CHANGES IN SENSORIMOTOR FUNCTION ASSOCIATED WITH THE DEGREE OF BRADYKINESIA OF PARKINSON'S DISEASE

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SUMMARY

Changes in coordinated eye and hand movements associated with the progress of bradykinesia were studied in 31 parkinsonian patients and 8 age-matched healthy subjects. Among the parameters expressing the changes in motor behaviour, the interval between the onset of eye and hand movements was most sensitive. This parameter reflected the difference in the progress of the symptom in the two motor systems. An increase in the reaction time of the hand response appeared in patients of grade II bradykinesia; this was observed for eye movements only in patients with grade III (severe) bradykinesia. While the changes in ocular reaction time remained within the physiological range, a lengthening of the reaction time, a reduction in peak velocity, a decrease in the open-loop gain, a prolongation of movement duration, and a slow build-up in EMG activity, appeared from an early stage in hand movement. These signs of motor disturbance may appear eventually in every motor system at an advanced stage, but their development is not synchronous in different motor systems. An analysis of the responses recorded simultaneously from the two motor systems examined made it possible to evaluate the changes in the sensorimotor processes with different grades of bradykinesia. A comparison between reaction times for eye and hand movements may be useful for assessing the degree of bradykinesia in parkinsonian patients.

INTRODUCTION

Parkinson's disease is characterized clinically by a variety of symptoms represented by tremor, rigidity and bradykinesia (Hoehn and Yahr, 1967; Selby, 1968). Although evaluating the degree of tremor and rigidity is relatively easy, an objective measurement of the severity of bradykinesia is difficult. Bradykinesia is a complex symptom that cannot be expressed simply in terms of the slowness of motor functions. In assessing bradykinesia, therefore, consideration must be given to the multitude of symptoms, including not only the slowness of movement but also

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disturbances in higher motor function. Many attempts have been made to quantify bradykinesia (Draper and Johns, 1964; Angel et al., 1970; Cassell et al., 1973; Flowers, 1976; Evarts et al., 1981; Beppu et al., 1984; Bloxham et al., 1984), but it is not yet established as to what parameter or parameters may contribute best to a realistic appraisal of bradykinesia.

In the present study, we attempted to characterize and quantify bradykinesia based on parameters measured by electrophysiological methods. Eye and hand movements during an aiming performance were analysed by recording electro-oculograms (EOGs), EMGs, and potentials representing the angles of a joystick. The parameters which reflected the time for information processing in the sensorimotor pathways were evaluated in the motor responses and were correlated with the clinical grades of bradykinesia that were originally suggested by Hoehn and Yahr (1967).

**METHODS**

**Subjects**

Thirty-one subjects were selected from patients with idiopathic Parkinson's disease. They were informed of the purpose and procedures of the experiment to which they consented. The criteria for selecting the subjects were: (1) patients whose primary symptom was bradykinesia and whose other symptoms such as tremor or rigidity were relatively mild; (2) no signs of obvious mental disorder, complaint of vertigo or visual disturbance; and (3) uncorrected binocular visual acuity of 20/40 or better. Studies were performed without correction. Patients with akinesia, cardiovascular disturbances, or other conditions which might have interfered with successful trials were not selected. Furthermore, those patients whose symptoms fluctuated daily in response to L-DOPA treatments were also not included.

Table 1 summarizes the clinical features of the patients with their degrees of bradykinesia, rigidity, and tremor, together with their medications at the time of experiments. Based on the grades of bradykinesia suggested by Hoehn and Yahr (1967), the patients were classified into four groups: I, slight; II, moderate; III, severe; and IV, maximum. Fifteen healthy subjects aged 40 to 67 years were also included as a control group.

**Procedure**

A subject was asked to make a laser-beam spot, which was operated by hand, follow a target displacement as quickly and accurately as possible. The visual target was a series of red light-emitting diodes (LEDs), vertically rectangular (width 0.05 deg, height 0.4 deg), which had been placed at seven positions in a horizontal plane at 10 deg intervals. They were aligned at the height of the eyes of each subject on a plane 1.8 m away from the eyes. The seven LEDs were lighted one at a time; at irregular intervals as each was extinguished, it was replaced simultaneously by another LED. The hand driven laser spot response marker (0.3 deg in diameter) was arranged to move along a line connecting the tops of the rectangles. The marker spot never covered the target even when it was superimposed on the rectangle.

