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THE EFFECT OF PARKINSON'S DISEASE AND LEVODOPA ON ADAPTATION OF ANTICIPATORY POSTURAL ADJUSTMENTS

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Abstract—Postural support alters anticipatory postural adjustments (APAs). Efficient adaptation to changes in postural support in reactive and centrally initiated postural synergies is impaired in Parkinson's disease (PD). This study examined whether APAs are affected differently by familiar and novel supports in people with PD, ON and OFF levodopa. The effect of PD and levodopa on the ability to immediately adapt APAs to changes in support and refine with practice was also investigated. Fourteen people with PD and 14 healthy control participants performed 20 single rapid leg lift tasks in four support conditions: unsupported, bilateral handgrip (familiar), bite plate (novel) and a combined handgrip + bite plate condition. APAs, identified from force plate data, were characterized by an increase in the vertical ground reaction force under the lifted leg as a result of a shift of weight toward the stance limb. Results showed the ability to incorporate familiar and novel external supports into the postural strategy was preserved in PD. Controls and PD patients in the OFF state further refined the postural strategy with practice as evidenced by changes in amplitude of vertical ground reaction forces and forces applied to support apparatus within conditions between the initial and final trials. In the ON state, people with PD failed to refine the use of postural supports in any condition. The results suggest that immediate postural adaptation is intact in people with PD and unaffected by levodopa administration but the ability to refine postural adaptations with task experience is compromised by dopamine therapy.

Key words: Parkinson's disease, anticipatory postural adjustments, levodopa, postural support, adaptation.

INTRODUCTION

Postural control is compromised in Parkinson's disease (PD) and can worsen with levodopa administration. Although the mechanism is complex, deficits in ''central set'' have been implicated. Central set refers to the central representation of a task, its biomechanical consequences and planning of appropriate postural adjustments to overcome them (Horak et al., 1989). ''Set'' allows timely implementation of appropriately scaled postural adjustments (Horak, 1996) and is thought to be mediated, at least in part, by basal ganglia networks based on compromised ability to change central set in PD as evidenced by studies of postural reactions to floor translation (Horak et al., 1996). These reactive postural adjustments are initiated in response to sensory information, but can be adjusted if constraints of the task change in a predictable manner (e.g. expected change in speed of support translation). In PD these reactions are inefficiently adapted when the context of the perturbation changes (e.g. increased velocity) and is unchanged by levodopa (Horak et al., 1992, 1996; Chong et al., 2000). Changes in central set rely on recognition of altered task demands and require a new strategy to accommodate. This dependence of accurate sensory information (which may be compromised in PD (Klockgether et al., 1995)) regarding new conditions complicates the interpretation of adaptation of the postural adjustment.

Incomplete adaptation to changes in postural demand has been argued in terms of difficulty changing central set (Horak et al., 1996; Chong et al., 2000), but interpretation is clouded by other deficits in PD that are known to affect the sensory system (Klockgether et al., 1995; Jobst et al., 1997). Investigation of another class of postural adjustments, anticipatory postural adjustments (APA), which prepare for predictable challenges to the postural control (such as those from voluntary movements), may provide greater clarity for investigation of central set as it is not complicated by the potential involvement of sensory pathways as the adjustment is initiated prior to movement rather than in response to sensory input induced by a perturbation.

APAs are specific to the movement, adapt to changes in external postural support by changing APA timing and magnitude, and are mediated by a range of supraspinal regions including cortical (Gahery and Massion, 1981), cerebellar (Bouisset and Zattara, 1987) and basal ganglia (Burleigh-Jacobs et al., 1997) networks. Addition of external support redistributes APA muscle activity to

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Abbreviations: ANOVA, analyses of variance; APA, anticipatory postural adjustment; BP, bite plate; FO, foot off; H & Y, Hoehn and Yahr scale; HG, bilateral handgrip; MDS-UPDRS, Movement Disorder Society-Sponsored Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; US, unsupported stance.

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segments that contact it (e.g. hands, jaw) (Slijper and Latash, 2000; Hall et al., 2010). Appropriate central set ensures immediate incorporation of familiar and novel supports with little/no further refinement with repetition (Hall et al., 2010). Evaluation of changes in APAs with modification of external support would establish the integrity of central set in PD.

