EVIDENCE FOR MOVEMENT PREPROGRAMMING AND ON-LINE CONTROL IN DIFFERENTIALLY IMPAIRED PATIENTS WITH PARKINSON'S DISEASE

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Investigated were those aspects of motor planning and execution underlying movement dysfunction in patients with Parkinson's disease (PD). Specifically examined was the effect of disease severity on these processes. An experiment is reported that dissociates preprogramming processes from on-line programming processes in a simple motor task that varies in movement complexity. Dependent measures included reaction time, movement time, as well as kinematic measures of peak velocity, peak acceleration, peak deceleration, and their respective time values, plus inter-trial variability and EMG activation. While PD patients as a whole were able to pre-program movements, inter-trial variability for these measures was increased for more severely affected PD patients. Nonetheless, evidence for on-line programming occurred for all PD patients in later intervals of more complex movements. Further, EMG impulses correspond with acceleration trace deviations. The data as a whole support the hypothesis that disrupted basal ganglia function influences the consistency of cortical activation and the selection of motor program components.

INTRODUCTION

In this paper we investigate motor planning and programming, aspects of motor control thought to be cognitive in nature, in differentially impaired patients with Parkinson's disease. Research has indicated that motor planning is strongly associated with premotor

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cortical areas, including the supplementary motor area (SMA), and that the basal ganglia influence motor planning processes through their thalamocortical connections (Alexander & Crutcher, 1990; Chesselet & Delfs, 1996; Cunnington, Bradshaw, & Iansek, 1996). Parkinson’s disease (PD), produced by impaired functioning of the basal ganglia and their related neural circuits, provides a window into how cortical and subcortical processes interact to produce coordinated, accurate movement. We use a paradigm designed to separate motor planning, or preprogramming, and on-line programming components of the motor control process in PD patients. To relate these findings to possible neural mechanisms and determine whether these processes are affected by different degrees of basal ganglia dysfunction, we investigated the effects of disease severity on motor programming.

Parkinson’s disease is a progressive disease that affects approximately 1% of the population (O’Brien & Shoulson, 1992). The average age of onset is 60 years and incidence increases with age. It is characterised by tremor at rest, rigidity (increased muscle tone simultaneously in extensor and flexor muscles), difficulty in initiating movement, paucity of spontaneous movements (akinesia), and slowness in the execution of movement (bradykinesia).

Although motor execution deficits are characteristic of PD, researchers disagree whether they result from impaired motor programming or planning (e.g. Flowers, 1978; Marsden, 1982; Robertson & Flowers, 1990). In situations where information is provided about the required movement, PD patients can plan and prepare simple movements relatively normally (Stelmach, Worringham, & Strand, 1987). Longer movement times are more commonly associated with PD than are prolonged reaction times (Phillips, Bradshaw, Iansek, & Chiu, 1993). However, researchers report mixed findings about PD patients’ ability to plan complex movements or to change movements midstream (Harrington & Haaland, 1991, 1996; Jennings, 1995; Rafał, Inhoff, Friedman, & Bernstein, 1987; Stelmach et al., 1987). For example in a delayed reaction time task, normal participants produce increases in reaction time (RT) with the number of movement components in a sequence but PD patients may not (Stelmach et al., 1987). Other studies have shown that PD patients were able to prepare a sequence of finger taps in advance only when there was a compatible relationship between stimulus and response (Harrington & Haaland, 1991). This difficulty in preparing complex movement sequences in advance suggests that the basal ganglia have a role in engaging subsequent movements in a movement sequence (Marsden, 1982). The different results may stem from the fact that different researchers use different measures to indicate preprogramming and by ignoring important information available in alterations of ongoing movement.

Differing results regarding motor preprogramming in PD may also arise from the patient groups’ disease severity. PD-related deficits in motor function are associated with a degeneration of neurons in the substantia nigra with subsequent reductions of dopamine.
(DA) in the substantia nigra and its projection sites (e.g. striatal and limbic regions) as well as other neurochemical abnormalities. Recent research has indicated that it is not only the presence and utilisation of DA that is critical for planning accurate movement, but also the timing of its release (Graybiel, 1990). Although disease progression corresponds to decreasing dopamine levels, PD symptoms vary widely among patients. This variability in the patient population implies a complexity in the underlying neural circuitry that organises the components of movement.

One way that disease severity and decreased DA production can influence movement is through the underactivation of cortical regions involved in motor programming and planning. Decrements in DA production in the basal ganglia affect motor planning through the activation of premotor brain regions, including the SMA and ventral premotor cortex (PMv). The SMA appears to be involved in motor programming, especially for internally generated movements (Decety, Kawashima, Gulyas, & Roland, 1992; Decety et al., 1994; Goldenberg et al., 1992; Jeannerod, 1995; Roland, Larsen, Lassen, & Skinhoj, 1980). The SMA has been implicated in the programming of motor subroutines prior to movement initiation (Roland et al., 1980), in the timing and initiation of submovements in terms of selecting the correct movements, and in the integration of these submovements into ongoing movement sequences (Kornhuber et al., 1989; Cunnington et al., 1996). A major cortical input to the basal ganglia is from SMA and a major cortical output of the basal ganglia is to SMA (Wickens, 1993). The basal ganglia modulate motor program outflow via the SMA and motor cortex via a complex interplay of excitatory and inhibitory pathways (e.g. Albin, Young, & Penney, 1989; Alexander & Crutcher, 1990; DeLong, 1990). Basal ganglia dysfunction alters activation in the SMA. In PD patients, decreased dopamine production decreases activation of SMA. Data from PET neuroimaging studies of PD patients confirm hypoactivation of the SMA (Shinotoh & Calne, 1995; Snow, 1996). As a result, underactivation of the SMA may lead to disrupted motor planning.