During the test, the subject was seated in an armchair with the head and the right arm restrained. Hand movements and extension and flexion of the right wrist were measured by a target tracker which converted the signals from wrist movement into the movement of the laser spot by a potentiometer, a driver amplifier, and a mirror-attached galvanometer in series. The amplification of laser spot movement was maintained so that it produced a 0.65 deg horizontal movement in response to a 1 deg wrist movement. Eye movements were recorded with silver-silver chloride electrodes attached to the
TABLE 1. GRADES OF BRADYKINESIA, RIGIDITY AND TREMOR IN PARKINSONIAN PATIENTS AND THEIR MEDICATION

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Course (yrs)</th>
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<th>Rigidity*</th>
<th>Tremor*</th>
<th>Treatment**</th>
<th>Case</th>
<th>Age (yrs)</th>
<th>Sex</th>
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* Score of bradykinesia, rigidity and tremor: 0, none; 1, slight; 2, moderate; 3, severe; 4, maximum. ** Treatment: A, trihexyphenidyl; B, amantadine HCl; C, levodopa or levodopa in combination with dopa decarboxylase inhibitor.
forehead and to the inner and outer canthi of the right eye. The d.c. EOG was recorded with an upper frequency limit of 100 Hz. EMGs were recorded from the extensor and flexor muscles of the right forearm with surface electrodes.

Two experimental paradigms were used. In the first, the subject was asked to follow a target with the laser spot; in the second, the target LED was extinguished for 1 s immediately after the onset of a saccadic eye movement. For this purpose, the circuit for the target light was interrupted by a pulse of 1 s duration that was triggered by a sudden shift of the EOG potential. This paradigm was inserted into the latter part of the sessions with the first paradigm at random intervals which were longer than 30 s. All the tests were completed with each subject within 30 min, including the 15 min periods for dark adaptation. This limitation minimized both fatigue in the subject and possible effects of predictability after repeated practice.

The data were stored on magnetic tapes and played back later on a digital memory scope (Nihon Denki San-Ei 7S07). The velocities of both eye and hand movements were obtained by electronic differentiation of the signals through an RC-coupled analog circuit and the differentiation of the responses shown in the figures were performed by digitizing the potentials by a PDP 11/23 computer. The onsets and peak velocities of the eye and hand movements were determined in these velocity signals. The completion of the hand movement was determined at the time when the laser spot reached and was maintained within 0.5 deg of the target location. The reaction times, the movement durations, and the total performance times were then evaluated. Target displacements of 10, 20, 30, and 40 deg to either right or left were randomly executed, and motor responses to 10, 20, and 40 deg displacements were later selected from the continuous records. Target positions at the centre, 10 deg right and left, and 20 deg right and left were commonly used. The targets 30 deg at right and left were used only occasionally in order to randomize the trials and to minimize the predictability of the sequence. Significance levels of the differences in patients with grades I, II, and III bradykinesia were compared with those of the age-matched healthy subjects, using analysis of variance.

RESULTS

In response to the instruction to match the laser spot (response marker) to a new visual target as quickly and accurately as possible, most subjects learned to move the eyes and hand almost simultaneously. Although the instruction did not particularly suggest moving the eyes to the new target, the manual responses were always associated with saccadic eye movements. The motor responses of parkinsonian patients were markedly different from those of healthy subjects, particularly in hand movements.

Fig. 1 shows typical motor responses of a 60-year-old healthy subject (A) and of a 55-year-old parkinsonian patient (B) to a 40 deg target displacement to the right. A remarkable difference can be seen in the manual responses. The peak velocity of the hand movement was 300 deg·s\(^{-1}\) for the healthy subject (A), while that for the parkinsonian patient was only 65 deg·s\(^{-1}\) (B). In response to a 40 deg target displacement, the normal subject could complete the hand movement in less than 0.5 s, but the parkinsonian patient needed more than 1.5 s. Furthermore, there was a considerable delay in the reaction time (B-2). The low peak velocity of the initial saccade (B-1), the long reaction time of the hand movement (B-2), the decrease in hand velocity, and the slow build-up of the flexor EMG activity (B-3) are demonstrated in the motor responses (fig. 1B). These abnormalities are characteristic of parkinsonian
FIG. 1. Eye and hand movements (1 and 2) in response to a 40 deg target displacement, recorded from a 60-year-old healthy subject (A) and a 55-year-old parkinsonian patient (B); 3, extensor EMG; 4, flexor EMG.

FIG. 2. Reaction times of eye movements (A) and hand movements (B) in parkinsonian patients and the age-matched controls. Each data point represents the mean reaction time of the group in response to 10, 20, and 40 deg target displacements. The SDs are listed in Table 2. Open triangles = 40 deg. Closed circles = 20 deg. Open circles = 10 deg.
patients with bradykinesia and frequently described in the literature (see Wiesendanger et al., 1969).

