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RESEARCH ARTICLE

The Effects of Dual-Task Cognitive Interference and Environmental Challenges on Balance in Huntington's Disease

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ABSTRACT: Background: Huntington's disease (HD) is characterized by chorea, balance and gait impairments, and cognitive deficits, which increase fall risk. Dual task (DT) and environmentally challenging paradigms reflect balance related to everyday life. Furthermore, the impact of cognitive deficits on balance dysfunction and falls in HD is unknown.

Objective: To determine the impact of DT interference, sensory feedback, and cognitive performance on balance and falls in HD.

Methods: Seventeen participants with HD (55 ± 9.7 years) and 17 age-matched controls (56.5 ± 9.3 years) underwent quantitative balance testing with APDM inertial sensors. Postural sway was assessed during conditions of manipulated stance, vision, proprioception, and cognitive demand. The DT was a concurrent verbal fluency task. Neuropsychological assessments testing multiple cognitive domains were also administered.

Results: HD participants exhibited significantly greater total sway area, jerk, and variability under single-task (ST) and DT conditions compared to controls (P = 0.0002 – <0.0001). They also demonstrated greater DT interference with vision removed for total sway area (P = 0.01) and variability (P = 0.02). Significantly worse postural control was observed in HD with vision removed and reduced proprioception (P = 0.001 – 0.01). Decreased visuospatial performance correlated with greater total sway and jerk (P = 0.01; 0.009). No balance parameters correlated with retrospective falls in HD.

Conclusions: HD participants have worse postural control under DT, limited proprioception/vision, and greater DT interference with a narrowed base and no visual input. These findings may have implications for designing motor and cognitive strategies to improve balance in HD.

Introduction

Huntington's disease (HD) is a progressive, autosomal dominant, neurodegenerative disease caused by an expanded CAG repeat (>40) in the gene for the huntingtin protein (*HTT*). Motor system involvement in HD typically begins with incoordination and progresses to chorea, rigidity, and akinesia. Neuronal death in the striatal division of the basal ganglia[1] causes chorea, the hallmark motor deficit in HD,[2] resulting in gait and balance dysfunction, falls, and morbidity.[3,4] The basal ganglia also helps integrate proprioceptive, visual, and vestibular signals critical for maintaining balance.[5] Balance impairments in HD are thus highlighted by difficulty utilizing sensory cues to maintain postural control.[6] The striatum also plays a role in cognition via networks with the prefrontal cortex.[7] Cognitively, HD patients have difficulty holding, shifting, and dividing their attention and struggle when responding to multiple stimuli simultaneously,[8,9] which may further exacerbate motor deficits.

Dual-task (DT) cognitive-motor paradigms are used to evaluate difficulty-dividing attention between multiple tasks,

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movement automaticity, and the effects of cognitive interference on motor tasks.[10,11] As HD progresses, automaticity changes, such that previously automatic tasks, including walking or balancing require increased cognitive resources.[12–14] Ultimately, this progressive neurodegeneration increases fall risk in HD.[8,13] The loss of automaticity in HD is also seen with fine motor skills.[15] However, a prior DT study utilizing a circle-tracing task did not find significant cognitive interference on the speed of this task in HD.[16]

Patients with HD show the greatest cognitive deficits in the domains of executive function, processing speed, attention, visuospatial ability, and short-term memory.[14,17,18] In other movement disorders, such as Parkinson's disease (PD) and multiple sclerosis (MS), cognitive deficits negatively impact balance and gait, leading to falls and progressive disability.[19,20] Furthermore, current understanding of postural control suggests it is an active process, requiring attentional resources.[21] Previous studies found HD participants demonstrate decreased gait speed, cadence, and stride length while dual-tasking.[13,22] However, the extent to which dual-tasking and cognitive deficits exacerbate balance dysfunction in HD is unknown.

Previously, difficulties in DT gait performance were associated with increased falls in PD[23] and HD.[22] We hypothesize that DT balance assessments and knowledge of how cognition impacts balance will provide important information about fall risk in HD. DT training programs have shown success in enhancing gait, balance, and cognitive processing while reducing fall risk in the elderly and in PD.[24–26] Therefore, this study could lead to treatment interventions targeted at motor and cognitive impairments in HD. The goals of this study were to: (1) determine the impact of altered sensory input, stance, and DT cognitive interference on postural control in HD; (2) identify which cognitive deficits might be associated with balance deficits and falls in HD; and (3) examine whether challenging balance conditions, including the DT, are associated with a retrospective history of falls in HD participants.

Methods

Study Participants

HD participants were recruited from the Rush University Medical Center (RUMC) Movement Disorders HD clinic; age- and sex-matched healthy controls were recruited from the RUMC community or friends of the HD participants. Inclusion criteria were, (1) clinical diagnosis of HD by a movement disorders/HD expert (JGG) for HD participants,[27,28] (2) >21 years of age, (3) ability to stand unsupported for ≥30 seconds, (4) ability to ambulate without an assistive device, and (5) the ability to follow protocol-specific directions as confirmed by a family member and/or caregiver. Participants diagnosed with juvenile HD, those who had lower limb orthopedic surgery within the past year, or those who had any additional neurological or musculoskeletal disorders negatively affecting balance were excluded from the study. The exclusion criteria for controls were the same, but also excluded individuals with cognitive impairment. Participants were classified as having a choreatic, hypokinetic-rigid, or mixed phenotype as previously described.[29] All participants provided informed consent in accordance with the RUMC Institutional Regulatory Board.

