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THE PROGRAMMING AND EXECUTION OF MOVEMENT SEQUENCES IN PARKINSON’S DISEASE

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Parkinsonian and neurologically normal subjects performed a finger-tapping task in which different sequence lengths had to be executed as rapidly as possible. For each response sequence, reaction time (RT), inter-tap-intervals (ITIs) and error patterns were recorded. It was found that the RT-sequence length relationship as well as the group ITI data were different for the two groups, indicative of impaired programming in the Parkinsonian subjects. This conclusion was supported by a relative dissociation of the first and subsequent taps and by a pattern of progressively increasing errors with longer tap sequences in the Parkinsonians.

Keywords: Parkinson’s disease, reaction time, movement sequences

The cardinal symptoms of bradykinesia, rigidity and tremor which characterize Parkinson’s disease are readily observable and very striking. What are less well understood are the ways in which this disease may affect preparatory processes in movement control (e.g., motor programming and/or planning). The basal ganglia clearly play an important role in premovement processes, but what this role is remains controversial. Marsden (1982) has proposed that the basal ganglia are responsible for “the automatic execution of learned motor plans,” and has argued that Parkinson’s disease offers the best available window on abnormal basal ganglia function (Marsden, 1984). Cools (1984a, 1984b) has suggested that the basal ganglia perform hierarchically structured motor programming functions, and that they are involved in “switching” motor programs when new types of behavior are required. There is a relative dearth of detailed studies, however, on which to base such speculation about the motor function of the basal ganglia. Apart from broadly focused studies of motor planning in Parkinsonism such as the investigation of symbolic and nonsymbolic movement representation by Sharpe, Cermak and Sax (1983) preparatory movement processing in Parkinson’s disease has not been much studied. The exceptions have dealt either with continuous movements under visual control, such as tracking, where an initial finding that Parkinsonians cannot use predictable stimulus information to plan movements (Flowers, 1978) has recently been disputed (Bloxham, Mindel & Frith, 1984; Day, Dick & Marsden, 1984); or with single, discrete movements e.g., Flowers (1976) who found impairment in open-loop aiming. We have studied rapid, discrete hand movements in our own

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laboratory (Stelmach, Garcia-Colera & Martin, in preparation), and found that Parkinsonians are able to use partial or complete advance information about the direction and extent of an upcoming movement, as well as about the hand to be used, to initiate movement with shorter latencies than when performing the same movements without advance information. This finding contradicts that of Bloxham et al. (1984) (experiment two), and shows that this aspect of motor planning is not completely disrupted. Rafal, Posner, Walker and Friedrich (1984) also found that valid advance information can be used by Parkinsonians to initiate movements more quickly (experiment three), and that medication, while reducing reaction times, does not affect that RT component which reflects use of the precue. In our own study, however, estimates of the time taken to specify values for the nonprecued parameters when the target is displayed did reveal some slowing relative to normals, so that these premovement processes appear to be intact but slowed (Stelmach, Worringham & Strand, 1986).

There are no detailed studies of preparatory processes in rapid movement sequence production by Parkinsonians, although it has been reported that rhythm formation may be abnormal in Parkinson's disease (Nagasaki & Nakamura, 1982; Nakamura, Nagasaki & Narabayask, 1978). The present study was designed to determine if Parkinsonians show deficits in such rapid movement sequence programming, by which we mean the preparation on motor commands necessary to execute a predefined set of movements. Such programming occurs when the movements are simple, of short duration, and when the individual knows in advance precisely what movements are required (Klapp, 1977; Stelmach & Requin, 1980). Programmed movement sequences have certain characteristics when performed by neurologically normal subjects: the reaction time is prolonged if the movement sequence is more complex (Henry & Rogers, 1960; Stelmach, Mullins & Teulings, 1984; Sternberg, Monsell, Knoll & Wright, 1978). Programmed movement sequences tend to be executed as a single unit, with minimal kinematic discontinuities such as prolonged pauses (Vrtunski & Patterson, 1985). In the study reported here, a finger-tapping task in which sequences of different lengths were performed, was used to examine whether Parkinsonian subjects program rapid movement sequences in the same way as normals. Our primary interest was in determining whether Parkinsonians programmed a tap sequence as an unit without any abnormal disruptions or discontinuities. We hypothesized that this would not occur as we believe that Parkinsonians have impaired motor programming process.

