OCULAR MOTOR DEFICITS IN PARKINSON’S DISEASE

III. COORDINATION OF EYE AND HEAD MOVEMENTS

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SUMMARY

Eye-head coordination was measured in patients with Parkinson’s disease as they made horizontal gaze shifts in response to predictable and unpredictable target steps and to targets moving smoothly with either constant or sinusoidally varying velocity. Patients preferred not to move their heads for both large and small amplitude gaze shifts. Both eye and head movement reaction times were prolonged. Saccades were hypometric and, frequently, slow. Head movements were also slow, hypometric, and varied in amplitude for target shifts of a given amplitude. Compensatory eye movements (CEMs) that normally stabilize gaze direction during head movement varied in gain from zero to greater than unity, and often drove the eyes off target. CEM abnormalities occurred most commonly in patients with abnormal vestibulo-ocular reflex (VOR) gain in darkness. We attribute these abnormalities of programming combined eye-head saccades to dysfunction of striatonigral-collicular circuits.

Smooth gaze pursuit gain, the ratio of gaze velocity to target velocity, was lowered in patients while tracking sinusoidal targets at 0.3, 0.5 and 1.0 Hz. Some patients could track these targets with the head fixed but not with the head free. We attribute this to abnormal suppression of the vestibulo-ocular reflex. The results indicate that Parkinson’s disease impairs motor programming of coordinated eye-head gaze saccades and disrupts normal interaction between head movement and the VOR.

INTRODUCTION

Rapid gaze shifts with the freely moving head are achieved by saccades coordinated with rapid head movements. Like saccades, the peak velocity of these head movements is proportional to their amplitude (Zangemeister et al., 1981). Head movements are considerably slower than saccades and continue after fast eye movements have brought the target onto the fovea. Gaze direction, defined as the sum of eye position in the orbit and head position in space, is stabilized by the generation of smooth eye movements in the opposite direction to head movement. These smooth
eye movements drive the eyes from the eccentric orbital position achieved by the saccade back towards the midorbital position as the head aligns with the target (Bizzi et al., 1972; Zangemeister and Stark, 1981). The compensatory smooth eye movements (CEMs) are normally generated by the vestibulo-ocular reflex (VOR) (Bizzi et al., 1971) but on occasion may be preprogrammed (Kasai and Zee, 1978; Zangemeister and Stark, 1981).

During pursuit, the head provides a platform from which smooth eye movements are generated (Gresty and Leech, 1977). Head motion causes vestibular smooth eye movements in the opposite direction, which drives the eye off target. Thus the VOR must be cancelled in order to maintain the target on the fovea during head-free pursuit (Lanman et al., 1978).

Patients with Parkinson's disease have impaired saccadic initiation and accuracy, low smooth pursuit velocities, hypoactive VOR and impaired visual suppression of the VOR (White et al., 1983a, b). Kennard et al. (1982) found that parkinsonian patients tend to avoid head movements during gaze shifts. When instructed to move their heads, the initiation of head motion is usually delayed until after onset of saccade. Our study was designed to analyse ocular motor function during rapid gaze shifts and during pursuit with the head free to move.

METHODS AND SUBJECTS

Six patients with idiopathic Parkinson's disease and 1 with posthypoxic parkinsonism, all of whom participated in previous oculomotor investigations with the head fixed (White et al., 1983a, b), were studied. Criteria for clinical assessment have been published previously. Briefly, tremor, rigidity and bradykinesia were graded from zero (absent) to 3 (severe). A score of 2 or more for each of two signs, or a score of 2 for one sign in addition to a duration of disease greater than 5 yrs, was sufficient to classify a patient as having advanced disease. All patients were fully mobile and independent. Four patients had advanced and 3 mild disease (Table 1), according to these criteria. The mean age of the patients was 56 yrs (range 39–74); 5 were men. Their results were compared with those of 5

