Motor Program Memory Storage in Parkinson's Disease Patients Tested with a Delayed Response Task

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Summary: We used a delayed response paradigm to test the hypothesis that the prolonged reaction time in patients with Parkinson's disease (PD) is related to a deficiency in their ability to store a motor program in memory while waiting to move. PD patients, both on and off medication, were compared with age-matched normal subjects during arm movements directed toward a target light. The target light was displayed either during a 3- to 9-s delay or for only 1 s followed by a 2- to 8-s delay before the go signal. At the end of the delay, subjects were required to begin movement rapidly. The reaction time of PD patients was longer than normal and increased slightly when the patients were off medication. The patients had no excessive increase in reaction time with delay in either task compared with the control subjects. We conclude that patients with PD can hold a motor program in memory storage for at least 8 s. **Key Words:** Reaction time—Delayed response task—Parkinson's disease—Memory storage—Motor program.

The most prominent voluntary motor disturbance in patients with Parkinson's disease (PD) is slowness of movement. This phenomenon has at least two components: bradykinesia and akinesia. Bradykinesia refers to slowness of ongoing movement, whereas akinesia refers to failure of willed movement to occur. The study of reaction time movements can give information about akinesia. In reaction time experiments, a stimulus is presented to a subject who must make a movement as rapidly as possible. Studies confirm that reaction time is prolonged in PD (1–8).

In order to understand reaction time studies, it is useful to consider, from a theoretical point of view, the tasks that the brain must accomplish (9). The starting point is the movement "set," which includes the environmental conditions, the initial positions of the body parts, the understanding of the nature of the experiment, and, in particular, an un-

derstanding of the expected movement. In the simple reaction time condition, the expected movement is described completely. Although the movements can be fully planned in advance, the movement requirements must be held in memory until movement initiation is requested. In the choice reaction time condition, the set does not include a complete description of the required movement. The description of the requisite movement is completed when the stimulus calling for movement initiation occurs. In this circumstance, the brain processing required to select muscle activity compatible with the direction and extent of the requisite movement occurs in the time between the stimulus signaling initiation and the response. Without prolonged practice, choice reaction time is longer than simple reaction time, and the time difference is due to this movement programming.

In virtually all studies, simple reaction time of PD patients is significantly prolonged compared with that of normal subjects (4,7,8,10,11). On the other hand, many studies have found that patients with PD have normal choice reaction times (4,8,10,11),

or, at least, the increase of choice reaction time over simple reaction time is the same in PD patients and normal subjects (6,12,13). If the difference between simple and choice reaction time is no different in PD patients than in normal subjects, then movement programming would appear to be normal in PD, and therefore the problem must lie either in storage of the motor program in memory or in execution of the movement.

The present study tested the hypothesis that the prolonged reaction time in PD patients is related to impairments in the process of holding movement signals in a temporary memory storage buffer. There is reason to believe that PD patients might have difficulty in maintaining such a memory trace, because neurons in the monkey substantia nigra, pars compacta, and caudate nucleus discharged preferentially during an instructed delay period before a saccade (14,15), and neurons in the putamen discharged while monkeys waited for a go signal to move the arm (16). If reaction time is longer than normal in PD patients when a target location must be retained in memory, then it might be concluded that the akinesia in PD is related to disruption of memory function. We studied reaction time in a delayed response paradigm in which the subjects had to remember a target location for up to 8 s.

SUBJECTS AND METHODS

We studied 10 patients with idiopathic PD (six men and four women; aged 44–75 years, mean 63.2 years) and seven normal control subjects (three men and four women; aged 44–78 years, mean 66.6 years). All patients were tested while on medication, including levodopa/carbidopa, trihexyphenidyl, and bromocriptine, and five of them (three men and two women; aged 52–75 years, mean 64.6 years) were retested in the morning after overnight withdrawal of medication. Each patient was clinically evaluated and rated with the Hoehn and Yahr Scale (17). The PD stages ranged from 1.5 to 4 (on or off states). None of the patients exhibited dementia. All control subjects had a screening medical history and physical examination. The patients and subjects were all right handed.