METHOD

Subjects

Six adults with diagnosed Parkinson's disease and six adults with no history of neurological disorders served as subjects for this experiment. Only subjects who could clearly comprehend the instructions were included: A seventh Parkinsonian subject was excluded on this basis. The Parkinsonian subjects ranged in age from 58 to 74, with a mean age of 64.7 yr. All Parkinsonian subjects were evaluated by a neurologist at the University of Wisconsin Clinical Sciences Center to ensure that they were free from secondary signs not typically associated with Parkinson's disease. The neurologist also graded the Parkinsonian symptoms of tremor and rigidity on a five point scale. The subjects varied as to the predominance of rigidity and tremor as well as in severity. Symptom profiles, including medications, are listed in Table 1 for each of the Parkinsonian subjects.
The normal (control) group ranged in age from 60 to 72 with a mean age of 67.6 yr. The six normal subjects, who had no reported history of neurological disease, were also evaluated by the neurologist prior to the experiment and were found to exhibit no signs of any neurological disorders.

Each of the Parkinsonian subjects was stabilized on L-dopa and carbidopa (Sinemet) in combination with either dopamine agonists or anticholinergic drugs, for several years. In an effort to reduce drug dosage related response fluctuations, the experimental sessions were scheduled at the end of each Parkinsonian subject's dosage cycle and during the time when the medication effects on symptom profile were minimal.

**Apparatus**

Each subject was seated before a table with his or her dominant forearm resting comfortably on a styrofoam surface to keep the wrist and hand level with a response key on which the index finger lightly rested. The key was a Cherry momentary contact switch that required a force of 125 g for closure. Custom software for use on the laboratory LSI-11/03 computer was used for presentation of warning, precue and response signals, and for data acquisition (Stelmach et al. 1984).

**Procedure**

The experimental task was to tap the response key a precued number of times as quickly as possible following a response signal. A precue signal, consisting of either 1, 2, 3, 4 or 5 characters (R, RR, RRR, RRRR, or RRRRR) was presented in the center of the computer screen for 2 s. A rehearsal period of 2.5 s occurred after removal of the precue. An auditory warning signal (two "bleeps," 0.5 s apart) was then given, followed by a row of asterisks in the center of the screen. Subjects were required to tap out the precued sequence as rapidly as possible after this response signal. The sequence of precue, warning and response signals for a trial on which three taps were required is illustrated in Figure 1.
Stimuli were presented in blocks of 32 trials, with six trials of each condition (1, 2, 3, 4 or 5 taps) presented in random order. In order to ensure that subjects were not learning to anticipate the appearance of the asterisks, each block also contained two catch trials in which no response signal appeared. Subjects failed the catch trial if the response key was triggered. A practice session of between 15 and 30 trials followed, with instructions repeated and an additional practice block given when necessary, until each subject fully understood the procedure. Testing then began, with one- to two-minute intervals between blocks, and a five- to ten-minute break after every third block of trials. Since error rates were not evenly distributed across conditions and were higher for the Parkinsonians and for one normal subject, these subjects were given additional blocks of trials to ensure comparable numbers of correct trials. Thus, the normal subjects averaged nine blocks of trials, while the Parkinsonians averaged 16 blocks.

Four error types were defined and recorded during data collection: anticipation errors, responses which were too slow, too few and too many taps. Reaction times of less than 100 ms were defined as anticipation errors, and those greater than 650 ms were defined as too slow. Those responses which did not match the correct number of precued taps were noted to be either too few or too many.

Reaction Time (RT), the time interval from the appearance of the response signal to the initiation of the first tap, was recorded for each trial. Movement Time (the duration of the entire movement sequence) and Inter-Tap Intervals (ITIs) were also recorded (ITIs were defined as the intervals between successive depressions of the response key). Data were then analyzed in a $2 \times 5$ factorial mixed design (Keppell, 1982) where the first factor was between groups (Parkinsonians vs. normals) and the second was within subjects (1, 2, 3, 4 or 5 taps).

