ABNORMAL OCULAR MOVEMENTS IN PARKINSON’S DISEASE

EVIDENCE FOR INVOLVEMENT OF DOPAMINERGIC SYSTEMS

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SUMMARY

Quantitated automated electro-oculographic data from 45 parkinsonian patients were compared with those from 30 normal control subjects. Patients were selected with idiopathic Parkinson’s disease without other associated neurological disease or dementia; 20 had never received antiparkinsonian drugs and in 25 such treatment had been stopped for at least 2 days. Saccade latency, amplitude and peak velocity, smooth pursuit peak velocity, optokinetic nystagmus (OKN) maximal and mean velocities and vestibulo-ocular reflex (VOR) suppression by vision or imagination were significantly altered in patients, whereas VOR gain in darkness was normal. Alterations of saccade latency and smooth pursuit peak velocity were more severe in the more advanced stages of the disease and saccade latency directed towards the symptomatic side was slightly delayed in hemiparkinsonian patients. Saccade amplitude improved 90 min after a single oral dose of L-DOPA. These results suggest a possible dopaminergic control of some ocular movements.

INTRODUCTION

Qualitative oculomotor abnormalities have been reported in parkinsonian patients for many years (Corin et al., 1972). Quantitative data have been presented in a few recent studies, but conflicting opinions on several aspects have been obtained. Some authors, for example, found that saccade velocity was preserved (DeJong and Melvill Jones, 1971; Teräväinen and Calne, 1980a, b; Shimizu et al., 1981; Bronstein and Kennard, 1985) while others did not (Shibasaki et al., 1979; White et al., 1983a). Shimizu et al. (1981), although not measuring the vestibulo-ocular reflex (VOR) gain, suggested that this might be adequate since they observed that gaze in their patients was very stable during head movement. Conversely, vestibulo-ocular function has been reported by Reichert et al. (1982) and White et al. (1983a) to be altered. As pointed out by Bronstein and Kennard (1985), methodological differences can explain some of these discrepancies: first, in all except studies (DeJong and Melvill Jones, 1971; Gibson et al., 1987), the tests were performed while most patients were under treatment with various antiparkinsonian drugs. Other studies provided no data about the treatment (Teräväinen and Calne, 1980a, b; Shimizu et al., 1981). An effect of antiparkinsonian medication...
on ocular movements cannot therefore be excluded and may explain some of these conflicting findings. Secondly, it is likely that the severity of the disease influences abnormalities of ocular movement (White et al., 1983b; Bronstein and Kennard, 1985). In some studies, the clinical status was not detailed (DeJong and Melvill Jones, 1971; Shibasaki et al., 1979; Teräväinen and Calne, 1980a, b); in others, only mildly (Bronstein and Kennard, 1985; Gibson et al., 1987) or only severely affected patients (Teräväinen and Calne, 1980a, b; Shimizu et al., 1981) were studied. This heterogeneity could also lead to differing results. Thirdly, the number of patients in several studies was rather limited, often less than 10, and differences between patients and controls were perhaps too slight to be significant in these small groups since variances have proved to be rather large in parkinsonian patients (White et al., 1983b). Fourthly, some disagreements might also be due to nosological differences. In recent years, more attention has been given to the diagnosis of pure idiopathic Parkinson's disease while in older studies some other extrapyramidal diseases were not as clearly distinguished from it. Moreover, in addition to the Parkinson's disease, some of the published cases also presented focal lesions which could interfere with ocular movements.

These reasons justified the reappraisal of oculomotor function in parkinsonian patients. Moreover, this work provided the opportunity to study some aspects which had not been extensively investigated before, such as optokinetic nystagmus (OKN) and the relationship which may exist between electro-ocularographic data and (1) the laterality of the disease, (2) the severity of the disease, and (3) different features of the disease (e.g. tremor, akinesia, rigidity and stability). Furthermore, it must be remembered that ocular movements are often chosen as a simple but relevant example of general motor function (Robinson, 1986). As the effect of L-DOPA in parkinsonian patients may be striking, it was thus of interest to investigate the effects of L-DOPA on the quantitative parameters of different ocular movements in Parkinson's disease.

