SHORT REPORT

Motor overflow in Huntington's disease

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We investigated both motor overflow and ability to control voluntary movement in patients with Huntington's disease (HD). We hypothesised that, compared with controls, overflow would be significantly greater in HD participants and that they would exhibit poorer control of voluntary movement. In a finger flexion task, participants had to maintain target forces representing 25, 50, or 75% of the maximum strength capacity for whichever finger was performing the task; overflow was measured in the corresponding finger of the non-responding hand. HD participants exhibited significantly greater motor overflow than controls, and more difficulty controlling the target force with the active hand. In addition, the degree of overflow in HD participants positively correlated with overall UHDRS motor symptom severity.The presence of exacerbated motor overflow in HD, and its correlation with symptom severity, is an important finding worthy of further investigation.

Huntington's disease (HD) is a neurodegenerative disorder characterised by progressive atrophy of the basal ganglia [1 2] and chorea, and is associated with abnormalities both in initiating and in executing movement.[3–6] Excessive production of unintentional movements is also characteristic of motor overflow, which has not been previously investigated in HD.

Motor overflow refers to involuntary activity in the homologous muscles of the opposite side of the body during voluntary muscle contraction.[7] Overflow is not usually observed in normal adults, although it is exhibited by children under 10 years of age,[8] normal adults under effort induced conditions,[9] and people with certain neurological dysfunctions.[10] There are essentially two competing theories regarding the mechanism of motor overflow, both implicating dysfunctional cortical inhibition.[7 8 11] The transcallosal facilitation hypothesis states that activation of a cortical region associated with voluntary movement facilitates activation of the corresponding area in the opposite hemisphere, via inter-hemispheric connections.[7] This facilitation results in motor overflow unless inhibited. The transcallosal inhibition theory suggests that overflow occurs as a result of the removal of inhibition within the ipsilateral corticospinal tract; movements produced by the contralateral hemisphere then result in a degree of ipsilateral overflow movement.[8 11 12]

The excessive production of unintentional movements in HD appears consistent with the probable manifestation of motor overflow, with previous research reporting difficulties in inhibiting competing motor programmes, especially during voluntary movements, resulting in involuntary muscle activity.[6] This study investigated the presence of motor overflow in HD, controlling for the established confounding factor of strength,[13 14] while also examining participants' ability to control voluntary movements. It was hypothesised that, overall, overflow would be significantly greater in HD participants, and that they would exhibit poorer control of voluntary movement compared with normal healthy controls.

METHOD

Participants

There were 11 participants with HD and 11 normal controls, all right handed (Edinburgh Handedness Inventory).[15] There was no difference in age between HD participants (mean (SD) 54.18 (10.47)) and controls (51.09 (11.96)), ($t_{(20)} = 0.53$, $p>0.05$), or in gender (HD 7M, 5F; controls 5M, 6F; $\chi^2_{(1,\ n=20)} = 4.00$, $p>0.05$). HD participants were diagnosed and assessed by a neurologist (AC), and screened for symptom severity using the Unified Huntington's Disease Rating Scale (UHDRS),[16] which gave a mean (SD) score of 29.50 (16.40). All were gene positive, with average illness duration of 4.10 (4.68) years. Nine HD participants were medicated, with six on antidepressants (citalopram hydrobromide, moclobemide, and sertraline hydrochloride), three on antipsychotics (quetiapine fumarate, haloperidol, and olanzapine), and four on movement disorder or anticonvulsant medication (benserazide hydrochloride, tetrabenazine, propranolol hydrochloride, and sodium valporate). HD and control participants were rated for cognitive status using the Mini Mental State Examination (MMSE)[17] (27.10 (2.51) and 29.45 (0.68), respectively); for premorbid IQ using the National Adult Reading Test (NART)[18] (113.58 (2.98) and 117.89 (4.27), respectively); and for depressive mood using the Montgomery and Asberg Depression Rating Scale (MADRS)[19] (9 (7.47) and 3.45 (3.63), respectively).

Apparatus

The apparatus, described in detail elsewhere,[13] consisted of two linear variable differential transformer (LVDT) units (Lucas Schaevitz model FTD-G-5K) measuring absolute force (g/weight).

