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RESEARCH ARTICLE

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Control of manipulative forces during unimanual and bimanual tasks in patients with Huntington's disease

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Abstract The aim of the study was to investigate grip-load force regulation in Huntington's disease (HD) patients as compared to control subjects during the performance of a manipulative task that required rhythmical unimanual or bimanual isodirectional/non-isodirectional actions in the sagittal plane. Results showed that the profile of grip-load ratio force was characterized by maxima and minima that were attained at upward and downward hand positions, respectively. Minimum force ratio was higher in patients than in controls, which points to an elevated baseline that may be related to the inherent bradykinesia observed in HD. Maximum force ratio was also increased in patients, but this effect depended on the performance condition, with largest amplifications occurring during non-isodirectional movements. The latter rescaling may be associated with the complexity of the coordination mode and its asymmetrical load characteristics. In addition, the temporal delay between the grip and load force peaks was augmented in patients versus controls, indicating a disturbed coupled activation of both forces. Furthermore, the interval was largest during non-isodirectional movements followed by isodirectional and unimanual movements, which denotes that the grip-load force coupling deteriorated as a function of coordinative complexity. Together, these data indicate a deficit in the grip-load force constraint due to HD and illustrate the degrading effect of striatal dysfunction on (bi)manual manipulative function.

Keywords Precision grip · Manipulation · Grip force

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Introduction

Huntington's disease (HD) is an inherited neurodegenerative disorder with an established basal ganglia pathology. The disease is associated with a degeneration of the striatum, resulting in progressive motor, cognitive and behavioral abnormalities. With respect to motor control of manual function, the symptoms of HD are characterized by involuntary movements (chorea) and unstable voluntary actions that particularly become evident in the execution of sequential (Hefter et al. 1987) and combined tasks (Brown et al. 1993; Thompson et al. 1988). This indicates that HD patients have additional difficulties in controlling complex movements and points to an impaired ability for producing coordinative motion. This impairment has recently been extended for bimanual rhythmical patterns that are performed according to an in-phase (mirror) or anti-phase (parallel) mode (Johnson et al. 2000).

The lack of coordinated behavior in HD is further manifested in the fine motor organization of object manipulation (Gordon et al. 2000; Quinn et al. 2001; Schwarz et al. 2001; Serrien et al. 2001). In particular, grasp stability is disturbed in HD patients and an inappropriate degree of grip force (normal to the surface) is generated in relation to load force (tangential to the surface). These observations contrast with performances of control subjects who couple both forces tightly and in a synchronized manner when executing a manipulative task. Moreover, an effective grip-load force mechanism ensures that a suitable grip force is generated in relation to destabilizing load force (Flanagan and Wing 1993; Johansson and Westling 1988; Serrien et al. 1999). In dynamic conditions during which varying load fluctuations are present, the grip-load force ratio is continuously adjusted and balanced across task execution (Flanagan and Wing 1995; Serrien et al. 1999). This implies that an adjustable safety margin is exploited in order to maintain grasp stability whenever a hand-held object is actively moved.

To evaluate more in detail the deteriorating effect of coordinative complexity on movement execution, the aim of the present study was to examine grip-load force

Table 1 Clinical features of the patients. Disease severity was staged according to the Unified HD Rating Scale (UHDRS). Motor assessment included selected items (tapping speed, rigidity, chorea, dystonia) and was summed for both hands. A unimanual score of 0 represented normal behavior whereas a score of 4 referred to severely impaired functioning. Tapping speed: 0 = normal (15/5 s), 1 = mild slowing (11–14/5 s) and/or reduction in amplitude, 2 = moderately impaired with occasional arrests in movement (7–10/5 s), 3 = severely impaired with frequent hesitations in initiating movement or arrests in ongoing motion (3–6/5 s), 4 = can hardly perform the task (0–2/5 s). Rigidity: 0 = absent, 1 = slight or present only with activation, 2 = mild to moderate, 3 = severe with full range of motion, 4 = severe with limited range of motion. Chorea: 0 = absent, 1 = slight/intermittent, 2 = mild/common, 3 = moderate/intermittent, 4 = moderate/common. Dystonia: 0 = absent, 1 = slight/intermittent, 2 = mild/common, 3 = moderate/intermittent, 4 = moderate/common. Disease duration in years since onset of symptoms

