available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

BRAIN RESEARCH

Research Report

Bradykinesia is not a "systematic" feature of adult-onset Huntington's disease; implications for basal ganglia pathophysiology

Alison Fenney[a], *Mandar S. Jog*[b], *Christian Duval*[a,*]

[a]*Département de kinanthropologie, Université du Québec à Montréal, Montréal, Québec, Canada*
[b]*Clinical Neurological Sciences, University of Western Ontario Health Centre–University Hospital, London, Ontario, Canada*

ARTICLE INFO

Article history:
Accepted 3 December 2007
Available online 8 December 2007

Keywords:
Whole-body involuntary movement
Chorea
Basal ganglia
Huntington
Kinetic
Dyskinesia
Parkinson

ABSTRACT

Our goal was to determine whether bradykinesia is present in choreic adult-onset Huntington's disease (HD) patients, and determine the impact of chorea on their voluntary movements. We recorded whole-body involuntary movements (WBIM) and voluntary motor acts simultaneously, using a magnetic tracker system, in 15 choreic HD patients and 15 healthy age- and gender-matched control subjects. Participants were asked to perform two distinct tasks; a manual-tracking (MT) task yielding a measure of chorea intrusion during accurate movements, and a rapid alternating movement (RAM) task, yielding measures of bradykinesia. Results show that patients with HD presented with deviations from the target that hindered their ability to match the target velocity during the MT task. Furthermore, error in performance was correlated with the amplitude of whole-body chorea (*Rho*=0.67), illustrating the deleterious effect of chorea during accurate movements. However, patients with choreic HD presented with significantly higher RAM range and velocity than matched controls, therefore ruling out the idea that bradykinesia is a systematic feature of HD even when chorea is predominant. The present results imply that patients may have benefited from an intact direct pathway ("select ON" pathway in the focused attention model of basal ganglia function) that allowed them to supersede any dysfunctions associated with the progressive alteration of the "control function" (striatal–globus pallidus–subthalamic) pathway responsible for generating the chorea. Finally, the present results suggest that patients with adult-onset HD having chorea would greatly benefit from improved treatments aiming at reducing their involuntary movements while maintaining proper motor function.

1. Introduction

Huntington's disease (HD) is usually considered a mixed movement disorder due to the presence of both hypokinetic and hyperkinetic symptoms, the most significant clinical feature of which is chorea (Weeks et al., 1997; Bilney et al., 2003; Gardian and Vecsei, 2004). The amplitude of chorea and its location within the body (motor

* *Corresponding author*. Département de Kinanthropologie, Université du Québec à Montréal, C.P. 8888, succursale Centre–Ville, Montréal (Québec) Canada H3C 3P8. Fax: +1 514 987 6616.
E-mail address: duval.christian@uqam.ca (C. Duval).

0006-8993/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.brainres.2007.12.005

