THE EFFECT OF TREATMENT ON EYE-HEAD COORDINATION IN PARKINSON'S DISEASE*

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Abstract — Eye-head movements to target steps of amplitude 3.75° to 30° were analyzed in 9 untreated patients with idiopathic Parkinson's disease. Testing was performed before and after the introduction of a dopaminergic drug (L-dopa or bromocriptine) and compared with 9 normal controls. The patients showed a significantly greater scatter of mean head latencies prior to treatment, although their mean latencies were not significantly prolonged. When compared to controls, the patients' head movements were of reduced peak velocity and gain. Treatment resulted in an improvement of gain but not velocity. Analysis of the frequency of gaze types showed no significant effect of treatment.

Keywords — eye/head coordination; L-dopa; saccades; basal ganglia; Parkinson's disease.

Introduction

When James Parkinson published his observations in 1817, he focused his attention on the clinical signs of bradykinesia and tremor in the trunk and limbs. He made no mention of any altered strategy for gaze target acquisition, although in clinical practice it is often apparent that Parkinsonian patients, particularly those severely affected, do not move their head as much as normal subjects.

Abnormalities of eye movements in Parkinson's disease (PD) were not described until 1925 by Krebs, although oculogyric crisis in postencephalitic Parkinsonism had been reported earlier (1,2). It was not until 1972 that any observation on eye-head coordination was reported by Corin et al (3). In a large qualitative assessment of patients they noted examples of dissociation in sequences of eye-head movements in which the head moved ahead of the eyes, but they did not mention the frequency of occurrence. However, in view of the high frequency with which they observed vertical gaze abnormalities, it is likely that a number of their patients had progressive supranuclear palsy or a striatonigral degeneration rather than PD (4). In the subsequent quantitative studies of combined eye-head movements that have been reported, there is a lack of agreement concerning the extent of head movement made by Parkinsonian patients. When subjects with their heads free are instructed to follow a step target "as quickly as possible," that is time-optimal movement, both Kennard et al (5) and White et al (6) observed that patients chose not to move their heads, or to move their heads with a small amplitude, less than 25% of the step. This was observed regardless of the amplitude of the target movement, and was markedly different from the controls who moved their heads under identical circumstances without instruction. In a forced head movement paradigm, Weinrich et al (7) also found reduced head movement in PD. By contrast Shimuzu et al (8) observed the opposite responses. Their normal controls scarcely moved their heads whereas the Parkinsonian subjects al-
ways had an overt head movement with a mean amplitude of 11.4° for a 30° step. This is surprising since all their patients were at the more severe end of the clinical spectrum and therefore would have had marked axial rigidity. Examining the recording techniques and experimental design fails to uncover a satisfactory explanation for this discrepancy.

All other data analysis in these studies was carried out in relation to forced head movements in which the subjects were instructed to actively move their heads. Under such conditions both Kennard et al (5) and White et al (6) agree that Parkinsonian patients show prolonged latencies for the onset of head movements. As a result the mean lead time of the eye saccade in advance of the head movement increases by at least 2 to 3 times. Such a noticeable change in the interval between head and eye onset was found by Shimizu et al (8), although their patients showed marked overall latency prolongation for both the saccade and the head. A further feature of both the eye and head latencies of Parkinsonian patients was their marked variability compared with controls. Analysis of coordinated eye-head movements into gaze types (9,10) showed an increase in the type 2 (delayed head onset, 330°0) when compared with the controls (4%), although the normal controls were not age-matched (5).

In an attempt to determine the value of objective motor performance measurement in assessing the effects of dopaminergic therapy on previously untreated PD patients, Gibson et al (11) studied saccadic eye movements with head fixed and compared this with manual tracking. In the clinically improved group, there was an increase in saccadic gain but none of the parameters of manual tracking showed a significant improvement.

These same patients also performed eye-head movements, and we have now analyzed their records, which were taken under head-free conditions, and have compared them with the age-matched controls to form the basis for this report.

The only previous study of the effects of drug treatment on eye-head coordination in Parkinson's disease investigated head oscillations in response to whole body sinusoidal oscillations (12). Untreated patients showed essentially the same well-coordinated response as controls. After administration of L-dopa, PD patients developed large increases in the amplitude of their head movements while fixating a stationary target. This increase was proportional to disease severity.

