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## Sensorimotor mapping affects movement correction deficits in early Huntington's disease

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**Abstract** Huntington's disease (HD) is associated with early voluntary movement problems linked to striatal dysfunction. In pointing movements, HD increases the irregularity of the terminal part of movements, suggesting a dysfunction in error feedback control. We tested this hypothesis in movements requiring continuous feedback control. Patients in the early stages of HD and controls traced as fast and accurately as possible circles within a 5-mm annulus on a digitizing tablet when visual feedback of the hand and the circle was direct or indirect (through a monitor). Patients deviated more often from the annulus and showed larger corrections toward the circle than controls when using indirect visual feedback but not with direct visual feedback. When velocity requirements were removed, patients showed little change in these control problems. These results suggest that HD does not affect error feedback control in all movements and that the striatal contribution to voluntary movement is sensitive to sensorimotor mapping.

**Keywords** Huntington's disease · movement · visual feedback · tracing · striatum

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### Introduction

Huntington's disease (HD) produces deficits in the control of voluntary movements (Bonfiglioli et al. 1998; Smith et al. 2000; Quinn et al. 2001; Schwarz et al. 2001; Serrien et al. 2001). Movements in HD are often slower than controls, and they are also variable and inefficient, showing multiple acceleration–deceleration phases to reach a target (Georgiou et al. 1995; Phillips et al. 1996; Smith et al. 2000). In rapid pointing movements toward a target, patients with HD generate aberrant responses to self-generated error and movement irregularity is especially exaggerated in the terminal portions of the movement, suggesting a deficit in error feedback control (Smith et al. 2000). If a general deficit in error feedback control is present in HD, it should be observed in all movements which require error feedback. The present study tested this hypothesis in a continuous movement requiring constant error feedback control.

The error feedback deficit in HD could be specific to movements requiring complex sensorimotor transformations. In the study by Smith et al. (2000), movements were displayed on a vertical screen in front of the participants, without direct vision of the hand. Thus, a sensorimotor transformation was required to transform visual and proprioceptive information into a common frame of reference (Messier and Kalaska 1997). It has been shown that sensorimotor transformations are prone to errors, which at least partially explains why aiming movements performed without vision of one's hand are less accurate and more variable than movements performed in a normal visual context (Soechting and Flanders 1989a,b; Vindras and Viviani 1998). Sensorimotor transformations could be more detrimental to patients with striatal dysfunction (Abbruzzese and Bernardelli 2003) either because of a proprioception deficit (Kuwert et al. 1993; Fellows et al. 1997; Boecker et al. 1999) or because of the additional processing involved.

In Smith et al. (2000), participants were also asked to perform the movements as fast as possible. Patients with

HD are known to take longer to initiate and perform a motor task (Hefter et al. 1987; Girotti et al. 1988; Bradshaw et al. 1992). In that context, it is possible that velocity requirements are more detrimental for patients with HD than controls, causing delays and irregularities in the execution of their movement.

Thus, the error correction deficit observed in HD may be linked to specific movement requirements such as sensorimotor mapping or movement velocity. The present study examined whether error feedback control is affected in HD in movements involving no or minimal sensorimotor transformation and with no velocity requirements. We evaluated the performance of HD patients during a continuous circular movement guided by visual boundaries. This movement involves continuous feedback control and errors are easily detectable. More importantly, continuous movement allows comparison of the use of feedback for the online control of a movement with no or minimal error correction (inside the circle) and error feedback correction (outside the circle). Finally, by segmenting the portions of the movement directed away from and toward the circle's boundaries, the time related to drifting, error detection and planning of the correction (away from the boundaries) can be compared to the time related to the implementation of the correction (toward the boundaries).

## Materials and methods

### Participants

Thirteen genetically confirmed patients with HD were compared to 13 controls with no history of cerebral damage matched in age (patients: mean = 44.9, SD = 8.2, controls: mean = 42.2, SD = 9.1) and education (patients: mean = 14 years, SD = 3.2 years, controls: mean = 14.5 years, SD = 3.2 years). Patients were in the early stages of the disease (less than 6 years and score of 0 or 1 on the item maximal chorea in the motor section of the Unified Huntington's Disease Rating Scale

(UHDRS)). Table 1 presents clinical data on the HD patients. All participants had normal or corrected-to-normal vision and were right handed, except for one HD patient. For all participants, written informed consent to participate in the study was obtained according to the rules of the hospital.