Procedure

The procedure has been described in detail elsewhere.[13] Participants exerted maximum pressure on the LVDT surface, using either their index or little finger; values were then used to compute the target forces for the experimental trials. Participants were instructed not to involve the wrist or other body parts; this was observed and monitored by the experimenter throughout each trial.

Participants were then required to sustain a force that represented either 25, 50, or 75% of their maximum force for each finger. For each trial, the computer provided a real time force display, which participants observed in order to maintain their target force. The same finger of the opposite hand rested on the opposite LVDT throughout each trial, thus motor overflow in the passive hand was determined.

Abbreviations: LVDT, linear variable differential transformer; MADRS, Montgomery and Asberg Depression Rating Scale; MMSE, Mental State Examination; NART, National Adult Reading Test; UHDRS, Unified Huntington's Disease Rating Scale

Data inclusion criteria

The data inclusion criteria have been described in detail elsewhere.[13] Generally, trials were excluded if participants were unable to generate a period of stable force production of within 10% of the target force, or if the level of force exerted by the passive hand was below baseline, indicating that the participant had lifted the passive finger off the LVDT. A number of trials were conducted to ensure that a minimum of three trials was included for each condition. Overall, for each group, 25% of trials were excluded

Data analysis

To control for the effect of larger absolute forces producing larger amounts of overflow, mean relative motor overflow was analysed; the mean absolute motor overflow was expressed relative to the target force.

To determine if differences in overflow production related to patterns of force variability, measurement of relative force variability was also computed. For each condition, the mean and standard deviation of the force exerted by the active hand across acceptable trials was calculated. SD was then taken to represent the absolute force variability for that condition, and was expressed as a percentage of the overall average force on acceptable trials.

Finally, relative force control variability was calculated. For each condition, the mean of the standard deviations of the force exerted by the active hand across acceptable trials was calculated, representing the absolute force control variability. This was expressed as a percentage of the overall average force, therefore relative force control variability measured participants' force control.

Although the data initially included separate measures for the index and little fingers, these separate finger data were pooled for all the analyses because there was no significant difference in overflow between fingers.

Statistical analyses

Owing to the high degree of variance (and violation of homogeneity of variance) log transformation of the data was required. Data were submitted to a mixed three factor analysis of variance. A series of Pearson's bivariate correlations were also performed.

RESULTS

Relative motor overflow data

The untransformed means for the relative motor overflow (table 1) revealed a significant main group effect ($F_{(1,\ 20)} = 4.55$, $p<0.05$), with mean relative motor overflow significantly greater in the HD participants ($M = 13.69$) than the controls ($M = 5.23$). There was also a significant main effect of target force ($F_{(2,\ 40)} = 166.82$, $p<0.01$). Post hoc analysis revealed that significantly more mean relative motor overflow occurred for the 25% condition ($M = 13.56$), compared with both the 50% ($M = 8.49$) and 75% ($M = 6.34$) conditions ($t_{(21)} = 12.19$, $p<0.01$ and $t_{(21)} = 16.21$, $p<0.01$), respectively, the latter two conditions of which also significantly differed ($t_{(21)} = 6.64$, $p<0.01$). There was no significant main effect of hand or significant interactions.

Force variability data

The means for the relative force variability data (table 2a) showed no significant main effect of group or active hand; there was a significant main effect of target force ($F_{(2,\ 40)} = 16.93$, $p<0.01$). Post hoc analysis revealed significantly greater force variability in the 25% ($M = 9.46$) condition compared with both the 50% ($M = 6.52$) and 75% ($M = 5.83$) conditions ($t_{(21)} = 3.28$, $p<0.01$ and $t_{(21)} = 3.79$, $p<0.01$), respectively, although the latter two conditions did not differ. No significant main effect of hand or significant interactions were observed.

Table 1 Means (SD) of relative % motor overflow for HD participants and controls recorded in the contralateral passive hand for each experimental condition

	Left hand active			Right hand active		
Group	25%	50%	75%	25%	50%	75%
HD	23.77 (30.20)	15.41 (22.34)	13.43 (19.32)	14.02 (12.91)	9.87 (12.52)	5.67 (4.39)
Controls	8.96 (3.48)	4.36 (1.52)	3.45 (1.01)	7.51 (4.25)	4.31 (2.54)	2.79 (1.51)

When the left hand is active, measurements relate to overflow occurrence in the right hand and vice versa; the larger the number the greater the degree of overflow.