**Methods**

Head movements of 9 mildly affected untreated patients (mean age 63 years, range 48 to 72) were studied and compared with 9 normal control subjects (mean age 58 years, range 49 to 66). The patients were then commenced on dopaminergic therapy, either bromocriptine or L-dopa with a dopa-decarboxylase inhibitor. They were re-studied either after their weighted Webster scale clinical rating score had improved by at least 33%, or after 6 months if they had not reached this level of improvement (11). Seven patients attained the 33% clinical improvement. The patients and control subjects were asked to move their heads "as quickly as possible."

Eye movements were recorded using the infrared limbus reflection technique. Head movement was measured using mechanical linkages and a low torque potentiometer attached to a light plastic helmet worn by the subject. Two runs of 40 random steps in which timing varied between 1.5 and 3 s, and amplitude between 9 possible positions (15°, 12.25°, 7.5°, 3.75° to left and right of center) were recorded during approximately 3 min. This generated 8 different step amplitudes: 3.75°, 7.5°, 12.25°, 15°, 18.75°, 22.5°, 26.25°, and 30°. The metrics of the eye and head movements were analyzed from the chart records using a digitizing tablet that yielded latency, duration, and peak velocity data for both the eye and the head traces.

**Results**

All but 2 patients showed a clinical improvement as defined above at the time of the second recording. There was no difference in the mean latency to random targets of the eye saccades, although there was a small but not
significant reduction after treatment (Table 1). With the head fixed, the same group of patients showed a greater scatter of latencies than did the controls (11). This was not apparent in the head-free situation. However, the mean latency of the onset of head movement did show a very high standard deviation (±229 ms), which significantly reduced after treatment, although the mean latency reduction (from 288 to 270 ms) was not significant. There was no measurable difference between the treated patients and the controls.

The overall mean gain of all the eye saccades was similar in both the patients and the controls, and treatment had no effect. There was a typical range effect with the highest gains found for the smallest step amplitudes. The controls showed larger head gains than the patients, and there was an increase in the mean gain from 1.2 to 1.3 after treatment in the patients who did not reach that of the controls (1.9). The compensatory eye movement (CEM) velocity gain (the ratio of smooth eye movement velocity to head velocity) was not significantly different in the 3 groups, although the controls were slightly higher.

As a result of these combined eye–head movements, calculation of the gaze error showed in the PD patients a very small mean undershoot of 0.3° which changed with treatment to a mean overshoot of 1.4°. The mean gaze error in the controls was an undershoot of 1.0 degrees.

The peak velocities of all saccades and head movements were plotted against amplitudes for each patient, before and after treatment, and for each control subject. The velocity–amplitude relationship was expressed by computing a best-fit curve to the scatter of points: \( PV = V (1 - \exp(-A/C)) \), where \( PV \) is peak velocity at any point on the curve, \( A \) is saccade or head velocity at that point, \( V \) is velocity at the asymptote of the curve, and \( C \) is a constant. There was no difference in group mean \( V \) values of saccades in untreated and treated patients or the controls. Although

### Table 1. Metrics of Eye and Head Movements

<table>
<thead>
<tr>
<th></th>
<th>S Latency (ms)</th>
<th>H Latency (ms)</th>
<th>S Gain</th>
<th>H Gain</th>
<th>CEM Gain (°/sec)</th>
<th>VEL (°/sec)</th>
<th>GAZERR (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD patients untreated</td>
<td>n = 9</td>
<td>207 ± 48</td>
<td>288 ± 229</td>
<td>1.0 ± 0.4</td>
<td>0.8 ± 0.6</td>
<td>1.2 ± 0.6</td>
<td>412</td>
</tr>
<tr>
<td>PD patients treated</td>
<td>n = 9</td>
<td>199 ± 48</td>
<td>270 ± 64</td>
<td>1.0 ± 0.4</td>
<td>1.3 ± 3.0</td>
<td>1.0 ± 0.7</td>
<td>422</td>
</tr>
<tr>
<td>Normal controls</td>
<td>n = 9</td>
<td>211 ± 51</td>
<td>271 ± 73</td>
<td>0.9 ± 0.3</td>
<td>1.4 ± 1.0</td>
<td>1.3 ± 0.4</td>
<td>434</td>
</tr>
</tbody>
</table>

S = saccade; H = head; CEM = compensatory eye movement; VEL = peak velocity asymptote; GAZERR = Gaze error; Mean ± SD.