### Apparatus and procedure

Movements were performed with a pen on a digitizing tablet (Wacom, 30 cm×30 cm) connected to a computer. The position of the pen was sampled at 100 Hz. Participants traced circles 90 mm in diameter with a 5 mm error margin indicated by a white annulus on a gray background. Movements were performed in the clockwise direction with the dominant hand and began at the vertical apex of the circle. Participants sat upright in a chair and were directed to maintain a consistent initial position before each trial. Participants were first instructed to perform one rotation of the circle to familiarize themselves with the task and additional rotations were performed if the experimenter considered that the task was not understood properly, i.e. when (1) direction of the movement was incorrect, (2) no deliberate effort was made to remain between the boundaries of the circle, and (3) the velocity requirement was not respected. These practice trials were not considered in the analysis. Next, participants performed three 45-s trials in each of three conditions. In the Direct condition, participants performed the tracing task on the horizontal tablet with direct vision of their hand and the circle display. In the Indirect condition, movements were performed in the horizontal workspace but the circle and the movement of the endpoint were shown on a vertical screen in front of the participants (ratio 1:1), without direct vision of their hand, the moving arm hidden from view by an occluding screen. In both Direct and Indirect conditions, participants were asked to trace circles as fast and accurately as possible. To test the role of the velocity requirement, participants also performed a control condition (Indirect-Precise condition), in which they

**Table 1** Demographic and clinical variables from the patient group. UHDRS Unified Huntington's Disease Rating Scale. In cognitive scores, higher values indicate better performance. The cognitive scale is the sum of scores on three tests: the verbal fluency test, the symbol-digit test and the Stroop interference test

No.	Age (years)	Sex	Duration of symptoms (years)	UHDRS cognitive score	Medication
1	54	F	2	–	Temazepam, quineprox
2	43	F	6	312	Uniquinone
3	42	M	1	214	Olanzapine, procyclidine
4 <sup>a</sup>	47	F	1	327	Citalopram, clonazepam, venlafaxine
5	30	F	4	281	Citalopram
6	41	M	4	345	Citalopram
7	47	F	1	–	Nil
8	54	F	4	250	Clonazepam, valproate
9	44	F	0.5	302	Nil
10	45	F	1	258	Nil
11 <sup>a</sup>	63	M	4	205	Citalopram
12	38	M	6	176	Valproate
13	36	M	2	200	Nil

<sup>a</sup> Participants removed from the analyses

were asked to execute the same tracing movements as in the Indirect condition but as accurately as possible without velocity constraints. The order of presentation of the three conditions was randomized across participants. Trials were separated by short pauses.

#### Data reduction

Independent analyses were conducted on global measures as well as on the portions of the trajectory traced inside and outside the circle boundaries. The dissociation between Inside and Outside portions allowed us to compare the performance in a situation of error correction to that of normal feedback control. Deviations were defined as segments in which the trajectory strayed outside of the boundaries for more than 100 ms. Deviations shorter than 100 ms are less likely to be detected and corrected at these relatively slow velocities (Glen-cross and Barrett 1992), making them less relevant for the present study.

Movement segments traced outside the circle boundaries and directed away from the circle were dissociated from segments directed toward the circle. These measures were used as estimates of the time related to drifting, error detection and planning of the correction (away from the circle) and the time related to the execution of a correction (toward the circle). Changes in direction were determined in the following manner: (a) the perpendicular distance between the trajectory and the circle was computed (b) if a point had a distance that was higher than that of the 10 following points; it was considered as a change in direction. A visual inspection of the data revealed that the use of 10 points best reflected the changes in direction.