<table>
<thead>
<tr>
<th>Case</th>
<th>Age yrs</th>
<th>Sex</th>
<th>Severity</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>58</td>
<td>F</td>
<td>Advanced</td>
<td>L-DOPA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>trihexiphenidyl</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>M</td>
<td>Advanced</td>
<td>L-DOPA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>benztropine mesylate</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>F</td>
<td>Advanced</td>
<td>Trihexiphenidyl</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>amantidine</td>
</tr>
<tr>
<td>6</td>
<td>75</td>
<td>M</td>
<td>Advanced</td>
<td>None</td>
</tr>
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<td>7</td>
<td>39</td>
<td>M</td>
<td>Mild</td>
<td>L-DOPA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>benztropine mesylate</td>
</tr>
<tr>
<td>11</td>
<td>67</td>
<td>M</td>
<td>Mild</td>
<td>L-DOPA</td>
</tr>
<tr>
<td>12</td>
<td>44</td>
<td>M</td>
<td>Mild</td>
<td>None</td>
</tr>
</tbody>
</table>

Case numbers identify patients who participated in the previous studies of head-fixed oculomotor control (White et al., 1983a, b).
normal subjects (mean age 51 yrs; range 42–65; 3 men). All subjects had the protocols fully explained to them and gave informed consent. No patients were demented as determined by neuropsychological criteria.

Horizontal eye movements were recorded by infrared reflection oculography and d.c. electro-oculography (EOG) simultaneously, as previously described (White et al., 1983a). EOG was used to measure eye movements beyond the linear range of the infrared system (±20°). Head movements were recorded using a lightweight helmet connected to a precision quality potentiometer by a torsionally rigid cable. All data were stored on magnetic tape for off-line digitization. The full system frequency response was 0–100 Hz after digitization.

Compensatory eye movement (CEM) gain (the ratio of smooth eye movement velocity to head velocity) during active head movements was compared to the VOR gain (the ratio of vestibular smooth eye movement velocity to whole body rotational velocity) recorded during passive whole body rotation in darkness in the same patients (White et al., 1983a).

Targets for gaze shifts were light-emitting diodes arrayed on a stimulus arc. The head-free pursuit target was a rear-projected laser reflected from computer-controlled, galvanometer-mounted mirrors (Sharpe et al., 1979). All tests were performed first without and then with instructions for subjects to move their heads.

**Saccadic gaze shifts**

**Predictable target steps.** The target was stepped from 30° left to 30° right at predictable intervals greater than 2 s. Responses to at least 40 target steps were analysed for each subject.

**Unpredictable amplitude target steps.** The target was stepped 5°, 10°, 15°, 20°, 40° or 60° to the left or right at predictable intervals (3 s) with direction amplitude varied pseudorandomly. The largest amplitude steps were centre-crossing. Responses to more than 100 target steps were examined for each subject.

**Head-free pursuit**

**Ramp targets.** The target moved predictably at constant velocities of 10°, 20° or 40°/s from 10° left to 10° right, with 3 s intervals between ramps. Twenty-five ramps in each direction, at each velocity, were analysed for each subject.

**Sinusoidal targets.** Smooth pursuit of sinusoidally moving targets was measured at frequencies of 0.25, 0.5 and 1.0 Hz with peak-to-peak amplitude of 20°. We analysed 25 half-sinusoids at each frequency for each subject.

Data editing and analyses were carried out with a PDP 11/23 computer using interactive programs as previously described (White et al., 1983a, b). Significance of results was evaluated by using the Mann-Whitney U test.

**RESULTS**

It was a striking finding that none of the patients chose to move their heads unless continuously encouraged to do so, regardless of the amplitude or velocity of the target movement. There was no difference in results between the patient with posthypoxic parkinsonism and patients with idiopathic disease. Normal subjects moved their heads through varying amplitudes under the same circumstances, without instruction. With instruction they made full amplitude head movements with each gaze shift. Thus all data reported here refer to protocols in which the subjects were instructed to move their heads.
Saccadic gaze shifts

Normal subjects. Two patterns of eye-head coordination were observed. When target steps were predictable, the eye and head movement usually started almost simultaneously towards the target; mean latency for both was similar (Table 2). Head movements sometimes preceded eye movements. Once target foveation had been achieved by the saccadic eye movement, a CEM stabilized gaze position in space while the head continued to move (fig. 1A).