**Reaction Time of Eye and Hand Movement**

The latencies of saccadic eye movements to a new target position were always longer when associated with a larger displacement. The extension of the time was also closely related to the degree of bradykinesia in parkinsonian patients. Fig. 2A shows the mean values of oculomotor reaction times for groups of healthy subjects and of parkinsonian patients with bradykinesia of grades I, II, III, and IV, obtained from saccades in response to 10, 20, and 40 deg target displacement in either direction. Fig. 2B shows the group means of the manual reaction times. In contrast to the ocular reaction times, the change in the manual reaction times has already appeared in patients of grade I bradykinesia. The extension was particularly large in 20 and 40 deg hand movements. For clarity, the standard deviations (SD) are not shown in figs 2 and 3, but they are summarized in Table 2.

![Graph showing oculomotor and manual reaction times](image)

**Fig. 3.** Oculomotor and manual reaction times for the four groups of parkinsonian patients and the age-matched healthy subjects. The SDs are listed in Table 2. Symbols as for fig. 2.

**Oculomotor Onset Latency**

When healthy subjects tried to superimpose a response marker on a target as quickly as possible, the eyes and hand tended to move almost simultaneously. The average oculomotor onset latency (the interval between the onset of eye and hand
movements) for aged healthy subjects was as short as 45 ms. This latency was significantly larger in parkinsonian patients with bradykinesia. Changes in the average onset latencies from healthy subjects to parkinsonian patients with an increasing grade of bradykinesia are illustrated in fig. 3, for 10, 20, and 40 deg movements. The average latencies of grade I bradykinesia for 10, 20, and 40 deg movements were almost twice as great as those of the healthy subjects. The latencies were 3.1, 4.1 and 9.3 times the value of healthy subjects, in parkinsonian patients with grades II, III, and IV bradykinesia, respectively.

![Image](https://via.placeholder.com/150)

**Fig. 4.** Original eye and hand movement recordings (A, B, C) and their computed velocities (D, E, F). A and D, responses from a normal subject; B and E, responses from a parkinsonian patient with grade I bradykinesia; C and F, responses from a parkinsonian patient with grade II bradykinesia. 1, eye movement; 2, hand movement.

**Peak Velocities of Eye and Hand Movements**

A remarkable change in the parameters of eye and hand movements in parkinsonian patients was the reduction of peak velocity in the initial movement. Fig. 4 illustrates typical motor responses recorded from a healthy subject (A) and parkinsonian patients with grade I (B) and grade II (C) bradykinesia and the velocity traces which were derived from the individual motor responses (D, E, F). The average peak velocities of eye movements for the control, grade I, and grade II bradykinesia patients were 367, 273, and 241 deg·s⁻¹ respectively. The average peak velocities of hand movements for the same subjects were 196, 109, and 47 deg·s⁻¹, respectively.
As compared with the reduction in the peak velocity of eye movement, that in the peak velocity of hand movement was devastating in parkinsonian patients. Fig. 5 shows the average peak velocity of hand movement for the four groups of parkinsonian patients measured during 10, 20, and 40 deg movements. Open circles connected by broken lines indicate the group means of the healthy subjects. Except for 1 patient with grade III bradykinesia, there was a consistent reduction in the peak velocity of hand movement associated with the progress of bradykinesia.

**Amplitudes of Initial Hand Movements**

Hand movements in normal subjects consisted of two consecutive actions driven by two distinct processes. One was a ballistic initial movement and the other was a slow or a step-wise error-correcting movement. Fig. 6 illustrates the paradigm and eye and hand movements, designed to separate the initial movement from the correcting movement. The visual target was turned off approximately 15 ms after the onset of saccadic eye movement (see Methods). As the target had disappeared when the gaze approached it, the corrective movement did not take place; the motor responses resulted from the position-error information which had been sampled before the eye movement (the open-loop mechanism).
On

Off

500 ms

Fig. 6. The paradigm and eye and hand movements to show the fast initial movement (the open-loop component). The target was extinguished for 1 s by a pulse triggered by a saccadic eye movement. As the target reappeared 1 s, the corrective movements (the closed-loop component) started with 1 s delay.

The open-loop gain was defined and computed as the amplitude of the initial movement during the blackout period divided by the amplitude of target displacement (see Methods). The average open-loop gains for 8 healthy subjects are shown with open circles in fig. 7. Those for parkinsonian patients with grades I, II, III and IV bradykinesia are represented by filled circles. The fine line connects the group means for the control and the grades I-IV bradykinesia.

