Temporal movement control in patients with Parkinson’s disease

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Abstract

Patients with Parkinson’s disease (PD) have been reported to be unable to modify their movement velocity to adapt to changing environmental demands. For example, when movement amplitude is varied, PD patients usually exhibit a nearly constant peak velocity, whereas elderly subjects show an increase of their peak velocity with increased amplitude. The experiment examined the ability of PD patients to vary the duration of their movement (four different percentages of their maximum) under conditions where temporal, but not spatial, control was emphasised. PD patients had longer movement times than control subjects, but were able to vary the duration of their movement with comparable temporal accuracy to that of elderly subjects. For both groups, the agonist EMG activity increased with decreased movement duration. For the PD patients, the number of agonist bursts increased with increased movement duration.

A cardinal manifestation of Parkinson’s disease (PD) is slowness in the execution of a movement. Subjects with PD patients are not slow, but that they are also seriously limited in their ability to modify movement velocity to meet changing environmental demands. For example, Draper and Johns reported that, contrary to elderly subjects who showed an increase in their peak velocity with increased movement amplitude, PD patients exhibited a nearly constant peak velocity across movements of different amplitudes. When under drug therapy, PD patients increased their peak velocity, but it was still smaller than that of elderly subjects by a more than five-fold difference. Flowers also reported that PD patients made movements of different amplitudes with constant duration, whereas the other groups made cycles of different amplitudes with constant velocity. Thus, there exists a general consensus that PD patients can only execute movements of different amplitudes at a single, slow velocity and cannot increase their movement velocity when they are cued to do so. These experiments provide valuable information on how movement amplitude affects PD patients’ control of movements. It is also of interest to determine whether and how PD patients can vary the duration of a movement when amplitude is kept constant. Indeed, movement time is an important parameter in movement behaviour and an inability to modify the temporal structure of a movement would suggest fundamental underlying deficits in movement organisation. Thus it is useful to determine the mechanisms by which PD patients vary the duration of their movements.

The underlying mechanisms of bradykinesia have been addressed by Hallett et al. They attempted to understand bradykinesia by examining abnormalities in PD patients’ EMG during voluntary movements. In normal individuals, simple arm movements are usually initiated by a burst of EMG in the agonist muscles and decelerated by a burst in the antagonist muscles; the movement is sometimes followed by a second and smaller burst in the agonist muscles. For bradykinetic patients, additional cycles of alternating bursts in the agonist and antagonist muscles have been observed. Hallett suggested that this is because the amount of EMG activity that can be put into a burst is limited in PD patients and that bradykinesia is a saturation problem, that is, a failure to appropriately energise the agonist muscle. Subsequently, Berardelli et al. showed that the first agonist burst does not saturate and suggested that in PD there is a breakdown of the link between “perceptual appreciation” of the goal and “delivery of the appropriate instructions” to the motor cortex. It follows from these two experiments that PD patients require more bursts of EMG to produce both faster and longer movements.

In previous experiments, however, movement amplitude covaried with movement duration so that movements of longer amplitudes were also of longer durations. Hence, it is not known whether the additional cycles of EMG activity previously observed in PD patients were the results of the longer movement amplitudes or of the longer durations associated with the movements of longer amplitudes. A resolution of this question is essential to a better understanding of the physiological mechanisms underlying the production of multiple cycles of EMG activity in PD. The aim of this experiment was thus twofold: 1) to examine the degree to which PD patients can vary the duration of their movements, and 2) to determine whether the increased cycles of EMG activity observed in PD patients are associated with the production of slow or fast movements.
Materials and methods

Eight patients with idiopathic PD (mean age = 66.2 years) and eight age- and sex-matched elderly subjects (mean age = 68.7 years) were examined. The clinical features of the patients are presented in table 1. Patients followed their normal schedule of medication during the day of testing, but the attempt was made to manage the effects of medication by testing the patients within the same relative temporal period of their drug cycle. Control subjects were free from any signs or symptoms of neurological disease. All subjects gave informed consent and performed movements.