A length and a duration index were computed as precision measures. We postulated that inefficient corrections would be detectable by an increase in their duration (duration index) and in the distance traveled before reaching back the boundaries (as determined by the length index). Both indexes were normalized according to the number of rotations performed in order to control for the effect of movement velocity on these measures. The length index (cm/rotation) is defined as the length of the trajectory traced outside the circle (away or toward the circle's boundaries) divided by the number of rotations. The duration index (s/rotation) refers to the duration of the trajectory traced outside the circle (away or toward the circle's boundaries) divided by the number of rotations.

Kinematic analyses examined several derivatives of the displacement including mean tangential velocity, the number of transitions between acceleration and deceleration, and the number of jerk events. Derivatives were obtained by applying a 4th-order Savitsky–Golay filter on a 250-ms window of displacement raw data. Acceleration transitions and jerk were determined on the vertical axis and were used as a measure of movement smoothness (Teulings et al. 1997). In circle-tracing, it has

been proposed that optimal and smooth control is achieved by minimizing discontinuities in velocity and its higher-order derivatives such as acceleration and jerk (Ivry et al. 2002). Acceleration–deceleration transitions cause a segmentation of the movement, resulting in an intermittent, less efficient and less smooth movement.

Jerk events correspond to qualitative changes in the jerk profile (Fimbel et al. 2003). There is an inverse relationship between the number of jerk events and the smoothness of a movement. Movement irregularity has often been quantified using total jerk, the total amount of jerk for a given movement (Schneider and Zernicke 1989; Alberts et al. 2000; Smith et al. 2000). However, there is evidence that this global parameter may not be an optimal measure of irregularity in slow or ballistic movements (Nagasaki 1989; Rohrer et al. 2002). When velocity profiles are complex, detection of specific jerk events may give a more precise index of irregularity (Fimbel et al. 2003). Normalized jerk was first obtained by dividing the amplitude of the jerk vector by the mean acceleration amplitude during the movement. This normalization was done because in a perfect movement, i.e. a circular movement performed at constant angular velocity, normalized jerk should be equal and independent of velocity. Then, the average normalized acceleration plus one standard deviation of the average was determined in control participants. This value was used as a threshold over which values of jerk were considered as an irregularity in movement or jerk event.

The number of jerk events as well as the number of acceleration–deceleration transitions were divided by the distance traveled. This normalization was done to compare the performance of the two groups on the tracing of a movement of a given distance, independently of the time used to travel that distance. The number of acceleration–deceleration transitions/cm and the number of jerk events/cm were determined for segments of the movement traveled inside and outside the circle.

The first downstroke was not considered in the analysis because of a high level of variability in the trajectory observed at the beginning of the movement. The results of one control participant and two HD participants were withdrawn from the analyses because their data differed by more than two standard deviations from the mean of their respective group.

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## Results

### Global measures

The global measures were submitted to a 2 (Group)×3(Condition) ANOVA with repeated measures on the last variable. Only the significant effects are reported. All significant effects and interactions were further analyzed using the Scheffé procedure with a threshold of  $P < 0.01$ . Sample trajectories for one control and one HD patient are presented in Fig. 1. Table 2

summarizes the average values of global measures in each condition.

Patients generally showed more frequent and larger deviations when feedback was indirect. Participants were predictably faster in the Direct condition than in the Indirect condition, and also faster in the Indirect condition than in the Indirect-Precise condition [number of rotations:  $F(2,42)=130.9$ ,  $P<0.0001$ ; time per rotation:  $F(2,42)=46.4$ ,  $P<0.0001$ ; movement velocity for the trajectory traced inside the circle,  $F(2,42)=118.3$ ,  $P<0.001$ ].

We examined variables focusing on the trajectory traced inside the circle boundaries which reflect the efficiency of feedback control when no major correction is required. Movements were smoother in the Direct than in the Indirect condition and smoother in the Indirect condition than in the Indirect-Precise condition [acceleration transitions,  $F(2,42)=42.5$ ,  $P<0.00001$ ;