SUBJECTS

Subjects

A total of 45 patients (29 males, 16 females, mean age 60.5 ± 9, range 40–75 yrs) with idiopathic Parkinson's disease were selected as the experimental group. All patients underwent full neurological examination by one of the authors (O.R.). Subjects with a history of head injury or neurological disease other than Parkinson's disease such as cerebrovascular disease, otoneurological pathology or neurosurgery (including thalamotomy) were excluded. Absence of clinical evidence of intellectual impairment was verified by a neuropsychological assessment including at least a Folstein mini-mental scale and a Benton visual retention test. Of these 45 patients, 20 had never received treatment with antiparkinsonian drugs; the other 25 were currently on antiparkinsonian therapy (dopaminergic as well as anticholinergic medication). In these 25 patients, the antiparkinsonian treatment was stopped at least 48 h before clinical and EOG tests. This temporary drug interruption was arranged in order to perform an L-DOPA test because of difficulties in adjustment of drug therapy, as proposed by Esteguy et al. (1985), or after informed consent for the purpose of the experiment. No subject was taking any psychoactive drug. All 45 patients were evaluated clinically for motor impairment by one of us (O.R.) according to the Hoehn and Yahr (1967) classification and the motor examination of the Unified Rating Scale for Parkinson's disease (URSP) (version 1, 1984;
TABLE I. MOTOR EXAMINATION OF THE UNIFIED RATING SCALE FOR PARKINSON’S DISEASE*

<table>
<thead>
<tr>
<th>Item Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Speech</td>
</tr>
<tr>
<td>2. Facial expression</td>
</tr>
<tr>
<td>3. Tremor at rest</td>
</tr>
<tr>
<td>4. Action or postural tremor of hands</td>
</tr>
<tr>
<td>5. Rigidity</td>
</tr>
<tr>
<td>6. Finger taps</td>
</tr>
<tr>
<td>7. Hand movements</td>
</tr>
<tr>
<td>8. Rapid alternating movements of hands</td>
</tr>
<tr>
<td>9. Foot agility</td>
</tr>
<tr>
<td>10. Arising from chair</td>
</tr>
<tr>
<td>11. Posture</td>
</tr>
<tr>
<td>12. Postural stability</td>
</tr>
<tr>
<td>13. Gait</td>
</tr>
<tr>
<td>14. Body bradykinesia or hypokinesia</td>
</tr>
</tbody>
</table>

* Version 1, Fahn et al., 1987. Each item was scored from 0 to 4.

Fahn et al., 1987). This scale (Table 1) allowed us to quantify global (items 1–14), tremor (items 3, 4), akinesia (items 2, 6–10, 14), rigidity (item 5) and instability (item 12) scores.

Thirty normal volunteers (19 males, 11 females, mean age 58.5 ± 6, range 46–70 yrs) were selected as controls. No statistical difference existed between patients and controls considering sex ratio and mean age. All controls were free of any known pathology and denied use of psychoactive drugs. If hypnotic drugs (such as benzodiazepines) were used, they were stopped 2 days before the tests. In order to eliminate educational bias, we recruited individuals with a wide range of social and cultural backgrounds. Half of the healthy volunteers were recruited from retired employees in various capacities in an aircraft company; the other half came from people working in the hospital, totally unfamiliar with the EOG technique. Informed consent was obtained from all patients and controls before the study after full explanation of the experimental nature of the project.

METHODS

Eye movement recordings

Eye movement recordings were made with a Pathfinder II (Nicolet Biomedical Instruments) and the automated electronystagmography package. Electro-oculographic (EOG) recordings were obtained using silver/silver chloride electrodes placed near the eyes, recording the summed horizontal movements of both eyes and the vertical movements of the left eye. Calibration (10° eccentricity) and EOG data were registered in total darkness, the subject following an illuminated target (Nicolet LT 100 lightbar stimulator). The Pathfinder II provided linear recordings over a range ±20°; a.c. EOG amplifiers were used, with a long time base (time constant 15.9 s) and a band width of 0.01–40 Hz. The sampling rate of the computer was 100 Hz. Only horizontal eye movements were analysed.

