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POSTURAL STABILITY LIMITS IN MANIFEST AND PREMANIFEST HUNTINGTON'S DISEASE UNDER DIFFERENT SENSORY CONDITIONS

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Abstract—Increasing evidence indicates that Huntington's disease (HD) produces postural control impairments even before the clinical diagnosis. It has been suggested that postural disorders of HD patients are explained by deficits in the processing and integration of sensory information, but this hypothesis has been under-explored. In the present study, we evaluated the amplitude of the center of pressure (COP) displacement during maximum leaning in four directions (forward, backward, rightward and leftward) and under three sensory conditions (eyes open, eyes closed and eyes closed standing on foam). We assessed the stability limits in 20 individuals with a positive HD genetic test (12 premanifests; eight manifests HD) and 15 healthy controls. The COP displacements were analyzed during the first and second phases of maintenance of the maximum leaning position. Manifest HD patients showed significantly greater COP ranges than healthy controls in both learning phases and all sensory conditions, but the greatest deterioration of their performance was found in the foam condition. In contrast, premanifest HD patients displayed larger COP ranges than controls only during the second phase of maximum learning, especially in the foam condition. Furthermore, both HD groups had significantly smaller limits of stability than healthy subjects during the second phase of maximum learning. However, their ability to maintain the maximum leaning position was degraded during both learning phases. Together, these findings demonstrate that HD reduces the limits of stability even before the clinical disease onset. Furthermore, our results indicate that dynamic postural tasks with high demand for sensorimotor integration and especially the use of proprioception are highly sensitive to early HD disease processes. This dynamic postural task may become a useful biomarker of HD progression.

Key words: stability limit, postural control, Huntington's disease, basal ganglia, sensorimotor integration.

INTRODUCTION

Huntington's disease (HD) is an autosomal dominant inherited neurodegenerative disorder affecting basal ganglia (BG) from the earliest stage of the disease, even before the clinical diagnosis ('premanifest') (Jurgens et al., 2008; Middelkoop and Roos, 2008). Manifest HD is characterized by progressive cognitive, behavioral and motor impairments such as involuntary movements and postural instability (Tian et al., 1991; Rao et al., 2009a,b; Panzera et al., 2011).

The perception of the limits of stability is critical for efficient postural control and to avoid falls. Such a mechanism involves the processing and integration of multiple sensory modalities including tactile, proprioceptive, visual and vestibular signals. BG networks are important for multimodal sensory integration (Nagy et al., 2006; Takakusaki et al., 2008; Patel et al., 2014). Thus, one major hypothesis that has been proposed to explain the postural control deficits in BG damage patients is abnormalities in the processing and integration of sensory information, particularly proprioceptive signals (Abbuzzese and Berardelli, 2003; Visser and Bloem, 2005; Patel et al., 2014). This hypothesis is widely supported by studies in Parkinson's disease patients (Mancini et al., 2008; Konczak et al., 2009; Tagliabue et al., 2009; Carpenter and Bloem, 2011). However, very few researchers have investigated this question in HD patients using a postural control paradigm with different sensory conditions.

Several postural anomalies have been reported in manifest HD patients. Notably, significant deficits were found in anticipatory postural adjustments (Delval et al., 2007, 2008), in reactive postural responses (Huttunen and Hömberg, 1990; Tian et al., 1992; Goldberg et al., 2010) as well as in quiet standing (Huttunen and Hömberg, 1990).

Of particular interest, several clinical tests such as the Unified Huntington's Disease Rating Scale, the Functional reach test, the Timed up and go and the Berg balance

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Abbreviations: ANOVA, analysis of variance; BG, basal ganglia; COP, center of pressure; EO, eyes open; EC, eyes closed; EC + F, eyes closed standing on a foam; HD, Huntington's disease.

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scale were shown to be not sufficiently sensitive in identifying motor deficits in the stage before clinical onset (Witjes-Ané et al., 2007; Rao et al., 2009a). Likewise, premanifest HD individuals displayed a similar performance as healthy subjects in a quiet standing task (Huttunen and Hömberg, 1990). Therefore, these postural tests cannot be used as motor biomarkers of HD progression.