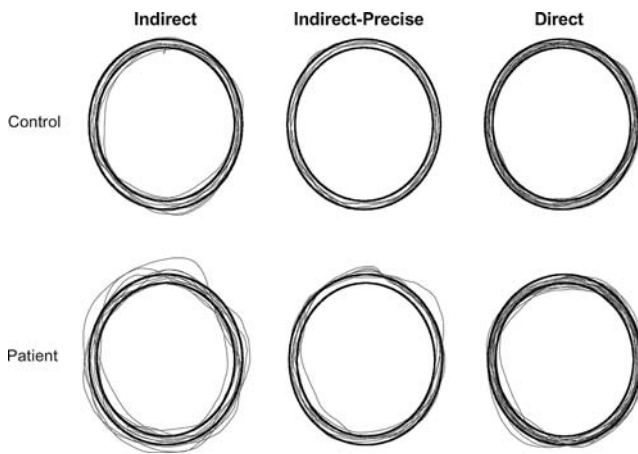
jerk events,  $F(2,42)=39.2$ ,  $P=0.00001$ ]. No differences were observed between groups for all the previous measures. However, the proportion of time spent inside the boundaries of the circle was lower in patients than controls [ $F(1, 21)=19.9$ ,  $P<0.001$ ] and lower in the Indirect condition than in the other conditions [ $F(2,42)=8.4$ ,  $P<0.000001$ ]. Also, patients deviated more often from the circle boundaries than controls in the two conditions with indirect feedback while no significant group difference was observed in the Direct condition [ $F(2,42)=19.4$ ,  $P<0.00001$ ].

#### Analyses of the trajectory traveled outside the circle

Variables related to the trajectory traveled outside the circle were analyzed using ANOVAs with three factors (2 Groups $\times$ 2 Conditions $\times$ 2 Directions relative to the circle) with repeated measures on the last two factors. It was proposed that feedback processing is mostly affected during the correction of an error. The Indirect-Precise condition was discarded for these last analyses because many participants showed few or no deviations for that condition.

As illustrated in Fig. 2, when visual feedback was indirect, patients but not controls traveled a greater distance and took more time when moving back toward the circle than when moving away from the circle, while no such differences were observed in the direct condition [duration index:  $F(1,21)=18.6$ ,  $P<0.001$ ; length index:  $F(1,21)=2.8$ ,  $P<0.01$ ].

Movements were also performed faster [ $F(1,21)=106.5$ ,  $P<0.00001$ ] in the Direct (9.67 mm/s  $\pm$  3.14) condition than the Indirect condition (5.54 mm/s  $\pm$  2.11). There were significant group differences in velocity, especially in the part of the trajectory directed toward the circle. Specifically, patients moved



**Fig. 1** Sample trajectories for one control and one patient in the three conditions

**Table 2** Average values and SD of global measures in the three conditions

	Indirect	Direct	Indirect-Precise
<i>Number of rotations</i>			
Controls	7.22 (2.7)	12.33 (2.88)	3.11 (1.45)
HD	5.94 (2.35)	10.48 (2.88)	3.55 (1.43)
<i>Duration of rotations (s)</i>			
Controls	6.04 (2.89)	3.28 (0.73)	13.55 (5.58)
HD	7.8 (4.4)	3.9 (1.13)	11.86 (4.86)
<i>Number of deviations per rotation</i>			
Controls	2.54 (0.89)	1.28 (0.72)	1.17 (1.09)
HD	4.72 (0.98)	2.63 (0.6)	5.18 (1.17)
<i>Percent time spent within the boundaries</i>			
Controls	76.77 (11.04)	90.23 (6.03)	94.32 (5.66)
HD	57.36 (13.72)	74.75 (15.72)	68.89 (13.93)
<i>Average velocity within the circle (mm/s)</i>			
Controls	5.82 (2.16)	10.25 (3.01)	2.5 (1.03)
HD	4.81 (1.84)	8.49 (2.59)	2.92 (1.08)
<i>Number of acceleration transitions within the circle</i>			
Controls	0.76 (0.5)	0.3 (0.15)	1.32 (0.69)
HD	0.51 (0.39)	0.16 (0.08)	1.53 (0.73)
<i>Number of jerk events within the circle</i>			
Controls	3.27 (3.53)	0.72 (0.53)	12.41 (6.53)
HD	5.29 (3.96)	2.1 (1.28)	10.35 (6.32)

