Akinesia, Hypokinesia, and Bradykinesia in the Oculomotor System of Patients with Parkinson's Disease

J. David DeJong and G. Melvill Jones

Parkinson's Project, Queen Mary Veterans' Hospital, Montreal 247, Quebec, Canada

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Detailed characteristics of voluntary saccadic eye movement were measured in 14 Parkinsonian patients and 12 age-matched controls by d-c electrooculography (5% attenuation at 450 Hz). Subjects performed rapid, alternating gaze shifts between two fixed visual targets separated horizontally by 25° of arc. On average, the patients took about twice as long as the controls (p < .001) to complete a cycle of the alternating task. Since the dynamic characteristics of the patients' saccadic movements were normal for the amplitude achieved, the fault was not due to a reduced ability to make fast, coordinated, muscle movements. The slowed performance was found to be due to two main factors: an increased target fixation time manifest as delayed initiation of voluntary movement (akinesia); and increased transit time between targets (bradykinesia) due to the normal delays of about 200 msec between corrective saccades which were necessitated by an abnormal (p < .001) tendency to undershoot the target (hypokinesia). The marked akinesia found in this investigation of voluntary eye movements contrasts strongly with the normal latency of saccadic response to sudden target movement found in the same patients during a previous investigation. The present findings support the previously drawn conclusion that peripheral neuromuscular components of the oculomotor system are unimpeached by the disease. Comparison with observations of other authors suggests that the impairment of oculomotor performance described here may be similar to that found in skeletal muscle systems during Parkinson's disease.

Introduction

Impairment of motor performance is a major clinical feature of Parkinson's disease, and a number of attempts have been made to measure such impairment. For example, Draper and Johns (5) demonstrated slowed manual tracking of a suddenly displaced visual target, and DeJong and

1 This research was supported by the Canadian Department of Veteran Affairs Grant in Aid of Research, No. 14-57. Dr. DeJong is Co-ordinator, Parkinson's Project, Queen Mary Veterans' Hospital, 4565 Queen Mary Road, Montreal 247, Quebec, Canada. Dr. Melvill Jones is Professor, Department of Physiology, and Director, DRB Aviation Medical Research Unit, McIntyre Medical Sciences Building, McGill University, Montreal, 109, Quebec, Canada.
Burns (3) showed reduced maximum frequency of alteration between two fixed targets using a wide range of different skeletal muscle systems.

This report describes the second of a series of studies of oculomotor performance in Parkinson's disease (9), designed to extend the above observations made on skeletal muscle. The oculomotor system was chosen for these studies since it exhibits unusually rapid neuromuscular response characteristics (2) making it possible to discriminate fine detail in the patterns of experimentally induced eye movement. Furthermore, data for the different components of normal eye movement have been well established in the literature (4,6–8,10–15).

**Methods**

The methods used to generate the visual target and to record eye movement have been described in detail in a previous article (9). Briefly, a bright spot on the short-persistence face of an oscilloscope was projected onto a screen 180 cm in front of the seated subject whose head was held still in a firm chin rest. The oscilloscope spot was driven by a square-wave generator at a frequency of 25 Hz, so that two apparently stationary spots appeared on the screen in front of the subject. These spots were symmetrically placed 12.5° either side of the direct line of forward vision and so always subtended 25° at the subject's eyes. This rather elaborate method of generating two stationary visual fixation spots ("targets") was employed to conform with the methods of other experiments in this series in which fast and accurate control of spot movement was required.

Binocular eye movement was recorded by DC electrooculography (EOG) using an ultraviolet galvanometer recorder to obtain a high-frequency response (5% attenuation at 450 Hz).

Subjects were allowed time to become familiar with the procedure and then, after calibration, they were asked to shift their gaze back and forth between the two stationary target spots as rapidly and as accurately as possible. At least 12 completed gaze shifts were recorded in each direction. Any fixation within ±2° of the target spot was accepted as "on target." The eye movements induced by this procedure are almost invariably saccadic in nature since, with the head still, it is almost impossible to make smooth pursuit-type eye movements in the absence of a moving target.

