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Clinical assessment of mobility and balance impairments in pre-symptomatic Huntington's disease

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Abstract

Background—Quantitative movement analysis can detect impairments in mobility and balance in persons with pre-symptomatic HD (pre-HD); however, it is not known whether clinical tests can also detect such impairments. Given the ease of administering clinical tests, and the importance of assessing mobility and balance, we examined whether clinical tests can detect motor impairments in individuals with pre-symptomatic HD.

Methods—Two clinical tests (Functional Reach Test [FRT] and Timed Up and Go [TUG]) and the Unified Huntington's Disease Rating Scale (UHDRS) were administered, along with quantitative gait analysis, to 15 individuals with pre-symptomatic HD and 15 controls.

Results—There was no difference in FRT and TUG scores across groups. Neither test was correlated with years to predicted disease onset or with quantitative gait analysis measures.

Conclusion—Clinical assessments such as FRT and TUG are not sensitive in detecting motor impairments in individuals with pre-symptomatic HD. The subtle nature of impairments provides a rationale for the use of quantitative gait analysis in pre-symptomatic HD.

Keywords

Huntington's disease; Pre-symptomatic; Clinical assessment; Mobility and balance

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Conflict of interest statement

None of the authors reports a conflict of interest with respect to financial or personal relationships with organizations that may have an influence on the work.

Huntington's disease (HD) is diagnosed on the basis of clinically observable motor impairments [1]. Interestingly, motor impairments are observed through quantitative movement analysis, well before diagnosis, in individuals who are pre-symptomatic HD mutation carriers (pre-HD) [2–4]. It is unclear whether clinical assessments can similarly detect impaired mobility and balance in pre-HD [5].

Since impaired mobility and balance are associated with functional limitations and falls later in the course of HD, it is important to determine whether clinical assessments can detect impairments in the pre-symptomatic stage. Clinical assessments are easy to administer across clinical settings, do not require extensive training, and are inexpensive compared with the instrumentation needed for quantitative movement analysis.

The most commonly used clinical assessment is the Unified Huntington Disease Rating Scale (UHDRS), which demonstrates high reliability and validity [6]. While motor items of the UHDRS can reliably detect impairments and their progression in symptomatic HD, there is little evidence that UHDRS items are able to reliably detect mobility and balance impairments in pre-HD [5].

The purpose of this paper was to examine whether clinical assessments of balance and mobility (Functional Reach Test [FRT] and Timed Up and Go [TUG]) can detect impairments in pre-HD. If clinical assessments detect impairments in pre-HD, they would be important to include in routine neurological examination. If clinical assessments were unable to detect impairments in pre-HD, it would highlight the need for quantitative motor examination in pre-HD [2].

1. Methods

1.1. Subjects

We estimated sample size based on quantitative gait analysis in pre-HD subjects [2]. Mean (SD) gait velocity for healthy controls was 1.43 (0.14) m/s, and for pre-HD was 1.27 (0.15) m/s. Assuming 80% power and significance level of 0.05, we required at least 14 subjects per group to demonstrate significant differences. In the current study, we enrolled 15 pre-HD (nine women) subjects. All 15 were participants in the PREDICT-HD study. Pre-HD subjects, each of whom had the HD gene mutation [1], were included if they did not meet clinical criteria for diagnosis of HD by a movement disorder specialist. Each pre-HD subject received a diagnostic confidence rating of 0 or 1 (out of 4), indicating respectively, no motor signs or presence of non-specific motor signs [1]. We also recruited 15 age-matched (± 2 years) controls from among mutation negative family members, students or staff through advertisement. Control subjects were included if there was a negative family history of HD or they had genetic confirmation of absence of the HD mutation (if they were members of known HD families). The mean (SD) age of pre-HD subjects was 38.9 (10.5) years, and they were, on average, 6.9 (7.1) years from predicted onset of symptoms, computed from a parametric survival model [7]. Mean (SD) age for control subjects was 39.5 (9.1) years. The local Institutional Review Board (protocol #9865 Columbia University) approved study procedures and all subjects signed an informed consent before participation.

