Centrally Initiated Postural Adjustments in Parkinsonian Patients On and Off Levodopa

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Received 27 December 1999; accepted in final form 20 July 2000

Frank, J. S., F. B. Horak, and J. Nutt. Centrally initiated postural adjustments in parkinsonian patients on and off levodopa. J Neurophysiol 84: 2440–2448, 2000. This study investigates the effects of parkinsonism and dopamine replacement therapy (levodopa) on centrally initiated postural activity preceding rising onto the toes. The electromyographic (EMG) and force magnitude, scaling, sequencing, and postural stabilization were compared when rising-to-toes under two conditions, slow/low versus fast/high, for parkinsonian patients and elderly control subjects. Parkinsonian subjects were tested after withholding their levodopa medication for 12–16 h and again 1 h after taking their medication when parkinsonian signs were diminished. Parkinsonian subjects showed reduced magnitudes and delayed timing of the postural and voluntary components of the rise-to-toes task, as if they had difficulty turning off the postural, tibialis anterior (TIB) component and initiating the voluntary, gastrocnemius (GAS) component. Dopamine improved the relative timing, as well as the magnitude of both postural and voluntary components of rise-to-toes. Although the magnitude of dorsiflexion torque was smaller for parkinsonian subjects on and off than for healthy elderly controls, the parkinsonian subjects showed intact scaling of the magnitude of postural activity. Parkinsonian subjects do not perform the rise-to-toes task like normal subjects who are instructed to rise slowly; the relative timing of TIB and GAS activation was different even at comparable speeds of performance. Parkinsonian subjects, both on and off, exhibited greater risk of falling than elderly control subjects when rising to toes. This increased risk of falling was reflected in a smaller safety margin between the peak center of mass (CoM) and peak center of pressure (CoP) during the task. The magnitude of mean postural dorsiflexion torque in the rise-to-toes task was highly correlated with a clinical rating scale of gait and balance, suggesting that force control is a critical factor influencing postural control in patients with Parkinson’s disease.

INTRODUCTION

Control of upright stance posture involves multiple components of postural control including reactions triggered by external perturbations, antigravity muscle tone, and centrally initiated postural adjustments preceding or accompanying voluntary movements (Horak and Macpherson 1996). Our previous studies (Burleigh 1995; Burleigh-Jacobs et al. 1997; Chong et al. 1999b, 2000; Horak et al. 1992b, 1996) showed that Parkinson’s disease impairs externally triggered postural reactions, central set for adapting postural responses, postural tone, and centrally initiated steps. However, we found that levodopa replacement improved only muscle tone and centrally initiated steps, but not externally triggered postural reactions and central set. These studies also showed that despite significant bradykinesia, parkinsonian patients do scale their postural reactions proportionally to changes in perturbation velocity, although they have difficulty increasing the magnitude of postural reactions when the increase must come from centrally anticipated changes in perturbation amplitude, i.e., central set (Horak et al. 1996). Furthermore, the latencies and timing of muscle activation within an externally triggered postural response synergy were not affected by Parkinson’s disease. The current study examined whether parkinsonian patients have difficulty scaling or controlling the relative timing of postural perturbations and voluntary movement in a centrally initiated rise-to-toes task and the effects of levodopa. A rise-to-toes task was chosen because it is a centrally initiated task that involves sequencing of preparatory postural adjustments prior to a voluntary movement. Marsden (Marsden 1984; Marsden and Obeso 1994) described difficulties with relative timing of a sequence of actions in Parkinson’s disease. Does Parkinson’s disease and levodopa affect bradykinesia or scaling of the preparatory postural activity and the voluntary activity similarly? How is timing of the preparatory and voluntary activity and postural stability affected by Parkinson’s disease and levodopa.

Parkinson’s disease provides a model for studying the motor functions of the basal ganglia (Marsden 1984; Martin 1967). Patients with Parkinson’s disease show profound clinical deficits in postural control including falls or retropulsion in response to a nudge on the sternum, instability in gait and turns, and a flexed, rigid postural alignment in stance (Martin 1967; Nutt and Horak 1996). We were surprised to find that postural reactions triggered in response to translations of the support surface had normal onset times and normal scaling of magnitude to changes in velocity of surface perturbations in Parkinson’s patients both in the off- and on-levodopa state (Horak et al. 1996). Although the relative distal to proximal timing of muscle activation within a postural synergy was normal in Parkinson’s disease, the sequencing of hip- and ankle-synergy components was abnormal in Parkinson’s disease (Horak et al. 1992b). In addition, postural response magnitudes were weaker...
than in elderly control subjects and did not improve with levodopa replacement. In contrast, excessive levels of background muscle tone decreased and forces related to voluntary step initiation significantly increased with levodopa (Burleigh et al. 1995; Burleigh-Jacobs et al. 1997). The lack of effect of levodopa on externally triggered postural reactions concurs with clinicians’ observations of the resistance of balance performance to improvement with levodopa despite improvement in voluntary movements. Whether the magnitude, scaling, and timing of postural preparations and associated voluntary movement are affected similarly by Parkinson’s disease and levodopa therapy is unknown.