The 26 subjects examined were the same as in the previous experiment (9). Fourteen of these were patients with Parkinson's disease and 12 were age-matched controls. As before, both groups were free from drugs for at least 3 days prior to the experiment.

**Results**

Figure 1 shows two extracts from original records obtained from a control subject (A) and a severely affected patient (B). Typically, a normal
control subject would complete one cycle of the alternating movement in about 1 sec. Each cycle would include a fast saccadic jump from one target toward the other, with an amplitude of jump close to 25° and a duration of 80–90 msec. A variable period of fixation on the target (straight horizontal components of the record) would then be followed by another large saccade in the opposite direction, although sometimes this would be preceded by a small corrective saccade.

In the Parkinsonian patient (Fig. 1B), the initial saccade associated with each change of direction tended to be smaller than in the controls. As a consequence, one or more corrective saccades would then ensue, each being preceded by the normal physiological pause of about 200 msec. Mainly owing to these pauses, the time taken to move from one target to the other tended to be considerably longer in patients than in controls. The other characteristic feature seen in Parkinsonian patients was a prolongation of the fixation time on the target before the next voluntary movement in the opposite direction began (Fig. 1B).

Figure 2 illustrates diagrammatically a typical sequence of alternating eye movement, and defines the variables which were measured on the records, as follows: (a), the half-cycle time, namely, the time between arrival at one target and arrival at the other (T); (b), the fixation time, namely, the duration of arrest on target (t₁); (c), the transit time, namely, the time from leaving one target to arrival at the other (t₂); (d), the magnitude of the first saccade associated with each change in gaze direction expressed as a percentage of 25°; for example, if the first saccade in Fig. 2 was 15°, its magnitude would be expressed as 60%; and (e), the number of corrective saccades made by the subject during each
OCR MOTOR SYSTEM

![Diagram defining measured components in a sequence of saccadic eye movements alternating between two fixed visual targets 25° apart. T = half-cycle time; t1 = fixation time; t2 = transit time; CT = correction time. For actual values of these times, see Tables 1 and 2.](image)

completed gaze shift from one target to the other. For example, one corrective saccade is represented in Fig. 2.

**Half-cycle Time (T).** Because of the cyclical nature of the eye movements in these experiments, it is appropriate to label the time between arrival at one target and arrival at the other one as the half-cycle time (T). Table 1 gives the collected data for T as defined in Fig. 2. Separate values are given for half-cycle times to left (T_L) and to right (T_R), and for the two sets of data combined (T). Of incidental interest is the fact that the mean value of T_R was slightly longer than that of T_L both in the patients and the controls (.02 < p < .05). The main feature of this table, however, is that in all cases the mean half-cycle time of patients was approximately twice that of the controls, the difference between means being uniformly of high statistical significance (p < .001). This difference occurred despite the fact that all subjects were instructed to perform the test as rapidly as possible.

**TABLE 1**

<table>
<thead>
<tr>
<th></th>
<th>No. of subjects</th>
<th>T_L</th>
<th></th>
<th>T_R</th>
<th></th>
<th>T</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SE</td>
<td>Mean</td>
<td>SE</td>
<td>Mean</td>
<td>SE</td>
</tr>
<tr>
<td>Patients (P)</td>
<td>14</td>
<td>168</td>
<td>968</td>
<td>36</td>
<td>680</td>
<td>1076</td>
<td>39</td>
</tr>
<tr>
<td>Controls (C)</td>
<td>12</td>
<td>144</td>
<td>525</td>
<td>16</td>
<td>600</td>
<td>578</td>
<td>20</td>
</tr>
</tbody>
</table>

Significance of difference (P - C) p < .001 p < .001 p < .001

* Data are given for movements to left (T_L), to right (T_R) and for all data combined (T). SE = Standard error of the mean. All times in msec. N = Total number of values.
Fixation Time \( (t_1) \) and Transit Time \( (t_2) \). The next step was to examine quantitatively the relative contributions of Fixation and Transit times to the almost 2-fold increase in the average cycle time seen in the patients. The mean values for \( t_1 \) and \( t_2 \) are given in Table 2, together with relevant statistical data. Evidently both \( t_1 \) and \( t_2 \) were considerably greater in patients than in controls.

