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Gait Dysfunction in Huntington’s Disease: Parkinsonism and a Disorder of Timing

Implications for Movement Rehabilitation

Andrew J. Churchyard, Meg E. Morris, Nellie Georgiou, Edmond Chiu, Randall Cooper, and Robert Iansek

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Huntington’s disease (HD) is an autosomal dominant degenerative disease caused by 37 or more CAG triplet repeats of a gene located at sub-band 4p16.3 of the short arm of chromosome 4 (1). Huntington’s disease is manifest primarily as a combination of involuntary movements (chorea), parkinsonism (rigidity and akinesia and bradykinesia, slowness in initiating and executing movement, respectively), and predominantly “frontostriatal” cognitive impairment that may ultimately result in dementia (2). Rare cases of HD characterized by cerebellar ataxia occur (2). Hypokinesia of the limbs appears to be invariable, even in the absence of marked parkinsonism (3,4). As with Parkinson’s disease (PD), reaction (RT), and movement (MT) times in a variety of tasks are slowed in HD (3,5–8). Moreover, patients with HD are more impaired than controls in changing cognitive set and in holding and shifting attention (9,10). Whether or not upper limb MT and RT correlate with lower limb gait parameters is unknown.

The studies described in this chapter sought to quantify gait patterns in patients with HD and control subjects using spatiotemporal variables obtained from stride analysis, with the goal of providing an intellectual basis from which to develop rehabilitative strategies to compensate for abnormalities in walking. In addition, we tested the hypothesis that basal ganglia destruction is the major cause of gait dysfunction and abnormal postural control in patients with HD by examining the relationship between gait dysfunction and overall disease severity as measured by the Unified Huntington’s Disease Rating Scale (UHDRS), which is assumed to be an index of striatal and pallidal damage. A further aim was to examine whether abnormalities in gait correlated with deficits in cognition so as to quantify the impact of cognitive impairment on difficulties in walking.

METHODS

Symptomatic community-dwelling HD patients (more than 37 triplet repeats) were recruited by EC and by advertisement in the Huntington’s Disease Association of Victoria newsletter. Control subjects were cognitively intact (MMSE greater than 26), had no history of neurological, psychiatric, or rheumatologic disease and were matched to the patients for age and height.
Patients were examined by AC for severity of HD with the UHDRS. Upper limb motor parkinsonism was assessed objectively with RT and MT time tasks. MT was quantified by serially pressing buttons at choice points along a designated sequential pathway in response to visual stimuli (7). Varying the stimulus allowed the reliance on advance visual information to be examined (7). RT was measured as the difference in the time of onset of the overall response to relevant and irrelevant stimuli (Simon effect) (7). Cognitive function was determined with the Mini Mental State Examination (MMSE), Stroop test, Trails A and B, Controlled Oral Word Association, and Montgomery-Asberg Depression Scale (11–15). Scores obtained by patients and controls with each of the RT, MT, Trails, Controlled Word Association Test, MMSE, Stroop, and Montgomery-Asberg scales were compared with t-tests. An Interference score was calculated for the Stroop test and Trails B was subtracted from Trails A so as to obtain a switching score for each patient and control.

The spatial (distance) and temporal (time) parameters of gait were quantified by RC, MM and RG using a Clinical Stride Analyzer (CSA; B&L Engineering, Santa Fe Springs, CA, U.S.A.), which comprised four pressure-sensitive switches worn as inner soles in the subject’s shoes connected to a 0.5-kg microcomputer suspended from a belt (16–19). Data from each of the footswitches were sampled every 2 ms and stored prior to being analyzed (PCSA software, Version 6, B&L Engineering). Recording was activated and terminated by a hand-held trigger that was activated by the examiner at the beginning and end of the walkway. Five 10-m walking trials for free (preferred), slow, and fast walking were conducted; the order of the conditions were counterbalanced to control for series effects. The variables measured were gait velocity (m/min), stride length (m), cadence (steps/min), and duration of the double-support phase (expressed as a percent of the gait cycle). To determine if patients could utilize external cues to normalize gait, walking in time to a metronome (80 bpm) was also examined. In order to determine if attentional mechanisms have an impact on gait in HD, walking was examined while counting digits backward (distraction task).