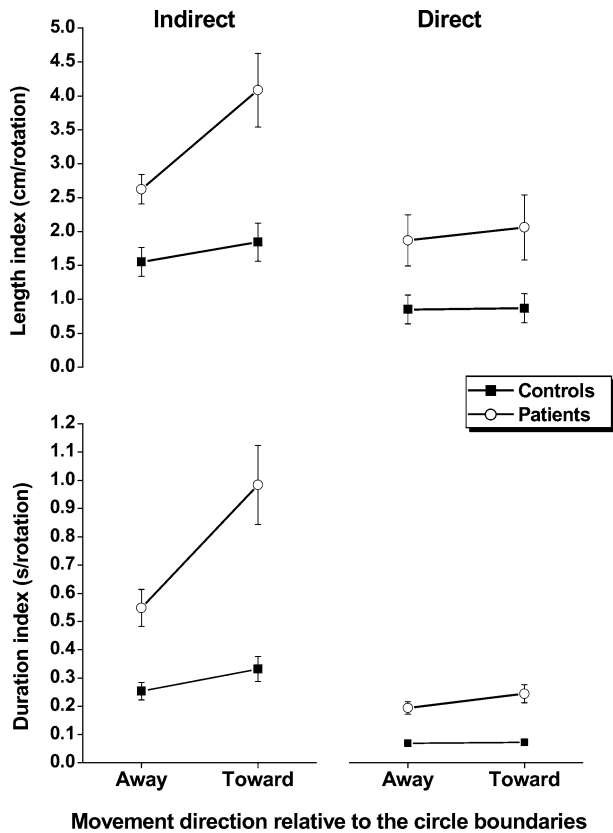


Fig. 2 Length and duration index for the trajectory outside the circle boundaries as a function of condition, direction and group

significantly slower when moving toward the circle ( $6.5 \text{ mm/s} \pm 3.64$ ) than away ( $7.3 \text{ mm/s} \pm 2.96$ ) and no such difference was observed for controls (toward:  $8.09 \text{ mm/s} \pm 3.64$ ; away:  $8.41 \text{ mm/s} \pm 3.49$ ) [ $F(1,21) = 9.9$ ,  $P < 0.01$ ]. Movements were smoother in the Direct condition (acceleration transitions:  $0.24 \pm 0.17$ ; jerk events:  $05 \pm 1.75$ ) than in the Indirect condition (acceleration transitions:  $0.56 \pm 0.43$ ; jerk events:  $5.88 \pm 6.92$ ) [acceleration transitions,  $F(1,21) = 17.6$ ,  $P < 0.001$ ; jerk events,  $F(1,21) = 8.1$ ,  $P < 0.01$ ], but no group differences were observed in these measures.

All dependent variables were specifically examined in four unmedicated patients and these patients showed performances that were similar to the medicated group average ( $P > 0.05$ ). In summary, patients were as efficient as controls when tracing inside the boundaries but deviated more often than controls when feedback was indirect. Moreover, during deviations in the indirect conditions, the trajectory traced toward the circle was less precise in patients than controls.

## Discussion

The goal of the present study was to investigate the performance of HD patients in a continuous movement requiring constant error feedback control. We postulated that more complex sensorimotor transformations

as required in indirect visual feedback conditions would affect movement execution. Results revealed that movements performed with indirect visual feedback were slower and showed more irregularities than movements performed with direct feedback confirming our proposition that movements performed with indirect feedback are more demanding than movements performed with direct feedback. More importantly, we also proposed that indirect visual feedback would be more detrimental to patients than controls. Patients showed little difficulty in movements using direct visual feedback but showed clear problems when the visual feedback was indirect. Specifically, when visual feedback was indirect, patients deviated more often outside the boundaries than controls even if their velocity was similar to controls and they took longer (both in time and distance) to move back toward the boundaries.

The difficulties of HD patients in error feedback control in the Indirect condition were not related to velocity demands. First, no change of performance was observed between the Indirect condition and the Indirect-Precise condition in HD patients, which differed only in the level of velocity required. Secondly, patients deviated less often in the Direct condition than the Indirect condition, even if movements were more rapid in the Direct condition.