Random saccades (fig. 1). Patients were asked to follow as rapidly as possible 28 target jumps moving in a random amplitude sequence (6–32°), a random jump interval and a random direction. Three parameters were analysed. The saccade latency (or delay) represented the mean time (in ms) from the target jump to the start of the subsequent saccade. The saccade accuracy, expressed as a percentage of the target amplitude, was an indication of how closely the amplitude of the primary saccade followed the amplitude of the target jump. These parameters were calculated from the 28 saccades. An analysed data graph displayed the peak velocity against the amplitude of the 28 saccades (see fig. 1). A quantitative indication as to how well peak velocity versus saccade amplitude compared with normal was given by the peak velocity performance index. For that purpose, the mean amplitude and mean peak velocity were computed for the 5 largest saccades to each side. The peak velocity performance index gave the ratio between this calculated mean velocity and the mean velocity for a standard group of normal subjects calculated by Baloh et al. (1975). Thus an ideal normal subject is assumed to have a mean velocity equal to this theoretical mean value and a peak velocity performance index equal to 1. If saccade velocity versus amplitude is impaired, the peak velocity performance index will fall below unity.

Smooth pursuit tracking. The stimulus was a sinusoidally moving target that the subjects were asked
FIG. 1. Examples of random saccade tests. A, normal control. An analysed data graph displays the peak velocity versus the amplitude of the 28 saccades. The graph is separated into left moving saccades on the left, and right moving saccades on the right. The dotted curved lines represent the mean ± 2 SD of a group of normal subjects (Baloh et al., 1975). The statistical results (delay, accuracy and performance index) are displayed below this graph and above the graph displaying eye position versus time. B, parkinsonian patient (stage IV of Hoehn and Yahr). Note that the delay (saccade latency) is increased, the accuracy (saccade amplitude) is decreased and that the peak velocity versus the amplitude of the saccades is markedly reduced. In the first graph many points are situated under the dotted lines (which represent the theoretical mean ± 2 SD); the performance velocity index is considerably below unity. This abnormality can also be seen in the graph displaying eye position versus time with an unequivocal reduction of the slope of the saccades. Although no histological proof is available to confirm the diagnosis of idiopathic Parkinson's disease, the long clinical history, the absence of a defect in vertical eye movements, the absence of dementia, and the efficacy of L-DOPA exclude other diagnoses (such as progressive supranuclear palsy) which could have been suggested by this graph.
Fig. 2. Examples of smooth pursuit tests (40 deg/s, 0.4 Hz). A, normal control. An analysed data graph displays eye velocity versus time. The statistical results for magnitude (peak eye velocity) and THD are displayed below this graph and above that for eye position versus time. B, parkinsonian patient (stage IV of Hoehn and Yahr). Note that the smooth pursuit eye velocity is markedly decreased. This explains the low value for peak eye velocity at the frequency of the stimulus (magnitude) and the high THD which illustrate the patient's difficulty in matching his eye movement correctly with that of the target. This difficulty makes him to catch up the target with small saccades, explaining the saccadic or cogwheel aspect of the pursuit observed on the graph displaying eye position versus time.
to follow as closely as possible (fig. 2). Two series were studied with an amplitude of 32°, the first with a 0.2 Hz frequency and a 20 deg/s velocity (4 cycles) and the second with a 0.4 Hz frequency and a 40 deg/s velocity (8 cycles). Saccades which occurred during pursuit were detected and removed according to Baloh et al. (1980). Analysed results (obtained from all cycles) included peak eye velocity at the frequency of the stimulus and total harmonic distortion (THD), which provided an index of data integrity (a THD > 15% indicates either an eye movement signal containing excessive artefacts or that the patient's eye movement failed to match target movement).

Optokinetic nystagmus. OKN was obtained from a constant velocity pattern of 3 rows of lights produced by the light bar (80x8° viewing field, velocity 40 deg/s, target spacing 10.24") in either a right or left direction. Patients were instructed to look at the middle row of lights, to watch them as they passed the centre, to count them but not to follow them (stare OKN). After some 30 s of stimulation, OKN was recorded for analysis during 20 s. The statistical results obtained were the maximal slow component velocity and the mean slow component velocity (mean velocity of all the accepted slow components) in each direction and in both directions taken together.

