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Risperidone and the treatment of psychiatric, motor, and cognitive symptoms in Huntington's disease

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Abstract

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 an open label, retrospective study to evaluate the effectiveness of risperidone on motor, psychiatric, and cognitive functioning in HD, 17 patients taking risperidone 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 (Huntington Study Group, 2003, 2006; Puri et al., 2005; van

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Vugt et al., 1997). The treatment of psychiatric symptoms, however, may be particularly important in HD due to their deleterious effects on everyday functioning and quality of life (Marder et al., 2000). Given its beneficial effects on agitation, aggression, and psychosis in other dementias (Brodaty et al., 2003; De Deyn et al., 2005), 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 (Parsa et al. 1997, Erdemoglu & Boratav 2000, Madhusoodanan et al. 1998). Similarly, in a series of five patients with HD, Dallocchio et al. (1999) reported improved motor and/or psychiatric symptoms across six months. The current study improves on prior work (e.g., greater sample size, longer period of observation, assessment of cognition and functional capacity, control group) to examine 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. Retrospective chart analysis identified 17 patients diagnosed with HD who were prescribed risperidone 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). 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., "control" group). The control group was matched to the risperidone group on age, education, and 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 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 control group, a similar period of time was identified for these individuals.

Following informed consent, all patients were administered the UHDRS. Several summary measures from the UHDRS were used as outcome variables: Total Motor score, Total Functional Capacity, Total Psychiatric score, and three cognitive tests (verbal fluency, symbol digit modalities, and Stroop interference). 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 (Shoulson et al., 1989) 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 (Beglinger et al., 2006) 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 cognitive scores (verbal fluency, symbol digit modalities, and Stroop interference) independently tap 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 $p < 0.05$.

Results

The average dose of risperidone for the risperidone group was 2.5 (1.9) mg daily, with a range of 0.75 – 6.0 mg. The average time period from the pre-test to the post-test evaluation was 14.8 (8.2) months. The control group had an average time from the pre-test to the post-test of 11.0 (3.7) months.

As seen in the Table, the control group displayed a trend of worsening Total Motor scores across time (p=0.053), 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 = 0.028), whereas there is no significance change in the control group's psychiatric functioning (p=0.539). Both groups displayed significant declines in functional capacity (p=0.023 and 0.042, respectively), and stable or worsening cognitive functioning on follow-up.

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 (Erdermoglu & Boratav, 2001; Madhusoodanan et al. 1998; Parsa et al., 1997) and other dementias (Brodaty et al., 2003; De Deyn et al., 2005). 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.

Psychiatric manifestations of HD have been widely reported (Marder et al., 2000), and the usual course of this disease is associated with a worsening of these symptoms (Beglinger et al., 2006). Consistent with its effect in other psychiatric conditions (e.g., Potkin et al., 2006), 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 literature focuses upon risperidone's effects upon motor control, Dallocchio et al. (1999) 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 (Marder et al., 2000). Whereas our control 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 (Huntington Study Group, 2003, 2006; Puri et al., 2005; van Vugt et al., 1997), they are somewhat inconsistent with existing literature that has reported risperidone-related *improvements* in motor functioning (Dallocchio et al., 1999; Erdermoglu & Boratav, 2001; Madhusoodanan et al. 1998; Parsa et al., 1997). 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 Dallocchio et al.). The anticipated declines in functional capacity and cognition were observed in both our control 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 study suggest that randomized, clinical trials are needed to better assess the effect of risperidone upon patients with HD.

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Table 1

Pre- and post-test outcome measures in risperidone and control groups.

	risperidone Pre-test	risperidone Post-test	risperidone p-value	Control Pre-test	Control Post-test	Control p-value
Total Motor	38.6 (22.3)	40.3 (19.5)	0.578	39.5 (24.6)	45.6 (25.4)	0.053
Total Psychiatric	34.9 (30.2)	17.9 (19.5)	0.028	23.2 (17.9)	20.1 (23.8)	0.539
Functional Capacity	8.9 (3.9)	7.3 (3.8)	0.023	9.6 (3.1)	8.8 (3.0)	0.042
Symbol digit modalities	23.8 (12.5)	19.6 (10.1)	0.077	22.0 (9.9)	22.2 (14.6)	0.917
Stroop interference	26.9 (12.5)	20.1 (10.7)	0.008	25.5 (12.3)	23.5 (12.8)	0.365
Verbal fluency	17.3 (9.3)	14.7 (8.8)	0.210	18.2 (12.2)	15.1 (11.5)	0.001

Note. Means and standard deviations are reported for pre- and post-test scores. P-value are from dependent t-tests within each group.

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