Open-loop gains in the healthy subjects ranged from 0.9 to 1.0. It is clear from fig. 7 that a significant reduction in open-loop gains was observed in patients with a
higher grade of bradykinesia. In grade IV bradykinesia patients, the initial hand movement was either extremely small (gain 0.2) or did not appear at all (gain 0).

**Movement Duration**

The reduction in the velocity of movement observed in parkinsonian patients with bradykinesia was accompanied by a lengthening of movement duration for both eye and hand movements. Average duration of hand movements, evaluated in each group of healthy subjects and patients with bradykinesia of different grades, is shown in fig. 8. It is important to note that, when tested with 10 deg displacements, the duration of the hand movement in patients with grade I bradykinesia was almost comparable to that of healthy subjects. Even in these patients, however, the increase in duration was significant when tested with 20 and 40 deg displacements ($P < 0.001$).

Three major factors caused the extension of movement duration in parkinsonian patients: (1) reduction in the peak velocity of the initial movement; (2) reduction in the average velocity of the correcting movement; (3) reduction in the open-loop gain.

Fig. 9 illustrates how the duration of hand movement was related to the reduction in the open-loop gain. Open circles represent the average movement durations for 8 healthy subjects plotted against the average open-loop gains for the same individuals. Filled circles compile the data of grades I–III bradykinesia patients. The smaller the open-loop gain of hand movement, the longer was the duration of hand
FIG. 9. Relation between the open-loop gain (amplitude of the initial hand movement/target displacement) and duration of hand movement. The reduction in the open-loop gain is associated with an extension of hand movement. Open circles = healthy subjects; closed circles = parkinsonians.

FIG. 10. Changes in the total performance time in the different groups of parkinsonian patients and in the age-matched healthy subjects. Symbols as for fig. 2.
movement. In combination with the data presented in fig. 7, it was concluded that the degree of bradykinesia was positively related to the reduction in the open-loop gain (the amplitude of the initial movement) and hence to the extension of the movement duration.

**Total Performance Time**

Total performance time is the time needed to complete the aiming task. This period, rather than the time to the onset of movement, has been more frequently designated as the reaction time in the literature of behavioural studies. Fig. 10 shows changes in the total-performance time in response to 10, 20 and 40 deg target displacement, measured in healthy subjects and in the four groups of parkinsonian patients.

**Table 2. Means and SD's of Reaction Times of Eye and Hand Movements, and Oculomanual Onset Latencies (ms)**

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<thead>
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<th>Amplitude of movement</th>
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<th>Grade I (11)</th>
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<td>SD</td>
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Controls: 60-69 yrs old (mean 63 yrs)

Table 2 summarizes the means and SDs of the reaction times and the oculomanual onset latencies. Each figure (in ms) represents the responses from all members of the subgroup in response to 10, 20, and 40 deg displacements. It is clear from the relatively small SDs that the means shown in figs 2 and 3 represented the consistent changes which occurred in the motor systems of the individual subjects, except for those of grade IV bradykinesia.

Table 3 compiles the significance levels in the changes in the parkinsonian patients as compared with the age-matched healthy subjects. In applying the analysis of variance, the data from grade IV patients were not included because their motor behaviours were considerably different from those of the other subgroups. This is indicated also by the large SDs in Table 2.

**DISCUSSION**

As quantitative measures of the degree of bradykinesia in Parkinson's disease, the reaction time and the duration of motor responses during various aiming tasks have been evaluated. These values, however, did not always show significant
### Table 3. Significance Levels of the Changes in the Response Parameters

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<tr>
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— = not significant; + = $P < 0.05$; ++ = $P < 0.01$; +++ = $P < 0.001$.

differences between parkinsonian patients and age-matched controls (Schwab et al., 1954; King, 1959; Cassell et al., 1973; Flowers, 1976; Heilman et al., 1976; Evarts et al., 1981). The inconsistent observations resulted partly from the wide range of symptomatology which can exist within any group of parkinsonians and even within a single subject depending on the kind of movement which the patient had to perform. It is generally agreed that bradykinesia is more pronounced when the patient executes a larger movement than a smaller one, and also when he executes a more complex movement than a simpler one (Talland and Schwab, 1964; Perret et al., 1970; Horne, 1973). Flowers (1975), for example, has shown that parkinsonians were not able to produce accurate initial movements when tested with aiming tasks requiring a high order of coordination. Evarts et al. (1981) have pointed out the need for more carefully designed studies in which various factors of movement must be programmed. Therefore, it is important to take the degree of complexity and difficulty of the task into account in the objective assessment of bradykinesia.