For each subject, the mean of trials 2 and 3 from a series of five successive trials for each gait condition were entered into an SPSS (Version 6) data file. Distributions of each of the variables for each condition were inspected and the descriptive statistics obtained. Normality of distribution of velocity, stride length, cadence and duration of double stance in free walking was confirmed with the Kolmogorov-Smirnov and Shapiro-Wilks statistics. Velocity, stride length, cadence, and duration of double stance in the HD and control groups were compared using univariate analyses of variance and t-tests.

Objective parameters of gait (velocity, stride length, cadence, and duration of double stance) were related to the UHDRS motor score, RT, and MT, all measures of cognitive function, and the duration of symptoms with Pearson’s correlation.

The relationship between gait dysfunction and disease severity was explored to test the hypothesis that basal ganglia destruction is a major contributing factor to gait disorders in HD by relating the UHDRS motor score to gait velocity, stride length, cadence, and duration of double stance, RT, and MT.

RESULTS

Data from 20 patients with symptomatic HD (chorea with 37 triplet repeats) were compared to 16 age-matched controls (Table 37.1). The initial presentation of HD was with chorea in 15, psychiatric disease in three, and cognitive impairment in two. Inheritance was maternal in 13, paternal in four, and unknown in three. Six patients received neuroleptics for suppression of chorea and seven were taking antidepressants. The mean duration of symptomatic disease was 9.9 years (range, 1 to 27). The mean UHDRS motor score was 44.1. The UHDRS motor score and duration of symptomatic illness correlated (r = 0.67, P < 0.05).

Preferred Gait (Free Walking)

The preferred velocity of free walking for HD subjects was slower than for control subjects. Whereas control subjects walked on average at 84.5 m/min, those with HD had an average

<table>
<thead>
<tr>
<th>Veloctiy (m/min)</th>
<th>Stride length (m)</th>
<th>Cadence (step/min)</th>
<th>Duration of double support (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>HD</td>
<td>Controls</td>
<td>HD</td>
</tr>
<tr>
<td>HD subjets</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.001
TABLE 37.1. Demographic characteristics of Huntington's disease and control subjects (mean [SD])

<table>
<thead>
<tr>
<th></th>
<th>Gender</th>
<th>Age (yr)</th>
<th>Disease duration (yr)</th>
<th>UHDRS</th>
<th>MMSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huntington's disease</td>
<td>16M</td>
<td>58.2</td>
<td>8.9</td>
<td>44.1</td>
<td>24.6</td>
</tr>
<tr>
<td></td>
<td>4F</td>
<td>(12.9)</td>
<td>(6.6)</td>
<td>(25.5)</td>
<td>(3.8)</td>
</tr>
<tr>
<td>Controls</td>
<td>13M</td>
<td>55.4</td>
<td>NA</td>
<td>NA</td>
<td>29.4</td>
</tr>
<tr>
<td></td>
<td>3F</td>
<td>(10.5)</td>
<td>—</td>
<td>—</td>
<td>(0.7)</td>
</tr>
</tbody>
</table>

HD subjects and controls were matched for age. The mean duration of symptomatic disease was 9.9 years and the mean United Huntington's Disease Rating Scale (UHDRS) motor score was 44.1.

SD, standard deviation; MMSE, Mini-Mental Examination; NA, not applicable.

velocity of only 59.7 m/min [F(3,5) = 19.3, P < 0.005] (Table 37.2). Velocity is the product of stride length × cadence × 1/2. Double stance is the time when both feet are on the ground at the beginning and end of the gait cycle. For preferred (self-selected) speed of walking, the mean stride length in HD of 1.16 m was significantly less than the controls (1.51 m) [F(3,5) = 17.5, P < 0.005] (Fig. 37.1; Table 37.1). That is, parkinsonism of gait (reduced velocity and stride length) occurred in HD (16,20). Notably, cadence was reduced in HD to 100.6 steps/min compared with 111.7 steps/min in the control subjects [F(3,5) = 8.4, P = 0.006] (Fig. 37.2). Of note, the variability of velocity, stride length, and cadence in HD was markedly increased. The standard deviation of each gait parameter was in excess of twice that of the control subjects. The duration of DS was unaffected by HD.