n	Age (years)	Sex	CAG	Duration disease (years)	UHDRS					
					Tapping	Rigidity	Chorea	Dystonia	Cognitive evaluation	Medication
1	51	F	44	10	4	0	0	0	78	–
2	44	F	47	3	4	3	0	0	137	–
3	48	M	>37	3	3	0	0	0	220	–
4	55	F	44	2	4	0	0	2	210	–
5	43	F	45	2	4	0	0	2	174	Paroxetine

regulation during various manipulative assignments in HD patients as compared to control subjects. This evaluation would allow the determination of the significance of task difficulty on prehensile forces during precision grip. In this respect, it can be proposed that planning of grasping forces will become increasingly crucial during more complex tasks in order to avoid inappropriate object manipulation. In the present experiment, subjects were required to execute rhythmical unimanual and bimanual movements with grasped hand-held objects in the vertical dimension. Bimanual patterns were performed according to an isodirectional or non-isodirectional mode. It was hypothesized that grip-load force organization would be most demanding for the non-isodirectional configuration as this performance condition enhances the likelihood of object loss because both hands move in opposite directions and therefore experience dissimilar loads. Accordingly, comparing the grasping forces during unimanual and bimanual movements in HD patients versus control subjects would permit the delineation of the role of the basal ganglia in the control and coordination of manipulative events.

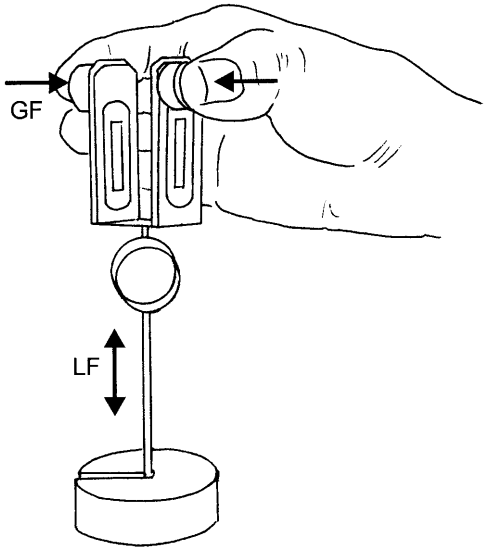

Fig. 1 Picture of a test object held in a precision grip. During the tasks, subjects produced upward/downward movements; grip force (*GF*) and load force (*LF*) are generated in a horizontal and vertical direction to the surface, respectively

Materials and methods

Subjects

Five HD patients (mean age 48±6 years) participated in the study. The diagnosis of the patients was confirmed genetically by determination of CAG trinucleotide repeat lengths >37. Disease severity was evaluated according to the Unified HD Rating Scale (UHDRS) (Huntington Study Group 1996). Motor assessment with respect to selected items for both hands (tapping speed, rigidity, chorea, dystonia) and cognitive evaluation are summarized in Table 1. All patients were right handed. Five control subjects (mean age 47±10 years) also participated in the study. None had a history of neurological pathology. All subjects gave informed consent and the procedures had been approved by the local ethics committee.

Experimental setup and recording

A test object consisted of a U-shaped gripper frame (6×4 cm) with two parallel grip surfaces on top of each side (see Fig. 1). The grip surfaces had a diameter of 2 cm. At the bottom and center of the framework was a 13-cm-long rod on which a mass of 400 g was added. A ball joint connected the gripper frame with the rod. The test object was instrumented with two pairs of strain gauges to measure grip force (normal to the surface), which represented the mean of the forces exerted by the fingertips. Load force (tangential to the surface) referred to the vectorial sum of the gravitational force and inertial force (proportional to the acceleration of the object) and was measured by a strain gauge attached at the top of the rod. Grip and load force were recorded at 400 samples/s. Data acquisition and analyses were performed by the SC/ZOOM program (Department of Physiology, Umeå University, Sweden).