RESULTS

Reaction Times

Each group's mean reaction times for the five conditions are shown in Table 2. The mean RT for the normal group increased for the sequence lengths up to three taps, but did not increase consistently beyond this point. The Parkinson's disease group RTs showed a more modest rate of increase for the first four sequence lengths and a decrease for the longest sequence, five taps. There was no statistically significant
difference in mean RTs between the two groups, as determined by analysis of variance, \((p<.05)\), the normal group's mean RT being 337 ms and the corresponding value for the Parkinsonian group being 329 ms.

### TABLE 2
Mean, median and fastest 25% RTs for normals and Parkinsonians as a function of tap sequence length

<table>
<thead>
<tr>
<th>Sequence Length</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>All data</td>
<td>Normals</td>
<td>318 (84)</td>
<td>337 (68)</td>
<td>348 (63)</td>
<td>338 (68)</td>
</tr>
<tr>
<td>Mean RT (± 1 SD)</td>
<td>Parkinsonians</td>
<td>320 (61)</td>
<td>327 (60)</td>
<td>332 (59)</td>
<td>338 (79)</td>
</tr>
<tr>
<td>All data</td>
<td>Normals</td>
<td>307 (98)</td>
<td>327 (69)</td>
<td>341 (71)</td>
<td>335 (69)</td>
</tr>
<tr>
<td>Median RT (± 1 SD)</td>
<td>Parkinsonians</td>
<td>300 (61)</td>
<td>313 (66)</td>
<td>319 (62)</td>
<td>338 (87)</td>
</tr>
<tr>
<td>Mean of Fastest 25% trials (± 1 SD)</td>
<td>Normals</td>
<td>235 (59)</td>
<td>261 (47)</td>
<td>271 (48)</td>
<td>267 (55)</td>
</tr>
<tr>
<td>(± 1 SD)</td>
<td>Parkinsonians</td>
<td>219 (46)</td>
<td>220 (43)</td>
<td>225 (44)</td>
<td>238 (65)</td>
</tr>
</tbody>
</table>

There was a difference between the the groups in how closely the data approximated the hypothesized sequence length-RT relationship. A linear trend was statistically significant for the normal group \(F(1,20)= 5.96, p<.05\), but not for the Parkinsonian group \(F(1,20)= 1.06, p>.25\). The regression equation for the normal group's linear trend was calculated to be \(RT = a + bX\) where \(a = 320\) ms, \(b = 5.6\) ms and \(X = \) number of taps in sequence. No other trends (quadratic, cubic or quartic) were evident in the data from either group. These results suggest that the normal group's RTs conformed to a linear increase of RT with increasing tap sequence length, but that no such conclusion may be drawn for the Parkinsonian group. When the same analyses were repeated using median RTs instead of means (Table 2), similar results were found, with a linear trend in the normal group's data, but not in that of the Parkinsonian group.

Since there was no evidence of programming in the overall data set for the Parkinsonian group and the RTs for both groups were generally slower than expected, it was decided to inspect separately the fastest trials for evidence of programming, since slower trials may represent instances in which subjects failed to program the response fully. Thus, the RT data were sorted and only the 25% fastest times were examined and analyzed. The mean data are also reported in Table 2. The results of this analysis essentially replicated the results from the all trial data; however, the slope of the normal group increased substantially. A significant linear trend was observed for the normal group, \((F(1,20)= 24.86, p<.001)\), the slope of which is given by the equation \(RT = a + bX\) where \(a = 237\) ms and \(b = 8.0\) ms. Statistical analysis revealed no linear trend for the Parkinsonian group, however, \((p >.25)\), neither were any other trends found. Thus, for normals, the trials with the shortest response latencies also showed a linear relationship between sequence length and RT, with a steeper slope than the overall data set. On the other hand, the corresponding data subset for the Parkinsonians provides no evidence for programming the required tap sequence length as a unit. This being the case, it should be expected that the ITI's for the Parkinsonians should reveal some discontinuities when compared to normals.
Inter-Tap Intervals and Movement Times

The ITIs of Parkinsonian subjects were, on the average, 63 ms longer than those of the normal group, and MTs were some 103 ms longer. Neither of these differences attained statistical significance at conventional levels (\(p > .25\)) for ITIs, (\(p > .11\)) for MTs. These measures are depicted in Figures 2 and 3 respectively.