The UHDRS motor score correlated with velocity (R = −0.53, P < 0.05) and stride length (R = −0.60, P < 0.05), but not cadence (R = −0.31, P > 0.05) or double stance (R = 0.20, P > 0.05). The duration of symptomatic disease did not correlate with any of velocity, stride length, cadence, or double stance (data not shown).

In summary, the preferred gait velocity was slowed in HD because both the rhythmical stepping rate (cadence) and stride length were reduced in comparison to control subjects. Moreover, step-by-step variability of cadence and stride length were increased, indicating a disturbance of both timing and amplitude regulation of gait.

**Fast and Slow Walking**

When instructed to walk either quickly or slowly, HD patients could modify velocity and stride length, but each remained less than for the control subjects in both conditions (Fig. 37.1; Table 37.2). Velocity at fast walking was 84.6 m/min for those with HD versus

### TABLE 37.2. Mean (SD) velocity, stride length, cadence, and duration of double stance in Huntington's disease (HD) and control subjects during all gait conditions

<table>
<thead>
<tr>
<th></th>
<th>Normal walking</th>
<th>Fast walking</th>
<th>Slow walking</th>
<th>Digits backward</th>
<th>Metronome (60 bpm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HD</td>
<td>Control</td>
<td>HD</td>
<td>Control</td>
<td>HD</td>
</tr>
<tr>
<td>Velocity (m/min)</td>
<td>59.7</td>
<td>84.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>84.6</td>
<td>109&lt;sup&gt;a&lt;/sup&gt;</td>
<td>45.5</td>
</tr>
<tr>
<td>(21.3)</td>
<td></td>
<td>(9.1)</td>
<td>(26.4)</td>
<td>(12.0)</td>
<td>(18.2)</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>1.16</td>
<td>1.51&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.43</td>
<td>1.74&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.00</td>
</tr>
<tr>
<td>(0.32)</td>
<td></td>
<td>(0.11)</td>
<td>(0.34)</td>
<td>(0.15)</td>
<td>(0.31)</td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>100.6</td>
<td>111.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>120.6</td>
<td>128.5</td>
<td>95.1</td>
</tr>
<tr>
<td>(13.6)</td>
<td></td>
<td>(7.7)</td>
<td>(15.0)</td>
<td>(11.4)</td>
<td>(10.4)</td>
</tr>
<tr>
<td>Duration of double limb support (%)</td>
<td>34.8</td>
<td>31.0</td>
<td>20.3</td>
<td>28.9</td>
<td>36.2</td>
</tr>
</tbody>
</table>

<sup>a</sup>P < 0.05.

Velocity, stride length and cadence were reduced in HD in all gait conditions. Duration of double stance was the same in the HD and control subjects. Variability of all gait parameters was markedly greater in the HD subjects than in the controls.
109.7 m/min in the controls \( [F(1,35) = 12.3, P < 0.005] \) and stride length was 1.43 and 1.74 m \( [F(1,35) = 11.7, P < 0.005] \), respectively, in the HD and control subjects. In the slow walking condition, velocity was only 45.5 m/min for those with HD compared with 59.1 m/min for the control subjects \( [F(1,35) = 8.2, P = 0.007] \). Stride length was 1.00 and 1.28 m \( [F(1,35) = 11.9, P < 0.005] \) in the HD and control subjects, respectively. Cadence in both groups varied according to the demands of the task, but was not significantly different in HD from the controls (Fig. 37.2). The duration of double stance was similar for the two groups. As with free walking, there was markedly more variability in velocity, stride length, and cadence in the HD subjects than the control subjects, with standard deviations in the former being generally twice that of the latter.