<table>
<thead>
<tr>
<th></th>
<th>Eye (ms ± ISD)</th>
<th>Head (ms ± ISD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predictable target steps</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normals</td>
<td>260 ± 60</td>
<td>280 ± 50</td>
</tr>
<tr>
<td>Patients</td>
<td>350 ± 140</td>
<td>380 ± 90</td>
</tr>
<tr>
<td>Unpredictable amplitude target steps</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normals</td>
<td>270 ± 40</td>
<td>330 ± 40</td>
</tr>
<tr>
<td>Patients</td>
<td>310 ± 140</td>
<td>430 ± 120</td>
</tr>
</tbody>
</table>

When the amplitude and direction of target steps were unpredictable, normal subjects still attempted to anticipate target shifts, but less frequently. Eye movements (mean latency 270 ms) led head movements in these normal subjects by 60 ms on average (Table 2). Again, CEMs were generated with the eyes returning towards the primary orbital position as the head moved. The end point of saccades made when the head was moving was difficult to judge due to the flattening of the eye position trace. We used the point when eye movement velocity, obtained from the computer differentiation of the position trace, returned to zero, to determine termination of the saccade and thus measure saccade amplitude.

Head movement amplitudes varied at each target amplitude despite encouragement to generate head movements actively. Target shifts of 60° were used for the predictable amplitude and direction protocol, thus generating the largest amount of data at a single amplitude. For these target shifts, the mean amplitude of head movement was 37° (SD 13°). Peak head velocity increased with increased amplitude of head movement (fig. 3c).

Patients. Saccadic gaze shifts were frequently composed of small slow head movements having gradual onsets and terminations. Patients most frequently attained the targets by using multiple hypometric saccades (fig. 1C, D, E, fig. 2B). When the target shifts were predictable, eye and head movements tended to coincide, both at prolonged latencies (eye 350 ± 140 ms; head 380 ± 90 ms; Table 2; fig. 1B). When target movements were unpredictable in amplitude and direction, saccades led head movement by an average of 120 ms, again at prolonged latencies compared with normals (Table 2). Saccade latencies were similar to those recorded in these patients with their heads fixed (330 ± 85 ms). These differences were not statistically significant when the whole patient group was compared with normal subjects; however, patients with advanced disease had the longest saccadic latencies
Fig. 1. Examples of head-free gaze shifts to targets predictable in amplitude, direction and timing. A, normal subject. B, mildly affected patient: note the high gain CEM and small corrective saccade. C, severely affected patient: multiple hypometric saccades take the eye to the target. Head movement occurs in the absence of CEMs and is responsible for gaze shift. D, severely affected patient: note the high gain CEMs, in both the eye and gaze traces, taking the eye off target and necessitating corrective saccades. E, severely affected patient: hypometric saccades and low velocity head movement. F, normal subject: this exhibits a reduced VOR gain during the final stage of a large gaze shift so that gaze shift is completed by head movement alone. Upward deflections signify rightward eye, head and target movements.

and frequently made no head movement at all, despite forceful encouragement and despite the fact that they had not foveated the target.

The small slow head movements made by patients were too variable in amplitude for calculation of significant differences in peak velocity/amplitude relationships
FIG. 2. Examples of head-free gaze shifts to targets moving pseudorandomly in direction and amplitude. A, normal subject; B, patient with advanced disease. Note the long latency to head movement by comparison with normal subjects. No compensatory eye movements are generated and a large part of the patient’s gaze shift is achieved by the head movement alone.