Vestibulo-ocular system

Fixation was explored in darkness by asking subjects to fixate a target on the light bar at 30° to the left or right of the centre. Vestibular nystagmus was recorded while subjects were turning on a rotating chair with sinusoidal stimulation (0.05 Hz, 60 deg/s maximal velocity). Three different situations were tested: (1) in darkness for 80 s when arousal was maintained by continuous mental activation (fig. 3); (2) in light while asking the subjects to fixate a target moving with the chair during 30 s (in order to quantify the visuovestibular suppression); and (3) in darkness while asking the subjects to imagine during 30 s that they were fixing the target exactly as they had done in the light (in order to quantify their ability to suppress voluntarily their vestibulo-ocular reflex by imagination). The analysed data graph displayed the slow component velocity against time and the average eye velocity of each beat of nystagmus; the mean maximal slow component velocity of the nystagmus for each direction was then calculated manually. Its ratio to the maximal velocity of the chair indicated the gain of right and left vestibulo-ocular reflex (VOR).

Experimental protocol and L-DOPA test

If patients were on treatment, all antiparkinsonian drugs (L-DOPA, anticholinergics, dopaminergic agonists) were stopped for at least 2 days. This delay was sufficient for the reappearance of extrapyramidal symptoms. The investigation began at 9 a.m. on the third day of drug withdrawal with the subject fasting, and consisted of an initial motor evaluation (including a Hoehn and Yahr rating and a URSP assessment) and the initial EOG. Controls did not undergo motor evaluation.

After this 'drug-free' study, 22 patients were submitted to an L-DOPA test; 12 had never previously been treated, and in 10 treatment had usually been with L-DOPA. The L-DOPA test has already been described (Esteguy et al., 1985; Rascol et al., 1988). Briefly, after the 2 days of antiparkinsonian drug withdrawal, a single 200 mg dose of L-DOPA (with 50 mg benserazide) was given orally; 90 mm later, when motor improvement was maximal, a new motor evaluation and a new EOG were performed in order to quantify the L-DOPA effect. Each new assessment with the URSP motor score and EOG was made blind, i.e., without the previous rating scale score and EOG available to the physician. Ten other patients underwent exactly the same protocol but received a placebo instead of L-DOPA in order to evaluate the test-retest effect.

Analysis

Parkinsonian patients, mildly affected patients (group A) and controls were compared by the Behrens-Fisher test because the variances in the control and patient groups differed markedly (Tables 2, 3). For smaller groups, nonparametric tests were used: the Mann-Whitney U test to compare mildly (group A) and severely (group B) affected patients (Table 3) and to compare the changes in EOG data observed after L-DOPA with the changes observed after placebo (Table 4). The Wilcoxon sign rank test was used to
TABLE 2. COMPARISON OF THE ELECTROOCULOGRAPHIC DATA BETWEEN 45 'DRUG-FREE' PARKINSONIAN PATIENTS (NEVER TREATED, OR DEPRIVED OF TREATMENT FOR 2 DAYS) AND 30 CONTROLS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls (n = 30)</th>
<th>Parkinsonians (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccades</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>168 ± 17</td>
<td>213 ± 49***</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>98 ± 8</td>
<td>86 ± 11***</td>
</tr>
<tr>
<td>Velocity performance</td>
<td>1.1 ± 0.1</td>
<td>0.9 ± 0.2***</td>
</tr>
<tr>
<td>Pursuit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 deg/s peak V (deg/s)</td>
<td>20 ± 1</td>
<td>18 ± 3***</td>
</tr>
<tr>
<td>THD (%)</td>
<td>11 ± 4</td>
<td>16 ± 9***</td>
</tr>
<tr>
<td>40 deg/s peak V (deg/s)</td>
<td>38 ± 4</td>
<td>33 ± 6***</td>
</tr>
<tr>
<td>THD (%)</td>
<td>12 ± 3</td>
<td>18 ± 7***</td>
</tr>
<tr>
<td>OKN (40 deg/s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>V max (deg/s)</td>
<td>35 ± 7</td>
<td>30 ± 7**</td>
</tr>
<tr>
<td>Mean velocity (deg/s)</td>
<td>33 ± 6</td>
<td>24 ± 7***</td>
</tr>
<tr>
<td>VOR gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darkness</td>
<td>0.6 ± 0.1</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Visual suppression</td>
<td>0.0 ± 0.0</td>
<td>0.1 ± 0.2</td>
</tr>
<tr>
<td>Imagination suppression</td>
<td>0.3 ± 0.1</td>
<td>0.4 ± 0.1***</td>
</tr>
</tbody>
</table>

Saccades, smooth pursuit, optokinetic nystagmus (OKN) and imagination suppression of vestibulo-ocular reflex (VOR) parameters were significantly altered in patients; *** = P < 0.01, ** = P < 0.01, * = P < 0.005, Behrens-Fisher test with Holm correction factor. Visual suppression of VOR gain was abnormal in 13 patients, but VOR gain in darkness remained unchanged. Saccade accuracy is expressed as a percentage of the target amplitude (hypometria = accuracy < 100%) and saccade velocity performance (index of peak velocity versus amplitude) in arbitrary units (theoretical normal = 1). V max = maximal OKN velocity.