Subjects were seated in front of a table on which two test objects were positioned, on both sides of their body midline. In the starting position, subjects held the objects with a precision grip between the tips of the index finger and thumb. They were asked to make vertical, straight-line cyclic arm movements 12 cm in amplitude, indicated between two markers, in an upward and downward direction. Movement rate was set at 98 beats/min and paced by a metronome. There were four protocols: (1) unimanual with

left arm, (2) unimanual with right arm, (3) bimanual according to an isodirectional mode, i.e., both hand-held objects were simultaneously moved in an upward as well as a downward direction, and (4) bimanual according to a non-isodirectional mode, i.e., one hand-held object was moved in an upward direction while the other hand-held object was moved at the same time in a downward direction. Each protocol consisted of five trials that lasted 10 s each. After each trial, there was a small break to avoid fatigue. In separate trials, the slip ratio was determined for each hand. During these trials (n=3), the object was raised a few centimeters above the table and the subjects were asked to slowly release the thumb and index finger until the object was dropped. The slip point was set as the initial detectable downward change in load force. This measurement was used to determine the safety margin which represents the difference between the slip ratio, i.e., the minimum value determined by the friction between skin and object, and grip-load force ratio employed by the subject (Johansson and Westling 1984). The slip ratio was analyzed in a 2×2 (group × hand) ANOVA with repeated measures on the last factor. The first factor indicated the HD patients versus control subjects whereas the second factor represented the right versus left hand. No significant differences were observed, P>0.05. The mean values were 1.06±0.19 for HD patients and 0.98±0.11 for control subjects.

Analysis

To examine grip-load force regulation in the different manipulative tasks, the magnitude of the coupling of both forces as well as the synchronicity of their combined activation was established.

Magnitude of grip-load force ratio

To evaluate scaling of the force constraint, the grip-load force ratio was estimated. This variable represents a load-independent index that permits the assessment of coupling between both forces across the movement cycle when load force is continuously varying. In this respect, the minimum and maximum values of the grip-load force ratio throughout the movement cycles were determined (see Fig. 2). The values were analyzed in a 2×2 × 3×2 (group × ratio position × condition × hand) ANOVA with repeated measures on the last three factors. The first factor indicated the HD patients and control subjects, whereas the second factor represented the minimum and maximum force ratio. The third factor referred to the unimanual, bimanual isodirectional, and bimanual non-isodirectional conditions, whereas the fourth factor specified the right and left hand. An additional analysis was conducted for the load force peaks in order to verify that similar changes in loads occurred for both groups during all performance conditions. The values were analyzed in a 2×2 × 3×2 (group × peak position × condition × hand) ANOVA with repeated measures on the last three factors. The first factor indicated patients and controls, whereas the second factor represented the minimum and maximum load force peaks. The third factor referred to the performance conditions, whereas the fourth factor specified the hands.

Synchronicity of grip-load force peaks

To investigate the synchronized activation of grip and load force, the temporal delay between the peaks of both forces throughout the movement cycles was determined and subjected to a 2×3×2 (group × condition × hand) ANOVA with repeated measures on the last two factors.

Results

Figure 2 illustrates grip force, load force and grip-load force ratio profiles when a control subject rhythmically moves a test object with one hand in the vertical dimension. It can be observed that grip and load force are tightly coupled while their respective peaks coincide in time, suggesting that grip force is regulated in a predictive manner with respect to load force (Flanagan and Wing 1995). However, grip-load force ratio is not constant throughout the movement cycles but tracks a reliable pattern that consists of regularly occurring maxima and minima. Maxima of grip-load force ratio are realized at load force minima when the loads of weight and inertia are subtractive, and happen at the higher reversal positions (hand upward). Conversely, minima of grip-load force ratio are attained at load force maxima when the loads of weight and inertia are additive, and take place at the lower reversal positions (hand downward). This indicates that force regulation depends on movement direction during vertically oriented actions due to the varying contribution of the load components.