FIG. 3. Velocity versus amplitude plots of A, normal subject, eye movements; B, Case 2 (advanced disease), eye movements; C, normal subject (from A), head movements; and D, Case 2 (advanced disease), head movements. Eye movements are saccades linked with head movements for 40° predictable target steps. A normal subject makes many saccades near full amplitude with smaller corrective saccades. A patient makes many hypometric saccades. The amplitude of both the normal subject’s and the patient’s head movements vary markedly, but generally the patient’s head movements are slower for a given amplitude of head movement. The asymmetry of saccadic function was not mirrored in general somatic function which was symmetrically impaired. Positive amplitude indicates rightward movements, and negative, leftward.
compared with normal subjects. Patients were able to generate head movements with metrics comparable to those of normal subjects but made a greater number of slow movements than normal subjects (fig. 3C, D). Saccadic peak velocities for matched amplitudes were lowered in patients but, like normals, there was no significant difference whether the head was fixed or free (Table 4; fig. 3A, B). Gaze velocities were not compared. The variability of saccade amplitude, in association with head movement, resulted in a very small sample of gaze shifts of amplitudes which could be compared with those of normals.

Between these hypometric saccades, patients generated smooth eye movements (fig. 1D) resembling the compensatory smooth eye movements that stabilize gaze in normal subjects. In our patients, the gain of these CEMs (the ratio of smooth eye movement velocity to head velocity) varied from near zero (fig. 1C, E) to greater than unity (fig. 1D). For example, in fig. 1E, after an initial hypometric saccade which failed to reach the target, a low gain CEM was generated during head movement. Thus final attainment of the target depended almost entirely on the head movement. Such behaviour was rarely observed with normals and then only during the largest amplitude gaze shifts (fig. 1F).

**Head-free smooth pursuit**

The gain of head-free pursuit was measured as the ratio of gaze velocity (eye velocity plus head velocity) to target velocity. Gaze pursuit gain was not significantly different from pursuit gain measured previously with the head fixed (White et al., 1983b), although mean gain at the lower sinusoidal target frequencies was lower than that of normals (Table 3). Normal subjects pursued ramp targets, with near unity gain, at ramp speeds up to 20 deg/s and sinusoidal targets at up to 0.5 Hz. Beyond these limits, pursuit gain deteriorated (Table 3; figs 4A, 5A, 6A). Patients made fewer smooth gaze pursuit movements, and at lower gain, for ramp targets at 10 and 20 deg/s (see fig. 6A, B), and had reduced pursuit gain during sinusoidal pursuit at all frequencies (Table 3).

With these targets, whether ramp (constant velocity) or sinusoidal, normal subjects tended to move their heads through the same or larger amplitudes than the target; thus the direction of image slip on the retina was occasionally reversed (figs 4A, 5A). Patients' head movements were more variable in amplitude and range than those of normal subjects. Even when head movement alone was inadequate to pursue the target, patients sometimes made smooth eye movements opposite to the direction of head movement. Such eye movements were counter-productive and rendered gaze pursuit even less accurate (fig. 5B).

Cases 3 and 7 were able to generate smooth eye movements during head-fixed protocols but were unable to pursue with the head free (Table 3). Both patients had impaired visual suppression of the VOR despite hypoactivity of the reflex in darkness and despite relatively preserved ocular smooth pursuit. They moved their heads minimally despite instruction and their results were not included in statistical analyses. On occasion, when they did move their heads, they were unable to pursue
TABLE 3. VOR GAIN DURING WHOLE BODY OSCILLATION*

<table>
<thead>
<tr>
<th>Frequency (Hz)</th>
<th>VOR gain darkness</th>
<th>VOR gain suppression</th>
<th>Frequency (Hz)</th>
<th>Pursuit gain (sinusoids)</th>
<th>Pursuit gain (sinusoids)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>0.3</td>
<td>0.68 ± 0.16</td>
<td>0.25</td>
<td>0.92 ± 0.07</td>
<td>0.80 ± 0.09</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>0.76 ± 0.19</td>
<td>0.5</td>
<td>0.90 ± 0.10</td>
<td>0.77 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.97 ± 0.13</td>
<td>1.0</td>
<td>0.55 ± 0.12</td>
<td>0.55 ± 0.13</td>
</tr>
</tbody>
</table>

Measured in darkness and during visual suppression, and of gaze pursuit gains with the head fixed and free. Values are mean gain ± 1 SD. NR = not recordable.