The basal ganglia also have strong thalamocortical connections to PMv (Hoover & Strick, 1993; Matelli, Luppino, Fogassi, & Rizzolatti, 1989; Passingham, 1993). The PMv has been implicated in the programming of externally generated movements. PET studies of PD patients performing motor tasks have found underactivation in this area as well as (Playford et al., 1992).

Alternatively, disease severity and DA production may affect motor programming and the functioning of these cortical areas by introducing noise or variability into the motor system through inconsistent premotor cortex activation. PD selectively impairs the activation or switching of motor sequences rather than the individual elements of the movement sequence. Thus, PD patients have difficulty in consistently activating the required sequence. Noise in the motor system would express itself, over the course of many movements, in terms of variability in both motor planning and movement accuracy (Sheriden & Flowers, 1990). For example, PD patients may be able to
generate sufficient force to execute the movement but be unable to activate the correct parameters for the movement. As a result, movements are inaccurate as the force varies erratically from trial to trial (Sheridan & Flowers, 1990). This unpredictability of limb placement forces patients to monitor each action while it is being made and to perform on-line corrections. Further, greater basal ganglia dysfunction would increase variability in PD patients' ability to plan and control movements.

Both inconsistent basal ganglia output and cortical underactivation correspond with the movement deficits observed in PD patients. These patients have relatively intact perceptual processes and do not exhibit obvious problems with the selection and sequencing of muscle activity (Hallett & Khoshbin, 1980). However, they tend to have variable delays in motor initiation and increased movement times. Further, kinematic analysis of movement execution in PD patients suggests that, relative to controls, these patients tend to have lower initial acceleration, lower overall velocity, and less accuracy in most movements, particularly lower-amplitude movements (e.g., Stelmach, Teasdale, & Phillips, 1992). They are also impaired when producing ballistic movements, varying movement acceleration and velocity, and executing movements without visual information.

Although it is clear from the literature that PD patients have motor execution problems that increase with disease severity, it is not clear whether motor programming processes are similarly affected. In the present study, we investigated whether disease severity influenced motor programming and, if so, what aspects of programming were disrupted. We modified a paradigm developed by Franks and colleagues to isolate motor processes involved in the preprogramming, on-line programming, and production of fast, accurate movements (van Donkelaar & Franks, 1991). In normal populations, these types of fast movements require little on-line monitoring. The separation of motor programming processes is achieved through multiple, kinematic-dependent variables that are sensitive to differences between preprogrammed and on-line prepared movements: movement initiation time (RT), acceleration traces, and EMG data from the triceps and biceps muscles of the arm. Although previous studies have used these measures to study preprogramming in PD, few have incorporated all of these measures in the same study to provide converging evidence for separate preprogramming and on-line programming processes.

The detailed level of analysis available from this paradigm and these measures permits insight into those motor programming mechanisms affected by disease severity and the role of the basal ganglia in motor control. For example, if disrupted basal ganglia function influences the consistency of selecting accurate motor components, then several explicit predictions in terms of motor control can be proposed: (1) variable motor parameter selection suggests evidence of on-line programming, but not necessarily a lack of evidence for motor preprogramming (i.e. one can plan an incorrect movement); (2) on-line programming should increase with sequence length because inaccu-
rate movements early in a movement sequence affect subsequent movement segments; and (3) increased disease severity and corresponding basal ganglia dysfunction will produce increased inter-trial variability of movement parameters.

In addition, specific predictions can be made regarding the effect of disease severity on specific dependent variables.

**Preprogramming**

Do patients with Parkinson’s disease preprogram stimulus-triggered movements? Is this ability affected by disease severity? Problems in programming a movement prior to execution can be revealed through the examination of the time necessary to initiate a movement. In this experiment, maximal speeds of movement were required. If participants can prepare upcoming actions in advance, then more complex movements should take longer to prepare and initiate than simple movements (Fischman, 1984; Henry & Rogers, 1960; Rosenbaum, Inhoff, & Gordon, 1984; Rosenbaum, Kenny, & Derr, 1983; Sternberg, Monsell, Knoll, & Wright, 1978). Thus, an increase in RT that is associated with an increase in movement complexity would be evidence for preprogrammed movement whereas a lack of increase in reaction time may imply that the movement is being controlled on-line (during its execution). However, inferences about movement programming from simple reaction time (SRT) have their problems due to the imprecise nature of the dependent variable. It is possible to partial out the programming aspects of the movement variable. It is also possible to partial out the programming aspects of movement preparation from the mechanical aspects of movement initiation using electromyography (EMG). SRT can be fractionated into premotor and motor time components (Botwinick & Thompson, 1966). Premotor RT is the time from the onset of the imperative stimulus to the beginning of EMG and has typically been associated with delays in central programming activity. On the other hand, motor RT is the time from the beginning of EMG activity to the start of external limb movement. This period is believed to reflect the duration of nonprogramming events, such as the electromechanical delay in the muscle and development of sufficient torque to initiate movement (Anson, 1982). Thus the use of premotor time as an indicator of movement programming enables valid interpretations of SRT differences across levels of movement complexity (Anson, 1989; Christina & Rose, 1985). If PD patients can preprogram stimulus-triggered actions, then simple movements should be faster to prepare and initiate than complex movements (Henry & Rogers, 1960; Sternberg et al., 1978). Normal preprogramming in PD patients has been found under some conditions (Harrington & Haaland, 1991; Rafal et al., 1987; Stelmach et al., 1987). Alternatively, if RT is invariant across levels of complexity, then on-line preparation is inferred; that is, the sequence is prepared in parts throughout the movement as opposed to entirely beforehand. In other words, if PD patients can only plan and initiate movements one at a time and not in combination (Marsden,
1982; Robertson & Flowers, 1990), then we should find no increase in RT or PMT with increases in movement complexity. PD has been found to disrupt the ability to preprogram a single movement or a series of movements (e.g. Flowers, 1978; Harrington & Haaland, 1991, 1996; Jennings, 1995; Stelmach et al., 1987).