Thus, in the patients, both the mean fixation time (759 msec) and the mean transit time (263 msec) were significantly prolonged compared to the corresponding values of 449 and 102 msec obtained from the controls \( (p<.001 \) for both \( t_1 \) and \( t_2 ) \). It may, therefore, be stated with good statistical assurance that the slowness of patients in their over-all performance \( (T \) in Tables 1 and 2) was attributable both to akinesia, defined as prolongation of the target fixation or "waiting" time, plus bradykinesia defined as a prolongation of the transit time.

It is evident from Table 2 that the fixation time, \( t_1 \), occupies approximately three-fourths of the total half-cycle time, \( T \), both in normal subjects (449 of 551 msec) and in patients (759 of 1022 msec). Thus, despite large differences in absolute values, the proportion of time taken by each component of the completed movement was on average similar in both patients and controls.

Accuracy and Corrections. The fixation time comprises a single entity, namely, the duration of arrest on target. However, the transit time between targets is the outcome of two interdependent factors, namely, accuracy of the saccadic jump, and the sequence of corrective jumps which usually follow an inaccurate one. These features are numerically displayed in Table 3, in which it can be seen that there was a highly significant tendency for patients to make smaller initial saccades than did the controls \( (p<.001) \). On average, the patients undershot the target by 14% of the required 25° full-scale movement, whereas the corresponding figure for controls was only 4%. Thus, on average the magnitude of the undershooting error in patients was roughly three times that in controls. Moreover,

<table>
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<th>TABLE 2</th>
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<tr>
<td><strong>MEAN FIXATION TIMES ( (t_1) ) AND MEAN TRANSIT TIMES ( (t_2) ) IN Milliseconds for Patients and Controls</strong></td>
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</table>

<table>
<thead>
<tr>
<th>No. of subjects</th>
<th>( t_1 )</th>
<th>( t_2 )</th>
<th>( T )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (P)</td>
<td>14</td>
<td>336</td>
<td>759</td>
</tr>
<tr>
<td>Controls (C)</td>
<td>12</td>
<td>288</td>
<td>449</td>
</tr>
</tbody>
</table>

Significance of difference \( (P - C) \) \( p < .001 \) \( p < .001 \)
the range of error magnitude was considerably wider in patients than in controls.

This tendency of the patients to undershoot was associated with an almost 3-fold increase in the average number of corrective saccades they made in one complete gaze shift between targets. Since each correction is associated with a normal delay of about 200 msec after the preceding saccade, the presence of corrections inevitably introduces a substantial delay in reaching the new target.

These results show that the more prolonged transit time ("bradykinesia") seen in patients is largely attributable to these intersaccadic pauses. In turn, the pauses result from the increased probability of undersized saccades in patients, as illustrated in Fig. 1B. This undershooting phenomenon, characterized as abnormally small saccades compared with the amplitude required to reach the target, is referred to from here on as hypokinesia.

Voluntary Saccade Dynamics. In this study, the average amplitude of measured initial saccades in the patients was 23°, as it was in a previous study on the same subjects in which they were required to follow the sudden 25° displacement of a visual target. Furthermore, the main variables characterizing saccade dynamics, namely, rise time and maximum eye velocity, were statistically indistinguishable between the two studies (p > .5 and p > .1, respectively). Thus, since the numerical values of these characteristics were considered normal in the first study, they are also considered physiologically normal in the present study.

Relation between Akinesia and Hypokinesia. The emergence of akinesia and hypokinesia as basic elements contributing to the measured impairment of oculomotor performance in the patients, raises the question whether they are correlated or independent phenomena. Plots of the relations between fixation times and magnitude of corresponding initial saccades showed no correlation between the two sets of data.

