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Short Communication

Domains and correlates of clinical balance impairment associated with Huntington's disease

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ABSTRACT

This study sought to (a) determine the domains of clinical balance impairments associated with Huntington's disease (HD), and (b) evaluate associations between balance test scores and other disease-related impairments. Eighteen subjects with genetically definite HD and 17 age-matched control subjects were evaluated on the Mini-BESTest for their clinical balance impairments as well as the Unified HD Rating Scale (UHDRS) motor and total functional capacity scales, Activity-Specific Balance Confidence (ABC) Scale-short form, Montreal Cognitive Assessment (MoCA), and Symbol Digit Modalities Test (SDMT). Results showed that subjects with HD exhibited significantly lower total Mini-BESTest scores than subjects without HD (mean (95% CI) = 76 (64–87)% with HD, 98 (96–99)% without HD; $p = 0.0011$). Mini-BESTest item scores were significantly lower for subjects with HD on one-leg stance, postural responses, standing with eyes closed on foam, and dual-task timed up-and-go. Mini-BESTest scores significantly correlated with UHDRS motor ($r^2 = 0.68$; $p = 0.00003$) and total functional capacity ($r^2 = 0.75$; $p = 0.000006$) scores as well as with scores on the ABC short form ($r^2 = 0.45$; $p = 0.0024$), SDMT ($r^2 = 0.42$; $p = 0.0036$), and MoCA ($r^2 = 0.23$; $p = 0.046$) assessments. This study, therefore, demonstrates that balance impairments associated with HD span domains of anticipatory postural adjustments, postural responses, stance in challenging sensory conditions, and gait. Although preliminary, clinical balance impairment appears to be an efficient proxy evaluation of multiple HD-related factors due to associations with functional capacity, other motor impairments, balance confidence, and cognitive abilities.

1. Introduction

Huntington's disease (HD) is a genetic neurodegenerative disease in which basal ganglia circuits degenerate, resulting in motor, cognitive and behavioral impairments [1]. Among the motor symptoms, patients with HD exhibit impaired balance and gait, which increases the risk for falls, injuries, and diminished participation in physical activity [2–9]. Thus, falls and mobility management represents a primary objective when treating patients with HD [2,10].

Balance impairments associated with HD span several domains of postural control that include (a) anticipatory postural adjustments during voluntary postural transitions, (b) postural responses to an externally induced loss of balance, (c) standing balance under challenging sensory conditions, and (d) gait [2,4–9]. Single domains have often been tested in isolation between different studies, and these balance impairments may have also been tested with clinically infeasible instrumentation. Thus, a comprehensive and clinically feasible evaluation of balance impairment with HD across all four domains is warranted.

The Mini-BESTest [11] represents a clinical exam of dynamic balance that evaluates multiple tasks within each of the above-listed domains of postural control and could, therefore, provide value to the care of patients with HD. Using the Mini-BESTest, this study sought to comprehensively evaluate the domains of clinical balance impairment associated with HD, as well as to evaluate associations among Mini-BESTest scores and other HD-related impairments. We predicted lower total Mini-BESTest scores for subjects with HD compared to subjects without HD and that lower scores would be evident on items across all four domains evaluated

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by the exam. We also predicted Mini-BESTest scores would correlate with other HD-related motor symptoms, cognitive impairments, balance confidence, and a functional capacity to participate in life roles.

2. Methods

2.1. Subjects

Eighteen subjects with genetically definite HD (confirmed trinucleotide repeat number of at least 40) and 17 age-matched subjects without neurological impairment (Table 1) participated in the protocol, which was conducted at two separate institutions. All subjects gave informed consent to participate in the protocol, and the local Institutional Review Boards of each institution approved the protocol as well as the sharing of data between institutions.

2.2. Protocol

Subjects with HD were recruited by a neurologist associated with a movement disorders clinic. Subjects without HD were recruited by advertisement. All subjects were evaluated on the Mini-BESTest, which includes 14 scored items examining dynamic balance during voluntary postural transitions (sit-to-stand, rise-to-toes, one-leg stance), postural responses to a loss of balance (forward, backward, and lateral push-and-release tests of compensatory stepping), stance under modified sensory conditions (eyes open on firm surface, eyes closed on foam surface, eyes closed on inclined surface), and gait (walking with changes in speed, with head turns, with pivot turns, over obstacles, and dual-tasked timed up-and-go) [11]. Examiners were personally trained by the test developer. Subjects also completed the Montreal Cognitive Assessment (MoCA; [12]) and the Activities-Specific Balance Confidence Scale-Short Form (ABCsf; [13]). The subjects with HD additionally completed the motor and total functional capacity (TFC) subscales of the Unified HD Rating Scale (UHDRS), as well as the Symbol Digit Modalities Test (SDMT) that is associated with the UHDRS exam [14].