Postural Sway Assessments

Quantitative balance analysis under single task (ST) and dual task (DT) conditions was performed using the well-validated, reliable inertial sensor instrumented SWAY (i-SWAY) system with balance metrics generated by Mobility Lab Software.[30,31] An Opal wearable inertial sensor was placed at the lumbar spine (L5), the approximate center of mass location.[31] Participants performed i-SWAY trials under increasingly difficult ST and DT conditions. Participants were asked to stand still for 30 seconds, barefoot, hands at their sides, and heel-to-heel distance set at 25 cm for those whose height was <165 cm, and 30.5 cm for those >165 cm, in accordance with the Neurocom Smart Balance Master system protocol, another quantitative, validated balance measurement system.[32] The main outcome variables selected for analyses were: (1) 95% ellipse sway area (m^2/s^4), (2) root mean square (RMS) sway (m/s^2), and (3) jerk (m^2/sec^5).[30] These variables were selected a priori out of 33 APDM-generated variables because these have been found to be sensitive measures of balance dysfunction in other movement disorders[30,31,33] and have good-to-excellent reliability.[31] A detailed description of selected sway variables are included in Supporting Table 1. Postural sway was assessed under various conditions of stance (feet apart/together), support surface (firm/on foam; foam pad was a Balance-pad Elite), and visual input (eyes open/closed), as well as with or without DT. The extent of DT interference, or the dual-task cost (DTC) in balance performance was defined as DTC (%) = (DT-ST/ST)*100, as previously described.[34] The ST conditions were based on the Modified Clinical Test of Sensory Integration in Balance (CTSIB-M), which is used clinically to determine aberrant sensory-motor integration.[35] The DT consisted of a simultaneous verbal fluency task (the Controlled Oral Word Association test, COWAT[36]), each with different letters for firm surface conditions. In the DT conditions, no instructions were given on which task to prioritize. The trials were conducted in a non-random order with increasing difficulty. Participants were carefully monitored during all trials for safety by the study investigator (NLP), standing directly next to the participant during the entire testing protocol.

Neuropsychological, Balance, and Clinical Rating Scale Assessments

Cognitive function was assessed with the following tests: (1) Montreal Cognitive Assessment (MoCA; global cognition)[37]; (2) Digit Span forwards, backwards, and sequencing (WAIS-IV) (attention and working memory)[38]; (3) Symbol Digit Modalities Test (SDMT; information processing speed)[39]; (4) Consortium

to Establish a Registry for Alzheimer's disease (CERAD word list memory with delayed recall; memory)[40]; (5) Judgment of Line Orientation (JLO; visuospatial perception)[41]; and (6) animal naming (verbal fluency).[42] This cognitive battery was chosen because it spans multiple cognitive domains known to be deficient in HD. The Unified Huntington's disease Rating Scale motor section was administered by a movement disorder/HD neurologist (JGG) and provided a total motor score (UHDRS-TMS).[27] Participants were asked to self-report the number of falls they had in the past 12 months. They were also administered the Berg Balance Scale (BBS)[43] and the Activities-Specific Balance Confidence Scale (ABC)[44] to obtain functional performance-based balance information and determine participant's perception of their balance impairment.

Statistical Analyses

Clinical characteristics were compared between HD participants and healthy controls using two-tailed Student t-tests for parametric and normally distributed measures, or the Mann-Whitney U test for variables that were not continuous or did not have normal distributions. Differences in i-SWAY variables under ST and DT conditions and the DTC for each of the primary outcome variables between HD participants and healthy controls were examined with the same statistical tests. Bonferroni corrections were applied to account for multiple conditions/outcomes on the i-SWAY (adjusted P value ≤0.0017). A two-way mixed ANOVA with Bonferroni corrections was performed with the within-patients factor being the four conditions of the CTSIB-M: (1) feet apart/eyes open/firm (AOF), (2) feet apart/eyes closed/firm (ACF), (3) feet apart/eyes open/foam (AOFo), and (4) feet apart/eyes closed/foam (ACFo) and a between-patients factor of group (controls versus HD).

Correlations between i-SWAY measures and cognitive test scores, UHDRS-TMS, ABC, BBS, and retrospective falls were examined in the HD group using Spearman's rho. The statistical significance for these comparisons was set at $P = 0.05$ given the exploratory nature of this work, the large number of variables tested, and correlations performed to reduce overlooking potential significant relationships due to Type II errors.

Results

Participant Characteristics

Seventeen individuals with HD and 17 age-matched controls participated in the study. Demographic and clinical features of the participant groups are in Table 1. UHDRS-TMS ranged from seven to 39 with seven participants in the seven to 20 group, and nine in the 21 to 40 group. Eight HD participants were mixed phenotype, four choreatic and four hypokinetic-rigid, with one participant not having a UHDRS-TMS recorded. HD participants scored significantly worse than controls on measures of global cognition (MoCA, $P = 0.0009$), response inhibition (stroop, $P = 0.007$), processing speed