Comparisons between ‘drug-free’ parkinsonian patients and controls

Table 2 shows the main quantitative results of the different horizontal oculographic data observed in controls and parkinsonian patients. Results are expressed as mean values ± SD.

All the three saccade parameters (fig. 1) were significantly altered in parkinsonian
Fig. 3. Examples of vestibular nystagmus tests in darkness (0.05 Hz, 60 deg/s maximal velocity, 80 s). The analysed data graph displays the slow component velocity versus time. Each asterisk on the graph represents the average eye velocity of the slow component of each beat of nystagmus. If the slow component contains an artefact such as eye blink, it is not included in the statistical analysis or the graph. The manually calculated VOR gain is normal (0.6) in both subject A (normal control) and subject B (parkinsonian patient, stage IV of Hoehn and Yahr).
TABLE 3. EOG RESULTS FOR CONTROLS AND MILDLY (GROUP A) AND SEVERELY (GROUP B) AFFECTED PARKINSONIAN PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 30)</td>
<td>(n = 29)</td>
<td>(n = 16)</td>
</tr>
<tr>
<td>Saccades</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>168 ± 17</td>
<td>193 ± 40***</td>
<td>248 ± 44+++</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>98 ± 8</td>
<td>87 ± 11***</td>
<td>83 ± 11</td>
</tr>
<tr>
<td>Velocity performance</td>
<td>1.1 ± 0.1</td>
<td>1.0 ± 0.1***</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>Pursuit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 deg/s peak V (deg/s)</td>
<td>20 ± 4</td>
<td>19 ± 3</td>
<td>17 ± 3</td>
</tr>
<tr>
<td>THD (%)</td>
<td>11 ± 4</td>
<td>15 ± 10</td>
<td>19 ± 7</td>
</tr>
<tr>
<td>40 deg/s peak V (deg/s)</td>
<td>38 ± 4</td>
<td>35 ± 5**</td>
<td>29 ± 5+++</td>
</tr>
<tr>
<td>THD (%)</td>
<td>12 ± 3</td>
<td>16 ± 6**</td>
<td>21 ± 7</td>
</tr>
<tr>
<td>OKN (40 deg/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V max (deg/s)</td>
<td>35 ± 7</td>
<td>30 ± 6**</td>
<td>30 ± 6</td>
</tr>
<tr>
<td>Mean velocity (deg/s)</td>
<td>33 ± 6</td>
<td>25 ± 7***</td>
<td>21 ± 7</td>
</tr>
<tr>
<td>VOR gain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darkness</td>
<td>0.6 ± 0.1</td>
<td>0.6 ± 0.03</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Visual suppression</td>
<td>0.0 ± 0.0</td>
<td>0.04 ± 0.03</td>
<td>0.1 ± 0.1</td>
</tr>
<tr>
<td>Imagination suppression</td>
<td>0.3 ± 0.1</td>
<td>0.3 ± 0.2</td>
<td>0.5 ± 0.2</td>
</tr>
</tbody>
</table>

Controls and group A patients have been compared by the Behrens-Fisher test with the Holm correction factor: •** = \(P < 0.001\), ** = \(P < 0.01\); groups A and B have been compared using the Mann-Whitney U test with the Holm correction factor: + + + = \(P < 0.001\), + + = \(P < 0.01\). For definition of groups, see text and for other explanations, see footnote to Table 2.