1.2. Apparatus and procedures

Clinical tests of mobility and balance, administered by an occupational therapist, and quantitative gait analysis, were performed during a single session. The UHDRS was administered to pre-HD subjects by a movement disorder specialist. Additional details are provided below:

1. Clinical tests of mobility and balance (FRT and TUG): The FRT measures the maximum distance a person can reach forward, beyond arm's length, while maintaining a fixed base of support in standing [8]. The TUG test measures the time taken (in seconds) to rise from a seated position, walk three meters, turn, walk back and sit then down again at a self determined comfortable speed [9]. We chose these tests because they examine mobility and balance and can be administered in a short period of time.
2. Quantitative gait analysis (GAITRite® CIR Systems, Inc.: Havertown, PA): Pre-HD subjects walked on an instrumented walkway at their preferred speed, stop three meters beyond the end of the walkway, turn around and walk back to the start (3 m from the beginning of the walkway). We analyzed seven measures: gait velocity, stride length and cadence (measures related to gait speed), double support percent and support base (measures of dynamic balance), and the coefficients of variation for stride length and step time (measures of gait patterning and fall risk).
3. UHDRS [6]: We analyzed four items: gait, tandem walk, retropulsion pull test (each scored from 0 [no disability] to 4 [maximum disability]), and total motor score (maximum score of 124, based on 31 test items, including chorea, dystonia, eye movements, hand movements, gait, tandem walk, and retropulsion pull test).

1.3. Analyses

To determine if clinical tests of balance and mobility (FRT and TUG) differentiated between pre-HD and controls, we used the Mann–Whitney *U* test for independent samples, because it does not make assumptions about the underlying distribution of the data. To test concurrent validity of clinical tests, we computed their Pearson's correlation with quantitative gait measures and with predicted years to symptom onset. All statistical analyses were conducted in SPSS version 16.

2. Results

The Mean UHDRS total motor score for pre-HD was 2.78 (SD 1.62). Total motor scores in these 15 pre-HD subjects were distributed as follows: 0 ($n = 2$), 1 ($n = 3$), 2 ($n = 3$), 3 ($n = 4$), 4 ($n = 2$) and 5 ($n = 1$), indicating that some subjects demonstrated non-specific motor signs. All pre-HD subjects scored zero on gait, tandem walk and retropulsion items, indicating that these items were unable to detect impairments in mobility and balance.

Statistical analysis (Mann–Whitney *U*) did not show differences in the performance of pre-HD and controls on the FRT (pre-HD = 0.413 ± 0.063 m, controls = 0.423 ± 0.063 m; $P = 0.696$) and the TUG (pre-HD = 6.5 ± 1.37 s, controls = 6.8 ± 0.67 s; $P = 0.33$). In addition, neither clinical test was significantly correlated with quantitative gait measures related to

gait speed, dynamic balance or falls and gait patterning (Table 1). Predicted symptom onset was not well correlated with FRT (Pearson's $r = 0.23$, $P = 0.44$), or with TUG (Pearson's $r = 0.37$, $P = 0.25$).

3. Discussion

Our current results indicate that clinical assessments such as FRT, TUG and UHDRS items (gait, tandem and retropulsion) do not detect mobility and balance impairments in pre-HD. In contrast, quantitative gait analysis (at sampling frequency of 60 Hz. using the GAITRite®) detected decreased gait speed, increased double support time and increased temporal variability in the same pre-HD subjects in a prior study [2].

One possible explanation for the inability of clinical assessments to detect impairments may be our small sample size. However, clinical tests (such as gait, tandem walk and retropulsion pull test items of the UHDRS) with larger numbers of pre-HD subjects have not been able to detect mobility and balance impairments [1, 5]. Secondly, a similar sample size was adequate to demonstrate significant differences between pre-HD and controls on quantitative gait analysis [2].

Another possible explanation for our results may be that we chose inappropriate clinical tests for measuring balance and mobility impairments. This is unlikely because FRT and TUG detect impairments in the early stages of symptomatic HD [10]. It may be useful to examine other sensitive assessment tools such as the Tinetti Performance Oriented Mobility Assessment, which have been validated for use in the elderly and individuals with Parkinson's disease [11].

A likely explanation for our results is that impaired mobility and balance in pre-HD is very subtle and difficult to detect through clinical assessment. Detection of subtle impairments in pre-HD may necessitate the use of quantitative gait analysis (such as the GAITRite®) with high rates of sampling for spatio-temporal data.

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Table 1

Pearson correlation coefficient (P value) of Functional Reach and Timed Up and Go with quantitative gait measures.

Quantitative gait measures	Clinical Assessments	
	Functional Reach	Timed Up and go
Gait speed		
Gait velocity	0.23 (0.59)	0.19 (0.64)
Stride length	0.20 (0.62)	−0.26 (0.53)
Cadence	0.06 (0.88)	0.87 (0.84)
Dynamic balance		
Double support percent	0.08 (0.86)	0.31 (0.39)
Support base	0.27 (0.52)	0.25 (0.56)
Falls and gait patterning		
CoV stride length	−0.29 (0.52)	0.03 (0.95)
CoV step time	−0.01 (0.98)	0.26 (0.48)