2.3. Statistical analysis

Differences between the subjects with and without HD in Mini-BESTest total scores, ABCsf scores, MoCA scores, and age were determined by two-tailed *t*-tests. Group differences in male-female composition were determined by Fisher's exact tests. Group differences in Mini-BESTest item scores were determined by Mann–Whitney *U* tests at the exact significance. Logistic regression on total Mini-BESTest scores was used to identify a cutoff score that best differentiated people with and without HD. Associations between Mini-BESTest total scores with UHDRS motor or TFC scores, SDMT scores, ABCsf scores, and MoCA scores were determined by Pearson correlation coefficients. Significance was defined as a *p*-value less than 0.05. Parametric statistics were used if Shapiro-Wilks tests indicated the assumption of normality was met, and statistics were adjusted for unequal variances if indicated by a Levene's test.

3. Results

The subjects with HD exhibited significantly lower total Mini-BESTest scores than the subjects without HD (Fig. 1). Item scores that were significantly lower for the subjects with HD (Fig. 1) included the one-leg stance test ($U = 69$, $p = 0.0043$), each direction of the push & release test ($U = 77$, $p = 0.010$ for forward step responses; $U = 84$, $p = 0.022$ for backward step responses; $U = 93$, $p = 0.049$ for lateral step responses), standing with eyes closed on foam ($U = 85$, $p = 0.025$), and the dual-task, timed-up-and-go test ($U = 67$, $p = 0.0038$). Mini-BESTest scores of the four subjects with minimal motor presentation (UHDRS motor scores <5 and TFC scores of 13) were all above 90% of the total possible score. Logistic regression of Mini-BESTest scores to differentiate subjects with and without HD identified an optimal cutoff score of 27 (96% score) on the Mini-BESTest to achieve 82% specificity, 78% sensitivity, and 80% accuracy (overall model $Chi^2 = 19.14$, $p < 0.0001$).

The subjects with HD also exhibited significantly lower ABCsf and MoCA scores than the subjects without HD (Table 1). Mini-BESTest total scores significantly correlated with UHDRS motor and TFC scores, as well as the ABCsf, SDMT and MoCA (Fig. 2).

4. Discussion

Balance impairments associated with HD spanned all four tested domains of postural control: voluntary postural transitions, postural responses to an induced loss of balance, stance in challenging sensory conditions, and gait. Consistent with previous research [5], gait impairments were most evident under dual-task conditions. In

Table 1
Group characteristics and outcomes.

Measure	Group		Statistic (*p*-value)
	With HD	Without HD	
# Female, # Male	13, 5	12, 5	Fisher's *p*-Value (1.00)
Mean (95% CI) Age (year)	45 (41–50)	45 (40–50)	$T_{33} = 0.08$ (0.933)
Mean (95% CI) Mini-BESTest (%)	76 (64–87)	98 (96–99)	$T_{17.7} = 3.87$ (**0.0011**)
Mean (95% CI) ABC_{sf} Score (%)	79 (66–91)	98 (96–100)	$T_{17.7} = 3.20$ (**0.0050**)
Mean (95% CI) MoCA Score	23 (20–25)	28 (27–29)	$T_{21.7} = 4.16$ (**0.00042**)
Mean (range) UHDRS Motor Score	13 (0–35)	Not evaluated	Not compared
Frequency of UHDRS Total Functional Capacity Scores By Stage*	Stage I = 9 Stage II = 6 Stage III = 3	Not evaluated	Not compared
Mean (range) Disease Burden Score	344 (215–485)	Not evaluated	Not compared
Mean (range) CAG Repeat #	43 (40–46)	Not evaluated	Not compared

* Stage I = Total Functional Capacity score 11–13; stage II = 7–10; stage III = 3–6.