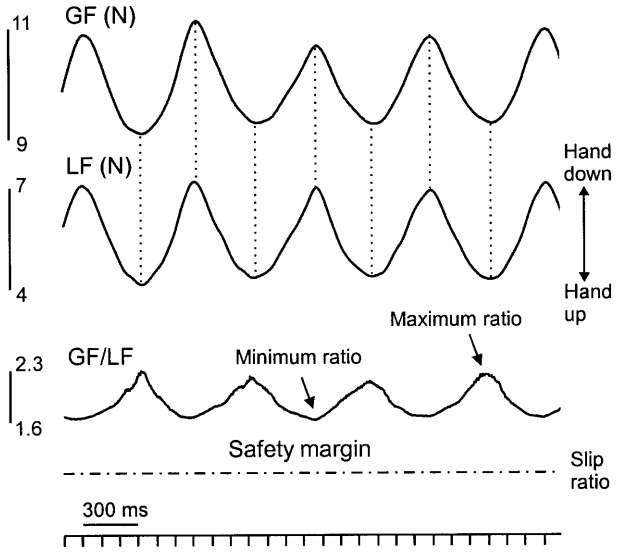

Fig. 2 Grip force (*GF*), load force (*LF*), and grip-load force ratio (*GF/LF*) profiles for rhythmical movements during a unimanual condition. *The arrow* indicates downward and upward motion of the hand. The safety margin represents the difference between the slip ratio, i.e., the minimum value established by the friction between skin and object, and the grip-load force ratio adopted by the subject

The analysis of grip-load force ratio revealed a significant main effect of group [$F_{(1,8)}$=10.1, P<0.02], ratio position [$F_{(1,8)}$=29.0, P<0.01], and condition [$F_{(2,16)}$=12.6, P<0.01]. The following two-way interactions were significant: group × ratio position [$F_{(1,8)}$=6.6, P<0.02], group × condition [$F_{(2,16)}$=5.7, P<0.01], and ratio position × condition [$F_{(2,16)}$=7.1, P<0.01]. The group × ratio position × condition interaction was also significant, $F_{(2,16)}$=4.3, P<0.02. Figure 3A demonstrates that minimum force ratio was lower for control subjects than for HD patients, but no additional difference was noted across the various performance conditions. Furthermore, Fig. 3B illustrates that maximum force ratio was inferior for control subjects than for HD patients. In addition, maximum force ratio of non-isodirectional movements was higher than that of

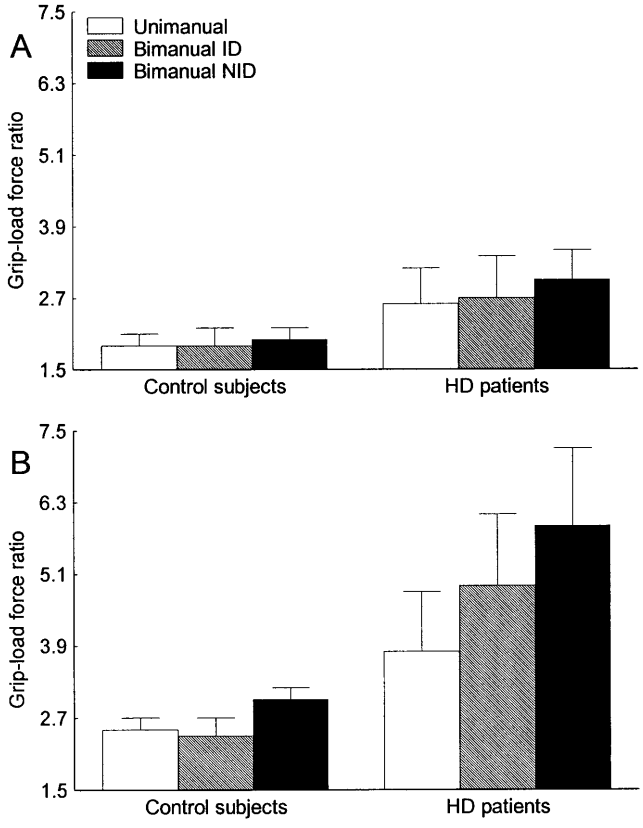

Fig. 3 Minimum **(A)** and maximum **(B)** grip-load force ratios for control subjects and HD patients when performing unimanual and bimanual isodirectional (*ID*) and non-isodirectional (*NID*) patterns. *The error bars* indicate the standard deviations from the means