Trend analysis of MTs showed strong linear effects (\(p < .0001\)) and (\(p < .0001\)) for Parkinsonian and normal groups respectively (see Figure 2). An interesting aspect of this analysis was the absence of any quadratic trend for either the Parkinsonian group (\(p > .25\)) or the normal group (\(p > .25\)). This finding indicates that there is no systematic slowing as a function of sequence length.

![Figure 2](image)

**FIGURE 2** Mean movement time as a function of sequence length.

A significant interaction between group and ITI (\(p < .001\)) was found to have its locus in differences between the groups in the duration of the first ITI, which was 60 ms longer in the Parkinsonian group (see Figure 3). Orthogonal contrasts showed that the first ITI was significantly longer than each of the subsequent ITIs for the Parkinsonian group (\(p < .01\)), but for the normals it was significantly longer than the second ITI only (\(p < .05\)).
Error Rates and Patterns

Rates and patterns for the four types of errors which were recorded (too few taps, too many taps, anticipation errors and responses which were too slow) are depicted in Figure 4 together with overall error rates. Parkinsonian subjects had higher overall error rates than did normals, and also showed rather informative error patterns. Of particular interest is the fact that sequence length errors, i.e., production of an incorrect number of taps, tended to become more prevalent for longer sequence lengths in the Parkinsonian group.

Anticipation errors were rarely made by members of either group, and the proportion of catch trials failed, while higher for the Parkinsonians, (10.7%) than for the normals (0.9%) was within acceptable limits and indicated that for the majority of trials, subjects did not anticipate the occurrence of the response signal.
DISCUSSION

When taken together, the Reaction Time, Inter-Tap Interval and error data indicated a deficit in rapid movement sequence programming in Parkinson's disease. The Parkinsonian group showed minimal evidence for sequence programming as evidenced by the absence of linearity in the RT functions. They showed an apparent dissociation between the first and any subsequent taps which is not compatible with notions of sequence programming, and finally, they had error patterns which indicated great difficulty in producing the appropriate sequence length, especially for longer sequences. We discuss each of these points in turn.

The absence of an overall RT impairment in the Parkinsonian group, can be accounted for in the following manner. If our interpretation of the Parkinsonians' deficit in programming is correct, then in only the one tap condition did both groups perform in a similar manner, since in the other conditions Parkinsonians
programmed a single tap, whereas the normals prepared a tap sequence. Consequently normals will have comparatively long RTs in these conditions. Note that the normals did indeed have longer RTs in the two, three, and five tap conditions (see Table 2).

Three RT analyses showed linear functions for normals but not for Parkinsonian subjects: mean and median RTs, and mean RTs considering only those data constituting the fastest 25% of trials. We interpret these data as lending support to the hypothesis that Parkinsonians have difficulty in rapid movement sequence programming. In agreement with this conclusion are the results of a recently completed experiment in our laboratory (Stelmach et al., in preparation), in which Parkinsonians performed a paced tapping task which required the stressing of one of the taps in both simple and choice RT conditions, as well as a no-stress, simple RT condition. Semjen, Garcia-Colera and Requin (1984) had previously shown with normal subjects that response latencies were higher in the choice RT-stress condition than either the simple RT-stress or simple RT-no stress conditions, between which there were no differences. The Parkinsonians showed elevated choice RT-stress latencies, but also had consistently longer latencies in the simple RT-stress condition than in the simple RT-no stress condition, when the required ITI was 200 ms. This suggests that the simple addition of the requirement to stress one of the taps in a rapid sequence requires additional programming time for the Parkinsonian, but not for the normal subject.