Patients. Mean latency was increased \(P < 0.001\) with a larger intrasubject variation; reduced accuracy \(P < 0.001\), i.e., hypometria, and reduced peak velocity performance index \(P < 0.001\), i.e., slower peak velocity versus amplitude were also observed. For smooth pursuit (fig. 2), at the two target velocities (20 deg/s and 40 deg/s) peak velocity was reduced \(P < 0.001\) and THD was increased \(P < 0.01\) and \(< 0.001\), respectively). Both maximal and mean OKN velocity were significantly reduced in patients \(P < 0.01\) and \(< 0.001\), respectively).

For the VOR, no patient and no control exhibited spontaneous nystagmus, and in darkness (fig. 3), mean VOR gain was identical in patients and normal subjects. All normal subjects were able to suppress the gain of their VOR and to reduce it to values virtually at zero. On the other hand, 13 patients were unable to decrease their VOR gain to such a value. No statistical analysis of this difference was performed as VOR gain and variance for controls was zero. It is obvious, however, that several patients did not behave in the same way as the controls. For voluntary visuovestibular suppression in darkness, controls and patients were able to decrease their VOR gain in darkness while imagining a stationary target moving with the chair. This voluntary suppression was less effective than the visual one in both groups. However, in parkinsonian patients the gain of the VOR after voluntary suppression was significantly higher than that for controls \(P < 0.001\): patients were unable to suppress as well as controls.
Clinical correlations

**Correlations between EOG parameters and severity of the disease.** Two different means were used in order to determine whether the severity of oculographic abnormalities paralleled the severity of the clinical state. Patients were first divided into two groups according to the Hoehn and Yahr (1967) scale. Stages I and II (29 patients), with mild disease, formed group A; stages III and IV (16 patients), who were more severely affected, formed group B. Group A was then compared with group B (Table 3). Secondly, we looked for linear correlations between oculographic parameters and the global score of the motor examination of the URSP.

Saccade latency was more severely altered in group B than in group A \((P < 0.001)\). Smooth pursuit peak velocity was also reduced at 40 deg/s \((0.4 \text{ Hz})\) in group B compared with group A \((P < 0.01)\). However, after application of the Holm (1979) correction factor, no correlations between the global score of the URSP and oculomotor parameters were significant.

Differences between mildly affected patients (group A) and controls were also sought. As shown in Table 3, saccade latency, accuracy and peak velocity performance were significantly altered in group A \((P < 0.001)\). Smooth pursuit peak velocity was significantly reduced at 40 deg/s \((P < 0.01)\) and maximal and mean slow component velocity of OKN was also slower than in controls \((P < 0.01 \text{ and } <0.001, \text{ respectively})\).

Conversely, the VOR gain in darkness and after imaginary suppression did not significantly differ between the two groups. The visual suppression of the VOR gain was imperfect (i.e., the VOR gain was not reduced to zero by fixation) in 6 mildly affected patients.

**Correlations between EOG parameters and specific extrapyramidal symptoms.** After applying a correction factor for multiple comparisons, no significant correlation was observed between oculographic parameters and akinesia, rigidity, tremor or instability URSP scores.

**Correlations between different oculomotor data.** No significant correlation was detected between any oculomotor abnormalities.

Hemiparkinsonism

Out of the 45 parkinsonian patients of this study, 20 presented strikingly asymmetrical manifestations: 15 had pure unilateral disease (stage I of Hoehn and Yahr); 5 others, while presenting mild contralateral symptoms (considered then as stage II of Hoehn and Yahr) had predominantly unilateral symptoms and were thus included in this group. Twelve had left and 8 had right hemiparkinsonism. In these patients the asymmetry of the 3 saccade parameters was studied.

In controls, saccades showed no significant asymmetry between the two directions of horizontal gaze. We analysed the data of 20 hemiparkinsonian patients in order to compare the parameters of saccadic movements directed towards or away from the symptomatic side of the body. Saccade latency directed towards the symptomatic side
TABLE 4. EOG RESULTS IN L-DOPA TEST