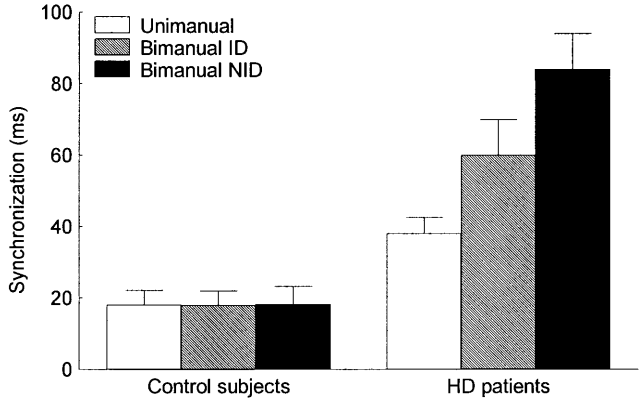

Fig. 4 Temporal delays between grip and load force peaks for control subjects and HD patients when executing unimanual and bimanual isodirectional (*ID*) and non-isodirectional (*NID*) patterns. *The error bars* denote the standard deviations from the means

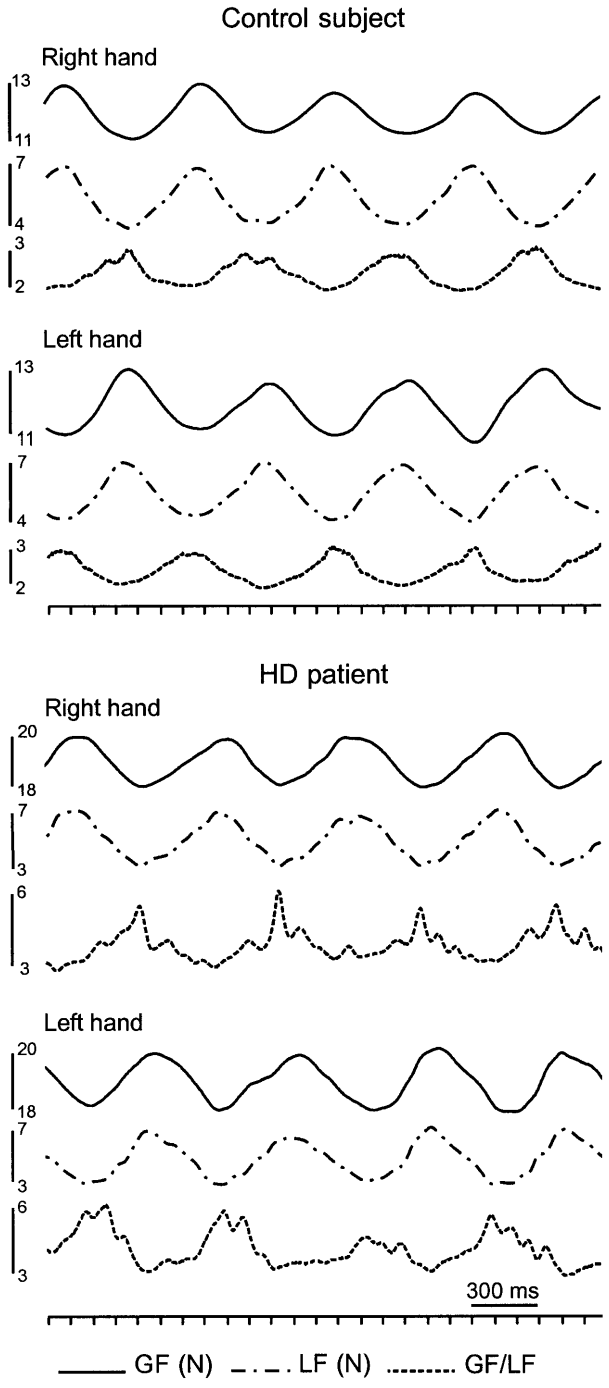

Fig. 5 Grip force (*GF*), load force (*LF*), and grip-load force ratio (*GF/LF*) profiles of the non-isodirectional mode for a representative control subject and HD patient. Single trial

isodirectional and unimanual movements for control subjects ($P<0.05$ for both), whereas it significantly differed across the various performance conditions for the HD patients ($P<0.05$ for all), resulting in an increased specification of grasping forces as a function of coordinative complexity due to striatal dysfunction.