Postural preparations accompanying voluntary movements serve to stabilize the body center of mass (CoM) or move it to a new position of support (Bouisset and Zattara 1987; Clement et al. 1984; Eng et al. 1992; Horak et al. 1984; Lee 1984; Nardone and Schieppati 1988). The timing and magnitude of the postural muscle activation appears to be scaled to the anticipated magnitude of the destabilizing force (Horak et al. 1984). Some tasks such as rising and maintaining balance on the toes and step initiation cannot be performed successfully without an initial postural adjustment that moves the CoM forward over a new base of support: i.e., the task begins with an initial postural destabilization. Several investigators (Clement et al. 1984; Diener et al. 1990; Nardone and Schieppati 1988) have reported an initial silencing of the gastrocnemius-soleus muscles and/or activation of the tibialis muscle prior to rising on the toes; this preparatory postural muscle pattern generates a dorsiflexor torque that moves the CoM forward to a new position of support. The timing of the postural and voluntary components is critical to the task. Early voluntary activation of the gastrocnemius would tip the body backward because the CoM would not be sufficiently forward to balance on the toes. Relative late voluntary activation of gastrocnemius would tip the body forward as the CoM would be too far forward to balance on the toes.

It is not clear whether postural preparations accompanying voluntary movement are absent or impaired in Parkinson’s disease. Bazalgette et al. (1986) and Rogers et al. (1987) reported that postural preparations are reduced or absent in patients with Parkinson’s disease when performing a task of rapidly elevating the arms to shoulder level. However, the slower arm movements of the parkinsonian subjects could explain these findings; slow arm movements do not create significant destabilizing force that requires anticipatory postural control (Horak et al. 1984). Kaneoke et al. (1989) found that parkinsonian subjects lacked early silencing of the gastrocnemius-soleus muscles prior to rising up onto the toes. However, this study provides only a partial description of the postural preparation during rise to toes. It is not known whether tibialis anterior activation, important for postural preparation, also is absent or impaired.

In this study, we investigated centrally initiated postural preparations in the same population of parkinsonian subjects as reported in two earlier studies (Burleigh et al. 1995; Horak et al. 1996) to gain insight to the role of the basal ganglia and dopamine replacement on various aspects of postural control. We tested the hypothesis that parkinsonian patients have difficulty scaling postural preparations prior to voluntary movement and controlling the timing of these events. Centrally initiated postural preparations were examined in a rise-to-toes task performed at two speeds: slow and fast. Preliminary results have been published as abstracts (Horak and Frank 1993; Horak et al. 1991, 1992a; Nutt et al. 1991).

METHODS

Subjects

Subjects comprised the same sample as an accompanying investigation of postural tone (Burleigh et al. 1995) and reactive postural control in parkinsonian subjects (Horak et al. 1996). Ten subjects with idiopathic parkinsonism (mean age 61 ± 6 yr, range 49–64 yr, 6 women and 4 men) were included in this study. The severity of parkinsonism ranged from stage III to stage IV on the Hoehn and Yahr scale. An 11-item clinical scale was used to rank their postural and gait disorders when OFF (i.e., off medication and with prominent parkinsonian signs); each item was rated on a three-point scale with 0 = normal, 1 = mildly abnormal, and 2 = severely abnormal (Table 1) (Horak et al. 1996). All subjects were able to stand independently during the testing session except the most severely involved parkinsonian subject (LH) who was completely “frozen” and unable to sit or sit while OFF levodopa. LH’s data were included only in the OFF condition.

Subjects with Parkinson’s disease reported to the laboratory in the morning having withheld their morning dose of levodopa (Sinemet) and were initially tested when OFF levodopa. Subjects then took their normal levodopa dose and were retested approximately 1 h later when ON (i.e., on medication and with diminished parkinsonian signs); all subjects showed diminished signs of parkinsonism 30 min following administration of levodopa as evidenced by an improved rate of finger and/or foot tapping; results are reported in an earlier study (Horak et al. 1996).