TABLE 1 *Participant characteristics*

	Health controls (n = 17)	Huntington's disease (n = 17)
Age (years)	56.47 ± 9.30 (37-69)	55 ± 9.66 (36-67)
Sex	8 Females, 9 Males	7 Females, 10 Males
BMI (kg/m)	26.29 ± 5.22 (20.8-37.8)	24.68 ± 3.79 (17.80-31.00)
Years of education	16.59 ± 2.82	15.59 ± 2.67
UHDRS-TMS	----	21.86 ± 9.86 (7-39)
Trunk chorea (subscore)	----	0.69 ± 0.79 (0-2)
Phenotype	----	4 choreatic, 4 hypokinetic/rigid, 8 mixed
Disease duration (years)	----	5 ± 2.8 (3-13)
ABC	95.38 ± 5.05 (83.7-100)	**81.20 ± 13.2 (50.31 – 100)*****
BBS (0-56)	55.88 ± .33 (55-56)	**51.18 ± 3.15 (44-56)******
One-year retrospective Falls (#)	0.176 ± 0.529 (0-2)	**2.29 ± 2.69 (0-10)*****
MoCA	26.47 ± 2.79 (20-30)	**22.70 ± 3.46 (12-28)*****
SDMT	99.34 ± 13.42 (80.4-131.1)	**70.89 ± 20.74 (45.5-105.9)******
Stroop-CW	45.5 ± 8.36 (35-59)	**37.19 ± 7.89 (25-52)****
CERAD-recall	6.35 ± 1.69 (4-10)	5.59 ± 2.24 (2-10)
JLO	12.35 ± 1.87 (8-15)	**10.06 ± 2.79 (5-14)****
Digit span total	11.12 ± 2.47 (5-14)	**8.23 ± 3.45 (1-15)****
Animal naming (#)	37.41 ± 8.44 (20-51)	21.76 ± 9.73 (8-53)

All values are mean ± SD with range in brackets unless indicated otherwise.
Abbreviations: ABC, Activity Specific Balance Confidence scale; BBS, Berg Balance Scale; BMI, Body Mass Index; CW, Stroop, Color-Word; CERAD, Consortium to Establish a Registry for Alzheimer's disease; JLO, Judgment of Line Orientation; MoCA, Montreal Cognitive Assessment; SDMT, Symbol Digit Modalities Test; UHDRS-TMS, Unified Huntington's Disease Rating Scale-total motor score.
Standardized Digit Span values were compared between Huntington's disease patients and controls. Note that the SDMT, Stroop-CW, CERAD-recall, and digit span were scaled to the patient's age and years of education. Significant differences are bolded.
#Self-reported in last year, 1 year fall history.
*$P < 0.05$;
**$P < 0.01$;
***$P < 0.001$;
****$P < 0.0001$.

(SDMT, $P < 0.0001$), verbal fluency (COWAT, $P < 0.0001$), visuospatial abilities (JLO, $P = 0.0083$), and working memory (digit span, $P = 0.0087$). Unexpectedly, performance on memory-delayed recall (CERAD word list) was not significantly different between HD participants and controls. HD participants reported having significantly lower balance confidence on the ABC ($P = 0.0001$), performed worse on the BBS ($P < 0.0001$), and had a higher number of falls within the past year ($P = 0.0007$) compared to controls.

Postural Sway Assessments

Single and Dual-Task Results

Because of the wide range of UHDRS-TMS scores in the HD group, we performed a sub-analysis examining potential differences in postural sway scores between participants with lower TMS scores (7–20) versus those with higher scores (21–40). There were no statistical differences in any balance parameters between these two subgroups; therefore, all data were combined for subsequent analysis. HD participants demonstrated greater total sway, jerk, and RMS sway under all i-SWAY conditions compared to controls, including both ST (Table 2) and DT conditions (Table 3; $P = 0.0002$ to <0.0001). HD participants also had significantly greater DTC for total sway area ($P = 0.01$) and RMS sway ($P = 0.02$) with feet together on a firm surface and eyes closed (TCF; Fig. 1).

Clinical Test of Sensory Integration and Balance-Modified (CTSIB-M) Results

There was a significant interaction effect between group and CTSIB-M conditions ($P = 0.0009$); therefore, the within-group comparisons were done separately for each group for all three postural sway parameters.

Between Group Comparisons

The HD group exhibited significantly worse total sway and sway variability in all four CTSIB-M conditions and worse total jerk on three of the four conditions compared to controls (Fig. 2; Table 2). Individuals with HD demonstrated significantly more sway than controls in the AOF ($P = 0.002$), ACF ($P = 0.004$), AOFo ($P = 0.0001$), and ACFo conditions ($P = 0.003$); significantly more jerk than controls in the AOF ($P = 0.005$), ACF ($P = 0.07$), AOFo ($P = 0.0008$), and ACFo conditions ($P = 0.001$); significantly more sway variability than controls in the AOF ($P < 0.0001$), ACF ($P = 0.0004$), AOFo ($P < 0.0001$), and ACFo conditions ($P < 0.0001$).

Within-Group Comparisons

Individuals with HD demonstrated greater total sway ($P = 0.001$), jerk ($P = 0.01$), and sway variability ($P = 0.001$) during the ACFo surface condition compared to ACF condition (Fig. 2). Additionally, HD participants exhibited greater total sway ($P = 0.001$), jerk ($P = 0.01$), and sway variability ($P = 0.001$) with ACFo, compared to AOF.