### Table 2. Head and Saccade Gain and Gaze Types Related to Target Step Amplitude

<table>
<thead>
<tr>
<th>Gaze types (%)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Head gain</th>
<th>Saccade gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.75, 7.5°</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gp1</td>
<td>48</td>
<td>41</td>
<td>9</td>
<td>2</td>
<td>1.6 ± 2.9</td>
<td>1.1 ± 0.4</td>
</tr>
<tr>
<td>Gp2</td>
<td>42</td>
<td>42</td>
<td>14</td>
<td>2</td>
<td>1.6 ± 1.8</td>
<td>1.1 ± 0.5</td>
</tr>
<tr>
<td>Gp3</td>
<td>40</td>
<td>45</td>
<td>11</td>
<td>4</td>
<td>2.8 ± 5.5</td>
<td>1.1 ± 0.3</td>
</tr>
</tbody>
</table>

| 18.75, 22.5°   |   |   |   |   |           |             |
| Gp1            | 36| 7 | 56| 1 | 0.9 ± 0.6 | 0.9 ± 0.3   |
| Gp2            | 36| 6 | 58| 0 | 1.0 ± 0.3 | 0.9 ± 0.3   |
| Gp3            | 27| 7 | 64| 2 | 1.1 ± 0.6 | 0.8 ± 0.2   |

| 26.25, 30°     |   |   |   |   |           |             |
| Gp1            | 7 | 4 | 82| 7 | 0.8 ± 0.2 | 0.8 ± 0.3   |
| Gp2            | 18| 3 | 76| 3 | 0.9 ± 0.2 | 0.8 ± 0.2   |
| Gp3            | 8 | 0 | 88| 4 | 0.9 ± 0.3 | 0.6 ± 0.2   |

Gp1 = untreated PD patients.
Gp2 = treated PD patients.
Gp3 = normal controls.
group mean $V$ values of head movements for both patient groups were no different, they were both significantly lower than that of the controls ($P < 0.05$, Wilcoxon). It is important to note that our normal controls demonstrated relatively low peak head velocities.

Analysis of the frequency of occurrence of the 4 different gaze types (10,13) showed no significant difference between untreated and treated patients. There was an interesting change for all 3 groups in the frequency of gaze types related to target step size (Table 2). For small step amplitudes, gaze types 1 and 2 predominated, whereas for larger amplitudes the frequency of these types decreased and type 3 predominated (increase from 9% to 82%). This general change from an eye-dominant to a head-dominant strategy was expected from earlier results (9,14). As reported previously (5), this change of gaze strategy proved to be significantly reduced ($P < 0.01$, Wilcoxon) when untreated PD patients were compared with normal age-matched controls. This difference is best seen for smaller gaze amplitudes (11.25° and 15.0°) that are normally performed using an eye-dominant strategy (Table 2). For gaze type 2 (eye-dominant) frequencies we found that $g_{p1} - g_{p3} = 15\%$, while for types 1 and 3 (head-dominant) the difference $g_{p1} - g_{p3} = -16\%$.

This implies that untreated PD patients demonstrate their preference for an eye-dominant strategy. Obviously, using a fast, time-optimal head movement is more difficult for them to perform than in larger gaze amplitudes (26.25°, 30°). Here, a similar but diminished difference shows up. After treatment started (Gp 2, Table 2), this difference becomes insignificant. We can infer from this that treatment had some effect on the distribution of gaze types, but our sample was too small to reach significance in this respect.