FIG. 4. Examples of smooth gaze pursuit following 20 deg/s ramp targets. A, normal subject and B, patient with advanced disease. The normal subject has made smooth head movements which exceed the amplitude of target shift. He has generated vestibular smooth eye movements in the opposite direction to maintain fixation of the target as evidenced by the gaze channel which is the sum of eye and head position. Only occasional small corrective saccades are required. The patient has considerably less head movement and is unable to suppress his VOR. The smooth eye movements seen take the eye off target necessitating frequent corrective saccades. Upward deviation indicates rightward movement, and down, leftward.
TABLE 4. SACCADIC PEAK VELOCITIES (IN DEG/s ± ISD) FOR SACCADES OF SELECTED AMPITUDES

<table>
<thead>
<tr>
<th>Saccadic amplitude</th>
<th>4°</th>
<th>10°</th>
<th>18°</th>
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<tbody>
<tr>
<td>Normals</td>
<td>157±37</td>
<td>286±83</td>
<td>375±79</td>
</tr>
<tr>
<td>Patients</td>
<td>140±34</td>
<td>248±65</td>
<td>291±119</td>
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<table>
<thead>
<tr>
<th></th>
<th>Head fixed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normals</td>
</tr>
<tr>
<td>Saccadic amplitude</td>
<td>176±15</td>
</tr>
<tr>
<td></td>
<td>142±37</td>
</tr>
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</table>

the target and were unable to regain fixation as long as the target continued to move, even if they ceased head movement.

Most patients showed similar pursuit gain values whether the head was fixed or free. However, Case 2, who had advanced disease and severe impairment of all eye movements with the head fixed, retained some capacity to suppress her VOR gain at higher frequencies of passive oscillation. This patient was unable to pursue a sinusoidal target at any frequency with the head fixed but, with her head free, she pursued targets smoothly, albeit at lower gain than for normals (Table 3). With the head free, all but one patient with mild disease (Case 12) had gaze pursuit gains lower than normal at all frequencies of sinusoidal target movement (Table 3). For ramp targets, patients’ normalized pursuit duration (summed duration of all pursuit movements divided by the summed duration of all target movements) was lower than normals. Furthermore, mean pursuit velocity was lowered at all ramp velocities (fig. 6A, B).

![Fig. 5. Examples of smooth gaze pursuit of sinusoidal targets at 0.5 Hz for normal subjects (A) and at 0.3 Hz for a patient (B) with advanced disease. The normal subject makes large amplitude head movements requiring smooth vestibular eye movements in the opposite direction to track the target accurately. The patient was unable to track a target at 0.5 Hz and at 0.3 Hz, pursuit was achieved by a combination of small amplitude head movement and frequent corrective saccades. Occasional smooth eye movements are seen opposing head movement. These may be generated by the VOR. Upward deviation indicates rightward movement.](image-url)
Fig. 6. Histograms of normalized smooth gaze pursuit duration (cumulative duration of smooth gaze movements at a specific velocity expressed as a percentage of the cumulative ramp duration) while tracking predictable target ramps, for a patient with advanced disease (dotted area) and a normal subject (open area). A, 10 deg/s ramps and B, 20 deg/s ramps. Note that the patient spends less time tracking at velocities near that of the target. Positive velocity indicates rightward tracking.

Cases 11 and 12 pursued targets better with their heads fixed than free. The mean pursuit gain for Case 12 was only minimally lowered but he made fewer pursuit movements with the head fixed than free (Table 3).

DISCUSSION

We have detected abnormalities of eye-head coordination not previously reported in Parkinson's disease. Normal subjects preferentially use saccades alone to achieve gaze shifts less than 20°. For larger gaze shifts, they initiate saccades towards the target and move their heads towards the new direction of gaze. Following the saccade, CEMs oppose head movement and stabilize gaze direction (Zangemeister and Stark, 1982a).