The apparatus consisted of a horizontal aluminium manipulandum; a force transducer was attached to the handle and reflected the force necessary to overcome the inertia of the mass lever system. In the initial position, the lever was electrically connected with a rigid starting plate; moving the lever from the initial position opened the circuit. Movement onset was defined as this initial drop in the voltage signal, and all the recorded data were synchronised with this event. Because almost no movement is required to deactivate the circuit, such a procedure allows for a more precise determination of movement onset than when it is determined from a displacement signal or its derivatives. Moving through a microswitch located at 20° closed the electrical circuit, and movement time was determined as the time interval for which the voltage signal was low.

Muscle discharge patterns from the biceps brachii and triceps lateralis were recorded using physiological amplifiers having a common mode rejection of 87 dB at 60 Hz (Therapeutics Unlimited). Pre-sampled (2.5 cm) Ag-AgCl surface electrodes were placed over the muscle bellies. The electromyographic (EMG) signals were pre-amplified at the source, full wave rectified, band-pass limited from 40 Hz–4 KHz, and filtered with a 2.5 ms time constant. All signals were digitised at 500 Hz.

The movement examined was a horizontal elbow flexion, with the shoulder abducted 90°. A display panel with two vertically aligned light-emitting diodes (LED) faced the subjects. The top light indicated a ready signal and was labelled as such, and the bottom light signified that subjects were to initiate the movement. A target indicated 20° but there was no spatial accuracy constraint. Subjects were instructed to follow-through their movement and encouraged to plan their movement in advance and to perform it without making on-line corrections. Thus the goal was to perform the initial 20° of movement in a pre-determined duration without stopping at that spatial location; in fact, for all temporal conditions, the instructions resulted in the limb stopping when the elbow was near hyperflexion (about 150°). There are many real life analogues to this task: for example, when throwing an object, one often needs to control the time interval between movement initiation and object release without actually stopping the throwing arm at the point of release. All patients were able to follow these instructions as no hypometric movements were observed.

In a baseline condition, subjects were instructed to produce ten maximum speed movements upon presentation of the visual stimulus. Temporal feedback was provided after every trial and subjects were encouraged to move fast; average movement duration was calculated from those trials. In subsequent conditions, subjects were trained to produce movements of similar duration, 30% slower, and 60% slower. To ensure that subjects would not perform additional movements as fast as they could, we added a "speed-plus" condition. In this condition, the goal duration was 10% faster than the Movement Time (MT) obtained for the baseline condition; subjects were unaware of this procedure. All subjects produced shorter average MTs for the "speed-plus" condition than for the "as fast as possible" condition (on average, 34 ms shorter for the PD patients and 15 ms shorter for the elderly). All conditions were presented by block. There were 10 practice trials followed by 25 experimental trials for each of the movement durations. Movement time feedback was presented verbally when it exceeded ±10% of the goal duration. EMG activity in the biceps and triceps muscles were also monitored on-line via an oscilloscope (Tektronix 5113) and background activity was minimised before the initiation of a trial. Each trial started with a ready signal (the top LED was turned on for 1 s), and a variable foreperiod (0.5 s to 1.5 s) preceded the stimulus (bottom LED) to initiate a movement.

Data Analysis

The trials obtained for the "speed-plus" condition and the slowest movement time condition were used to evaluate whether additional bursts of EMG activity were used to produce faster movements. An arbitrary temporal bandwidth from 100 ms before the initiation of the movement to 100 ms after the 20° displacement was first established. The number of agonist bursts included in the temporal bandwidth was determined by visually identifying (on a computer display) the onset and offset of the bursts for the background activity. Because of the procedure used to minimise background activity before trial initiation, there was little resting EMG activity preceding the movement, and therefore, a threshold was set for initial detection. The criterion for offset was when the EMG returned to baseline or near baseline activity (no higher than 20% of the peak EMG). Bursts initiated before the movement reached the 20° target, but which finished after it, were included in the analysis; bursts that started after the 20° target was reached were, however, not included. To determine whether the agonist burst was saturated and whether there was any extraneous activity in the antagonist muscle in PD subjects, the EMG envelope for the agonist and antagonist muscles was also calculated.