Discussion

In our study, the saccadic eye gain was similar in patients and control subjects and was not influenced by therapy, whereas the head gain (that is, head amplitude/target step) improved with therapy patients always showing a smaller head gain than controls, which can be interpreted as an equivalent of axial bradykinesia. Further analysis showed that it was especially the small target steps that were responsible for the relatively high mean gain values (above unity) obtained in this study. We consider that this might be due to the fact that the more everyday head movements usually lie in the range between 25° to 60° (9), which automatically biases towards overshooting in the experimental condition. This effect is more prominent in the patient group, whereas the eye gains (normally below 15°, see reference 15) are not influenced by the pathological process operating in PD in this particular target paradigm. In this way the smaller gaze jumps might have a tendency to overshoot the target, forcing the eye to make a final correction in the backward direction. Due to corrective saccades that could be observed as frequently in PDs as in controls, the slight gaze errors were not significantly different in this study. However, Shimuzu et al (8) have reported on the final eye position and found that Parkinsonian patients are more prone to make hypometric combined movements when compared with controls. They observed in about half of both the patient and control group that more accurate gaze was attained at the end of the initial saccade when both the head and the eye were moved, rather than in the condition with the eye alone (head fixed). Among their subjects, only the Parkinsonian subjects tended to move their heads. This led Shimuzu to the unlikely hypothesis that since the coordinated eye-head movement is phylogenetically older than voluntary saccades without head movement, Parkinsonian patients tend to achieve accurate gaze by using the older mechanism instead of the newer one used by controls.

Since in Parkinson's disease the major clinical abnormalities mainly affect movements of the limbs and axial structures, it is perhaps surprising that so few studies of combined eye and head movements have been reported. In such combined refixation movements in nor-
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mal subjects, the onset of the eye saccade usually precedes that of the head. The eye fixates the target, and, as a consequence of the continued head movement, smooth eye movements are generated in the opposite direction to the head movement to maintain gaze fixation. These slow compensatory eye movements are normally generated by the vestibular-ocular reflex (VOR) (16), although on occasions they may be preprogrammed (10,13,17). In PD the VOR gain has been measured in darkness during sinusoidal whole body rotation and appears to be normal (18,19), except in severely affected patients. In our mildly affected patients, we also found evidence for a normal VOR gain in that the compensatory eye movement velocity gain was normal.

Parkinsonian patients have been found to have slightly reduced peak head velocities (6), although Shimuzu et al (8) reported no difference. Our findings of significantly reduced head velocity in PD patients while performing forced head movements is in agreement with the recently reported study by Weinrich et al (7). Time optimal head movements in the amplitude range recorded should be faster in normal controls than reported in this paper. For example, Zangemeister et al (14,20) reported head peak velocities of 200° to 300° per sec for amplitudes of 30° in young as well as old normal subjects. Therefore, our difference may be even more significant when head movements of normal old subjects are performed in a more clearly forced task. Moreover, higher deviations of PD patients’ larger amplitude head movements (acceleration jerks) may be more instructive for detecting the defective fine movement structure and its possible improvement with therapy.

In the study by Weinrich et al (7), the patients had their l-dopa withdrawn overnight and were then tested before and after a single oral dose. They reported that the reduced head peak velocities of PD patients compared to controls did not significantly improve with l-dopa, while the distal limb motor function studied in the same group showed some response. The more clearly reduced peak head velocities in the more severely affected PD patients even seemed to decline after l-dopa administration. Studies of eye movements with the head fixed in PD have also shown some evidence for improvement with l-dopa (16,21,22). In the only study of the effects of drug treatment on eye–head coordination in PD, head oscillations in response to whole body sinusoidal oscillations were studied (12). Untreated patients showed essentially the same well-coordinated response as controls. After administration of l-dopa, PD patients developed large increases in the amplitude of their head movements while fixating a stationary target. This increase was proportional to disease severity.

In conclusion, we have found a variety of relatively minor abnormalities in the metrics of eye–head coordination in PD. These include increased head latency variability and reduced head gain and velocity in contrast to normal saccades. It should be emphasized that the patients in our study were all only mildly or moderately affected when tested before treatment was started, and it is likely that a more severely affected group would have shown more significant abnormalities. However, one of the aims of the study was to assess the value of measurement of eye–head coordination in PD as a quantitative measure of response to treatment. Unfortunately, we conclude that, because of these minor abnormalities and the considerable patient variability shown in this study as well as the failure to show significant changes with treatment, this does not appear to be a useful objective measure, at least in the early stages of the disease. Further studies of this topic will have to use more sophisticated methods of visual stimulation, for example, white-noise time distributions and larger target amplitudes (23,24), as well as the evaluation of the movements’ fine structure.

Acknowledgments—We are extremely grateful to Mr. Stephan Evans for his considerable assistance with the statistical evaluation of this data. Dr. Hansen was in receipt of a grant from the Deutscher Akademischer Austauschdienst.
REFERENCES