Shimizu et al. (1981) reported that parkinsonian patients, unlike control subjects, preferred to move their heads during head-free gaze shifts of 30° and were able to stabilize gaze direction in space. They assumed the VOR was normal and noted that saccades, although hypometric, had normal velocities. However, they did not report the relationship of velocity to amplitude. They concluded that eye-head coordination was normal in parkinsonism. Kennard et al. (1982) noted that patients preferred not to move their heads. Saccadic latencies were reported as normal but head movement latency was prolonged. Their patients generated CEMs opposed to head movement but sometimes preprogrammed opposing eye movements preceding the head movement.

In the experimental situation, expectations of performance may result in alter-
ation of the normal response. For this reason we standardized the instructions to all subjects and studied a range of gaze shift amplitudes and conditions. Differences between our study and those reported above may be attributable to differences in the severity of parkinsonism or the experimental protocols. From our observations, parkinsonian patients rarely move their heads spontaneously, and then only for the largest gaze shifts. Most patients exhibited prolonged eye and head movement latencies for all paradigms. Saccades during head movements were slow and hypometric, and smooth gaze pursuit gain was lowered. CEMs frequently had abnormal gain, ranging from zero to greater than unity, and resulted in gaze inaccuracy. Occasionally smooth eye movements preceded head movement.

**Saccadic gaze shifts**

*Latencies.* Normal subjects' eye and head movement latencies vary with the experimental paradigm, and are affected by neurological disease (Zangemeister and Stark, 1982a, b). For predictable target shifts, head movement latency can be reduced, coinciding with eye movement onset (Zangemeister and Stark, 1982a, b). We observed similar behaviour in our subjects.

The mean latencies of our patients' eye and head saccades were prolonged for both predictable and unpredictable gaze shifts (Table 2). The differences were not statistically significant but the longest latencies occurred in patients with severe disease. Despite instruction and encouragement, patients at all stages of disease frequently failed to make head movements or moved so slowly that precise determination on onset and offset was impossible. The necessary exclusion of these trials from statistical analysis biases mean latencies towards normal.

*Velocity.* The mean peak velocity of head-free eye saccades was lower, although not significantly, in all normal subjects than those of a similar amplitude made with the head fixed. Although patients can make saccades having normal peak velocity/amplitude relationships (Table 4), they make more slow saccades than normals.

Morasso et al. (1973) noted reduction of eye saccadic velocity during head movements made by monkeys, and attributed this to addition of the opposed VOR. Rapid head movements, made by our subjects, might slow saccades by activating vestibular smooth eye movements but, in our patients, the observed slowing of saccades during head movement was not significant (Table 4). Furthermore, patients with advanced parkinsonism actually had hypoactive VOR activity measured during passive whole body oscillation in darkness (White et al., 1983a). Opposing vestibular CEMs seem unlikely to reduce saccadic velocities appreciably.

Patients frequently, and normal subjects occasionally, made gaze shifts during which target foveation was achieved by head movement alone after the eyes ceased moving. Tomlinson and Bahra (1986b), in monkeys, and Laurutis and Robinson (1986), in humans, have demonstrated that the VOR is not subtracted from saccades during gaze shifts greater than 20°. In monkeys, the VOR is active during gaze shifts less than 20°. Tomlinson and Bahra (1986a, b) suggested that a separate
motor program was operative for large gaze shifts in monkeys and that the eye movements were analogous to vestibular quick phases which are slower than saccades of matched amplitude (Jurgens et al., 1981b). Laurutis and Robinson (1986) proposed that feedback of an efference copy of the gaze signal slowed the eye movements in their subjects.

In the cat there appear to be two gaze mechanisms. Stimulation of the anterior superior colliculus evokes retinotopically-coded saccades with variable small head movements (Guitton et al., 1980). Stimulation of the intermediate zone resulted in saccades to an orbital location associated with invariable, short-latency head movements during which the VOR was cancelled and gaze was the sum of the evoked saccade and head movement alone (Roucoux et al., 1980).

Our observations suggest that our patients frequently used a phylogenetically older motor program, akin to that used by afoveate animals, wherein the fast eye movements are analogous to the quick phases of vestibular nystagmus. Such a paradigm is used by normal subjects only for large gaze shifts.