The EMG activity obtained for the speed-plus, slowest and baseline conditions was integrated in four temporal bandwidths of 50 ms from the
onset of the agonist muscle.* The values obtained for each subject were normalised to the integrated EMG values obtained for the baseline condition. Analysis of variance was used to determine group and temporal requirement effects.

Results

Temporal characteristics of the movements

The data demonstrate that PD patients have the ability to vary the duration with which a movement is produced. The movement times obtained for the four temporal requirements are presented in table 2. PD patients produced slower baseline maximum movement times and as a result had slower movements at the four temporal requirements (on average, 249 ms versus 191 ms). The difference, however, was modest \((F(1,14) = 4.03, p < 0.06)\). PD patients were able to vary their movement time when required to do so (191, 225, 272, and 309 ms for the four temporal requirements; \((F(3,42) = 273.35, p < 0.001)\), for the effect of temporal requirement). When the movement times were transformed relative to each subject’s maximum (movement time \(\times 100)/\text{mean movement time of the baseline condition)}\), there were no group differences \((p > 0.05)\). Hence, both groups showed a similar ability to vary movement duration.

Table 1: Profile of Parkinson’s disease subjects

<table>
<thead>
<tr>
<th>Subject number</th>
<th>Age (years)</th>
<th>Duration of disease</th>
<th>Hoehn and Yahr</th>
<th>Predominant symptoms</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70</td>
<td>3</td>
<td>I</td>
<td>Mild tremor</td>
<td>Artane</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>23</td>
<td>III</td>
<td>Moderate bradykinesia, mild rigidity</td>
<td>Sinemet, Amanitadine</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>7</td>
<td>III</td>
<td>Severe bradykinesia, moderate rigidity, akinesia</td>
<td>Sinemet, Artane</td>
</tr>
<tr>
<td>4</td>
<td>72</td>
<td>17</td>
<td>II</td>
<td>Mild tremor, moderate rigidity</td>
<td>Sinemet</td>
</tr>
<tr>
<td>5</td>
<td>66</td>
<td>9</td>
<td>III</td>
<td>Moderate bradykinesia, mild tremor</td>
<td>Sinemet</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>5</td>
<td>II</td>
<td>Mild rigidity, moderate tremor</td>
<td>Artane</td>
</tr>
<tr>
<td>7</td>
<td>68</td>
<td>7</td>
<td>III</td>
<td>Moderate to severe rigidity</td>
<td>Sinemet</td>
</tr>
<tr>
<td>8</td>
<td>61</td>
<td>19</td>
<td>III</td>
<td>Moderate rigidity, severe akinesia</td>
<td>Sinemet, Pergafile, Imiprime</td>
</tr>
</tbody>
</table>

The temporal variability of both groups was computed (within-subject standard deviation of movement times at a given temporal requirement) to determine if PD patients were more variable than elderly subjects at achieving a given goal movement time. The data presented in fig 1 show that PD patients were slightly more variable than elderly subjects. For both groups, the variability increased with an increased movement time (from 16 ms to 31 ms for the elderly subjects and from 25 ms to 58 ms for the PD patients; \(F(3,42) = 6.58, p < 0.001)\). Temporal variability, however, increases with increased movement time, implying that the increased temporal variability for PD patients is not the result of different control processes but simply a reflection of longer movement times. Thus PD patients were slower than elderly subjects, but the overall linear relationship obtained between temporal variability and movement time implies that both groups were affected similarly by the different temporal requirements.