<table>
<thead>
<tr>
<th></th>
<th>After placebo</th>
<th>After L-DOPA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Saccades</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>+5 ± 6</td>
<td>-8 ± 6</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>-3 ± 2</td>
<td>+8 ± 2**</td>
</tr>
<tr>
<td>Velocity performance</td>
<td>-0.1 ± 0.0</td>
<td>+0.2 ± 0.0</td>
</tr>
<tr>
<td><strong>Pursuit</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 deg/s peak V (deg/s)</td>
<td>0 ± 0</td>
<td>+1 ± 0</td>
</tr>
<tr>
<td>THD (%)</td>
<td>-3 ± 3</td>
<td>-1 ± 1</td>
</tr>
<tr>
<td>40 deg/s peak V (deg/s)</td>
<td>-1 ± 1</td>
<td>+3 ± 1</td>
</tr>
<tr>
<td>THD (%)</td>
<td>-2 ± 2</td>
<td>-2 ± 1</td>
</tr>
<tr>
<td><strong>OKN (40 deg/s)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V max (deg/s)</td>
<td>+1 ± 2</td>
<td>+1 ± 2</td>
</tr>
<tr>
<td>Mean velocity (deg/s)</td>
<td>-1 ± 2</td>
<td>+1 ± 1</td>
</tr>
<tr>
<td><strong>VOR gain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Darkness</td>
<td>-0.01 ± 0.00</td>
<td>0.00 ± 0.00</td>
</tr>
<tr>
<td>Visual suppression</td>
<td>0.01 ± 0.01</td>
<td>-0.02 ± 0.01</td>
</tr>
<tr>
<td>Imagination suppression</td>
<td>0.01 ± 0.00</td>
<td>0.00 ± 0.00</td>
</tr>
</tbody>
</table>

Comparison of the changes induced by 200 mg of L-DOPA (n = 22) and placebo (n = 10) in EOG data. Note that L-DOPA significantly improved saccade accuracy (Mann-Whitney U test with Holm correction factor, ** = P < 0.01). For other explanations, see footnote to Table 2.

was longer (196 ± 39 ms) than that directed towards the other side (182 ± 34 ms). This difference was at the limit of the significance (P < 0.02; 0.016 required after application of Holm correction factor). Saccade peak velocity performance towards the affected side was also slightly reduced, but this difference was not significant (1.0 ± 0.1 vs 1.1 ± 0.2; arbitrary units). Saccade accuracy did not differ between the two sides (89 ± 12% vs 85 ± 15%).

**L-DOPA test**

Twenty-two patients were tested before and after the ingestion of 200 mg of L-DOPA (with benserazide). All motor symptoms of the URSP motor examination improved significantly, namely global (18 ± 11 vs 9 ± 6, P < 0.001), tremor (2.1 ± 2.0 vs 0.7 ± 0.9, P < 0.001), rigidity (1.5 ± 1.0 vs 1.0 ± 0.6, P < 0.01), akinesia (10 ± 7 vs 5 ± 4, P < 0.001) and stability (0.9 ± 0.8 vs 0.3 ± 0.4, P < 0.001) scores. Ten patients were tested with exactly the same protocol but with placebo instead of L-DOPA. The URSP global score did not alter (15 ± 5 vs 17 ± 4). The same lack of effect of placebo was observed for each individual item (data not shown). As shown in Table 4, the difference induced by L-DOPA on saccade accuracy was significantly different from that induced by the placebo (P < 0.01). Saccade latency and smooth pursuit parameters were also mildly but not significantly improved. Saccade velocity performance, OKN and VOR values did not differ.
DISCUSSION

In this study, 45 carefully selected patients with idiopathic parkinsonism deprived of antiparkinsonian treatment were tested, and alterations in ocular movements were assessed quantitatively after a single oral dose of L-DOPA. Before discussing the potential role of a dopaminergic deficit in the genesis of the oculomotor abnormalities of parkinsonian patients, the possibility that these results might be caused by other differences must be addressed. Two main hypothesis should be considered.

Cognitive impairment could explain some abnormalities of ocular movement. While all patients underwent psychometric tests (Folstein minimental scale and Benton's visual retention test), we concede that a subtle neuropsychological deficit may have been overlooked. It is well known that dementia (Fletcher and Sharpe, 1986) or simply distraction (Kaufman and Abel, 1986) can alter oculographic results. However, very mildly affected parkinsonian patients in whom cognitive deficits are unlikely showed significant oculomotor abnormalities (Table 3). It must also be emphasized that VOR gain in darkness rapidly decreases in the presence of any fall in attention or vigilance. As it was normal in our patients, we assume that they did not manifest a deficit in alertness.