Whether evidence for preprogramming is found or not, evidence for inconsistent parameter selection may be found in the variability of preprogramming as well as movement measures. If the extent of subcortical dysfunction is related to parameter inconsistency, then within-subject variability should increase with disease severity.

Movement Execution

Does the severity of the disease affect movement execution? Execution variables reflect movement and movement monitoring processes. Execution deficits are characteristic of all PD patients. We expect that disease severity will influence these variables given that severity is largely defined in terms of execution difficulties. In addition, we predict that movement execution becomes more variable with increased disease severity, because it is the output of variable motor parameter selection. Previous studies indicate that the movement of PD patients differs from that of normal patients in terms of lower initial acceleration, lower overall velocity, and lower accuracy, particularly in larger amplitude movements (e.g. Flowers, 1975, 1976). PD patients are also impaired when executing movements without visual information, suggesting that they are more dependent on "on-line" visual guidance to achieve a spatial target.

On-line Programming

Does the severity of PD affect the degree of on-line movement control? Kinematic profiles of the acceleration trace are used to parse aiming movements into two phases: the initial impulse and the error correction phase. The initial impulse is assumed to be preprogrammed and is characterised by a rapid, continuous change in the position of the limb. In normal populations, fast movements performed under 200msec were predominantly programmed in advance with no use of feedback to detect and correct errors (Abrams, Meyer, & Kornblum, 1990; Meyer, Abrams, Kornblum, Wright, & Smith, 1988; Woodworth, 1899). The initial impulse does not contain movement modifications and is therefore comprised of one submovement. The correction phase begins if the endpoint of the initial impulse misses the target. Error corrections are indexed by discontinuities in the position, velocity, and acceleration of the moving limb, which are said to reflect the presence of the initial adjustments to a movement, or error reduction. Error correction phases may consist of only a single submovement or they may contain multiple submovements (see Crossman & Goodeve, 1983; Meyer et al., 1988; Meyer, Smith, Kornblum, Abrams, & Wright, 1990, for more in-depth discussions on the number of submovements). Parsing of movements into their initial impulse and error correction phases has been accomplished by
locating the first moment at which one of the following movement modifications occurs: a positive to negative zero-line crossing velocity, a negative to positive zero-line crossing in acceleration, or a significant deviation in acceleration. Positive-to-negative transitions in velocity correspond to reversals in the direction of the movement, going from a forward to backward direction. Zero-line crossings in the acceleration trace represent an increase in the velocity of the movement after it was slowing down. Significant deviations are relative minimums in the absolute value of acceleration while the acceleration is negative. In contrast to zero-line crossings, significant deviations represent abrupt changes in the acceleration trace that reflect a decrease in the net braking force of the limb without an increase in velocity.

If disease severity affects movement planning and accuracy, we would expect to find evidence for increased on-line control, as indicated by an increased incidence of significant deviations of the acceleration trace for later segments of the more complicated movement overall, and in particular, for more severely affected patients. Few zero-line crossing differences are expected given that the data analysis is constrained to accurate movements. On-line processing may be reflective of a movement strategy employed by patients with PD, among others. If one cannot be certain of the endpoint of a limb movement, a good strategy would be to visually monitor movements. In addition, inaccuracies in the endpoints of early movement segments may warrant additional monitoring of later movement segments. As a result, early movement segments may be preprogrammed, but later segments may be subject to on-line control.

**METHOD**

**Participants**

Twelve participants diagnosed with idiopathic PD (9 male, 3 female; age range 48–76 years; mean age = 57.5 years; mean years from diagnosis = 6.75) volunteered to participate in this study. All were tested during their normal medication cycle, that is, they were taking medication for their PD symptoms and participated in the experiment during periods of good dose effectiveness. All participants were right-handed and had no history of stroke, heart attack, or serious medical problems. All were able to follow verbal instructions. They were classified into two groups, based on the severity of PD symptoms indicated by their Hoehn-Yahr motor rating: PD1 = less severe (Stages I–II), PD2 = more severe (Stages III–IV) (Table 1).

In addition, three participants from the Vancouver community (1 male, 2 female; aged range 47–71 years; mean age = 59.67 years), matched for age and education, volunteered to participate as control participants. All control participants were right-handed and had no history of stroke, heart attack, or serious medical problems. Given that the primary predictions concern differences among PD patients, the data from control participants is reported primarily for broad comparison purposes. In
Table 1. Patient Information

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Years Since Diagnosis</th>
<th>Medication</th>
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<tbody>
<tr>
<td>F</td>
<td>48</td>
<td>5</td>
<td>Sinemet, Elderyll</td>
</tr>
<tr>
<td>M</td>
<td>49</td>
<td>3</td>
<td>Sinemet, Tolcapone</td>
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<tr>
<td>F</td>
<td>49</td>
<td>4</td>
<td>Artane, Amantadine</td>
</tr>
<tr>
<td>M</td>
<td>52</td>
<td>6</td>
<td>Sinemet</td>
</tr>
<tr>
<td>M</td>
<td>52</td>
<td>3</td>
<td>Sinemet</td>
</tr>
<tr>
<td>M</td>
<td>66</td>
<td>9</td>
<td>Sinemet, Amantadine, Selegiline</td>
</tr>
</tbody>
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PD2

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Years Since Diagnosis</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>48</td>
<td>7</td>
<td>Sinemet, Lisuride</td>
</tr>
<tr>
<td>M</td>
<td>57</td>
<td>9</td>
<td>Sinemet, Bromocryptine</td>
</tr>
<tr>
<td>F</td>
<td>58</td>
<td>8</td>
<td>Sinemet, Amitriptyline, Deprenyl, Permax</td>
</tr>
<tr>
<td>M</td>
<td>63</td>
<td>8</td>
<td>Sinemet</td>
</tr>
<tr>
<td>M</td>
<td>72</td>
<td>9</td>
<td>Sinemet, Deprenyl, Bromocryptine</td>
</tr>
<tr>
<td>M</td>
<td>76</td>
<td>10</td>
<td>Sinemet, Tolcapone</td>
</tr>
</tbody>
</table>

*PD1: Less affected by PD.
*PD2: More affected by PD.