The temporal structure of the force-time curves was also analysed to determine if changes in movement duration affect the underlying temporal movement organisation. PD patients needed more time to achieve peak force than elderly subjects (on average, 160 ms versus 100 ms; \(F(1,14) = 14.26, p < 0.005)\). Peak force also occurred relatively later in time (ratio time-to-peak force/MT) for the PD patients than for the elderly subjects. On

![Figure 1: Movement-temporal variability (within-subject standard deviation of the movement times at a given temporal condition) for the PD patients and the elderly subjects.](http://jnnp.bmj.com/)

*Burin offsets are usually easily identifiable. The exact temporal location of the endpoint, however, is often arbitrary. The temporal requirements in the present experiment accentuated this problem. For this reason, we arbitrarily determined temporal bandwidth of 50 ms from the agonist offset. The selection of a 50 ms bandwidth was based on previous experiments that have estimated the first agonist burst duration to be in the 50-80 ms range.\(^{18,19}\)
average, time-to-peak force occurred at 65% of the total MT for the PD patients, whereas it occurred at 52% for the elderly (F(1,14) = 4.61, p < 0.05). Thus peak force occurred absolutely and relatively later in time for the PD patients. Nevertheless, PD patients modulated their time-to-peak force, as did the elderly subjects. For the four temporal requirements, PD patients needed 118, 131, 176, and 213 ms to achieve peak force whereas elderly subjects needed 76, 77, 111, and 136 ms (F(3,42) = 51.87, p < 0.001, for the main effect of temporal requirement).

**EMG**

Hallett and Khoshbin suggested that PD patients can put a limited amount of EMG activity in a burst and as a result they need multiple bursts of EMG to produce movements of greater amplitude. An examination of the integrated agonist EMG activity for the “speed-plus” and the slowest MT conditions (Fig. 2) shows that our PD patients did not exhibit this saturation problem (p > 0.05 for the group effect). As in elderly subjects, PD patients modulated the amount of EMG activity produced so that faster movements were produced with much larger initial EMG activity than slower movements (F(1,14) = 14.33, p < 0.005, for the movement time effect).

Despite the ability to produce more EMG activity when faster movements were required, most of our PD patients (seven out of eight) showed multiple bursts of EMG. However, multiple bursts of EMG were not observed when faster movements were produced, but rather when slower movements were produced. Figure 3 has representative raw EMG agonist and antagonist records for the speed-plus and the slowest movement time conditions. From these records, it is clear that the number of bursts increased with an increased MT for the PD patient. On the average, elderly subjects had a constant number of bursts across the two conditions of movement time (1.2 and 1.5 for the speed-plus and the slowest movement time conditions), whereas PD patients needed more bursts and showed significantly more “bursting” over longer movement durations (2.0 and 3.51 for the speed-plus and the slowest MT).

Both the group effect (F(1,14) = 15.06, p < 0.001) and the interaction of temporal requirement by group (F(1,14) = 6.44, p < 0.05) were statistically significant. Hence, not only did PD patients require more bursts than elderly subjects to produce a movement, but they also showed an increased number of bursts with increased movement time. There was also a strong relationship between bradykinesia and the multiple bursts of EMG activity. Figure 4 shows the individual relationships between the number of bursts produced and movement time for the PD patients and the elderly subjects. For seven out of eight PD patients, an increased movement time yielded a significant increase in the number of bursts, which exceeded the “normal” two bursts of agonist seen in the triphasic pattern of EMG activity of normal individuals.

It does not appear that the additional cycles of EMG were the result of extraneous activity in the antagonist muscle as might occur if there were problems of reciprocal inhibition. For both groups (p > 0.05, for the group effect), the antagonist EMG activity, presented in fig 2, was larger for the speed-plus movements than for the slowest movements (F(1,14) = 15.51, p < 0.005). There was a tendency for the elderly to show an increased activity 150 ms after agonist onset, but this effect was not significant (p > 0.05). This supports Delwaide’s findings, using H-reflex techniques, that reciprocal inhibition is not impaired in PD.