The aiming task used in the present study required not only precise transformation of information in the sensory system but also fine coordination of the motor system. The performance in the task consisted of two consecutive actions which were controlled by two distinct sensorimotor mechanisms. One was a fast initial acquisition movement (open-loop or ballistic) and the other was a slow correcting movement, as suggested by Flowers (1975). These movements were distinguishable in both eye and hand movements in healthy subjects (T. Warabi, H. Noda, T. Kato, unpublished).
Ocular and Manual Reaction Times and their Onset Latencies

An important finding in the present study in correlation with the clinical grades of parkinsonian bradykinesia was the extension of the intervals between the onset of eye and hand movements (the oculomanual onset latency). This latency in healthy subjects was on the average 45 ms (T. Warabi, H. Noda, T. Kato, unpublished). In spite of the 45 ms delay in the wrist movements, the onset of burst activity in the flexor (or extensor) EMG was almost synchronized with the onset of saccadic eye movement. This suggested that in healthy subjects impulses necessary for programming appropriate angles of the wrist and eye movements had arrived at the respective motor systems almost simultaneously.

The oculomotor reaction time remained unchanged during the early stages of Parkinson's disease. The manual reaction time, however, increased significantly even in patients with grade I bradykinesia and extended further with the progress of the symptom. The normal oculomotor reaction time indicated that the function of the visual system was relatively well preserved.

Duration and Velocity of Hand Movement

A higher grade of bradykinesia was always associated with extended durations of hand movements. As can be seen in fig. 6, the hand movement during the blackout (the initial movement) was considerably longer than the saccadic eye movement. The slowing was caused entirely by a malfunction of the motor system which could not make quick associated movements in the forearm muscles. The velocity decreased further in association with the advancement of bradykinesia.

The second part of the hand movement depended on the error-correcting mechanism. In this movement, the velocity was related not only to motor function but also to sensory function which provides the feedback information concerning the position errors. This velocity also showed a remarkable reduction, reflecting the degree of deterioration of sensorimotor function.

The duration of hand movement varied, depending upon how much of the movement was executed by the fast initial movement. The milder the parkinsonian symptom, the larger was the percentage of the amplitude executed by the open-loop mechanism (fig. 7). The rest of the distance had to be reached by the error-correcting movement. The extension of movement duration in Parkinson's disease was, therefore, caused by a combination of the disturbed open-loop mechanism and the deterioration of the fine coordination of motor function of the hand. The larger the deterioration of these functions, the stronger was bradykinesia.

The precision in the programming of an appropriate motion before its onset also seems to deteriorate in parkinsonian patients. This deterioration, however, started at a later stage of bradykinesia as demonstrated by a reduction in the open-loop gain that manifested itself in patients of grades III and IV (see fig. 7). In characterizing bradykinesia, Flowers (1975) described his patients' loss of ability to produce accurate ballistic actions. Their patterns of movement on a step-function tracking typically showed a slow, steady movement towards the target rather than the normal
fast ballistic approach movement. This observation has been confirmed in our
dvanced patients (grades III and IV). In contrast to Flowers' observation, our
patients of grades I and II could use the information which was sampled before a
saccade to execute a hand movement towards the target (the initial movement),
although the accuracy and the speed of the initial movement were somewhat
impaired.

In our patients with grade III bradykinesia, the disturbances appeared also in the
oculomotor system. The initial saccadic eye movement frequently showed an
undershoot or overshoot, suggesting a malfunction of the oculomotor system in
translating the target position information into impulses necessary for correct eye
movements. Another important finding in the present study is that the oculomotor
system was affected only at an advanced stage of bradykinesia, confirming the
common observations in the literature (see White et al., 1983). The time lag in the
onset of symptoms in the oculomotor system behind the hand movement system is
apparently related to their anatomical differences. It is generally accepted that hand
movements are controlled by structures that include the basal ganglia, which are
affected at an early stage in Parkinson's disease. Eye movements are primarily
operated by the brainstem oculomotor nuclei in collaboration with the cerebellum
and the cerebral cortex, such as the frontal eye fields and association cortex. The
basal ganglia are least involved in oculomotor mechanisms.

The present study has shown that the most sensitive measure of bradykinesia was
the parameter which compared the abnormalities in eye and hand movements.
Parkinson's disease is a progressive degenerative disorder which gradually invades
one motor system after another until every motor system is finally involved. The
structures controlling the coordination of the extremities are anatomically in-
dependent from the oculomotor system. Structural differences cause the variations
in the onset of clinical symptoms. The electrodiagnostic method which compared
the responses recorded simultaneously from eye and hand movements was found to
contribute best to an objective appraisal of the bradykinesia of parkinsonian
patients.

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