**Metronome Gait**

When walking in time to a metronome set at 80 bpm, velocity remained less in those with HD than for the control subjects, but this difference was not statistically significant \( [HD 49.4 \text{ m/min versus controls 53.9 m/min; } F(1,35) = 1.8, P = 0.183] \). Stride length remained less in those with HD \( [HD 1.11 \text{ m versus controls 1.32; } F(1,35) = 17.7, P < 0.005] \) (Fig. 37.1). Cadence was modulated in response to the beat of the metronome to 88.1 steps/min in HD and 81.6 steps/min in the controls. However, cadence was different in the two groups \( [F(1,35) = 5.1, P = 0.031] \), implying that its regulation in response to an external cue is impaired in HD. Neither group was able to perfectly entrain foot step rates to the metronome as cadence in each was significantly greater than 80 bpm \( (P < 0.05 \text{ student's t-test for each group versus test value of 80.}) \). The duration of double stance remained the same in the two groups. Notably, there was markedly more variability in velocity, stride length, and cadence in the HD subjects than the control subjects with standard deviations in the former being invariably twice or more than that of the latter (Table 37.2; Fig. 37.2).
GAIT DYSFUNCTION IN HUNTINGTON’S DISEASE

**Condition**

FIG. 37.2. Cadence (steps/min) in Huntington’s disease (HD) and control subjects. Cadence was reduced in patients with HD in all the conditions. Variability of cadence was markedly increased in the subjects with HD. This variability was particularly prominent when walking in time to a metronome striking at 80 bpm. The abnormality of cadence is consistent with a disorder of timing of gait.

---

**Digits Backward Task**

When walking while counting backward, velocity [HD 57.7 m/min versus controls 65.4 m/min; F(1,35) = 2.6, P = 0.119] and cadence [HD 90.4 steps/min versus controls 95.2 steps/min; F(1,35) = 0.5, P = 0.488] remained less in those with HD than for the control subjects, but this difference was not statistically significant. Stride length remained less in those with HD [HD 1.16 m versus controls 1.36; F(1,35) = 5.8, P < 0.05]. The duration of double stance remained the same in the two groups. The variability in each gait parameter was greater in the HD subjects than the control subjects, but was most marked for stride length. Overall, reduced attention to walking (distraction) had little or no effect on stride length or duration of double stance, but reduced velocity and cadence when compared to free walking (Figs. 37.1 and 37.2; Table 37.2).

---

**Movement and Reaction Times**

Only 10 of the 20 HD subjects could perform the MT and RT tasks. Analysis is therefore confined to these patients, who were the least severely affected with respect to both motor and cognitive function. Only one of these patients was receiving a major tranquilizer and he was not overly parkinsonian (Webster score 5). In this relatively mildly impaired group, both MT and RT were significantly increased (Table 37.3). Thus, MT and RT were 299 and 858 msec, respectively, in the HD group and 177 and 584 msec, respectively, in the controls [MT: t(18) = 3.38, P < 0.01 and RT: t(18) = 2.13, P < 0.05].

RT failed to correlate with any gait parameter (velocity, stride length, cadence, and duration of double stance; P > 0.05 all). In contrast, MT correlated with velocity (R = −0.73, P < 0.05), cadence (R = −0.68, P < 0.05), and stride length (R = −0.73, P < 0.05), but not
TABLE 37.3. Mean (SD) reaction time (RT), movement time (MT) and scores for tests of frontostriatal cognitive function (Stroop, Trails A and B, Controlled Oral Word Association [COWA])

<table>
<thead>
<tr>
<th></th>
<th>RT (N = 10)</th>
<th>MT (N = 10)</th>
<th>Stroop Interference (N = 12)</th>
<th>Trails A and B (switching component) (N = 12)</th>
<th>COWA (N = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huntington’s disease</td>
<td>658 msec a</td>
<td>299 msec a</td>
<td>77</td>
<td>72 msec a</td>
<td>33 a</td>
</tr>
<tr>
<td></td>
<td>(393)</td>
<td>(106)</td>
<td>(37)</td>
<td>(34)</td>
<td>(12)</td>
</tr>
<tr>
<td>Controls (N = 16)</td>
<td>584 msec</td>
<td>177 msec</td>
<td>73</td>
<td>43 msec</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>(103)</td>
<td>(21)</td>
<td>(27)</td>
<td>(20)</td>
<td>(16)</td>
</tr>
</tbody>
</table>

RT and MT (examined in 10 Huntington’s disease [HD] subjects) were slowed and the variability of each was increased in HD. Performance on the Trails A and B and Controlled Oral Word Association was impaired in HD, but the Stroop test score was unaffected (12 HD subjects examined).