**Discussion**

Whereas previous experiments have focused upon the effects of movement amplitude on PD patients’ movement control, this experiment examined the extent to which PD patients could control their movement duration and

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1 In this experiment, the temporal location of the antagonist (when present) to the agonist activity was quite varied for both groups. For this reason, we will not refer to a specific locus causing "multiple cycles of tri-phasic patterns" (that is, agonist-antagonist-agonist) as Hallett and Khoshbin did, but simply to the mechanism of producing multiple bursts or cycles of EMG without reference to the activity in the antagonist muscle. The exact role and function of the antagonist burst in the control of simple movements is still a matter of debate. Nevertheless, there is a general consensus that it is involved in the deceleration of the limb. The task used in the present experiment did not have any specific deceleration requirements and as such was certainly different from the ones used in previous experiments, suggesting a task-dependent role for the antagonist muscle.

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**Figure 2** Integrated EMG for the agonist and antagonist muscles for the fastest and speed-plus temporal conditions. The labels on the abscissa correspond to the integrated EMG from agonist onset to 50 ms, 51 to 100 ms, 101 to 200 ms, and 151 to 200 ms after agonist onset, respectively.
how their pattern of EMG activity was affected by variations in movement duration. Despite slower minimum movement durations, PD patients were able to vary movement duration with comparable temporal accuracy relative to that of elderly subjects. The temporal structure of their movements, however, was different from that of elderly subjects. Peak force occurred both absolutely and relatively later in time for the PD patients, implying that the increased slowness in PD cannot be accounted for by a simple overall slowing of the motor programme. Rather, the results suggest a more fundamental problem, because PD patients generated forces at rates that were above and beyond a simple proportional slowing. This was the case for each of the four temporal conditions studied.

Contrary to previous experiments in which PD patients, even when under drug treatment, were unable to speed up their movements, PD patients in this experiment were able to produce movements that were 15% faster than during an initial "as fast as possible" condition. Obviously, this result implies that sub-maximal movements were initially produced despite the specific instructions to produce movements that were as fast as possible. This result, however, may also be interpreted as an important aspect of PD movement control. Indeed, it is possible that a portion of the slowness in movement, as well as the limited ability to modify movement velocity (hence, movement duration when amplitude is constant), shown in previous experiments, was the result of a reluctance among the PD patients to emphasise movement speed at the expense of movement accuracy.

Because of the specific task requirements previously used, however, this aspect of PD motor control might have been overlooked. Indeed, previous experiments that have examined the velocity control problem in PD have used very similar tasks in which spatial accuracy was always emphasised (either imposed by the task or perceived by the patients).
For example, in the Berardelli et al\textsuperscript{11} experiment, subjects were required to join three or four small dots in order to draw a triangle or a square. PD patients, in this experiment, were slower but were actually more spatially accurate than elderly subjects. In our experiment the task did not have any spatial accuracy requirements and agrees with our suggestion that PD patients showed a significant decrease in their movement time (thus increased velocity) when they were required to reduce it (15\%, decrease versus 9\% for the elderly). Also, Sanes\textsuperscript{25,26} recently showed that, for an alternating tapping task (Fitts-task), PD patients performed as quickly and accurately as elderly subjects when the task had a low index of difficulty (that is, large targets, small amplitude). Movement impairments were induced only when spatial accuracy and/or movement amplitude were increased. Thus, task requirements appear to be an important determinant of the movement performance and control of PD patients. Similarly, there is an increasing amount of evidence suggesting that, for normal subjects, the context in which a movement is performed is a major determinant of movement organisation.\textsuperscript{27-31}

This context-dependent hypothesis suggests that the expression of the velocity and temporal control deficits in PD varies as a function of task requirements. Thus, it is important that future research needs to vary systematically the context in which a movement is performed to determine where and how the performance of PD patients breaks down. The determination of these breakdowns along the varying continuum of movement constraints should yield insights into the underlying neuro-control principles in PD.\textsuperscript{32}

\textbf{Multiple cycles of EMG activity in Parkinson's disease}

While some studies\textsuperscript{17, 18, 21, 22} have suggested that PD patients require more cycles of EMG to produce movements of short durations, we found that PD patients required more bursts to produce those movements. Rather than producing movements of longer durations by increasing the duration of their first agonist EMG burst,\textsuperscript{19, 20, 32-35} seven out of eight PD patients required additional cycles of EMG activity. Further, there was no indication that PD patients had problems appropriately "energising" the agonist muscle; indeed, the integrated EMG data showed that the first agonist burst did not saturate in PD patients. As in elderly subjects, PD patients modulated the EMG activity so that faster movements required more EMG activity that did slower movements. Berardelli et al\textsuperscript{21} also reported that the duration and amplitude of the first agonist burst in a wrist flexion task does not saturate in PD but increases with increased movement amplitude.