Thirteen healthy elderly subjects (mean age 65 ± 6 yr, range 48–66 yr, 7 women and 6 men) were included as control subjects in this study. Subjects were administered a complete neurological examination by one of the authors. All subjects were free of orthopedic, psychological, or other neurological constraints that could affect posture. All subjects provided informed consent for protocols approved by the Institutional Review Board.

Procedures

This study examined the magnitude, scaling, and relative timing of postural adjustments that accompany rising up onto the toes. Subjects stood with their arms folded across the chest, eyes open, and feet comfortably positioned 6–9 cm apart at the heels. Scaling of the response was examined by instructing subjects to perform the task under two conditions: rising to the toes as high and as quickly as possible and maintaining balance on the toes. Relatively late voluntary activation of gastrocnemius would tip the body backward as the CoM would not be sufficiently forward to balance on the toes. Subjects then took their morning having withheld their morning dose of levodopa (Sinemet) and were initially tested when OFF levodopa. Subjects then took their normal levodopa dose and were retested approximately 1 h later when ON (i.e., on medication and with diminished parkinsonian signs); all subjects showed diminished signs of parkinsonism 30 min following administration of levodopa as evidenced by an improved rate of finger and/or foot tapping; results are reported in an earlier study (Horak et al. 1996).

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TABLE 1. Clinical stability test

<table>
<thead>
<tr>
<th>Score</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing posture (A/P, Lateral)</td>
<td>Moderate-severe</td>
<td>Mild</td>
<td>Normal</td>
</tr>
<tr>
<td>Standing posture (Fwd/Back)</td>
<td>Absent</td>
<td>Minor</td>
<td>WNL</td>
</tr>
<tr>
<td>Trunk mobility range (A/P, Lateral)</td>
<td>Absent</td>
<td>Small</td>
<td>WNL</td>
</tr>
<tr>
<td>APA with arm raise</td>
<td>Severe</td>
<td>Mild</td>
<td>WNL</td>
</tr>
<tr>
<td>Sit-to-stand</td>
<td>Unable</td>
<td>Arm/falls*</td>
<td>WNL</td>
</tr>
<tr>
<td>Gait initiation speed</td>
<td>Freezes</td>
<td>Slow</td>
<td>WNL</td>
</tr>
<tr>
<td>Gait step length</td>
<td>Shuffles</td>
<td>Short</td>
<td>WNL</td>
</tr>
<tr>
<td>Gait step speed</td>
<td>Festinating</td>
<td>Slow/shuffling</td>
<td>WNL</td>
</tr>
<tr>
<td>Gait arm swing</td>
<td>Absent</td>
<td>Minimal</td>
<td>WNL</td>
</tr>
<tr>
<td>Turning strategies</td>
<td>Small Steps</td>
<td>Cross over</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Maximum instability possible = 22. APA, anticipatory postural adjustment; WNL, within normal limits. * Uses arms to push off or falls.

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possible (fast) and rising to the toes slowly with low elevation (slow).

Under both performance conditions, subjects were instructed to hold the elevated position for 5 s. Subjects performed a block of seven trials in each condition; each trial was initiated following a verbal command from the experimenter. Unsuccessful trials were discarded and replaced; these occurred in <2% of all trials for the parkinsonian group and <0.5% for the control group. The order of presentation of conditions was the same for all subjects: fast and slow. All trials preceded a series of reactive postural perturbations that occurred in the same experimental session and previously has been reported (Horak et al. 1996).

Subjects stood with each foot on custom-built force platforms throughout the experiment. Each force platform was instrumented with a strain gauge mounted at the corner of the platform. Surface reactive torque primarily due to the ankle was determined from the difference between the front and the back strain gauge vertical force outputs. Center of pressure (CoP) was calculated by dividing the summed ankle torques by body weight and multiplying this value by the distance from the center of the platform to the location of the strain gauge.

Movement of the limbs and trunk were determined from displacements of markers positioned at five joint locations on the right side of the body: metatarsal of the small toe, ankle, knee, hip, and shoulder. A Watsmart System recorded the displacements of these markers at a frequency of 100 Hz. Movement of the body CoM was calculated from the kinematic and anthropometric measures using a three-segment model (Koozekanani et al. 1983).