RT and MT did not correlate with duration of disease or the UHDRS motor score (data not shown, P > 0.05 both).

Neuropsychological Studies

Only 12 of the 20 HD subjects were able to perform the neuropsychological tasks (Stroop, Trails A and B, Controlled Oral Word Association) and therefore could be analyzed. The remaining eight cases were too cognitively impaired (MMSE < 22) to successfully complete these tasks. HD and control subjects were matched for age [HD: 54 ± 10 versus controls: 53 ± 10, t(22) = 0.39, P > 0.05] and years of education [HD: 13 ± 2 versus controls: 14 ± 3, t(22) = −1.57, P > 0.05]. However, the HD subjects were more depressed as measured by the Montgomery-Asberg Depression Scale [HD: 9.8 ± 6.4 versus controls: 1.4 ± 1.7, t(22) = 4.42, P < 0.001] and their MMSE was lower [HD: 27.0 ± 1.7 versus controls: 29.4 ± 0.8, t(22) = −4.48, P < 0.001].

The HD patients took longer to switch between tasks on the Trail Making test [HD: 72 msec ± 34 versus controls: 43 msec ± 20, t(16) = 2.21, P < 0.05] and achieved a lower score on the Controlled Oral Word Association test than the controls [HD: 33 ± 12 versus controls: 50 ± 16, t(22) = −2.88, P < 0.01] (Table 37.3). However, performance of the Stroop task was similar in both groups [Interference score: HD 77 ± 37 versus controls 73 ± 27, t(22) = 0.29, P > 0.05]. There was no correlation between either the Trail Making test score or the Controlled Oral Word Association test score and any of velocity, stride length, cadence, and duration of double stance (data not shown).

The UHDRS score correlated with the Controlled Oral Word Association test score (R = −0.62, P < 0.05), but not the Trail Making test score (R = −0.11, P > 0.05) or the MMSE for all 20 HD subjects (R = −0.39, P > 0.05). The MMSE score correlated with the Controlled Oral Word Association test score (R = 0.55, P < 0.05), but not the Trail Making test score (R = 0.33, P > 0.05). The MMSE score did not correlate with the duration of disease in the full sample of 20 HD patients (R = −0.43, P > 0.05). Correlations were not attempted for the Stroop test scores.

DISCUSSION

The major finding of this study is that locomotion in HD is abnormal because of a combination of hypokinesia, evidenced by reduced stride length, and disordered regulation of rhythmic stepping manifest as reduced stepping rates, poorly modulated cadence, and increased variability of velocity, stride length, and cadence.

The gait velocity of the HD subjects was very slow for free (preferred speed) walking (Table 37.2). Patients with HD could voluntarily vary their speed of walking yet remained significantly slower during the fast and slow walking tasks than the control subjects. The velocity of walking in time to an external auditory cue and in a distraction task was also less than for controls. That is, although HD patients could vary the velocity of walking, they were unable to do so to the same degree as controls. This pattern may vary from one patient to another, and presumably depends on the degree of disorganization of the frontal and striatal components of locomotion. The gait velocity was decreased relative to controls (21–22) and was correlated with HD duration (R = 0.32, P < 0.05) in HD patients. The MMSE score, which was also correlated with HD duration (R = 0.55, P < 0.05), was also significantly related to gait velocity.

The bradykinesia is likely to be the result of degeneration of the nigrostriatal dopamine system. Initial studies have shown that dopamine depletion in the neostriatum is inversely related to the amount of DA loss. A similar pattern of results has been observed with other neurotransmitter systems. For example, a number of studies have shown that the rate of progression of HD is related to the rate of dopamine depletion in the neostriatum (28). It has been suggested that the abnormalities of gait in HD are related to the dopamine depletion in the neostriatum. The gait abnormalities in HD are likely to be related to the dopamine depletion in the neostriatum.