<p>| TABLE 3 |
|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>No. of subjects</th>
<th>Mean size of 1st saccade (% of 25°)</th>
<th>Mean error (% of 25°)</th>
<th>Average no. of corrective saccades per half-cycle</th>
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<tbody>
<tr>
<td>Patients</td>
<td>14</td>
<td>168</td>
<td>86</td>
<td>14</td>
</tr>
<tr>
<td>Controls</td>
<td>12</td>
<td>144</td>
<td>96</td>
<td>4</td>
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<tr>
<td>Significance of difference</td>
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Variability. The results in Tables 1, 2, and 3 indicate that the Parkinsonian patients were more variable in their performance than the controls. Thus, the standard errors of the mean values of saccade size, fixation time \( t_1 \), transit time \( t_2 \), and half-cycle time \( T \), were all greater in patients than in controls. However, these increases for the standard errors of the mean values were nearly proportional to the corresponding increases in the mean values themselves. This apparent correlation between the mean values of these parameters and their standard errors is substantially confirmed in Table 4 which shows no great differences between the coefficients of variation \( (V) \) in patients and controls where,

\[
V = \frac{\text{Standard deviation}}{\text{mean}} \times 100.
\]

Reproducibility of Results. One subject was examined on two occasions separated by 5 months, using the same methods. None of the measured variables were significantly different on the second occasion.

Discussion

Characteristics of Impairment of Oculomotor Performance. The two aims of these experiments were to extend the observations of DeJong and Burns (3) to the oculomotor system, and to examine in detail the various factors contributing to any motor impairment seen. DeJong and Burns expressed their results in terms of the average frequency of completion of an alternating goal-directed task. Expressed in this way, the mean frequency of completing one cycle of eye movement in the present experiment was 0.49 Hz in the patients and 0.91 Hz in the controls. Hence, the average frequency achieved by the patients was reduced to 54% of that of the controls. A corresponding average value of 58.5% was obtained by DeJong and Burns from skeletal muscles tested in 12 different parts of the body. While two different groups of patients were examined using different methods in these two studies, the close similarity of results suggests that in

<table>
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<tr>
<td>COEFFICIENTS OF VARIATION *</td>
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<td>---------</td>
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<tr>
<td>( V_E )</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Patients</td>
</tr>
<tr>
<td>Controls</td>
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</tbody>
</table>

* Expressed as \( V = \frac{\text{standard deviation}}{\text{mean}} \times 100 \) calculated from data in Tables 2 and 3. The suffix \( E \) denotes error in saccade size (Table 3). \( T, t_1, \) and \( t_2 \) are as in previous tables, and in Fig. 2.
Parkinson's disease impairment of motor performance in the extraocular muscles is similar to that in skeletal muscles.

Detailed examination of the various factors contributing to this marked slowing of the rate of over-all task achievement in the Parkinsonian patients, revealed the rather surprising feature that the slowing was not due to reduced speed of individual saccadic movements. Both the maximum angular velocities and the times for completion of individual saccadic eye movements (rise times) were normal for the amplitudes of movement achieved, as indeed was the case in an earlier study of eye movements driven by a moving visual target (9).

The major contribution to the increased time required by the patients to complete the sequence of events in one gaze shift between targets was found to be due to an increase in the average time per cycle during which the eye was stationary. This in turn was found to be attributable to two main factors: akinesia and hypokinesia. Akinesia is here defined as prolongation of the normal delay in initiating voluntary movement. In this study, it was characterized by prolongation of the time on target (fixation time), before the initiation of the next voluntary movement toward the alternate target. Hypokinesia defined here as abnormal smallness of movement relative to the amplitude of movement required, was characterized by an abnormal tendency to undershoot the target in both initial and corrective saccades. This undershooting led to an increased probability of corrective saccades occurring in each cycle of movement. But each corrective saccade is almost inevitably preceded by a pause of about 200 msec and hence the increased number of saccades per cycle gave rise to bradykinesia, defined as abnormal slowness in the average speed of movement (inverse of the transit time) between targets. Note that the origin of this sequence of events is to be found in the measured hypokinesia, or tendency to undershoot the target. This tendency was also seen in our control subjects (once in every four initial saccades) but was three times as frequent and nearly four times as great in magnitude in the Parkinsonian patient of this experiment.