topography) are known to fluctuate over short periods of time such as seconds or minutes (Fenney et al., in press). There is ample evidence to suggest that the chorea itself negatively affects motor function, specifically accuracy (Bilney et al., 2003; Phillips et al., 1996), reaction time (van Vugt et al., 2003, 2004; Jahanshahi et al., 1993; Kim et al., 2004), sequencing and submovement cueing (Agostino et al., 1992; Curra et al., 2000), timed motor tests (Garcia-Ruiz et al., 2002) and gait regulation (Bilney et al., 2005). Although there is extensive variability in motor symptom expression, the clinical features of typical adult onset HD are characterized by a progression from hyperkinetic to hypokinetic movements (Berardelli et al., 1999). Then, motor symptoms of HD may include rigidity, dystonia, akinesia and bradykinesia (Thompson et al., 1988; Berardelli et al., 1999; Bilney et al., 2003; Hamilton et al., 2003; Gardian and Vecsei, 2004). Aggravation of bradykinesia has been associated with a decrease in chorea, which in turn is related to a worsening of reaction time (van Vugt et al., 2004). However, the time course of the appearance of bradykinetic features is still debated, especially since clinical and laboratory observations suggest that the two symptoms may coexist in both early and late stages of HD (Thompson et al., 1988; Joel, 2001; Hashimoto et al., 2001; Kim et al., 2004). Interestingly, past basal ganglia models suggest that bradykinetic and choreic features are the result of opposite neural disturbances (Albin et al., 1989; Alexander et al., 1986). More recently, Mink (2003) has suggested that chorea would be the result of impaired inhibition of competing motor pattern generators, and the presence of bradykinesia would be the result of the superposition of desired and undesired motor pattern generators. If this is indeed true, bradykinesia may simply be a result of biomechanical effect due to low signal-to-noise ratio, where the signal is the intended movement and the noise represents the involuntary movements. It then becomes important to make a distinction between "core" bradykinesia, which is the consequence of improper activation of cortical structures by the basal ganglia–thalamo–cortical output, as seen in Parkinson's disease, and bradykinesia that is caused by mechanical disturbances, such as the intrusion of involuntary movements. Since the main treatment modality for chorea is to deplete dopamine with the potential side effect of drug-induced parkinsonism (Bonelli et al., 2004), determining whether "core" bradykinesia is a symptom of early HD, or simply the consequence of a low signal-to-noise ratio as described above, is imperative to assess whether accepted treatment may actually worsen an already existing and important feature of HD. Accordingly, the goals of the present study were to isolate the impact of chorea on motor performance in patients with HD, and determine whether "core" bradykinesia is being co-expressed with chorea during performance. In order to achieve this goal, whole-body involuntary movements (WBIM) were simultaneously quantified during two distinct motor tasks; a manual-tracking (MT) task that allowed for the quantification of choreic intrusions during accurate movements, and a rapid alternating movement (RAM) task that provided a measure of bradykinesia.

2. Results

Subject characteristics are presented in Table 1.

Fig. 1 illustrates the changes of WBIM amplitude during the rest and active conditions of MT and RAM. ANOVA reveals a *group* effect for WBIM during MT ($F=17.111$, $p<0.05$) and RAM ($F=39.790$, $p<0.05$) confirming the presence of significant chorea at rest and during voluntary movements in the HD group. RAM movements generated a *condition* effect that was present in both groups ($F=10.530$, $p<0.05$), but not during MT, which suggests that the increase of WBIM amplitude with voluntary movement is related to the velocity of the performed motor act.

Fig. 2 illustrates the amount of error (performance minus target) present during MT. In displacement, the difference did not reach the threshold for statistical significance ($t=250$, $p=0.481$), despite a clear trend toward more deviation from the target. The HD group exhibited high variability in error as well as WBIM amplitude; therefore, a correlation was done to determine if a relationship existed between these variables. Results indicate that indeed patients with higher WBIM presented with increased deviations from target ($Rho=0.67$, $p<0.05$). Error in velocity (difference between the target velocity and performance velocity) was significantly higher for the HD group ($t=340$, $p<0.05$), suggestive of a difficulty in matching the target velocity during the different phases of movement.

Fig. 3 illustrates the RAM performance for RANGE and VELOCITY. Patients with HD had significantly higher RANGE ($t=4.398$, $p<0.05$) and VELOCITY ($t=3.072$, $p<0.05$) than control subjects, suggestive of hypermetria.

Fig. 4 shows examples of MT and RAM performance from one patient with HD who had higher amplitude chorea and showed clear choreic intrusions in their MT performance, but slightly better performance then the control subject during RAM.

3. Discussion

3.1. *Chorea*

Patients had significantly greater WBIM compared to controls, confirming the presence of chorea. Beyond this confirmation, the effect of voluntary motor activity on amplitude of WBIM in patients with chorea is well demonstrated. Patients and controls both exhibited increased WBIM amplitude during motor activity, especially during RAM, with the HD group providing the most dramatic example of this trend. While the increased WBIM in the control group could be characterized as motor overflow, the increased WBIM in the HD group is the result of increased chorea. These results are similar to those of dyskinetic PD patients, where increased dyskinesias were observed during voluntary motor acts (Ghassemi et al., 2006; Lemieux et al., 2007). This may imply that both PD and HD hyperkinetic symptoms are sensitive to increased cortical facilitation brought about by neural activity related to voluntary movements.