11)). Additionally, risperidone was likely prescribed for presenting psychiatric difficulties and not motor problems. The anticipated declines in functional capacity and cognition were observed in both our comparison and risperidone groups. While risperidone might help improve some symptoms, it does not appear to aid all areas affected by HD.

In conclusion, this study suggests risperidone might be improving or preventing some symptoms associated with the progression of HD, specifically psychiatric symptoms and motor functioning. It also appears that while risperidone improves some areas, functional capacity and cognition are not included. The current study is consistent with prior literature, with deviations possibly due to varying doses of risperidone. Future studies could build on weaknesses in the current investigation by including a more formal assessment of the psychiatric symptoms and a more comprehensive cognitive battery. Additionally, with the exception of antipsychotics, other medications were not controlled for, but these could also have affected results. Nonetheless, the results from this retrospective chart review suggest that randomized, clinical trials are needed to better assess the effect of risperidone upon patients with HD. It should be noted that risperidone is not currently approved by the Food and Drug Administration for HD and has been linked to increased mortality in dementia patients, but controlled

clinical trials could provide the necessary information to accurately determine its safety and efficacy in HD.

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