Muscle activation patterns were determined by recording surface electromyographic (EMG) activity from the right side: gastrocnemius (GAS) and tibialis anterior (TIB) muscles. Muscle activity was recorded from bipolar, surface electrodes (2.5 cm diam) positioned 2–4 cm apart over the muscle belly. EMG activity was band-pass filtered (70–2,000 Hz), rectified, and low-pass filtered with a time constant of 10 ms. EMG activity could not be calibrated reliably on an absolute scale; however, amplifier gains were fixed throughout all experimental sessions for all subjects, and skin resistance was kept below 5 KΩ.

**Data analysis**

For all trials, torque at the surface, EMG, CoP, and CoM data were recorded for 5 s beginning with a verbal instruction to the subject to rise up onto their toes. Prior to analysis, all trials were aligned at the peak of ankle dorsiflexion torque to provide an equivalent time base and cut to retain an interval extending from 1 s before to 2 s after this landmark. The peak of ankle dorsiflexion torque defined time “0 ms,” and events occurring prior to this were interpreted as preparatory for rising up onto the toes.

Torque was quantified by calculating the integral below the baseline torque (quiet stance) until it recovered above this level, i.e., dorsiflexion torque. EMG onset times were identified from individual rectified trials using an automatic search program that identified the earliest time that EMG activity increased beyond the baseline (quiet stance) activity by 2 SD and remained above this level for 50 ms. EMG baseline activity was determined from a 200-ms sample recorded at the onset of data collection, just prior to the instruction to rise to the toes. EMG offset times were identified with the same automatic search program, but identified when EMG returned to baseline level. EMG onset and offset times were recorded with an accuracy of 2 ms. Integrated areas under the rectified, filtered EMG were quantified over the first 250 ms after EMG onset for individual trials. The integration interval (250 ms) was chosen to examine EMG scaling during the early period of the postural response in a similar manner to our earlier investigation of triggered postural reactions (Horak et al. 1996). Although integrated EMG (IEMG) was never directly compared between individuals, unnormalized group means were compared with the assumption of no systematic difference in skin impedance between our groups of age-matched parkinsonian and control subjects.

A $2 \times 2$ ANOVA was used to examine subject group (elderly controls vs. parkinsonian subjects ON) and task speed (slow vs. fast) influences on the magnitude of dorsiflexion torque and IEMG, EMG onset, and EMG duration. Separate ANOVAs were conducted to examine the difference between 1) healthy elderly controls and parkinsonian subjects OFF and 2) parkinsonian subjects OFF and ON.

![FIG. 1. Torque associated with rising onto the toes high and fast. A: 3 sample trials from a representative control and a parkinsonian subject OFF and ON. All torque responses are aligned at the peak of dorsiflexion torque (0 ms) responsible for preparatory postural adjustment. Shaded areas reveal the time over which the torque integral was measured. B: histogram of the mean and standard error of the dorsiflexion torque integral for each group. Parkinsonian subjects OFF showed less dorsiflexion torque than control subjects and torque increased for parkinsonian subjects when ON. Asterisks (*) denote $P < 0.05$ or greater for this and the following figures. C: correlation between the parkinsonian OFF subjects’ mean dorsiflexion torque in the rise to toes high and fast task and their Clinical Instability Index.](http://jn.physiology.org/)

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RESULTS

Magnitude and scaling

Parkinson’s disease reduces the magnitude of centrally initiated postural preparations. Figure 1 displays torque profiles and integrals during fast rise to toes. Figure 1A shows smaller than normal initial dorsiflexor torque (shaded area), responsible for moving the body CoM forward over the toes, in three trials from a representative patient with Parkinson’s disease compared with an elderly control subject. The subsequent plantarflexor torque (voluntary movement) acts to both arrest the forward body motion and lift the body up onto the toes. Figure 1B displays differences in mean torque generation when rising up onto the toes fast for the elderly control and parkinsonian groups. Parkinsonian subjects OFF displayed significantly less dorsiflexor torque than healthy elderly controls (−36%; P < 0.05). Dorsiflexor torque was significantly greater for parkinsonian subjects ON when compared with OFF (+40%; P < 0.05). The magnitude of the mean dorsiflexion torque (fast task) was highly correlated with the clinical balance instability index (Table 1) for parkinsonian subjects OFF (Fig. 1C). The parkinsonian subjects with the largest dorsiflexion torque were rated lowest in clinical instability, and the patients with the smallest torques were rated highest in clinical instability.