In addition, the performance of normal participants on these tasks is reported in van Donkelaar and Franks (1991).

Task, Apparatus, and Procedure

Participants performed two simple motor tasks: horizontal arm extension and horizontal arm extension and flexion. They gripped a vertical handle at the free end of a horizontal level attached to a vertical shaft such that the elbow was coaxial with the axis of rotation. The movement of the frictionless level controlled a cursor on an oscilloscope screen. On the screen were two target boxes located ± 22.5° (± 5 cm) from the centre of the screen for a total movement of 45° or 10 cm. The left start target was ± 1.225° for a total of 2.25° or 0.5 cm on the screen. The right end target was ± 2.25° for a total of 4.5° or 1 cm on the screen. Before each trial, participants heard a 200 msec warning tone at 100 Hz and saw a brightening of the targets to indicate that the trial was about to begin. The foreperiod between the warning tone and “go” tone varied from 500–2500 msec. Upon hearing a 300 msec “go” tone at 700 Hz, participants moved the cursor (and their arm) as quickly and accurately as possible to the right target. Catch trials, during which participants heard a warning tone without a subsequent “go” tone, occurred on 10% of the trials to ensure that movement onset was not anticipated. Data was collected for 5000 msec.

The within-subject independent variable was complexity of movement (task complexity), as indicated by the number of changes in direction of movement: extension and extension-flexion. In the extension task, participants extended their arm at the elbow joint to move the cursor to the right target, without exceeding its bounds. For the extension-flexion task, participants extended then flexed their arm to move the cursor within the bounds of the right target and then move the cursor within the bounds of the left target. Trials were blocked by task. This manipulation provides evidence of preprogramming in that RTs should increase with additional movement segments being programmed.

To distinguish between central and on-line processing components of movement, only fast and accurate movements were acceptable for analysis. Participants received feedback
regarding RT, movement time (MT), and accuracy; they were encouraged to “beat their best times.” After completing 10 accurate practice trials, participants completed 10 accurate experimental trials.

During each trial four components of data were collected at a sample rate of 1000Hz: angular displacement, acceleration, triceps EMG, and biceps EMG. After data collection, the angular displacement was calculated. All data were stored on-line during a trial, analysed, and reviewed; they were then saved in a data file on the computer hard disk. Angular displacement was sampled from a custom optical encoder interface card (Nagelkerke & Franks, 1996). Angular acceleration traces were obtained from an accelerometer filtered at 50Hz, then sampled via a 12-bit Analogue-to-Digital Converter. EMG activity was sampled using surface electrodes placed on the biceps brachii and triceps brachii muscles. The raw EMG signal was amplified, and then sampled via the 12-bit Analogue-to-Digital Converter. Angular velocity was calculated by copying the displacement data into a temporary array, low-pass filtering the data at 10Hz and then differentiating into the velocity data array.

Dependent Variables

Reaction time (RT). RT, or movement initiation time, is the time between the onset of the imperative stimulus tone and the subject’s first movement. If the ability to preprogram upcoming actions are relatively intact in PD, then simple movements should be faster to prepare and initiate than complex movements. A less accurate motor program/plan would mean that RTs would be more variable for more complex movements and for more severe PD patients.

EMG recordings. From EMG recordings, RT may be divided into premotor time, associated with central planning activity, and motor time, associated with the electromechanical delay of the muscle overcoming the inertia of the limb. Thus, like RT, an increase in premotor time with movement complexity would be indicative of movement preprogramming (e.g. Kasai & Saki, 1992). A possible outcome of a noisy motor program/plan is the finding of more variable premotor times for more complex movements and for more severe PD patients.

Acceleration traces. Two aspects of the acceleration trace indicate on-line adjustments to movement: the number of zero-line crossings within a movement segment, and significant deviations in the shape of the trace. Whereas preprogrammed movements produce acceleration traces that cross the zero-line only once during each movement segment, movements in which adjustments are prepared on-line produce acceleration traces with multiple zero-line crossings. Zero-line crossings in the acceleration trace represent an increase in the velocity of the movement after it was slowing down and vice versa.

In addition, on-line prepared adjustments can be inferred from an acceleration trace through significant deviations in its shape. In contrast to zero-line crossings, significant
deviations represent abrupt changes in the acceleration trace which reflect a decrease in the net force of the limb without an increase in velocity (Kahn, Franks, & Goodman, 1996). A significant deviation is a peak or valley in the data between successive maximum points of positive or negative acceleration, that are preceded or followed by a minimum of 10 data points (e.g. 20msec) (van Donkelaar & Franks, 1991). Typically, preprogrammed movements result in smooth acceleration traces; however, adjustments made during movement appear in the acceleration trace as deviations from the normally smooth curve. In normal participants these fast movements show little on-line adjustments; they are only seen when moving at slower rate (van Donkelaar & Franks, 1991). If the motor program is often inaccurate, one would expect evidence of increased on-line processing, especially for more complex movements.