The abnormalities of gait in HD are likely to be related to the dopamine depletion in the neostriatum. The abnormalities of gait in HD are likely to be related to the dopamine depletion in the neostriatum. The abnormalities of gait in HD are likely to be related to the dopamine depletion in the neostriatum.
velocity of locomotion, it was invariably slowed. Similarly, stride length was decreased relative to the control subjects in all the gait tasks and again could not be "normalized" in response to varying requirements. Reduced velocity in association with a shortened stride length and impaired capacity to change either according to the requirements of different gait tasks is characteristic of PD and is indicative of gait hypokinesia (16–20). Reduced velocity of gait and stride length has previously been described in HD (21–23). Upper limb RT and MT were decreased in HD as in previous studies (Table 37.3) (3,4). MT, but not RT, correlated with velocity, stride length, and cadence. These findings are consistent with current concepts that MT, which comprises most of the gait cycle as distinct from the brief RT of each step, is a long-duration preprogrammed motor act.

The pathophysiologic substrate of hypokinesia in HD appears likely to be basal ganglia degeneration, which is centered on the caudate nucleus (Cd) and subsequently putamen (Pu) (24). Initially, GABAergic striatal projection neurones are selectively destroyed, but as the disease progresses other striatal neurones degenerate and involvement of the globus pallidus (GP) is invariable in advanced HD (24,25). Marked loss of neurones in the substantia nigra pars compacta occurs rarely. Gross parkinsonism may occur without severe loss of dopaminergic nigral neurones, and striatal dopamine receptors are equally affected in the choreic and rigid variants (24,26,27). Current theories suggest that the basal ganglia form part of partially segregated, parallel functional loops that run from cortex to striatum to GP to thalamus to cortex (28). Because the associative loop includes the Cd, and the motor loop the Pu, both are likely to be dysfunctional in HD. Functional positron emission tomography studies have related upper limb bradykinesia in HD to reduced activation of the striatum and key frontal premotor cortices that comprise the corticobasal gangliothalamocortical motor circuit (24,28,29). Rigid HD has been associated with a greater loss of GABA in the internal GP and more severe destruction of GABAergic striatal neurones projecting to this nucleus than the choreic form (26,30). Thus, it appears that hypokinesia in HD is caused by destruction of the striatal neurones that project to the GP and causes disinhibition of inhibitory pallidal outflow. Chorea is thought to be a consequence of overactivity of the subthalamic nucleus as a result of reduced inhibition of the lateral GP.

The symptomatic severity of HD has been shown to correlate with the degree of striatal and pallidal destruction (24). We found that the UHDRS motor score correlated well with stride length and velocity of free walking. That is, the severity of gait hypokinesia correlated with the overall degree of motor disability and, by implication, the extent of basal ganglia damage, as would be predicted by the hypothesis that hypokinesia in HD is caused by loss of inhibitory striatal neurones projecting to the GP. We found no relationship between the UHDRS motor score and the two objective indices of upper limb hypokinesia (RT and MT) studied; however, the numbers of cases studied was small (N = 10). Larger studies with adequate power are required to determine if upper limb hypokinesia correlates with UHDRS score.

Cadence of free walking was reduced in HD as previously described (Table 37.2) (21,23,32). The proportion of the gait cycle spent in double stance was unaffected (32). Thus, the abnormalities of locomotion in HD differ from those of PD, where the proportion of the gait cycle spent in double stance is increased and cadence is unaffected (18). The deficits in cadence were more profound than a simple reduction of the rate of stepping alone. HD patients could vary cadence cruelly in keeping with the requirement to voluntarily increase or decrease the speed of walking. However, since gait velocity and stride length were reduced in all tasks, by implication the HD patients were unable to increase the rate of stepping in compensation. The HD patients were less able to entrain stepping in time with an external auditory cue (metronome chiming at 80 bpm) than the control subjects as evidenced by a grossly inaccurate mean of 88.1 steps/min versus 81.6 steps/min, respectively, but also by the remarkable variability in the rate of stepping [standard deviation of 11.5 (13.1%) in HD versus 2.2 (2.6%) in controls] associated with this
task. Moreover, there was a striking variability of stride length, velocity, and cadence in all the gait tasks and of RT and MT. The marked variability observed by us has been described in the gait and upper limb movements in HD (21–23,33). That is, there is excessive variability of amplitude and timing of movement in HD.