When rising up to the toes, the initial dorsiflexor torque is generated by activation of TIB, and the subsequent plantarflexor torque is generated by activation of GAS and silencing of the TIB. Figure 2A shows smaller than normal EMG activity (shaded area) for three trials in a representative patient with Parkinson’s disease ON and OFF levodopa compared with an elderly control subject. Figure 2B displays the mean magnitude of activation of tibialis anterior and gastrocnemius muscles (fast task) for elderly control and parkinsonian subjects OFF and ON. The magnitude of both TIB and GAS activity in the parkinsonian patients OFF was a small fraction of the activity in the elderly control subjects (21 and 22%, respectively, P <
0.01). When parkinsonian subjects were ON, the TIB and GAS magnitude significantly improved ($P < 0.05$; 35 and 39% of control TIB and GAS IEMG).

Despite a reduction in force magnitude, parkinsonian patients could scale centrally initiated postural adjustments. The time to reach peak forward CoM displacement when rising to the toes fast versus slow decreased for all subject groups. Mean duration for slow versus fast performance for each group was 1,294 versus 1,122 ms for elderly controls, 1,685 versus 1,230 ms for parkinsonian subjects ON, and 1,849 versus 1,430 ms for parkinsonian subjects OFF. Figure 3 compares the magnitude of mean dorsiflexion torque, TIB activity and GAS activity for two speeds of task performance. All subject groups showed an increase in dorsiflexor torque when increasing the speed of performance from slow to the fast ($P < 0.001$). The amount of change in torque was similar for all groups, although the percent increase was larger for the Parkinson patients because their torque was so small: torque increased by 33, 63, and 65% for controls, Parkinson OFF, and Parkinson ON, respectively. All subject groups also showed a significant increase in TIB ($P < 0.003$) and GAS ($P < 0.001$) muscle activity during fast performance compared with slow performance. Changes in IEMG were similar for all three groups: TIB increased 56, 35, and 40%, and GAS increased 39, 34, and 38% for control, Parkinson OFF, and Parkinson ON, respectively.

**Relative timing**

Parkinson’s disease impairs not only force magnitude but also the relative timing of muscle activation underlying the postural preparations and subsequent voluntary movements. During fast performance (Fig. 4A), parkinsonian subjects OFF displayed an earlier onset ($P < 0.03$) and prolonged duration ($P < 0.004$) of TIB activation relative to elderly control subjects. The activation of GAS occurred close to the onset of plantarflexor torque ($\sim 2$ ms) for elderly controls. In contrast, Parkinson subjects OFF showed a delayed activation of GAS (77 ms following peak dorsiflexor torque) compared with elderly control subjects ($P < 0.03$). It is unlikely that GAS onset was delayed because of delayed TIB offset in parkinsonian subjects as the correlation coefficient between GAS onset and TIB offset was low and nonsignificant: $r = -0.14$ OFF and -0.18 ON. Parkinsonian subjects appeared to have difficulty turning off the postural, TIB component and initiating the voluntary, GAS component. This altered timing did not correlate strongly with the clinical balance instability index as was observed for the magnitude of dorsiflexion torque; correlation coefficients for TIB onset, TIB duration, and TIB-GAS duration ranged from 0.1 to 0.4.

Dopamine improved the relative timing, as well as the magnitude of muscle activation in parkinsonian patients during fast rise-to-toes. Temporal characteristics of muscle activation for parkinsonian subjects ON were more like elderly controls. The onset of GAS was significantly earlier (50 vs. 78 ms) for parkinsonian subjects ON than OFF ($P < 0.05$). Although there was a tendency for TIB onset and duration to shorten like controls when parkinsonian patients were ON, these differences were not significant OFF versus ON. Temporal properties of muscle activation always were more variable across parkinso-
nian subjects than elderly controls as can be noted by the larger standard errors. Parkinsonian subjects did not perform the fast rise-to-toes like elderly controls who are instructed to rise slowly, i.e., their performance was not normal for a slower speed of movement. Even when performing slowly, elderly controls displayed a later onset \( (P < 0.05) \) and shorter duration \( (P < 0.05) \) of TIB and earlier onset of GAS \( (P < 0.05) \) compared with the timing of these events during fast rise-to-toes by parkinsonian subjects OFF. The onset and duration of TIB and the onset of GAS did not differ for fast and slow performance in all groups (Fig. 4, A vs. B).

Despite an initial flexed posture, parkinsonian subjects did not use hip flexion as an alternate strategy for moving the CoM forward prior to rising to the toes. Figure 5A shows stick figures and CoM position of a representative control subject who stands with hip hypertension and a parkinsonian subject OFF and ON who stands with flexed hips, knees, and ankles in stance and when rising to toes. Despite more flexion at the hip throughout the task, the parkinsonian group showed a similar sequence of hip joint change: initial hip extension to move the CoM forward followed by hip flexion (Fig. 5B).