Compensatory smooth eye movements. CEMs during saccadic gaze shifts are thought to be vestibular in origin (Bizzi et al., 1971, 1972; Zangemeister and Stark, 1981, 1982b), but may be preprogrammed in labyrinthine-defective humans and monkeys (Bizzi et al., 1972; Kasai and Zee, 1978) and in normal humans (Roucoux et al., 1981). Our patients sometimes generate CEMs with low gain, but often with normal or high gain, despite a hypoactive VOR. Gain variation was vastly more variable than VOR gain, even in the same patient.

CEMs may be vestibular, preprogrammed or adapted cervico-ocular reflex movements, as observed in labyrinthine defective humans and monkeys (Kasai and Zee, 1978; Dichgans et al., 1973). In those studies, the cervico-ocular reflex did not fully compensate for an absent VOR, and preprogrammed CEMs were implicated. Preprogrammed CEMs did not seem to be an adaptive response to hypoactive vestibular eye movements in our patients, as the variation in CEM gain often produced gaze inaccuracy. Low gain CEMs may be explained by the hypoactive VOR observed in advanced disease (White et al., 1983a). However, patients with mild disease had normal VOR gains measured in darkness. Thus the low gain of CEMs during active head movement in our patients would indicate that they were preprogrammed.

It appears that our patients' program selection for small and large gaze shifts was frequently inappropriate and integration of motor activity with sensory (vestibular) information was impaired. Such disturbances indicate degeneration of higher executive functions in the saccadic gaze system.

Head-free pursuit

Normal subjects, during head-free pursuit, often moved their heads faster and further than the target. The VOR was appropriately suppressed and gaze pursuit gain was equivalent to the gain of head-fixed ocular pursuit. Gresty and Leech
suggested that head movements increase the effective ocular motor range but do not enhance pursuit performance otherwise.

In Parkinson's disease, head-free pursuit gain is similar to that measured with the head fixed (White et al., 1983b). When free to move their heads, patients, like normals, prefer to pursue with their eyes alone for the amplitude of target movement we have tested. When instructed to move their heads in pursuit of the targets, patients, unlike normals, chose not to move their heads most of the time. Gaze pursuit (the sum of eye movement and head movement) was predominantly saccadic in all patients.

The anatomical substrates for these deficits of the saccadic and smooth pursuit systems are uncertain. Schiller et al. (1980) demonstrated in monkeys that combined lesions of the frontal eye fields and the superior colliculus produced slowed hypometric saccades. The caudate nucleus sends axons to the medialis dorsalis and ventralis anterior nuclei of the thalamus which, in turn, project to prefrontal cortex and frontal eye fields (Alexander et al., 1986). Brinkman and Porter (1979) identified cells in the supplementary motor cortex of monkeys which activated with ipsilateral eye movements and which Schlag and Schlag-Rey (1985) showed to fire before gaze shifts, whether the monkey's head was fixed or free. This region is probably influenced by basal ganglia outflow. Striatal efferents also influence nigrostriatal pathways (Jayaraman et al., 1977; Hikosaka and Wurtz, 1983). Further studies have demonstrated that the substantia nigra pars reticulata inhibits neurons of the superior colliculus (Hikosaka and Wurtz, 1985a, b) and could thereby affect saccade and gaze saccade generation.

Ablation of the superior colliculus in cats impairs the VOR and its modulation for 3 to 4 weeks (Flandrin and Jeannerod, 1981). Boussaoud and Joseph (1985) injected the GABA agonist muscimol into the substantia nigra pars reticulata, which projects to the superior colliculus, thus reducing VOR gain for ipsilateral rotations. It seems that nigrocollicular pathways influence the VOR, although, the duration of effect of a fixed lesion is not certain. Parkinsonism may permanently disrupt these circuits.

ACKNOWLEDGEMENTS

Supported by MRC of Canada Grants MT5404 and ME5509, and by Physicians' Services Incorporated Foundation of Ontario (O.B.W. and J.A.S.).

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(Received December 19, 1986. Revised May 18, 1987. Accepted June 2, 1987)