However, while abnormal frequency of normal pre-saccade pauses is the principal factor causing bradykinesia, it is not the only one. A slight contribution derives from the reduction in saccade speed (angle of movement + rise time of saccade) normally associated with reduction of saccade size. The small effect of this contribution may be illustrated by the following example. The average rise time of a single saccade of 24° in our subjects was 88 msec (9). If this same angle of excursion was achieved by a series of three saccades (one initial and two corrective ones) each of about 8°, the sum of the times of actual movement (saccade rise times) would amount to about $3 \times 40 = 120$ msec (10), which amounts to an increase
of only 32 msec. But the sum of the two pauses (correction times) necessarily introduced before the two corrective saccades of this example, would amount to about 400 msec.

From these observations, we conclude that the impairment of oculomotor control seen in our group of Parkinsonian patients was primarily due to akinesia and hypokinesia, with the latter phenomenon introducing bradykinesia, mainly as a result of the inevitable pauses introduced before the corrective saccades which usually follow undershooting the visual target.

Comparison with Skeletal Muscle Performance. How applicable are these findings and conclusions to the impairment of skeletal muscle control in Parkinson's disease? As already seen, the impairment of the rate of performance of alternating goal-directed movements found in this experiment is close to that found in a wide range of skeletal muscle systems by DeJong and Burns (3). In another study, Draper and Johns (5) measured the movement of a manually driven pointer which was required to follow as rapidly as possible the instantaneous movement of a target from one location to another. Their patients showed similar akinesia with bradykinesia marked by a succession of steplike movements interrupted by pauses. The close similarity of our observations to theirs supports the view that similar mechanisms are at play in the disorganization of both skeletal and extraocular muscle control. However, whereas they concluded that " intermittency of motion is the major defect of movement control in Parkinsonism," we regard the intermittency of movement that characterizes bradykinesia as secondary to the primary fault of hypokinesia.

Draper and Johns also concluded that their Parkinsonian patients showed an inability to establish the normal increase of movement velocity associated with increase in the arc of movement. But this conclusion was based on their measurement of the total transit time from one target to another, including times of pauses as well as of movements. This provided information only about average speed of movement. They did not fully analyze individual movements alone, and we found these to be normal for their size in every way, including increasing their velocity with increasing amplitude of movement, at least up to the limit of 25° eye movement.

Unimpaired Features of Control. Although, on average, our Parkinsonian patients showed marked differences from the control subjects, manifest as akinesia, hypokinesia, and bradykinesia, the two groups showed several similarities. Thus, in accord with the observations of Angel, Alston, and Higgins on skeletal muscles (1), there was no evidence of impaired ability to recognize the direction of movement required. Moreover, on average, one in every four initial saccadic jumps achieved the correct amplitude of movement and hence it seems there was no inherent inability to recognize the required magnitude of response to the visual stimulus. In
addition, it has already been emphasized that for a given size of jump the
dynamic characteristics of an oculomotor saccade appear to be normal in
Parkinson's disease. Indeed, even the main features of discrepancy, namely,
akinesia and hypokinesia, can perhaps be looked upon as exaggerations of
normal phenomena seen in control subjects. Thus akinesia may be but a
prolongation of the normal and apparently inevitable pause before the initi-
ation of voluntary saccadic movement; and hypokinesia may be but an ex-
aggeration of the normal slight tendency to undershoot a visual target.

Akinesia and Latency. A particularly striking point of difference be-
tween the present results and those of a previous experimental study (9)
is seen in the time required to initiate movement. Whereas, in the present
investigations of voluntary eye movements, there was marked akinesia, the
previous experiments in which subjects followed the sudden displacement
of a visual target demonstrated a mean latency of response which was indis-
tinguishable from that of the age-matched controls. It seems that the
disease process responsible for akinesia during voluntary control must be lo-
calized outside the peripheral pathway and central mechanisms involved in
the oculomotor response to target movement on the retina.

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