TABLE 2 *Balance comparisons between controls and HD participants on the single task CTSIB-M i-SWAY conditions and narrowed stance condition*

CTSIB-M		
Condition 1: Feet apart–eyes open–firm surface		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.01 ± 0.009	**0.31 ± 0.28*** **
Total jerk (m^2/s^5)	0.56 ± 0.36	**19.78 ± 20.33*** **
RMS sway (m/s^2)	0.06 ± 0.02	**0.19 ± 0.08*** **
Condition 2: Feet apart–eyes closed–firm surface		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.02 ± 0.01	**0.31 ± 0.30*** **
Total jerk (m^2/s^5)	1.42 ± 1.55	**20.69 ± 30.25*** **
RMS sway (m/s^2)	0.07 ± 0.02	**0.19 ± 0.10*** **
Condition 3: Feet apart–eyes open–foam surface		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.05 ± 0.04	**0.62 ± 0.42*** **
Total jerk (m^2/s^5)	1.43 ± 1.30	**31.60 ± 25.81*** **
RMS sway (m/s^2)	0.08 ± 0.03	**0.26 ± 0.09*** **
Condition 4: Feet apart–eyes closed–foam surface		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.12 ± 0.06	**1.05 ± 0.93*** **
Total jerk (m^2/s^5)	4.26 ± 3.16	**56.15 ± 45.65*** **
RMS sway (m/s^2)	0.13 ± 0.03	**0.34 ± 0.12*** **
Narrowed base of support		
Feet together–eyes open–firm surface		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.06 ± 0.02	**0.48 ± 0.42*** **
Total jerk (m^2/s^5)	1.38 ± 0.77	**20.55 ± 13.77*** **
RMS sway (m/s^2)	0.08 ± 0.01	**0.24 ± 0.11*** **
Feet together–eyes closed–firm surface		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.10 ± 0.06	**0.91 ± 0.78*** **
Total jerk (m^2/s^5)	3.16 ± 3.16	**45.10 ± 40.62*** **
RMS sway (m/s^2)	0.10 ± 0.03	**0.30 ± 0.14*** **

Data reported as mean ± SD. 95% Ellipse sway area refers to the area of an ellipse covering 95% of the points in both the coronal and sagittal planes, putting more weight on regions more frequently visited. Root mean square (RMS) is the extent of postural sway calculated as RMS of the sway angle in both the AP and ML directions. Total jerk is method to quantify the amount of active postural corrections. Significant differences are bolded.
*$P < 0.05$;
**$P < 0.01$;
***$P < 0.001$;
****$P < 0.0001$.

TABLE 3 *Balance comparisons between controls and HD participants on the dual task (DT) i-SWAY conditions*

Condition 1: Feet apart–eyes open–firm surface–DT "C"		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.05 ± 0.07	**1.38 ± 1.96*****
Total jerk (m^2/s^5)	4.97 ± 7.09	**100.59 ± 133.61*****
RMS sway (m/s^2)	0.09 ± 0.04	**0.37 ± 0.24*****
Condition 2: Feet apart–eyes closed–firm surface–DT "L"		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.04 ± 0.03	**1.11 ± 1.75*****
Total jerk (m^2/s^5)	2.39 ± 2.05	**79.96 ± 98.22*****
RMS sway (m/s^2)	0.08 ± 0.03	**0.34 ± 0.23*****
Condition 3: Feet together–eyes open–firm surface–DT "A"		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.11 ± 0.09	**1.60 ± 2.06*****
Total jerk (m^2/s^5)	4.57 ± 4.36	**112.25 ± 148.97*****
RMS sway (m/s^2)	0.12 ± 0.05	**0.40 ± 0.25*****
Feet together–eyes closed–firm surface–DT "S"		
Variable	Controls	HD
95% Ellipse sway area (m^2/s^4)	0.09 ± 0.04	**1.67 ± 1.83*****
Total jerk (m^2/s^5)	3.41 ± 1.86	**95.68 ± 99.82*****
RMS sway (m/s^2)	0.11 ± 0.02	**0.41 ± 0.22*****

Mean differences between controls and HD patients' sway characteristics under dual task (DT) (controlled oral word association task [COWAT] letters C, L, A, S) reported as mean ± SD. Significant differences are bolded.
**P* < 0.05;
***P* < 0.01;
****P* < 0.001;
*****P* < 0.0001.

Correlations Between Cognition, i-SWAY, UHDRS, and Falls in HD (Table 4; Fig. 2)

Visuospatial function was significantly associated with certain i-SWAY variables under ST and DT conditions in HD participants (Fig. 3). Lower JLO scores were correlated with (1) greater total sway, under AOF, DT (r = -0.617; *P* = 0.0097), and (2) greater total jerk ACF under both ST (r = -0.551, *P* = 0.0443) and DT (r = -0.624; *P* = 0.0087). Additionally, impaired visuospatial processing was associated with greater DTC under feet together, eyes open, firm (TOF), resulting in increased total sway (r = -0.593, *P* = 0.014), jerk (r = -0.552, *P* = 0.023) and TCF conditions, resulting in increased total sway (r = -0.492, *P* = 0.047) and sway variability (r = -0.489, *P* = 0.048). Lower SDMT scores correlated with greater total sway (r = -0.574, *P* = 0.018) and greater RMS sway (r = -0.554, *P* = 0.023) under TCF, ST. UHDRS-TMS correlated with greater total sway under TOF (r = 0.679; *P* = 0.0048) and TCF (r = 0.644; *P* = 0.006) ST conditions, as well as greater RMS sway (r = 0.662; *P* = 0.006) with TCF, ST condition. UHDRS-TMS did not correlate with any balance variables under DT conditions. The number of falls self-reported in the previous year did not correlate with any cognitive test scores or balance parameters under either ST or DT conditions.