The analysis of load force peaks revealed a significant main effect of peak position, $F_{(1,8)}=2141.2$, $P<0.01$, which indicates that maximum load force (mean= 6.6±0.9 N) was higher than minimum load force (mean= 3.4±0.6 N). No other effects reached the level of significance, $P>0.05$.

The analysis of grip-load force delay showed a significant main effect of group [$F_{(1,8)}$=81.8, P<0.01] and condition [$F_{(2,16)}$=17.4, P<0.01]. The group × condition interaction reached significance, $F_{(2,16)}$=17.6, P<0.01. Figure 4 shows that the grip-load force interval was equivalent across the different performance conditions for control subjects, whereas the delay was higher for HD patients and increased progressively as a function of coordinative difficulty.

Figure 5 further illustrates the modulation in the specification of grasping forces that arise due to HD. The figure shows grip force, load force and grip-load force ratio for a control subject and a HD patient when performing the non-isodirectional mode. It can be observed that the grip-load force ratio profile is characterized by maxima and minima that occur in a reciprocal fashion. However, the values are higher for the HD patient as compared to the control subject, especially with respect to the maximum force ratio. Also, the grip-load force ratio profile is less smooth for the HD patient, illustrating the modified coupling between both forces and their concurrent adjustments that are critical for optimal control of precision grip.

Discussion

When manipulating an object, the synergistic activation of grip and load force corresponds to a constraint that not only reduces the number of controllable degrees of freedom but also ensures grasp stability as anticipatory grip force changes are generated in relation to destabilizing loads (Flanagan and Tresilian 1994; Johansson 1996). Furthermore, an optimal grip-load force regulation is important in order to avoid inappropriate grasping and likelihood of object loss. It implies that there is a functional necessity associated with response planning of a manipulative event. As the organization of grasping and manipulation depends on distributed neural circuits (Jeannerod 1996), it is of interest to examine modifications of control functions as well as motor deficits that arise from (sub)cortical damage.

Grip-load force control during a rhythmical manipulative task

When rhythmically moving an object, grip-load force ratio follows a regular pattern of maxima and minima throughout the movement cycles. Maxima of grip-load force ratio are realized at load force minima, whereas minima of grip-load force ratio are attained at load force maxima. The augmented degree of grip force during upward motion of the hand can be taken as a strategy for preventing slip/loss of the object when load force is progressively decreasing and going low. Conversely, moving the hand downward affords a tight grip-load force association, leading to a minimum force ratio that is kept stable across movement cycles. It suggests that minimum grip-load force ratio defines a baseline during cyclical manipulative actions (Flanagan and Wing 1995; Serrien and Wiesendanger 2001).

During all performance conditions, HD patients as compared to control subjects overscaled their motor output, extending previous work on discrete unimanual tasks (Gordon et al. 2000; Schwarz et al. 2001; Serrien et al. 2001). With respect to the rhythmical unimanual and bimanual assignments examined in the present study, this implied an increased minimum and maximum force ratio. The augmented minimum force ratio shows that patients adopted an elevated baseline. The underlying cause of this upward shift may be related to bradykinesia that represents a generalized motor disturbance in HD (e.g., Hefter et al. 1987; Sánchez-Pernaute et al. 2000; Thompson et al. 1988). This observation is also in line with the finding that control subjects increase their baseline ratio as a function of cycling frequency (Flanagan and Wing 1995). It indicates that the more dangerous the situation in terms of speed requirements, and therefore load force changes, the higher the minimum force ratio will be in order to maintain grasp stability. This signifies that the inherent slowness in HD is likely the responsible factor for the natural increase in baseline ratio.