Movement Analysis

Only data from accurate trials were analysed. Despite the many errors made by PD patients in these tasks, movements of accurate length were required to compare the dependent measures for simple and complex movements in which the initial movement was equated. Trials exceeding 1sec or 3 standard divisions (SDs) from the individual’s mean were also eliminated from the analyses. One patient’s performance exceeded 3 SDs from mean patient performance and, thus, was eliminated from numerical analyses.

Mean data for each subject was collected using an interactive graphics display. The graphic display included displacement as a function of time, velocity traces, acceleration traces, and biceps and triceps raw EMG traces. To determine the beginning of movement, the displacement profile, which was recorded by an optical encoder, was searched for the point in which the displacement value exceeded zero. This point was defined as the beginning of movement. The end of movement was defined as the point in time following peak velocity in which the absolute angular velocity of the change fell below 10 deg/sec for 150msec. A search was then performed from the acceleration profile for the possible initiation of an error correction phase, that is the occurrence of zero-line crossings and significant deviations. To qualify as a significant deviation the difference in the absolute values of acceleration between minima and maxima had to be at least 100 deg/sec. EMG traces were analysed for the time corresponding to the first significant burst of activity.

Data across participants was subsequently analysed using MANOVAs for Severity (PD1, PD2) and Task Complexity (extension, extension-flexion). Alpha was set at the .05 level unless otherwise reported.

RESULTS AND DISCUSSION

In the literature, PD patients are reported to reliably undershoot targets (e.g. the movement stops short of hitting the target). An analysis of error trials in this task indicated that both con-
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trol and Parkinson's patients did not reliably undershoot or overshoot the target, $F(1,12) = 1.64, P > .10$. No significant group differences were found between control patients and Parkinson’s patients when testing for a Group (control, PD) × Task (extension, extension-flexion) × Error Direction (undershoot, overshoot) interaction, $F(1,13) = 2.9, P > .10$. These results are different from the prevalent undershoot errors observed in many clinical settings and experimental studies. It is possible that the incidence of undershoot errors in our study was minimised by the external movement cue and by trial-by-trial error feedback. Typically, undershoot errors were immediately followed by overshoot errors.

Do Patients with PD Preprogram Stimulus-triggered Movements? Is This Ability Affected by Disease Severity?

To address the questions of whether patients with Parkinson's disease are able to preprogram stimulus-triggered movements and whether this ability is affected by the severity of the disease progression, we examined reaction time (RT) data and premotor time (PMT).

Reaction time (RT: time from the auditory signal to movement initiation as indicated by displacement, msec). An analysis of RT data revealed no significant effects of severity, $F(1,9), < 1$ (PD1: 256.77; PD2: 276.50; Ctrl: 222.4) and no interaction with task complexity. However, it did produce a significant effect of task complexity, $F(1,9) = 7.62, P > .03$ (Extension Task: 251.03; Extension-Flexion Task: 276.50). For tasks of different movement complexity, holding perceptual features constant and changing only the task requirement, PD participants are able to show evidence of preprogramming. This ability is not affected by the progression of the disease. PD participants’ RTs are in the same range as those of the control participants.

Premotor time (PMT: time from stimulus to onset of EMG, msec). No effect of disease severity, $F(1,9) < 1$ (PD1: 200.66; PD2: 212.20; Ctrl: 177.32) or interaction was found. A main effect of task complexity was significant, $F(1,9) = 9.86, P < .02$ (Extension Task: 189.64; Extension-Flexion Task: 222.17). Consistent with the RT data, PMT data provides converging evidence of preprogramming. Research with normal participants suggests that PMT represents delays associated with central programming (Anson, 1982; 1989).

Within-subject variability for preprogramming measures (inter-trial variability). Less severe patients tended to have less inter-trial variability than more severe patients. There was a significant severity effect for RT, $F(1,9) = 7.00, P < .03$, and a marginal effect for premotor time, $F(1,9) = 4.31, P < .07$. These findings imply inconsistent functioning of the basal ganglia, even in accurate movements.

In sum, PD patients can execute the tasks correctly and are able to preprogram at least some part of the movement. Disease severity did not appear to affect preprogramming process in terms of mean measures. However, disease severity did influence the within-subject
variability of the preprogramming measures, suggesting increasing inconsistencies in pre-
programming processes.

Does the Severity of the Disease Affect Movement Execution?

To address the question of how the severity of the disease affects movement execution, we examined the following kinematic variables related to execution: movement time (MT), peak velocity (first peak: deg/sec), time to peak velocity, peak acceleration (deg/sec/sec), time to peak acceleration (msec), acceleration and deceleration intervals for the extension task (msec), and within-subject variability (inter-trial variability).

Movement time (MT: time from movement initiation to end of first movement, to permit comparison between extension and extension-flexion tasks, msec). MT is reliably slowed in Parkinson’s patients as a result of rigidity and bradykinesia inherent in the disease symptoms. As expected, we found a severity effect, $F(1,9) = 14.11, P < .005$ (PD1: 345.00; PD2: 548.75; Ctrl: 363.72), but no task complexity effect, $F(1,9) = 3.48, P < .10$ (Extension Task: 411.79; Extension-Flexion: 463.86) or interaction.

Peak velocity (first peak; deg/sec). Peak velocity has also been found to be lower in patients with PD. The significant severity effect, $F(1,9) = 21.10, P < .002$ (PD1: 250.23; PD2: 159.29; Ctrl: 239.05) suggests that the lowering of peak velocity increases with greater basal ganglia dysfunction. There was also a task complexity effect, $F(1,9) = 7.22, P < .03$ (Extension Task: 224.20; Extension-Flexion: 193.59), with the single movement task producing higher peak velocities than the complex movement. There was no interaction.