The Parkinsonian group showed excessively long first ITIs, which are not compatible with the behavior expected when a movement sequence is programmed in advance as a whole unit. Two possible explanations may be advanced for this effect. The first involves the mode of control which would be necessary if these subjects did not or could not program the sequence in advance, as suggested by their response latency data. In this case, the first tap could have been produced as a distinct response common to all the conditions, while subsequent taps (if any) would be controlled through ongoing monitoring of the number of taps actually produced. If Parkinson's subjects have difficulty in advance preparation of movement sequences, such a mode of control would allow them to react and move reasonably quickly with only a single tap programmed. It would also lead naturally to a relatively prolonged initial ITI. This explanation would also account for the absence of a linear increase in Parkinsonian RTs with longer sequences.

The second explanation for this effect is also concerned with the special characteristics of the initial tap, and assumes that in Parkinsonism there is an impaired ability to regulate the force level necessary to initiate movement. Flowers (1978) has shown that large inaccuracies are typically found in rapid, open-loop aiming movements in Parkinson's disease, and we feel that impoverished force regulation on movement initiation may lie behind this finding in particular, and akinesia in general. In finger-tapping, a certain minimum force is necessary to depress the key, but there is no maximum level which must not be exceeded. The Parkinsonian subject may error on the side of using a force level well above what is necessary, in order to be sure that the first tap is made quickly. Excessive force would elongate the first ITI because of a longer "dwell" time on the key. In a related experiment (Stelmach et al., in preparation) we found longer dwell times for finger tapping in Parkinsonians when they made changes in required force levels.

Visual observation of the subjects during the tapping task as well as their high error rates relative to the normals led us to examine more closely the group error patterns. Parkinsonian subjects' difficulty in completing the correct number of taps is one manifestation of an impairment in the execution and/or programming of
rapid movement sequences, although it is difficult to attribute the deficit to preparatory or execution phase deficits solely on the basis or errors, since they may result from the correct execution of an incorrectly programmed response, or from the incorrect execution of a correctly programmed response. Nevertheless, it is apparent from Figure 4 that the Parkinsonians had a tendency to produce either too many or too few taps much more frequently than the normal subjects, and that this trend became more pronounced as the required number of taps increased. The difference between the groups was especially evident in the rate for too few taps, an error made by the normal group on less than 2% of trials in any one condition, but one which the Parkinsonians made with linearly increasing frequency, peaking at 20% when five taps were required. Interestingly, “too slow” errors and anticipation errors did not increase with sequence length, which argues against the notion that the Parkinsonians used a different and generally more error-prone strategy for long sequences, and hints at a specific problem in regulating sequence length. The Parkinsonians’ difficulty with producing correct sequence lengths is not simply the result of an inability to stop tapping quickly enough—an artifact which might arise from inadvertent switch activation caused by tremor at the end of the sequence. This is shown by the greater number of both “too few” and “too many” errors for longer sequences. Nor can it be a probability artifact: While the likelihood of random “too few” errors increases with sequence length, that of “too many” errors would be greatest for one or two taps, but hardly any occurred in these conditions. A third potential explanation for the sequence length error data, that the Parkinsonian subjects favored speed over accuracy the longer sequences, may also be ruled out. The linear relationship between sequence length and MT (Figure 4) shows that the speed of execution did not vary with sequence length for either group.

It is clear that much remains to be learned about preparatory movement processing in Parkinson’s disease, but these results suggest that there are deficits in the programming of rapid movement sequences, and that control over the length of a sequence of repeated movements is also disrupted. These results are compatible with the model put forward by Cools (1984), who ascribes specific and hierarchical programming functions to different levels of the basal ganglia, each of which adds successively more detail to the upcoming movement. Further, recent data from our laboratory by Stelmach and Worringham (in press) which shows a disproportionate slowing in motor programming for Isometric Force Production also supports a localized programming deficit in Parkinsonians. However, we feel that progress in understanding the exact function of the basal ganglia in the programming of movement will require more studies in which the exact nature of the movement, and therefore the amount and type of programming activity necessitated, is carefully controlled.

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