Postural stabilization

If the magnitude and relative timing of centrally initiated postural preparations and voluntary movements are important for postural stability when rising-to-toes, the differences in these parameters between control and parkinsonian subjects should be reflected in control of the CoP that acts to move CoM. Figure 6A displays sample records of the CoM and CoP from an elderly control and a parkinsonian subject OFF and ON when rising-onto-toes. The performance of the elderly control subjects is characterized by an initial backward displacement of the CoP, which moves the CoM forward. The CoM is guided to a new position of stability over the toes by a subsequent forward displacement of the CoP, which moves ahead of the CoM. The peak forward displacement of CoP (relative to the quiet stance position) normally exceeds the peak forward displacement of the CoM with a phase advance to decelerate the forward movement and prevent falling forward.

Despite improved postural adjustment when ON levodopa, parkinsonian subjects OFF and ON allow the CoM to fall further forward than elderly controls at the completion of rise-to-toes. Figure 6B shows a larger difference between peak CoP and peak CoM for elderly controls than parkinsonian subjects OFF and ON \((P < 0.05)\). The peak CoP displacements was similar for all groups; however, mean forward displacement of the CoM was significantly less \((P < 0.01)\) for elderly controls \((8 \pm 0.5 \text{ cm}, \text{ mean } \pm \text{ SD})\) than for parkinsonian subjects OFF and ON \((10 \pm 0.5 \text{ cm})\). The time to reach peak CoP was significantly longer \((P < 0.01)\) for parkinsonian subjects OFF \((449 \text{ ms})\) and ON \((404 \text{ ms})\) than elderly controls \((263 \text{ ms})\). The slower rate of CoP displacement would allow the CoM to move further forward to a less stable position.

DISCUSSION

Parkinsonian subjects were able to generate centrally initiated preparatory postural adjustments when attempting to rise-to-toes. They also could scale up the force of the postural adjustment when performing the task fast versus slow. The primary postural deficit in these subjects was impaired force magnitude and relative timing of the postural and voluntary components of the task. These deficits significantly impaired postural stability for rising-to-toes. Dopamine replacement therapy had a positive effect on both the postural and voluntary components of performance.

Magnitude is reduced but scaling of centrally initiated postural adjustments is preserved in Parkinson patients

Parkinsonian subjects OFF and ON generated significantly less dorsiflexion torque and displayed lower levels of muscle activation than elderly controls when rising-onto-toes. Nevertheless, most \((8 \text{ of } 10)\) parkinsonian subjects and all elderly controls were able to scale both the postural and voluntary components of the task when increasing the speed of perfor-
performance. Scaling TIB and GAS allowed them to move the CoM forward and upward more quickly. Parkinsonian subjects OFF and ON showed a greater scaling of dorsiflexion torque that was similar to elderly controls despite lesser scaling of TIB over the initial 250 ms of activation. It is possible that parkinsonian subjects generate more force for a lesser increase in TIB activity or that muscles other than those recorded, e.g., reduced soleus or increased tibialis posterior muscle activity, contributed significantly to the increased dorsiflexion torque.

Reduced force magnitude, but intact force scaling of centrally initiated postural adjustments in parkinsonian subjects is consistent with our findings for externally triggered postural reactions reported in an earlier paper (Horak et al. 1996). In this companion study, the same group of parkinsonian subjects scaled postural responses to different velocities of surface displacement, but at lower force levels than elderly controls. Reduced force control is a well-accepted symptom of Parkinson’s disease; however, the issue of scaling is controversial. Beckley et al. (1993) reported an inability of parkinsonian subjects to scale postural reactions to two amplitudes of toe-up ankle rotation, and Flowers (1976) reported scaling difficulty for different amplitudes of voluntary arm tracking movements. The findings of Beckley et al. (1993) could be explained by saturation of the postural responses at large perturbation amplitudes, as we found for responses to higher amplitudes of surface translation (Horak et al. 1996). Despite the interpretation by Flowers (1976) that parkinsonian subjects move at a single, slow speed for all amplitudes of arm movement, the mean peak velocity of arm movement increased by a factor of 4 with increasing amplitudes, similar to that of control subjects. Other investigators reported intact scaling in Parkinson patients consistent with our findings. Dietz et al. (1993) reported appropriate scaling of postural responses to different velocities of sinusoidal surface translations, and Berardelli et al. (1986) reported normal scaling for different velocities of voluntary arm movements.