Time to peak velocity (msec). The time to peak velocity reflected the peak velocity data. There was a severity effect, $F(1,9) = 19.57, P < .002$ (PD1: 156.13; PD2: 242.39; Ctrl: 173.78) as well as a task complexity effect, $F(1,9) = 6.57, P < .04$ (Extension Task: 180.65; Extension-Flexion Task: 210.04). There was no interaction.

Peak acceleration (deg/sec/sec). Peak acceleration data mirrored peak velocity data despite different measuring instruments. There was a group effect $F(1,9) = 21.96, P < .002$ (PD1: 270.45; PD2: 113.56; Ctrl: 227.58) and task complexity effect, $F(1,9) = 5.98, P < .04$ (Extension Task: 228.52; Extension-Flexion Task: 169.77). There was no interaction.

Time to peak acceleration (msec). Time to peak acceleration showed a group effect, $F(1,9) = 10.95, P < .01$ (PD1: 97.90; PD2: 146.21; Ctrl: 100.40), and a task complexity effect, $F(1,9) = 5.37, P < .05$ (Extension: 112.84, Extension-Flexion: 126.89), but no interaction.

Acceleration and deceleration intervals for extension task (msec). The acceleration and deceleration intervals for the extension task produced effects of severity, $F(1,9) = 18.54, P < .002$ (PD1: 212.3; PD2: 312.43; Ctrl: 225.77) and interval, $F(1,9) = 55.03, P < .0001$ (Acceleration Interval 1: 205.89; Acceleration Interval 2: 309.74), but
no interaction. Teasdale, Stelmach, and Mueller (1991) emphasise that the goal of most tasks is to initiate a movement and to decelerate a limb accurately to produce a skilled movement. In normal populations, equal acceleration and deceleration intervals are commonly found. Here we find greater deceleration intervals for the PD group.

Motor time (time from EMG onset to movement initiation, msec). No effect of severity, $F(1,9) = 1.18, P > .10$ (PD1: 56.09; PD2: 64.30; Ctrl: 45.08), or task complexity, $F(1,9) = 2.41, P > .10$ (Extension Task: 61.39; Extension-Flexion Task: 58.26), was found for motor time. The Severity x Task Complexity effect was significant, $F(1,9) = 12.64, P > .01$ (Extension: PD1 = 53.54; PD2 = 70.80; Extension-Flexion Task: PD1 = 58.64; PD2 = 57.80). This interaction does not have a clear interpretation. The longer motor time for the PD2 group in the extension task appears to be related to coactivation of both agonist and antagonist muscles at the beginning of the extension movement, thus requiring more time for the agonist to overcome inertia. Proportionately more coactivation was found for PD2 than for PD1. Figures 1a, 1b, 2a and 2b provide visual examples of this finding for typical patient performances on the extension and extension-flexion task. Both biceps and triceps are concurrently active at the initiation of movement.

Qualitative Analysis of EMG Activity
For normal participants performing a forearm extension movement, the characteristic pattern of EMG activity from triceps and biceps muscles is triphasic (Enoka, 1994): The triceps agonist activates to accelerate the arm to the target then the biceps antagonist provides a breaking force to the arm as it nears the target, followed by triceps reactivation to secure the arm in place. A slightly different pattern of activity is typically displayed during a continuous extension-flexion arm movement. The triceps initialise movement and the biceps slow the arm as it nears the target; however, in this case, the antagonists become agonists to move the arm in the opposite direction. The biceps remain active until the triceps stop the arm and then the biceps secure the arm at the start position (van Donkelaar & Franks, 1991).

This normal pattern of activity was not typically present in PD patients, as depicted in Figs. 1a, 1b, 2a, and 2b. Both within and between individuals, there was great variability of muscular activation patterns. Figures 1a and 1b illustrate an example of a participant from the less affected PD1 group, which displays EMG patterns similar to those of normal young adults. This participant’s performance was included for comparison purposes. This example displays triphasic muscular activity, although the amount of activation appears to be smaller than that of normal participants. Muscular activation is maintained to allow the switch from agonist to antagonist function. In contrast, Figs. 2a and 2b illustrate an example of a participant from the more affected PD2 group that displays very different EMG patterns. Participants in the PD2 group tended to show multiple weak phasic bursts of both agonist and antagonist muscles, in contrast to stronger, more sustained firing found in the perform-
ance of normal participants. Additional coactivation of biceps and triceps muscles is found as well as significant deviations in the positive acceleration portions of the acceleration curve, a finding never found in normal performance.

PD patients seem unable to maintain the long burst of the biceps as its role changes from antagonist to agonist at the reversal point of the movement. Previous research from Berardelli, Accornero, Argenta, Meco, and Manfredi (1986) and Hallett and Khoshbin (1980) suggests that PD patients require additional bursts of muscle activity (especially agonist muscle activity) to produce both faster and longer movements. This is consistent with our data. However, the multiple bursts of muscle activity also corresponds with a strategy for accurate movement strategies with PD. Compare the bursts of EMG activity with changes in the acceleration curves in the earlier figures. The largest bursts correspond with major maxima and minima of the trace. Note, however, how the additional bursts correspond in time with deviations of the acceleration trace that are indicative of on-line control. It appears that patients with PD are trying to impose control throughout the movement to produce an accurate movement. If PD patients have difficulty predicting the endpoint of a limb movement, a good strategy for producing an accurate movement would be to use smaller, more frequent bursts of muscle activity to control the movement.

Within-subject variability (inter-trial variability). Less severe patients were generally less variable than more severe PD patients in terms of movement time, $F(1,9) = 16.16, P < .003$, RT to peak velocity, $F(1,9) = 4.95, P < .06$, marginal, RT to peak acceleration, $F(1,9) = 4.90, P < .06$, marginal, and motor time, $F(1,9) = 16.76, P < .003$. However, there were two variables in which less severe patients were more variable than more severe patients: peak velocity, $F(1,9) = 8.12, P < .02$, and peak acceleration, $F(1,9) = 6.47, P < .04$.