Discussion

Postural stability was once thought to be under the control of a few balance centers in the central nervous system.[45] However, this view evolved to characterize balance as a complex motor skill controlled by a variety of sensorimotor and cognitive processes and their respective neural pathways.[45–47] Our study found that individuals with HD, compared to controls, have significant cognitive interference when visual input was eliminated and base of support was narrowed, resulting in impaired postural control. Furthermore, the increased postural instability under DT was associated with impaired visuospatial processing. To our knowledge, this is the first study to investigate key characteristics of postural control in HD using inertial sensors, and we found several postural sway domains compromised with reduced visual and proprioceptive input and during cognitive-motor DT. Our findings are in line with previous work demonstrating that vision is important for stabilizing balance by continually updating the nervous system on body position within a changing environment.[48] In the present study, removing vision and narrowing the base of support challenged the neuromotor control of balance, especially under DT, perhaps due to cognitive interference. More specifically, dual tasking produced a "jerkier," more variable postural sway in HD, which could lead to increased fall risk. These findings suggest that performing a verbal fluency task while balancing significantly interferes with the neural resources necessary to maintain postural control, suggesting competition for common neural networks that are deficient in HD, a theory previously proposed in PD[21,49] and older adults.[21,50]

Our findings are related to prior gait studies in HD where performing a cognitive-motor DT resulted in decreased stride length, cadence,[13] and gait speed,[13,22] with increased gait speed DTC.[22] Our findings are also consistent with the elevated DTC for combined cognitive and balance tasks in individuals with other neurodegenerative diseases, including MS and PD.[51,52]

Under ST conditions, individuals with HD exhibited greater total sway, jerkiness, and variability compared to controls. Our CTSIB-M findings highlight balance difficulties in HD when proprioception is reduced and when predominantly relying on vestibular information to maintain balance. These results are consistent with previous studies showing that HD participants demonstrate increased sway when proprioceptive and visual cues were altered.[6,53,54] However, our study is unique in that we characterized balance deficits in three specific domains that measure different aspects of postural stability.[31]

Our finding that impaired visuospatial perception in HD significantly correlated with a greater, jerkier sway path under DT, suggests that HD participants may depend heavily on their visuospatial system, especially during DT to maintain balance.

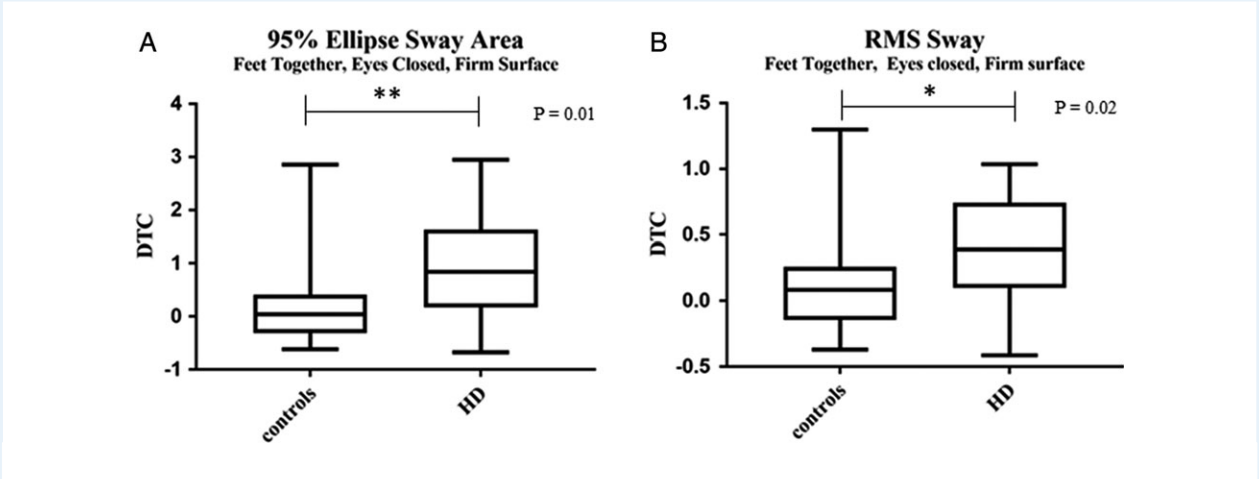

FIG. 1. Dual-task costs (DTC) on the instrumented sway (i-SWAY) for (A) total sway area and (B) root mean square (RMS) sway between controls and HD patients. DTC defined as (DT-ST)/ST scores x 100. Data expressed as mean ± SD. *$P < 0.05$, **$P \leq 0.01$.