Relative timing of postural adjustments and voluntary movement is impaired in Parkinson patients

The order of TIB and GAS activation was preserved in Parkinson’s disease; however, the relative timing of these events was impaired. Rising-toes and holding that position involves the precise coordination of postural preparation and the voluntary movement (Clement et al. 1984). The elderly control subjects showed activation of the TIB prior to GAS with very small variability in the relative timing of onset of these muscles or the offset of TIB. In contrast, Parkinson patients showed larger variability in the relative timing of TIB and GAS, especially OF levodopa. The relative timing of these muscles differed from elderly controls: TIB activation was prolonged, and GAS activation was delayed. The consequence of this impaired timing, as well as the reduced magnitudes, was a slower, less forceful postural adjustment and less stabilization at the completion of the task as defined by greater forward displacement of the CoM relative to the controlling CoP.

The altered timing of TIB and GAS activation for parkinsonian subjects did not reflect normal performance at a slower speed of movement. Parkinsonian subjects performed fast rise-to-toes at a speed comparable to elderly controls performing the task slowly. However, the speed of performance (fast vs. slow) did not influence the onset time of TIB and GAS activation or the duration of TIB activation for either elderly controls or parkinsonian subjects. Even at comparable speeds of performance, TIB activation was longer and GAS activation was later for parkinsonian subjects compared with elderly controls. Parkinsonian subjects appeared unable to turn off their postural component (prolonged TIB activity) and to activate their voluntary movement (delayed GAS onset) as swiftly as normal subjects, whether instructed to move fast or slow. Crenna et al. (1990) likewise reported that parkinsonian patients OFF levodopa displayed prolonged activation of TIB during anticipatory postural adjustments to initiate the first step in gait. Other investigators have reported difficulty with quickly terminating muscle activity during voluntary arm movement (Hallett and Khoshbin 1980; Hallet et al. 1977) and isometric contraction (Corcos et al. 1996) in patients with Parkinson’s disease. A tight temporal coupling between TIB offset and GAS onset does not appear to explain the delay onset of GAS in parkinsonian subjects. The delay between TIB offset and GAS onset was greater for parkinsonian subjects OFF (97 ms) than parkinsonian subjects ON (68 ms) and healthy controls (66 ms). Furthermore, the correlation between TIB offset and GAS onset times was low and nonsignificant for parkinsonian subjects OFF and ON.

Contrary to our findings, other investigations have reported that postural preparations are absent in parkinsonian subjects when raising the arms while standing (Bazalgette et al. 1986; Rogers et al. 1987). It is likely, however, that the absence of postural preparations resulted from the slower performance of the arm movement by parkinsonian subjects in these studies. Eng et al. (1992) have shown that postural preparations when raising or lowering the arms serve to counteract reactive forces acting at joints below the shoulder and hence, prevent collapse. When moving the arms slowly, which is characteristic for parkinsonian subjects, the destabilizing reactive forces are small, thereby minimizing the need for stabilizing postural preparations. The timing and magnitude of postural preparations is directly related to the velocity of arm movement (Horak et al. 1984; Lee et al. 1987); thus the task of slowly raising the arms does not require anticipatory postural preparations.

In contrast, tasks such as rising and maintaining balance on the toes and step initiation cannot be performed successfully, even slowly, without initial postural preparations that move the CoM forward. While we have shown that the timing and magnitude of muscle activation contributing to this postural preparation is impaired, it, nevertheless, is present. Similar to rising-toes, parkinsonian patients show anticipatory postural activity for step initiation (Burleigh-Jacobs et al. 1997). Gait initiation also involves early activation of TIB, which moves the CoM forward prior to voluntary push-off of the swing limb (Yuancheng et al. 1993). Parkinson’s disease results in reduced magnitude and prolonged duration of both the postural preparation and voluntary component of gait initiation (Burleigh-Jacobs et al. 1997). Crenna et al. 1990; Ingvarsson et al. 1986). Burleigh-Jacobs et al. (1997) reported that these postural deficiencies improved when parkinsonian subjects were ON-levodopa and when an external, cutaneous cue was used to trigger step initiation.