To summarise, both severity and movement complexity affect motor control in PD. First, the severity of PD affects all of the above variables in predictable ways. People with more severe PD are slower to move, producing movements of lesser velocity and acceleration. They also tend to be more variable in their movements. The task effects show increasing effects of dopamine deficits with complexity. Less severe patients with PD may have a

Fig. 1 (opposite). Performance data from patient no.3 of the less affected PD1 group. Figure 1(a) illustrates performance on the extension task. Figure 1(b) illustrates performance on the extension-flexion task. The top graph represents lever displacement in degrees as a function of time. The acceleration trace (degrees/sec/sec), and the rectified and filtered EMG activation trace (volts) for biceps and triceps follow. All traces correspond to the same function of time. Note that RTs are longer for the extension-flexion task than for the extension task and that MT for the first movement is similar for both tasks. In addition, note that although biceps activation appears to be smaller than that for normal participants, there is a triphasic pattern of EMG activity between biceps and triceps. Last, muscular activation is maintained as triceps switch from agonist function to antagonist function in the extension-flexion task. Overall, these examples are similar to EMG patterns of a normal, young person.
greater variability for faster movements (e.g., Sheridan & Flowers, 1990) because they have a larger repertoire of movement speeds available to them. The variability of movement would decrease if there are fewer movement speeds available, as seen in more severe patients with PD. In other words, the less severe group's greater within-subject variability can be explained by the range of velocities available to the control of patients more severely affected by PD. People in the less severe group may have greater within-subject variability because they have a larger range available to them given the status of the dopamine in the system. However, patients with less dopamine in the system have fewer options for movement velocity and acceleration.

Second, movement complexity (the difference between extension and extension-flexion tasks) affects execution variables differently. Movement times for the same segment are increased for the more complex task. In addition, peak velocity and peak acceleration are lower and time to peak velocity and acceleration are increased for the more complex task. Unlike the other measures, motor time was not significantly different for the two tasks. These effects do not interact with severity. This is also of interest because PD patients as a whole have performance that is in a similar range of our control participants.

Does the Severity of PD Affect the Degree of On-line Movement Control?

Zero-line crossings. Because we restricted our analyses to fast and accurate movements, we did not expect to find extraneous zero-line crossings. No severity effects were found for either the extension task, $F < 1$ (PD1 = 1; PD2 = 1) or the extension-flexion task, $F < 1.0$ (PD1 = 2.07; PD2 = 2.17). This result is to be expected given that we only analysed accurate movements that appeared to be, on the basis of smooth and bell-shaped displacement and velocity curves, single movements for each direction of movement. In addition, participants were instructed to move as fast as possible, which should have precluded zero-line crossings. These analyses confirmed that participants primarily programmed one or two movements, depending upon the task.

Significant deviations in the acceleration curve. For the extension task, there was no severity effect [$F(1,9) < 1$ (PD1 = .403, PD2 = .350; Ctrl = .067; PDoverall vs. Ctrl, $P < .08$)], interval effect [$F = 2.57$, $P > .10$], or interaction. However, for the

**Fig. 2 (opposite).** Performance data from patient no. 6 of the more affected PD2 group. Figure 2(a) displays performance on the extension task. Figure 2(b) displays performance on the extension-flexion task. The top graph represents level displacement in degrees as a function of time. The acceleration trace (degrees/sec/sec) and the rectified and filtered EMG activation trace (volts) for biceps and triceps follow. All traces correspond to the same function of time. In the PD2 group, note the coactivation of biceps and triceps. Multiple bursts of weak activity are evident in the EMG traces. As illustrated here, PD patients have difficulty maintaining muscular activation at the point at which the agonist muscle becomes the antagonist. Note that there are significant deviations in the positive acceleration portion of the acceleration curve that are never seen in normal performance.
extension-flexion task, there was an interval effect, \(F = 14.19, P < .0002\) (Interval 1 = .259; Interval 2 = .988; Interval 3 = .512]. The interval effect suggests that more on-line adjustments occur when a second movement is required. No effects were found for severity \([F(1,9) < 1\) (PD1 = .569; PD2 = .644; Ctrl = .211; PDoverall vs. Ctrl; \(F(1,9) = 6.94, PD < .03\]) or interaction. This general interval effect is not due to the severity of PD; however, there were significant differences between the PD patients and the controls; the PD group produced a greater number of significant deviations in the acceleration curve, especially on the extension-flexion task. As movements became more complex, PD patients overall made additional on-line adjustments.

**Mean significant deviations for extension and extension-flexion tasks.** No effect of severity \([F(1,9) < 1\) (PD1: .503; PD2: .505; Ctrl: .150)] was found. A task effect was significant \([F(1,9) = 5.42, P < .05\) (Extension: .399; Extension-Flexion: .609]. In contrast, there was a significant difference between the PD patients and the control group \([F(1,9) = 5.53, P < .04\]. The performance of the control group was significantly different from that of the PD groups for mean number of significant deviations, suggesting increased on-line control for people with PD. The greatest difference occurred at the end of the more complex movement. We would expect to find evidence for increasing on-line programming as movement because more complex if one postulates a noisy motor system.

In summary, patients with PD can preprogram movements, but on-line monitoring of movement is evident as well, especially in the more complex task. Disease severity appears to influence within-subject variability of the preprogramming measures, movement, and on-line processing despite evidence of preprogramming.