The basis of the excessive variability of both the amplitude and timing of movement in HD is unknown. Postural instability, which is common in HD, is a potential cause of excess variability of gait amplitudes and timing (34). We have not, thus far, quantified postural instability in the HD subjects, although it was impaired on the retropulsion test (UHDRS item 20) in 16 of 20 (mean score 1.7 ± 1.0). Because the duration of double stance was not increased in HD, postural stability might be thought to be intact in HD. However, it appears more likely that failure to increase the duration of double stance in the presence of postural instability represents another example of the inability of HD patients to appropriately adapt motor behavior to need. At the current level of understanding, the contribution of postural instability to the increased variability of gait parameters is unknown.

Timing of serial movements is thought to be a product of a distributed network which comprises many structures, including the basal ganglia, prefrontal and frontal cortices, brainstem premotor nuclei, and cerebellum (35–39). The basal ganglia are thought to regulate switching between learned motor acts, whereas the cerebellum controls timing and processes sensory feedback to optimize movement (35–39). Abnormal regulation of amplitude and timing of gait and upper limb movements occur in PD (21,32,40,41). However, such marked variability in velocity, stride length, and cadence in the different conditions studied and RT and MT is not found in PD and cannot be attributed to hypokinesia (16–19,21). Chorea appears unlikely to account for the observed variability because cadence did not correlate with the UHDRS score in this study or with the severity of chorea when examined by others (21). In this study, cadence during free walking could not be correlated with the UHDRS score in contrast to stride length. Since clinical disease severity is related to the extent of striopallidal degeneration, the deficits in timing and regulation of amplitude of gait parameters in HD observed by us might be unrelated to basal ganglia degeneration (24).

Cerebellar ataxia is associated with reduced stride length and increased variability of stride length and duration of stride with free walking, whereas cadence is only mildly reduced (40,42). Studies of postural control in cerebellar disease have also found increased variability of movement latencies (43,44). Cerebellar atrophy, unlike PD, results in increased variability of intertap intervals in a task requiring serial tapping (38). Increased variability of the timing and amplitude of movement is a fundamental consequence of cerebellar dysfunction. Mild to moderate destruction of cerebellar Purkinje cells has been detected in many HD patients even in the absence of gross degeneration and may be severe in a minority (24,45). We suggest that, although unproven, the deficits in the regulation of timing and amplitude of movement observed in HD might result from degeneration of cerebellar Purkinje cells.

The HD subjects were impaired in their ability to switch between tasks on the Trail Making test, achieved a lower score on Controlled Word Association test and showed a slower RT in a task that required discrimination between irrelevant and relevant stimuli (Simon effect, which depends on maintenance of attention) (Table 37.3) (7). Performance of these tasks is impaired with frontostriatal cognitive dysfunction (7,9,10). Surprisingly, another test of frontostriatal function, the Stroop test, was unaffected, and impaired attention while walking (counting digits backward) had a similar effect on gait in both the HD and control subjects. Nonetheless, this and many other studies demonstrate that frontostriatal cognitive impairment is an extremely common, if not invariable, result of even mild HD (46–48).

It is noteworthy that the neuropsychology tasks did not correlate with gait parameters, but that the score on Controlled Word Association test correlated with both the MMSE and the UHDRS motor score. There are three possible reasons to account for our failure to correlate frontostriatal cognitive impairment and motor dysfunction. First, the correlational studies were

confined to subjects with overt motor impairment. Second, the tasks involved the ability to maintain attention, a cognitive function that is not necessarily impaired in mildly affected subjects. Third, the Stroop test may be centered on an aspect of attention that is relatively unaffected by the cognitive impairments of PD and HD. This postulate is supported by observations of serial omission of overt motor responses in a task requiring sequential associations with digits (46). Hence, the attentional demands of the Stroop test with digits may be different than the attentional demands of a task with digits involved in calculation of RT and the MMSE score (46).
confined to a small subset of mildly affected subjects selected because they were able to complete the tasks; therefore, failure to detect any correlation might be an artefact attributable to limited statistical power. Second, no correlation between cognitive impairment might be expected in this mildly affected patient group because the corticobasal ganglia associative loop, which is centered on the Cd, regulates the direction and maintenance of attention, whereas the motor loop is centered on the Pu, and because the Cd is the focus of neuronal degeneration in early HD (24,28).