Relative force control variability data

The means for the relative force control variability (table 2B) revealed a significant main effect of group ($F_{(1,\ 20)} = 15.96$, $p<0.01$), with significantly greater force control variability in the HD participants ($M = 11.09$) than the controls ($M = 5.83$). No other significant main effects or interactions were observed.

Correlations

Overall UHDRS motor scores (for $n = 10/11$) were correlated with relative overflow measures using the transformed data ($r = 0.74$, $p<0.015$), suggesting a strong significant correlation. Individual chorea UHDRS scores showed a non-significant, yet moderate relationship ($r = 0.51$, $p>0.10$). There were no significant correlations between relative overflow and MMSE, NART, and MADRS scores. Owing to the limited number of HD participants off ($n = 2$) *v* on medication ($n = 9$), statistical analysis was deemed inappropriate.

DISCUSSION

HD participants exhibited significantly greater relative motor overflow than controls. When target force was at its lowest (25%) there was significantly greater relative overflow production and increased relative force variability, a finding in support of previous research.[14] Increased force variability is potentially associated with the degree of fine motor control required to complete the task at lower forces.[14] HD participants also exhibited greater relative force control variability, suggesting more difficulty in controlling the target force with the active hand, compared with controls. Finally, as indicated by the moderate (albeit non-significant) correlation between motor overflow and UHDRS chorea scores, chorea may play a role in overflow production. However, the significant positive correlation between overall motor UHDRS scores and motor overflow suggests that symptom severity may possibly be a stronger predictor of motor overflow occurrence in HD.

Significantly less intracortical inhibition has been noted in HD,[20] suggesting that increased overflow may be a result of an inability to inhibit the ipsilateral corticospinal tract. While other studies have failed to find abnormal intracortical inhibition in HD, they only examined involuntary movement with respect to chorea.[21 22] Interestingly, Hanajima *et al*[21] conceded that, while abnormal inhibition was not present with chorea, reduced inhibition occurs in several other types of movements, suggesting that the pathophysiology of chorea differs from other types of unintentional movements of HD. Results of the current study support this claim.

Results also revealed a greater degree of variability during voluntary movements in HD. Previous research has demonstrated a specific impairment in the ability to maintain

Table 2 Means and standard deviations (SD) for HD participants and controls for: relative force variability and % relative force control variability recorded in the active finger for each experimental condition

	Left hand active			Right hand active		
Group	**25%**	**50%**	**75%**	**25%**	**50%**	**75%**
RFV						
HD	11.24 (7.56)	6.02 (3.54)	5.72 (3.39)	10.41 (5.26)	8.01 (3.56)	7.11 (3.28)
Controls	7.44 (4.82)	6.61 (2.87)	5.93 (5.98)	8.77 (3.03)	5.46 (3.42)	4.55 (4.25)
RFCV						
HD	11.04 (4.91)	11.11 (4.60)	11.08 (2.77)	10.18 (4.38)	11.32 (6.36)	11.78 (6.06)
Controls	6.08 (1.68)	5.83 (1.56)	6.48 (2.19)	6.35 (2.17)	4.70 (1.12)	5.53 (1.78)

RFV, relative force variability; RFCV, relative force control variability.

isometric grip forces, in particular when lifting lighter weights, with significantly higher force variability compared with controls.[23 24] The aetiology underlying impaired motor control (voluntary or unintentional) in HD remains unclear, although previous research suggests dysfunctional feedback mechanisms.[3 5] Indeed, HD participants in this study were unable to utilise the visual feedback on display to effectively control their force, a finding also reported in other studies.[3 5]

While the current study provides a number of interesting findings, there are some limitations. The measurement of overflow required that participants use only their fingers, without including their wrists or other body parts. Although every attempt was made to ensure this, there was no objective measure to gauge that only fingers were used. Furthermore, the duration of 5 seconds for each trial may seem limited; however, motor overflow can be exacerbated if trials are prolonged.[9] In addition, clinically none of the HD participants had drug induced parkinsonism; increased motor overflow is unlikely to be due to medication. Exacerbated motor overflow, especially its correlation with overall motor UHDRS symptom severity, is an important finding worthy of further investigation.

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