**GENERAL DISCUSSION**

Parkinson’s disease can provide insight into the role of the basal ganglia in the planning and production of coordinated movement. The main goal of the present study was to examine motor planning processes in PD patients with varying degrees of severity and to infer neural function from behavioural measures. Specifically we investigated the differences between preprogrammed movements and those prepared on-line. In normal young populations movement initiation time, acceleration traces, and EMG data provide evidence as to the conditions under which preprogramming and on-line control processing occur within a movement sequence. Using a paradigm designed to separate motor control processes, we found that patients with PD are indeed able to preprogram movement, as evidenced through increased RT and PMT with movement complexity. However, there was also evidence for variable motor planning processes. All patients with PD showed increased on-line adjustments to their movements as the movement complexity increased. Furthermore, there were effects of disease progression that were consistent with a hypothesis of a variable motor system producing an inappro-
appropriate scaling of movement. Both preprogramming measures and execution measures showed an increase in within-subject (or intertrial) variability.

How do the current results address hypotheses regarding the role of the basal ganglia in motor control? The basal ganglia modulate motor program outflow via the supplementary motor cortex (SMA), premotor cortex, and motor cortex via a complex interchange of excitatory and inhibitory pathways. The basal ganglia receive excitatory input from all areas of cortex. In particular, the striatum (the caudate and putamen) receive cortical input from the SMA. In the direct, facilitatory pathway, cortical activity through the basal ganglia disinhibits thalamic activity, potentially facilitating one motor program while suppressing activation of other motor programs. An indirect, inhibitory nigrostriatal side loop modulates this activity. Dopamine further modulates thalamocortical activity through both facilitatory and inhibitory mechanisms. Research has indicated that the phasic release of dopamine in addition to its presence is critical for smooth voluntary motor control (Graybiel, Aosaki, Flaherty, & Kimura, 1994). Thus, the loss of dopamine and the dopamine cell activity produces the loss of smooth motor control. Thus, PD resulting from decreased dopamine from SNpc produces an overactive indirect pathway and an underactive direct pathway. Both decrease thalamic and cortical activation. The net result is decreased activation to SMA and other premotor areas (Chesselet & Delfs, 1996).

This study and clinical observations support the contention that the basal ganglia do more than simply modulate the activation of premotor areas. If PD simply produced an underactivation of these areas, then the preprogramming of movement should be increasingly disrupted with disease severity. However, that prediction was not born out by the data. Alternatively, if the basal ganglia are specialised to perform parallel processing in which certain movements are enhanced and others are suppressed, then their function may be to amplify the signal-to-noise ratio in the selection of appropriate parameters of movement. Many of the motor symptoms found in PD may arise from the dysfunctional operation of the basal ganglia that introduces additional noise into the motor system (Sheridan & Flowers, 1990). Noise in the motor system would manifest itself in increased performance variability and this is supported by our data.

A neurally based model of basal ganglia function in Parkinson's disease has been proposed by Wickens and colleagues (Wickens, 1993; Wickens, Hyland, & Anson, 1994). They describe a model in which neurons in cortical motor areas have functional groupings or cell assemblies. Complex movements are represented in cortical motor areas as a set of closely linked cell subassemblies, each representing a different element in the sequence of movements. Inhibitory connections between cells create a winner-take-all mechanism in which only the most strongly activated cell in the network fires. The process of motor planning would involve bringing each different subassembly to partial activation so that only a small amount of additional activation would bring...
the assembly to threshold and “ignite” it. The planning of more complex movements requires the activation of additional subassemblies and thus the activation of additional inhibitory neurons. Thus, longer sequences would produce more inhibition and slow the “ignition” time of the first subassembly of the sequence. Thus, this model would predict longer RTs for complex movements.

An additional consequence of this competitive network of cell assemblies is that the assembly that most closely matches the constraints of the input receives the most activation and ignites. Overall insufficient activation produced by excessive inhibition of the thalamus and premotor areas from the basal ganglia would produce consistently longer RTs. However, inconsistent basal ganglia operation could have two implications. First, it could affect the selection of motor cell assemblies in that no one motor cell assembly has dominance over several others, thereby allowing less optimal assemblies to reach threshold first and fire. Second, it could affect the time to ignite the correct subassemblies in that additional input is needed to reach threshold. Thus, basal ganglia dysfunction in PD patients could affect cell assembly firing rates. Inconsistent igniting could manifest itself in behaviour as variability in motor preparation and on-line programming where activation is insufficient to activate the rest of the subassemblies for complex movements. This type of mechanism is consistent with our findings that PD patients demonstrated increased RTs for more complex movements, that disease severity affected the variability of their increased RTs, and that more on-line programming was required for complex movements.

In addition, evidence for the on-line programming, as well as preprogramming of movement, provides support for the explanation that PD patients may initiate movement before programming is finished (Jennings, 1995). The initiation of movements before programming is complete is often found in the performance of normal populations when various loads are placed on performance (Ketelaars, 1995). If disease severity increases the likelihood of incomplete programming, then we would expect to find and do find corresponding differences in the variability of preprogramming measures with disease severity. Also, both a noisy motor system and incomplete programming would produce our finding of additional on-line adjustments at the end of complex movements. However, incomplete programming does not necessarily predict significant increases in preprogramming time for more complex movements. If movements are reliably initiated before programming is complete, then RT and PMT could be similar for simple and complex movements. Further, incomplete programming should produce corresponding increases in motor time. Our data do not support either of these outcomes.

In conclusion, the examination of Parkinson’s disease subpopulations provides insight into the influence of the basal ganglia on various aspects of motor control. The investigation of disease severity permits the formulation of hypotheses about subcortical influences on various motor control functions. Further in-
vestigation using such patient groups and sensitive paradigms, however, is necessary to confirm and support our conclusions as to the specific neural mechanisms involved in motor programming.

REFERENCES