This possibility is consistent with the repeated observation that cognitive impairment precedes overt motor dysfunction in HD and by the correlation of behavioral and cognitive abnormalities with the severity of metabolic changes in the Cd, but is difficult to reconcile with the correlation of the score on Controlled Word Association test with both the MMSE and the UHDRS motor score (46–49). Third, frontostriatal cognitive impairment may not contribute to gait dysfunction in HD.

MOVEMENT REHABILITATION IN PATIENTS WITH HUNTINGTON’S DISEASE

Although movement disorders are arguably the most common and disabling outcome of HD, little is known about the effects of movement rehabilitation strategies for people with this progressive basal ganglia disorder. To date there have been no randomized clinical trials (RCTs), comparative group outcome studies, or controlled single case studies investigating the effects of physical therapy treatment on movement disorders in HD. Apart from the data on external cues and dual task performance presented in this chapter, there is no information on the response of those with HD to interventions such as external cuing, attentional strategies, falls prevention programs, or even strengthening programs. Although physical therapists and occupational therapists play a role in educating people with HD and their caregivers on how to manage movement disorders and prevent falls, this has been done on a case-by-case basis without a theoretical framework from which to predict the likely effects of treatment. Currently, clinicians rely on general clinical decision-making strategies in order to determine the goals, priorities, and methods of movement rehabilitation for each individual, rather than a general paradigm of management suitable for the population of people with HD.

Working from first principles, as well as the findings on movement rehabilitation in PD, we suggest a model of movement rehabilitation for those with HD based on the following assumptions, which still need to be validated with RCTs.

1. Activity, participation, and independence in people with HD are compromised by movement disorders, postural instability, secondary adaptations to reduced activity, and cognitive impairment.

2. Physical therapy strategies can enable people with HD to retain their levels of activity, participation, and independence for longer periods compared with no therapy.

3. Physical therapy strategies can assist people with HD to reduce the number of falls and the severity of injuries from falls.

4. Physical therapy strategies can train people with HD to manage movement disorders such as hypokinesia, chorea, other forms of dyskinesia, weakness, and postural instability; and enhance independence and quality of life.

Given that hypokinesia is common in HD, it may be useful for therapists to teach people with HD strategies for overcoming hypokinesia that have been found to be useful in PD (3,4,16–19). These include attentional strategies such as focusing on walking with long steps, writing with large strokes, or reaching forward with a large movement of the hand (50). Avoiding dual-task performance or using external cues either in the form of visual markers or auditory stimuli can be effective in minimizing hypokinesia (50,51). Where postural instability and a history of falls are prominent, basic falls prevention strategies can be utilized (52,53). These strategies include modifications of the residential environment to make it safer as well as educating the person and their caregivers about the risk factors for falls. Moreover, general exercise programs to assist people with HD to maintain strength, endurance, and cardiopulmonary fitness may prove
to be useful in minimizing the secondary effects on the musculoskeletal and cardiovascular systems that seem to appear as a consequence of reduced activity and disuse [53]. Clearly, these suggestions need to be validated with controlled clinical trials. In addition, the capacity for people with HD to learn new ways to cope with their movement disorders and postural instability needs close scrutiny, given that the majority of people with HD will eventually develop significant cognitive impairment that may limit their capacity for new learning.

The role of allied health professionals in reducing severe or distressing chorea is uncertain. Although attentional strategies, such as thinking of keeping the part still or weight bearing through the affected part, appear to be effective in reducing dyskinetic movements in PD, the benefit is rarely prolonged [18]. This is particularly the case when the person attempts to perform a second motor or cognitive task [50]. In the absence of RCTs, neuroleptics remain the mainstay of the treatment of chorea despite the risk that these drugs will worsen hypokinesia.

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GAIT DYSFUNCTION IN HUNTINGTON’S DISEASE