Dynamic postural control is a major aspect of daily motor acts. To our knowledge, no previous study assessed dynamic postural control in the absence of external perturbation and in different sensory conditions in premanifest and manifest HD patients. Therefore, whether the postural anomalies of individuals with HD are exacerbated in more natural dynamic everyday life situations and whether these postural deficits are linked to impaired processing and integration of specific sensory information remain unresolved.

The present study was designed to extend previous findings in a number of ways. First, we used a dynamic stability limit task to compare the postural control of manifest and premanifest HD patients to healthy participants. The limits of stability were quantifies using the maximum voluntary inclined posture (Mancini et al., 2008). Second, we investigated the limits of stability of HD patients in three sensory conditions: eyes open (EO), eyes closed (EC) as well as eyes closed standing on a foam (EC + F) support surface (foam condition). The comparison between groups across sensory conditions will allow the evaluation of changes in sensorimotor processing during HD progression. In the EO condition, we assessed the postural stability limits of HD patients while all sensory modalities were available. This created high requirements for multimodal sensorimotor integration. In the EC condition, we evaluated whether patients with HD rely more on vision than healthy participants to maintain stability limits. Standing on a foam support surface decreases plantar pressure sensations and increases instability, especially at the ankle joint. Therefore, the foam condition was used to test if postural instabilities of HD patients increase when they are forced to use fine time-varying ankle proprioceptive signals to control posture.

If HD patients have globally impaired sensory processing and integration functions for dynamic postural control, then disorders in the ability to maintain stability limits compared to healthy participants should be observed in all sensory conditions. However, if the deficits of HD patients are primarily explained by altered proprioceptive processing, then HD patients should be impaired relative to healthy participants both in the EC and in the foam conditions with greater deficiencies when standing on a foam support surface.

EXPERIMENTAL PROCEDURES

Subjects

Eight manifest HD patients aged 35 to 60 years (52.1 ± 8.4 years), 12 premanifest HD participants aged 25 to 52 years (38.7 ± 9.3 years) and 15 healthy adults aged 24 to 65 years (40.8 ± 11 years) participated in this study after providing informed consent on a form approved by the institutional ethics review board. Exclusion criteria were a history of orthopedic disorders, other neurologic disorders and a recent chirurgical procedure. All HD subjects were genetically confirmed. Premanifest participants did not have motor signs classical of HD as measured by the motor exam subsection of the Unified Huntington's Disease Rating Scale. Manifest HD subjects presented the typical clinical symptoms of HD. A summary of the clinical features of manifest HD patients is reported in Table 1.

Experimental setup

Prior to the experiment, anthropometric measurements of the subject's feet (length and width) were assessed and their footprints were traced on the force plate to ensure that the feet position was consistent from trial-to-trial. The standard initial stance position established by McIlroy and Maki (1997) was used.

At the beginning of a trial, participants stood barefoot on a force plate with arms crossed on the chest. Participants were asked to maintain an upright quiet standing position until an auditory cue (5 s) instructed them to lean as far as possible in a different directions in each trial (forward, backward, rightward and leftward) without lifting their feet or flexing their hips. Participants were asked to maintain their maximum leaning position for 10 s and, thereafter, to return to the initial standing position (7 s).

This experimental task was tested in three different sensory conditions: (a) EOEO, (b) EC and (c) EC + F. The compliant foot support was a 5.5-cm-thick medium density foam. One trial was performed under each condition for each direction. Under the EO condition, participants were asked to fix a target (2 cm of diameter) on the wall 3 m ahead of them. During EC and EC + F conditions, participants were encouraged to remember the target's position in order to keep their head in the same position across trials. Before data collection, each subject performed a practice trial to ensure that task instructions were understood. No feedback about the performance was given to the participants during the testing session.

Data collection and data analysis

Ground reaction force data were collected at 200 Hz using an AMTI force platform and data processing was performed using the Balance Clinic software. The analysis of the center of pressure (COP) displacements during the maximum leaning position was subdivided into two phases (Fig. 1a). The beginning of phase 1 was defined as the first time the COP moved in the opposite direction to the voluntary leaning movement and ended at the 5th second of maximum leaning. Phase 2 was during the last 5 s of maximum leaning.

The total amplitudes (cm) of the maximum COP excursions along the AP (during forward and backward leaning) and ML axes (during rightward and leftward leaning) were analyzed during both phases. The amplitudes of the maximum COP excursions were