Experimental Procedures

The subjects were asked to perform two-dimensional step-tracking reaching movements with the right arm either 90° to the left, 90° to the right, or away from the center of the body by sliding an elec-tronic pen across a digitizing tablet (Super L II digitizing tablet, GTCO Corporation, Columbia, MD, U.S.A.). X,Y-Coordinate pairs were recorded at 100 Hz, from which reaction time and movement time were derived. Movements were initiated in response to visual signals provided by light-emitting diodes (LEDs) mounted underneath the tablet. The pen was positioned over a centrally located start LED and moved to one of the three target LEDs. The distance from the starting position to the left and right end targets was 13 cm and to the center target 18 cm.

The subjects were presented with two tasks. In the first task, called "no-memory," the subject held the pen over the start LED. After 1–3 s, the target LED appeared and remained illuminated. As the signal to move, the start LED was extinguished 3, 5, or 9 s later. The subject was asked to make the movement to the target LED as rapidly as possible.

The second task was the "memory" task. As in the no-memory task, the subject held the pen over the start LED. After 1–3 s, the target LED was illuminated for 1 s. As the signal to move rapidly toward the remembered target, the start LED was extinguished 2, 4, or 8 s later (for a total time of 3, 5, or 9 s).

Reaction time was measured from the time the start LED was extinguished to the time the velocity of the arm movement clearly exceeded baseline velocity variations. Patients with tremor were generally excluded from participation, but some patients did have mild tremor when off medication. The tremor made the assessment of reaction time slightly more difficult, but the start of the movement was generally unambiguous. Movement time was measured from the time reaction time ended to the time of a zero-crossing of acceleration, after which velocity stayed low.

In a single session, each subject had three experiments of 90 trials each. Each experiment paired a no-memory task and a memory task at each delay between the presentation of the target and the signal to move. The 90 trials in each experiment consisted of 30 directed to each of the three different targets, randomly intermixed. Of the 30 to each target, 15 were of the no-memory task and 15 were of the memory task, randomly intermixed.

Statistical Analysis

Comparisons were made by analysis of variance (ANOVA) with the level of significance set at p < 0.05.

RESULTS

The PD patients took significantly longer (p < 0.0001) to initiate movement than did the control subjects (Fig. 1). There was no effect of target position. For both groups, the reaction time was slightly longer when the delay was longer. The reaction time in both groups was slightly longer for the no-memory task, but the difference between the groups in the reaction time for the two tasks was not significant. Reaction time was slightly faster in patients who were on medication (p = 0.22), but reaction time for the memory task was not significantly different between patients on medication and those off medication.

The movement time was much more prolonged in the PD patients than in the control subjects (p ≤ 0.05). For both groups, the movement times were similar for the memory and no-memory tasks, and there was no influence of delay on movement time. Movement time was only slightly different between patients on medication and those off medication. Movements were faster when patients were on medication, and this effect was slightly greater when the delay was longer (p ≤ 0.05).

DISCUSSION

Our results fail to support the hypothesis that slowed reaction time in PD patients is related to deficiencies in temporary storage of motor signals necessary for voluntary movement. Instead, in comparison with normal subjects, PD patients had a general slowing of reaction time in all the movement conditions. Furthermore, withdrawal of dopamine replacement medication from the PD patients, thereby causing additional disruption of basal ganglia processing, did not increase the reaction time for the memory task. Together, these findings suggest that temporary memory of movement signals required for initiation of limb movements is not a function of the basal ganglia.