Visuospatial skills are important for gait and postural control[55,56] and are modulated by the posterior parietal and occipital cortices, areas of volume loss in HD.[57,58] The ability to identify and manipulate where an object is in space involves activation of the parietal lobes, primary motor and premotor cortices, and the basal ganglia.[57] Prefrontal cortical degeneration in HD[59] would likely

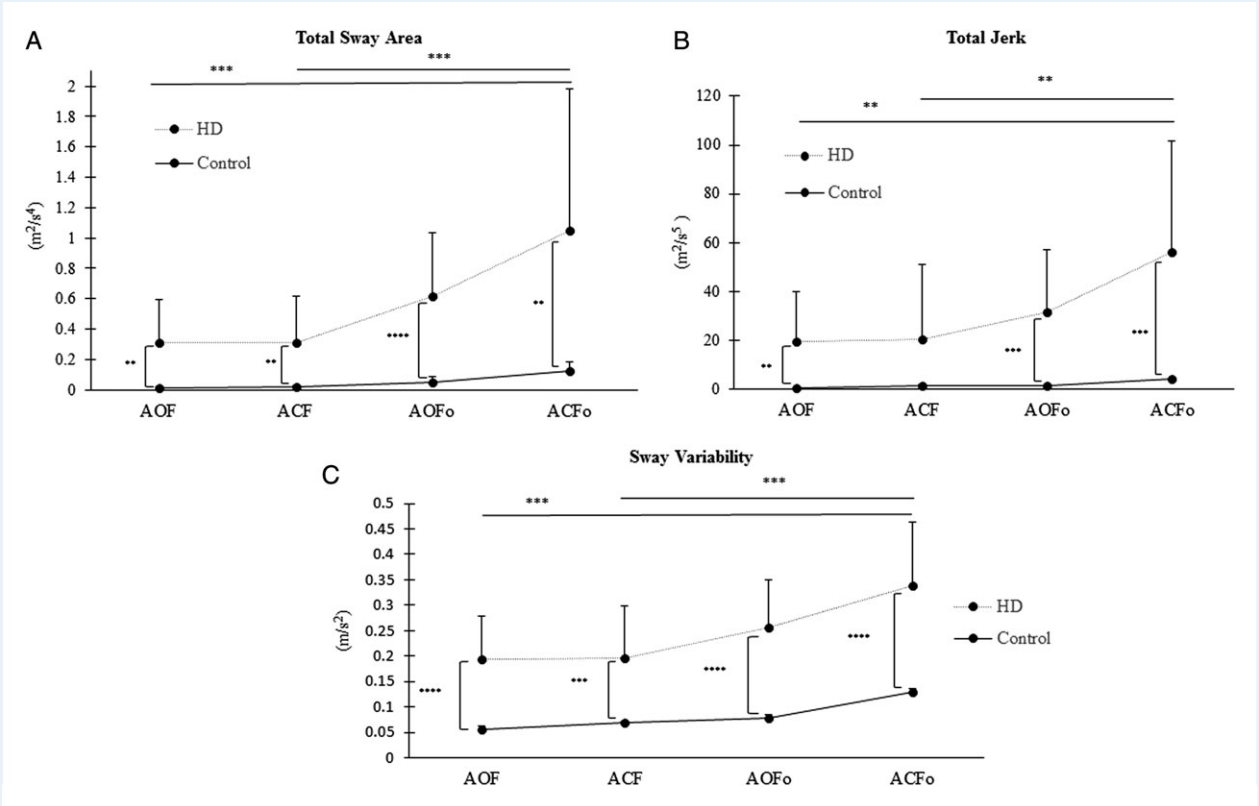

FIG. 2. Within and between group comparisons of (A) total sway area, (B) total jerk, and (C) RMS sway values of the HD and control groups under the four conditions of the (CTSIB-M) modified clinical test of sensory integration and balance; (AOF) feet apart, eyes open, firm surface feet apart; (ACF) eyes closed, firm surface; (AOFo) feet apart, eyes open, foam surface; and (ACFo) feet apart, eyes closed, foam surface. All values are expressed as mean + SD. **$P \leq 0.01$, ***$P \leq 0.001$, ****$P \leq 0.0001$.