Contrary to the deviations directed toward the circle, no group differences were observed for the part of the deviation directed away from the circle boundaries, which likely represents the time to detect a deviation and initiate a correction. Taken together, our results suggest that the correction deficit in patients with HD seems to be related to the execution of the correction rather than to the detection of the deviation. Because corrections were initiated at similar distances or times in the two groups, the execution of corrections cannot have been influenced by the distance required to correct the movement.

Contrary to the results of Smith et al. (2000) on discrete movements, HD patients showed no more irregularities than controls in both the direct and indirect conditions. This discrepancy may be linked to the nature of the tasks. For example, continuous circle tracing movements are intrinsically more irregular than discrete movements, requiring multiple changes in the acceleration profiles in order to maintain the cursor inside the circle. The efficiency of continuous circle tracing movements appears to be better reflected by precision measures.

Thus, movement corrections appear more problematic for HD patients when visual feedback is indirect. It could be argued that small involuntary movements may have affected the performance of patients. However, there were no group differences in acceleration transitions or jerk events, suggesting that involuntary movements did not significantly affect performance. Also, the number of deviations from the circle was similar between groups in the Direct condition, suggesting that patients could perform the task as well as controls when

direct vision of the target and the moving hand was available. Involuntary movements should affect all conditions and movement phases and only movements in the indirect visual feedback conditions and movements traveled toward the circle were affected in HD. In addition, involuntary movements are inhibited during attention to voluntary movements in HD and they are usually not correlated with voluntary movement control (Smith et al. 2000; Carella et al. 2003).

Smith et al. (2000) proposed that a proprioception deficit in HD may be involved in their difficulty in performing corrections. Participants might possibly rely more extensively on proprioceptive information when no direct visual information of the moving hand is available. It has been proposed repeatedly that seeing the hand before initiating the movement improves accuracy by permitting a multisensorial representation of the hand position (Desmurget et al. 1998). Direct vision could compensate for a proprioceptive deficit by comparing and updating the visual representation of the hand with its proprioceptive position.

An alternative explanation would be that correction difficulties observed in HD patients are linked to a faulty integration of different frames of reference. It has been proposed that the basal ganglia are involved in sensorimotor transformation (Abbruzzese and Berardelli 2003). Circle tracing requires that visual information from the circle and the moving arm as well as proprioceptive information concerning the location of one's hand during movement execution be transformed into a common frame of reference. These transformations are thought to induce systematic biases (McIntyre et al. 1998). Sensorimotor transformations are more complex in indirect feedback conditions and this may contribute to exacerbate the performance deficit of HD patients.

Finally, the observed difficulties of HD patients in error correction might also be related to a response selection deficit. Response selection deficits have been widely documented in HD (Agostino et al. 1992; Bradshaw et al. 1992; Jahanshahi et al. 1993; Georgiou et al. 1995; Sprengelmeyer et al. 1995; Curra et al. 2000; Gordon et al. 2000). This problem is especially severe in movement sequences or in movements which require a complex response selection rule. This deficit could explain our results at least partially. An indirect feedback increases response selection demands by increasing the complexity of the sensorimotor transformation. HD patients may have problems selecting movements in such conditions, leading to larger corrections. When an error takes place, a decision needs to be taken regarding the direction and amplitude of the correction. The success of such decisions depends on many factors such as the complexity of the task, novelty and precision demands (Richer and Chouinard 2000).

The difficulties of proprioception, response selection and sensorimotor transformations could be linked to a more general deficit of forward modeling in patients. A forward model is an internal model that predicts the relation between actions and their consequences

(Desmurget and Grafton 2000; Wolpert and Ghahramani 2000). Forward modeling is probably important in predictable tracing to reduce the time required to make a correction and to decrease the variability of the tracing movement. It could be proposed that because of deficient forward modeling, patients rely more extensively on closed-loop monitoring, making the correction longer and possibly more variable (Desmurget and Grafton 2000).

Overall, our results indicate that an error feedback control dysfunction in HD is not present when a direct visual feedback is used. Thus, the problem does not appear to be fundamentally linked to error feedback control per se, but rather to the inefficient use of error feedback in some situations such as indirect visual feedback which decrease the efficiency of voluntary corrections in HD patients.

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