Although levodopa improved the force and relative timing of centrally initiated postural adjustments and voluntary move-
ment during rise-to-toes, it did not necessarily improve postural stability. The magnitude of GAS activation, which provided the brake for forward CoM movement, was larger when ON levodopa, but remained well below normal values. Postural tone also was reported reduced for this same group of parkinsonian subjects when ON levodopa (Burleigh et al. 1995). Consequently, the parkinsonian subjects showed slower than normal forward CoP adjustments and larger than normal forward CoM movements during rise-to-toes. Dietz et al. (1993) also reported reduced activation of GAS and larger forward movements of the CoM for parkinsonian subjects compared with controls during sinusoidal translations of the support surface. The reduced safety margin between CoP and CoM at the end of movement increases the risk of falling.

Theoretical and clinical implications of levodopa effects on postural control

Parkinson’s disease is considered to be a good clinical model for the study of motor functions of the basal ganglia (Marsden 1984; Marsden and Obeso 1994). The findings of this study together with our previous investigations (Burleigh et al. 1995; Chong et al. 1999b, 2000; Horak et al. 1996; Nutt et al. 1992) show that Parkinson’s disease affects at least three different types of postural control: centrally initiated postural preparations, peripherally triggered postural reactions, and background postural tone. Generation of rapid force is a problem for patients with Parkinson’s disease for either centrally initiated postural movements such as rising onto toes and step initiation (Burleigh-Jacobs et al. 1997) as well as for peripherally triggered postural reactions to external displacements (Horak et al. 1996). This inability of patients with Parkinson’s disease to quickly develop muscle activation to generate forces at the surface to control the center of mass can be considered a reflection of their postural bradykinesia (Horak et al. 1992b, 1996). The relative timing of muscle activation within a postural synergy is intact for patients with Parkinson’s disease (Horak et al. 1996), although the relative timing between motor actions such as between postural preparations and voluntary movements for rise to toes and step initiation is impaired in Parkinson’s disease. Postural tone, as measured by background levels of EMG during quiet stance, is larger in patients with Parkinson’s disease, reflecting their rigidity (Burleigh et al. 1995; Horak et al. 1996). This rigidity makes it easier to resist external displacements of the center of mass but more difficult to self-initiate movements of the center of mass. Parkinsonian patients also suffer from inability to use central set to adapt both centrally initiated and peripherally triggered postural synergies based on changes in environmental context such as conditions of support (Chong et al. 1999a, 2000; Horak et al. 1992b). Despite the many types of motor deficits affecting postural control in parkinsonian patients, they do not have difficulty using the integrating vestibular, somatosensory, and visual information for postural orientation (Chong et al. 1999a).

The selective influence of levodopa therapy on different aspects of postural control suggests that the basal ganglia regulates the different types of postural control by separate neural circuits. The control of force and sequencing of centrally initiated postural preparations and postural tone appear to involve dopamine circuits because they improve with levodopa therapy (Burleigh et al. 1995; Horak et al. 1996). In contrast, the control of force of peripherally triggered postural reactions and ability to use central set appear to involve nondopaminergic circuits because they are unaffected by levodopa therapy (Horak et al. 1992b, 1996).

Clinicians often observe that speed and force for voluntary movement are improved with levodopa, whereas the ability to resist external perturbations (a push or pull) can be further impaired when Parkinson patients are ON levodopa. Our findings help to explain why some patients with Parkinson’s disease continue to be unstable and fall, although dopamine replacement clearly improves their voluntary movements. The failure of levodopa to increase the force of peripherally triggered postural reactions combined with reduced postural tone resulted in faster falls and greater instability in response to external perturbations (Horak et al. 1996). In contrast, the increased force for centrally initiated postural preparations combined with decreased postural tone facilitated movements of the CoM for rise to toes and step initiation. Patients who display improved stability in response to an external perturbation when ON levodopa likely are those who take advantage of stepping to recover balance.

Clinical evaluations of postural control in patients with parkinsonism necessarily examine a subset of potential postural control mechanisms. In this study, our clinical index of instability correlated well with dorsiflexion torque for voluntary rising to toes. That same clinical instability index, however, did not correlate with the plantarflexion torque for recovery of equilibrium following external perturbations in the same patients (Horak et al. 1996). Together, these findings suggest that even comprehensive clinical evaluations of balance and gait reflect primarily bradykinesia of voluntary movement and their accompanying postural preparations. More sensitive and specific clinical assessment sensorimotor function must take into account the multiple, independent and inter-dependent mechanisms responsible for motor and postural control.

Technical assistance from C. Jones and J. Knop and data analysis from M. Stephens is greatly appreciated.

These studies have been supported by grants from the National Institutes of Health (AG-06457 to F. Horak and NS-21062 to J. Nutt) and the Natural Sciences and Engineering Research Council of Canada (to J. Frank).

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