TABLE 4 *Correlations of cognitive/UHDRS-TMS and iSway parameters*

	MoCA	SDMT	Stroop	Digit span	CERAD-recall	Animal naming	JLO	UHDRS-TMS
Condition 1: Feet apart, eyes open, firm surface								
95% Ellipse sway area (m^2/s^4)	-0.258	-0.382	-0.366	-0.073	-0.018	-0.31	-0.32	**0.528***
Total jerk (m^2/s^5)	-0.174	-0.132	-0.293	0.105	0.089	-0.15	-0.328	0.251
RMS sway (m/s^2)	-0.248	-0.208	-0.464	0.032	-0.001	-0.275	-0.298	0.321
Feet apart, eyes closed, firm surface								
95% Ellipse sway area (m^2/s^4)	-0.136	-0.064	-0.135	0.099	0.089	-0.08	-0.343	0.189
Total jerk (m^2/s^5)	-0.14	0.128	-0.133	0.262	0.166	-0.086	**-0.497***	0.049
RMS sway (m/s^2)	-0.113	0.044	-0.281	0.162	0.089	-0.086	-0.344	0.027
Feet together, eyes open, firm surface								
95% Ellipse sway area (m^2/s^4)	-0.262	-0.439	-0.349	-0.266	-0.075	-0.364	-0.134	**0.679****
Total jerk (m^2/s^5)	-0.224	-0.196	-0.037	-0.006	0.063	-0.22	-0.209	0.478
RMS sway (m/s^2)	-0.248	-0.392	-0.319	-0.326	-0.131	-0.456	-0.094	0.557*
Feet together, eyes closed, firm surface								
95% Ellipse sway area (m^2/s^4)	-0.41	**-0.574***	-0.343	-0.309	-0.142	-0.448	-.033	**0.644****
Total jerk (m^2/s^5)	-0.348	-0.468	-0.133	-0.187	0.033	-0.255	-0.43	**0.525***
RMS sway (m/s^2)	-0.340	**-0.554***	-0.355	-0.318	-0.122	-0.43	-0.308	**0.662****
Feet apart, eyes open, foam surface								
95% Ellipse sway area (m^2/s^4)	0.032	-0.314	-0.419	-0.046	0.121	-0.084	-0.216	0.479
Total jerk (m^2/s^5)	0.113	0.039	-0.174	0.306	0.280	0.073	-0.264	0.062
RMS sway (m/s^2)	0.11	-0.203	-0.468	0.025	0.219	-0.066	-0.245	0.36
Feet apart, eyes closed, foam surface								
95% Ellipse sway area (m^2/s^4)	-0.230	-0.059	-0.038	-0.069	-0.058	0.081	-0.06	0.264
Total jerk (m^2/s^5)	-0.108	0.181	-0.034	0.248	0.023	0.213	0.009	-0.134
RMS sway (m/s^2)	-0.183	-0.042	-0.116	-0.108	0.001	0.07	-0.134	0.214
Feet apart, eyes open, dual-task "C"								
95% Ellipse sway area (m^2/s^4)	-0.176	-0.262	-0.302	-0.058	0.065	-0.304	**-0.617****	0.296
Total jerk (m^2/s^5)	-0.14	-0.066	-0.155	0.062	0.089	-0.23	**-0.549***	0.133
RMS sway (m/s^2)	-0.126	-0.228	-0.387	-0.064	0.102	-0.269	**-0.581***	0.23
Feet apart, eyes closed, dual-task "L"								
95% Ellipse sway area (m^2/s^4)	-0.143	-0.150	-0.234	0.111	0.152	-0.166	**-0.569***	0.186
Total jerk (m^2/s^5)	-0.216	-0.064	-0.138	0.159	0.131	-0.118	**-0.624****	0.035
RMS sway (m/s^2)	-0.049	-0.076	-0.205	0.178	0.253	-0.015	**-0.544***	0.102
Feet together, eyes open, dual-task "A"								
95% Ellipse sway area (m^2/s^4)	-0.142	-0.164	-0.059	-0.028	0.157	-0.122	**-0.527***	0.292
Total jerk (m^2/s^5)	-0.044	-0.047	-0.202	0.188	0.253	-0.15	**-0.507***	0.075
RMS sway (m/s^2)	-0.132	-0.137	-0.038	-0.042	0.116	-0.139	**-0.528***	0.165
Feet together, eyes closed, dual-task "S"								
95% Ellipse sway area (m^2/s^4)	-0.245	-0.267	-0.127	-0.112	-0.084	-0.175	**-0.557***	0.395
Total jerk (m^2/s^5)	-0.248	-0.216	-0.149	0.037	0.615	-0.114	**-0.634****	0.254
RMS sway (m/s^2)	-0.163	-0.275	-0.140	-0.109	-0.045	-0.196	**-0.551***	0.399

Abbreviations: CERAD, Consortium to Establish a Registry for Alzheimer's disease; CW, Stroop, Color-Word; JLO, Judgment of Line Orientation; MoCA, Montreal Cognitive Assessment; SDMT, Symbol Digit Modalities Test; TMS, Total Motor Score; UHDRS, Unified Huntington's disease Rating Scale.

Digit span values were correlated with HD patients' iSWAY performance under varying sensory conditions. Significant differences are bolded. All values are Spearman's rho (r).

*$P < 0.05$;

**$P < 0.01$;

***$P < 0.001$;

****$P < 0.0001$.

contribute to these deficits, given that this area mediates the ability to perform a cognitive motor DT involving executive function.[60] While our observations make sense for the eyes open condition, the correlations obtained with the eyes closed condition are not as clear. It is possible that even when HD participants have reduced visuospatial skills, they are likely to use whatever visuospatial capacity they have during balance control, such that eliminating any visual cues caused greater balance impairments. This scenario was made even more challenging by the verbal fluency DT. Future neurophysiological studies employing techniques such as functional near-infrared spectroscopy (fNIRS)[61] while performing balance tasks might help elucidate neural mechanisms for postural control deficits in HD. fNIRS was able to detect changes in prefrontal cortical activation during DT gait paradigms in PD.[62] Therefore, a DT fNIRS study could provide a better understanding of prefrontal cortical activation patterns when cognitive loads are imposed on postural control in HD.

We found a reduction in information processing speed was correlated with impaired postural control under the ST conditions of reduced base of support and removed vision, suggesting inadequate cortical processing did not allow HD participants to quickly adapt to these conditions. Lower processing speed has been found to be associated with worse postural stability and increased falls in MS,[63] worse turning in PD,[64] and slower gait speed in the elderly,[65] further highlighting the importance of this cognitive domain in the neural control of balance.[66] We did not find significant correlations between the domains of attention, executive function, memory, or global cognition and postural