The question remains as to why multiple cycles of EMG activity are observed in PD patients. To explain some of the slowness in PD, Berardelli et al\textsuperscript{31} raised the possibility that patients underestimate the muscle activity required for a particular movement because of a "breakdown of the link between the perceptual appreciation of the task requirements and the appropriate instructions to the motor cortex". This suggestion cannot explain why slower rather than faster movements were characterised by an increased number of EMG cycles. Because of their larger EMG requirements, faster rather than slower movements should have yielded an underestimation of the muscle activity and an increased number of EMG cycles. In our experiment, there was also a strong relationship between bradykinesia and multiple cycles of EMG activity so that the most bradykinetic patients were also the patients who exhibited the most cycles of EMG. Clearly, tremor is a likely explanation for these results. Action tremor has in fact been shown to be in the 6 to 9 Hz range, and higher frequencies (10–11 Hz) have also been observed.\textsuperscript{37} Nevertheless, the results shed more light on the physiological mechanism of producing multiple cycles of EMG. Because we found in a previous experiment\textsuperscript{18} that movement time covaried with movement amplitude, the results suggest that the multiple cycles of activity were not the result of movements of longer amplitudes but of longer movement times associated with the movements of longer amplitudes. Thus rather than having a problem calculating necessary forces\textsuperscript{31, 38} or an additional "energising" the agonist muscle,\textsuperscript{3} PD patients may experience problems controlling muscle activation. While the cortico-motor neuron connection has been shown to be intact in bradykinetic patients\textsuperscript{39} and the recruitment order of motor neurons is little affected,\textsuperscript{40} there are, however, motor unit abnormalities.

Milner-Brown et al\textsuperscript{41} reported that, even when PD patients made an effort to maintain voluntary force, some motor units stopped firing for prolonged periods; some of the units also fired at abnormally low frequencies (2–3 per second). Further, in agreement with our results showing greater EMG abnormalities for slower movements, their patients had difficulty in the recruitment of motor units at low threshold levels. Dietz et al\textsuperscript{42} also reported a prolonged postexcitatory inhibition between spike bursts for tremorous patients. Thus the mechanism of producing multiple cycles of EMG might be associated with an inability to maintain and regulate the EMG activity over time rather than with a "perceptual breakdown" or an inability to appropriately "energise" the agonist muscle.

Slowness of movement, on the other hand, might be induced by increasing the spatial accuracy requirements. In our experiment, the lack of spatial accuracy constraints resulted in seven out of eight patients being as fast or nearly as fast as elderly subjects. As previously mentioned, Sanes\textsuperscript{25, 26} also suggested that PD patients can produce nearly normal performance and that it is increased movement accuracy which induces movement impairments. This may be the case because increasing accuracy requirements creates a different control
problem. For example, Waters and Strick have shown that the antagonistic activity is nearly abolished when subjects are allowed to terminate their movement by hitting a mechanical stop as opposed to when they must decelerate precisely. Hence, it could be that impaired agonist-antagonist synergies induce slowness of movement.

Overall, the data demonstrate that when temporal control is emphasised, PD patients are able to vary movement duration with comparable temporal accuracy to that of elderly subjects. The movements were, nevertheless, characterised by more irregularities in the force-time and EMG patterns, implying that while PD patients have an accurate internal model of the forces required to produce movements, they have problems regulating and sustaining EMG activity. Indeed, slower (not faster) movements were characterised by a greater number of EMG bursts. It is possible that changes occur in the excitability of certain interneurons or that the impulse to the cortico-spinal system is impaired in PD.

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