PD has been characterized by reduced amplitude, increased duration and delayed onset of APAs in tasks such as gait initiation (Burleigh-Jacobs et al., 1997; Frank et al., 2000; Rogers et al., 2011); parameters thought amenable to levodopa therapy. The ability to scale APAs with changes in internal constraint (e.g. stance width) is preserved in PD, but the accuracy of rescaling is less than for healthy individuals (Rocchi et al., 2006). Although this may imply central set is preserved a problem is that in step initiation the focal movement contributes to the postural preparation (to shift the COP over the supporting leg) and this somewhat confounds the interpretation of the mechanisms of adaptability of the APA. A more detailed investigation of the issue may be possible by investigating more complex changes in postural demands, such as that imposed by changes in external constraint (e.g. additional postural support).

This study aimed to investigate the effect of PD and levodopa on adaptation of APAs to novel and familiar changes in external postural supports. Retention of central set would be supported if there was immediate adaptation to the new support, and the quality of central set could be interpreted from the amount of further refinement of the APA with practice, which would infer incomplete adjustment for modified task constraints.

EXPERIMENTAL PROCEDURES

Participants

Fourteen people with a clinical diagnosis of idiopathic PD (13 male, age 64.2 [9.4] (mean [SD]) years) and 14 healthy age (±3 years) and gender-matched Controls (age 65.4 [5.0] years) volunteered (Table 1). Participants with PD were included if they were aged <75 years, treated pharmacologically for their symptoms and had the ability to stand unaided for at least 10 min. Exclusion criteria included respiratory, circulatory or vestibular disorders, neurological conditions other than PD, previous spine, limb and face fractures/surgery, major postural deformities and false teeth.

PD participants were tested on two occasions: one hour after taking their normal levodopa medication (ON), and after a minimum 12-h medication washout period (OFF). Motor impairments were assessed using the motor subsection (III) of the Movement Disorder Society-Sponsored Unified Parkinson's Disease Rating Scale (MDS-UPDRS) in the ON and OFF states. Disease severity was rated using the Hoehn and Yahr scale (H&Y) (Table 1). Although disease severity was mild, and some participants had an H&Y score of 2 with no overt signs of postural instability, we have previously shown postural deficits using methods similar to that used here and this disease severity ensured bradykinesia was limited, thus enabling control of the experimental task. Procedures conformed to the Declaration of Helsinki, the Institutional Ethics Committee approved the study, and participants provided written informed consent.

Procedure

Procedures were identical to those reported previously Hall et al. (2010). In brief, participants flexed a leg at the hip in response to a visual cue. APAs were quantified from two force plates (Bertec Corporation, USA) as a vertical ground reaction force (Fz) increase under the lifted leg and changes in force applied to postural supports prior to foot off (FO). Adaptation of APAs was measured as the change from that associated with unsupported stance (US). Adaptation to familiar (bilateral handgrip, HG), unfamiliar (bite plate, BP), and complex supports (HG + BP) was studied (Fig. 1). The unfamiliar support of the BP was included to test the refinement of postural adaptation to a postural set that would be novel to the participants.

Participants wore a head-mounted laser and stood (heels 0.1 m apart, equal weight distribution [real-time feedback]) 1.5 m from an infrared-sensitive target and visual cue. Single rapid left or right hip and knee flexion (as indicated by a randomized visual left or right signal) to 75° was performed in four conditions. Instructions for the task were standardized and participants were asked to "in your own time, lift the appropriate leg as fast as possible to then return to your starting position". Audible feedback when the laser moved outside a 90-mm diameter target ensured head position remained similar between conditions with (BP, HG + BP) and without (US and HG) head constraint. The standard instruction was to "in your own time, lift the appropriate leg as fast as possible then return to your starting position". The task was designed to involve self initiated movement rather than a reaction time task as this can modify the characteristics of the APA (Burleigh-Jacobs et al., 1997; Jacobs and Horak, 2006). No instructions were given regarding support apparatus. For each condition, 20 leg lifts (each leg) were completed, separated by at least 10 s. Foot position was corrected between repetitions. There was 3 min rest between conditions and condition order was randomized.

Triaxial accelerometers (±3G, Dimension Engineering, USA) placed bilaterally over the patella measured leg acceleration. Hand grips (range 20 kg, CCT Transducers, Italy) and a bite plate were mounted to a support frame to record hand and jaw forces during support conditions. A force transducer (range 110 kg, Scale Components, Australia) in the frame recorded applied forces that were not the direct result of bite or grip, e.g. leaning on the frame. Data were sampled at 500 Hz using a Power 1401 Data Acquisition System (Cambridge Electronics Design, UK) with Spike2 software.

Data analysis

Data were analyzed from leg lifts contralateral to the dominant side (Controls) or side most affected by