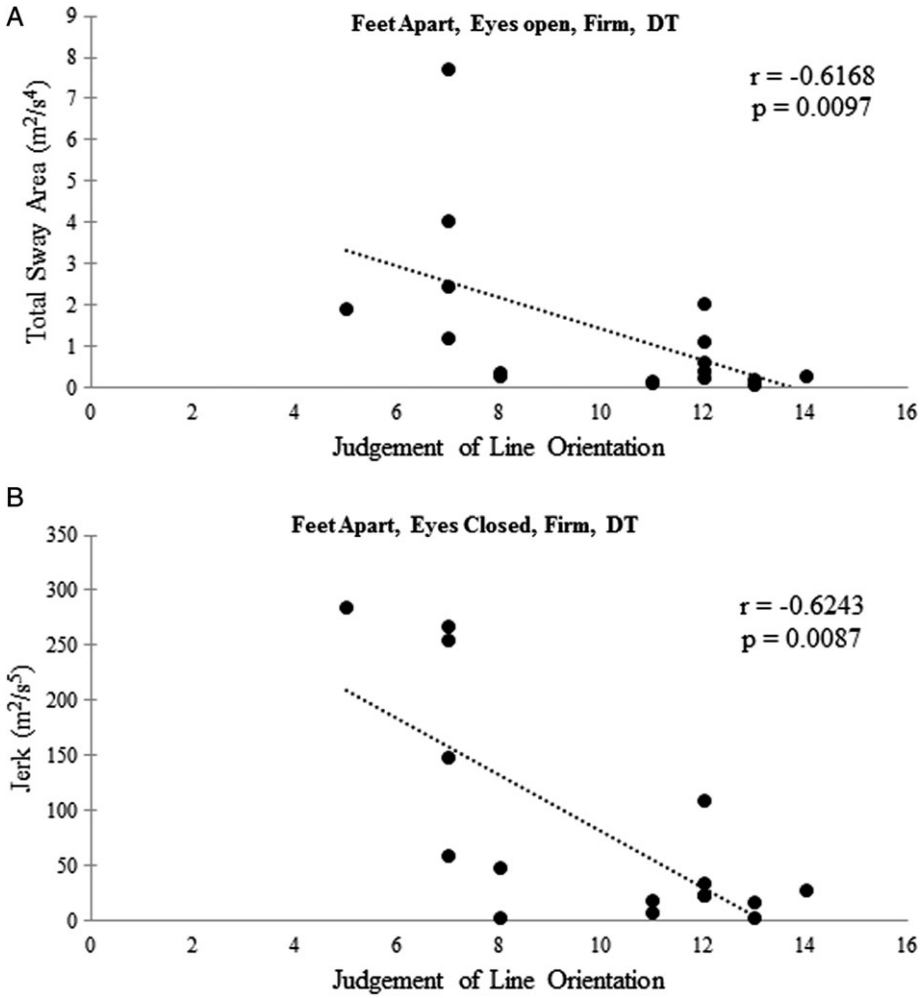

FIG. 3. Spearman's correlations (rho) between judgement of line orientation (JLO) scores and (A) total sway area and (B) total jerk under dual task (DT) conditions in HD patients.

instability. In the past, deficits in executive function were found to compromise a person's dual-tasking ability, negatively affecting gait and balance in both HD and PD.[67,68] We attribute our lack of significant correlations in the present study to our relatively small sample size.

Contrary to our expectations, the number of self-reported falls in the past year did not correlate with balance variables under any of the conditions. Retrospective self-report questionnaires, however, rely on the participants' self-awareness and long-term memory and are vulnerable to under-reporting. Future studies with prospective fall assessments, caregiver corroboration, or an activity-monitoring device might provide a more accurate fall report.

The strengths of this study are (1) the use of a sensitive, reliable inertial sensor system to measure balance control in HD under conditions reflecting everyday situations, including cognitive DT; (2) the use of an extensive neuropsychological testing battery that captures multiple cognitive domains and their potential correlations with postural sway and fall risk; and (3) examination of falls in HD, which to date has been understudied. Although this study highlights important negative consequences of DT cognitive interference and altered sensory input on postural control, there are limitations to address in future research. Subsequent studies would benefit from a larger sample size to strengthen potential associations between cognitive domains and balance impairments and stratify HD groups into various levels of motor and cognitive function. A more thorough investigation into visual-cognitive deficits by utilizing an extensive visual cognition test battery would be beneficial in providing insight into the relationship between visual and balance deficits in HD. Furthermore, incorporating eye-tracking technology into future balance and gait studies would address the impact of saccadic dysfunction, an early symptom of HD,[69] on postural control and fall risk.

In conclusion, HD participants exhibit the most detrimental effects of cognitive interference on postural control with a reduced base of support and vision eliminated. In addition, impaired visuospatial perception and processing speed was associated with worse postural control under DT and ST, respectively. These findings also identified potential future therapeutic strategies to improve balance and reduce fall risk in HD. For example, DT cognitive motor training paradigms,[70] virtual reality based rehabilitation,[71] and cognitive remediation therapies[72] have been shown to improve balance and turning and reduce falls in neurodegenerative disorders.[73] Future investigations on the impact of these therapeutic approaches in HD are warranted.

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Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

N.P.: 1A, 1B, 1C, 2A, 2B, 2C, 3A

J.G.: 1A, 1B, 1C, 2C; 3B

B.O.: 2C

B.B.: 1A, 3B

J.O.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

Disclosures

Ethical Compliance Statement: This study was approved by the Rush University Medical Center institutional review board (IRB); ID# 16050204. Informed consent was obtained from all study participants prior to testing. We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Supporting Information

Supporting information may be found in the online version of this article.

Supporting Table 1. iSWAY Variable Description
Expanded descriptive definitions of the three selected APDM™ iSWAY variables.