HD patients also employed an increased maximum force ratio, which probably denotes a disturbed grip-load force constraint. This notion is supported by the augmented temporal delay between the peaks of grip and load force, suggesting that their coupled activation is less strict. This also implies that grip-load force adjustments will be less tightly tuned to one another during object manipulation. Also, it might be that the augmented force output represents a compensatory strategy, especially in view of the spontaneous chorea that can disturb the grip in an unpredictable manner throughout task execution. Alternatively, a reduced efficiency of sensorimotor processing may induce an increased force specification. Disturbed sensorimotor activity in HD has been suggested because of a total suppression or reduced activity of the reactive EMG response (Fellows et al. 1997; Noth et al. 1985), an abnormal (sub)cortical activation during passive sensory stimulation (Boecker et al. 1999), changes in somatosensory evoked potentials (Noth et al. 1984; Töpper et al. 1993) and deficits in feedback control when external perturbations are introduced during reaching movements (Smith et al. 2000).

Force regulation as a function of coordinative complexity

In control subjects, maximum grip-load force ratio was higher in the non-isodirectional as compared to the isodirectional mode, which can be associated with its dissimilar load characteristics, necessitating increased processing and monitoring. Therefore, augmenting the force output during non-isodirectional coordination can be viewed as a safety mechanism for maintaining grasp stability in an asymmetrical load situation. As the temporal

delay between grip and load force peaks did not vary across performance conditions, it shows that a tight grip-load force coupling exists in control subjects that is independent of the complexity of the manipulative task.

HD patients experienced additional difficulties in organizing bimanual patterns, with a stronger effect for non-isodirectional than isodirectional movements. The marked increase in maximum grip-load force ratio in the non-isodirectional mode suggests that rescaling took place due to the complex control requirements of unequal force specifications for both hands. Also, the patients' temporal delay between grip and load force peaks was largest during non-isodirectional actions, which signifies that the coupling constraint that unites both forces degraded as a function of coordinative complexity. Together, these observations point to alterations in the magnitude and timing of prehensile forces during precision grip due to HD that depends on the difficulty of the task requirements.

Modulation of manipulative forces due to HD

The unstable planning of manipulative forces for HD patients when moving rhythmically hand-held objects extends previous findings of disturbed spatiotemporal behavior during bimanual activities (Hefter et al. 1987; Johnson et al. 2000) and sequential movements (Agostino et al. 1992; Georgiou et al. 1995). Overall, the present data demonstrate that regulation of movement components in unimanual and bimanual actions is disrupted in HD, resulting in modulated motor behavior. That HD patients have deficits in maintaining attention (Georgiou et al. 1997; Sprengelmeyer et al. 1995) may also contribute to abnormalities in control processes that require continuous monitoring, as for the cyclical tasks examined in the present study.

The movement irregularities that are observed in HD have been associated with damaged basal ganglia and consequences for the output areas. In particular, HD patients have an impaired activity of the striatum and its frontal motor projection areas when performing activities, indicating a malfunctioning of the basal ganglia-thalamocortical circuit (Bartenstein et al. 1997; Weeks et al. 1997). Previously, Houk and Wise (1995) proposed that basal ganglia are important for decoding specific contexts and states that are useful for organizing behavior. As a result, contextually related inputs can be exploited for selecting suitable responses while suppressing inappropriate outputs. In this respect, it can be hypothesized that failure to recognize a context of action will depend on the complexity of the task. This is in line with the relevant role of the basal ganglia circuits in the optimization of functional synergies (Hallett 1993), and is also in agreement with current theories of basal ganglia functions (Brooks 1995; Graybiel et al. 1994; Mink 1996). In view of the current results, it can be proposed that striatal dysfunction disrupted the neural network underlying the task-related processes and prevented the optimal planning of the manipulative action.

In conclusion, HD patients as compared to control subjects showed modulated grip-load force regulation during cyclical manipulative tasks using the precision grip. Alterations were stronger for bimanual than for unimanual actions, and more prominent for non-isodirectional than for isodirectional coordination patterns. These findings illustrate the deteriorating effect of striatal pathology on fine motor control involving (bi)manual function. Efficient regulation of grasping forces and coordination dynamics is reduced due to HD and is likely to degrade the proficiency of manipulative activities.

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