Our experimental data are consistent with the results of studies (18–20) showing that the latency to the initiation of remembered saccadic eye movements was not slowed in PD, but they apparently differ from those of other experiments in which visual memory was tested in a delayed response paradigm. In one experiment (21), reaction time was not measured, but errors were increased in the delay situation. This abnormal performance, how-
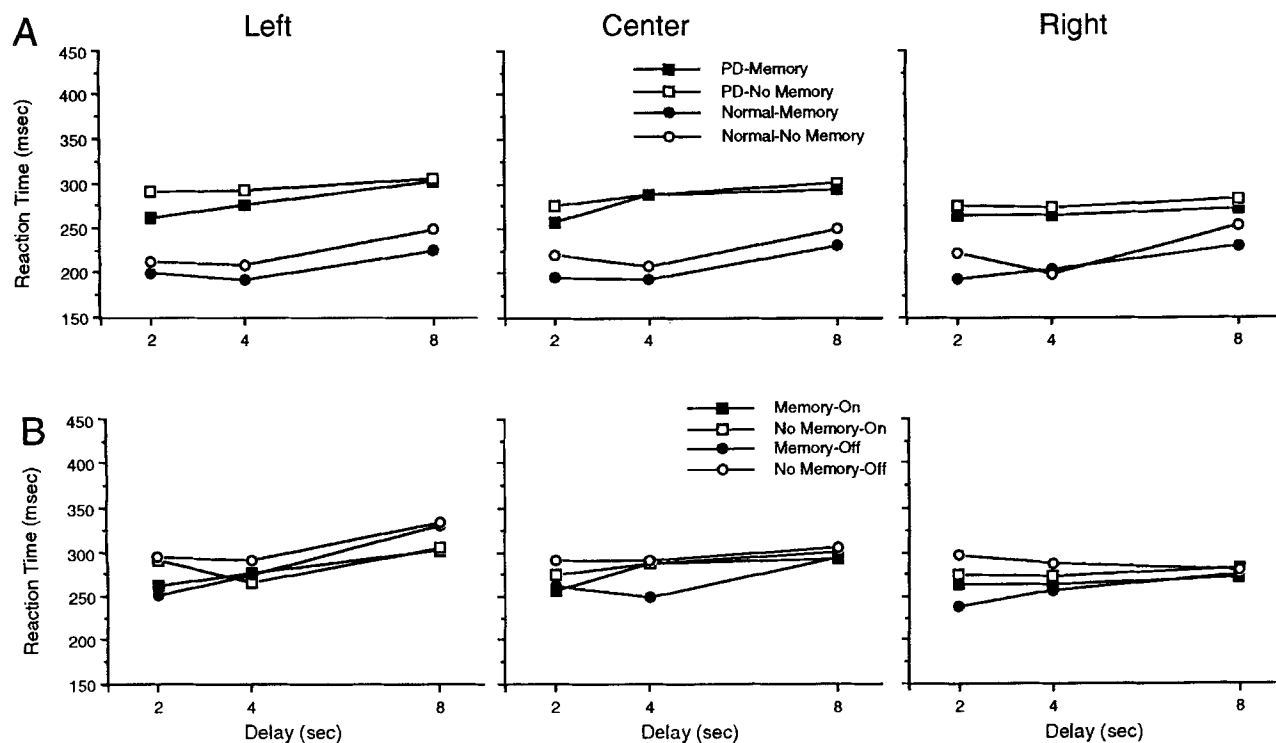

FIG. 1. Results of reaction time experiments in patients with PD and normal subjects. Each data point represents the mean group performance. A: Comparison of reaction time between PD patients and normal subjects for movement toward each target (left, center, right). B: Data are shown for the patients on and off antiparkinsonian medication.

ever, was found only in the group of PD patients with dementia. In another experiment (22), subjects had to recognize a Chinese character visually and respond by voice. There was no increase in errors, but PD patients were deficient only in the delay task. The patients, however, were all recovering from a thalamotomy, and their IQs were lower than those of the control subjects. Hence, the reported deficiencies of delayed response performance in PD might well be ascribed to dementia.

The role of the basal ganglia in learning and memory functions is controversial. Several studies, for example, have suggested that predictive movements are impaired in PD (10,23,24), yet patients benefit from advance information (5,10,25). Additionally, in PD patients, improvements in performance with repetition and learning a new motor skill have been impaired in some tasks (26,27) but not others (28).

The finding that reaction time was longer than normal for PD patients, but was not significantly increased when the patients were off medication, is similar to the results of previous reports (2,3,7,29–31).

If holding the motor program in memory storage is normal in PD patients, execution of the movement must be the fundamental problem in the akinesia. If movement execution is abnormal, however, it is difficult to understand how simple reaction time can be abnormal while choice reaction time is normal in PD. The explanation may be that in the choice reaction time situation both the motor programming and the motor execution can proceed in parallel (9). There is some evidence from psychophysical (32,33) and neurophysiological (34–36) data that such parallel processing does occur. In other work from our laboratory, we have done experiments in which the results are consistent with an abnormality in movement execution in PD (37,38). In studies using magnetic stimulation of the motor cortex, we have shown that patients with PD have a prolonged period of increased excitability of the cortex before the movement is generated. The prolonged movement time in patients with PD, confirmed by the present study, may well be another, and more prominent, aspect of the abnormality in movement execution.

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