Although a learning effect on retesting could have improved performance in the second EOG, this hypothesis can be excluded. Several subjects, controls and patients, did not understand the instructions perfectly or did not perform optimally at first. Several series of 28 saccades and of 4 and 8 smooth pursuit cycles were then necessary before obtaining optimal cooperation. For statistical analysis we only took into account the best series: in this way, patients were equally familiar with the protocol in the first as well as in the second EOG. The absence of a test-retest or placebo effect was confirmed by performing 2 EOG examinations at 90 min intervals in parkinsonian patients who received placebo instead of L-DOPA and compared the two series of patients.

Saccadic system

We studied visually-guided (random amplitude and random jump interval target) saccades. Saccade accuracy was decreased in parkinsonian patients and latency increased. Saccade hypometria is a common finding in parkinsonians (DeJong and Melvill Jones, 1971; Melvill Jones and DeJong 1971; Shibasaki et al., 1979; Shimizu et al., 1981; White et al., 1983b; Gibson et al., 1987). Almost all published data except those of Gibson et al. (1987) also univocally indicate delayed reaction times for random (White et al., 1983b; Bronstein and Kennard, 1985; Warabi et al., 1986) as well as nonrandom (Shibasaki et al., 1979; White et al., 1983b; Bronstein and Kennard, 1985) saccades. In the present study, latencies for controls and patients were shorter than those usually reported for subjects of this age group (e.g., Sharpe and Zackon, 1987). Our results also suggest that peak velocity versus amplitude of the saccades is reduced in the patients. Such velocity decreases have been much debated in the past. Several authors have reported normal saccade velocity in parkinsonian patients (DeJong and Melvill Jones, 1971; Melvill Jones and DeJong, 1971; Teräväinen and Calne, 1980a, b; Shimizu et al., 1981; Bronstein and Kennard, 1985; Gibson et al., 1987) while others have found it to be
reduced (White et al., 1983b; Warabi et al., 1986). As we do not have histological proof of the diagnosis of idiopathic Parkinson's disease, the possibility of the inclusion of patients suffering from other diseases (such as progressive supranuclear palsy), which are known to reduce the saccade velocity, could be raised. This criticism could be applied to all previous studies on the same topic. In the present study, we carefully selected patients in order to exclude clinical diagnoses other than Parkinson's disease. Although the data were not analysed here, we recorded vertical ocular movements in order to exclude patients with vertical gaze palsy; moreover, the efficacy of L-DOPA tests and L-DOPA treatment observed in our patients would be very atypical for nonparkinsonian extrapyramidal syndromes. Thus, in our opinion, other explanations must be sought in order to explain the conflicting results between the published studies on saccade velocity in Parkinson's disease. L-DOPA had no effect on the peak velocity performance index; this suggests that differences in antiparkinsonian treatment do not account for the discrepancies between previous reports. Differences in the severity of the disease could also provide an explanation (White et al., 1983b). Some authors who reported normal values did not specify how severely affected were their patients (DeJong and Melvill Jones, 1971; Melvill Jones and DeJong, 1971; Teräväinen and Calne, 1980a, b); others studied only mildly affected patients (Bronstein and Kennard, 1985; Gibson et al., 1987). However, in the present study, saccade velocity was significantly reduced even in mildly affected patients (Table 3) and the difference in the peak velocity performance index between mildly and severely affected patients was not significant (Table 3). Parkinsonian saccades were significantly slower than those of controls but saccade velocities in patients were within the normal range (normal mean −2 SD). This has already been pointed out by White et al. (1983b); the limited differences observed may then explain some of the conflicting data. Finally, in some studies, the large age range of the subjects investigated (from 20—70 yrs; Teräväinen and Calne, 1980a, b; Shimizu et al., 1981) might also account for negative results. Ageing affects saccadic function (Warabi et al., 1984; Sharpe and Zackon, 1987). Groups of patients or controls with a large age range could thus have such a high within-group oculomotor variability that differences between the means fell short of statistical significance.

Saccade abnormalities could be related to the pathogenetic process of the underlying disease and, at least in part, to the dopaminergic deficit. Several arguments support such an assumption.

1. L-DOPA improved saccade accuracy. Improvement of saccade function by L-DOPA in parkinsonian patients was suspected at quite an early stage (Highstein et al., 1969; Corin et al., 1972). However, these pioneering works lacked quantitative assessment. In a single MPTP-treated monkey (Brooks et al., 1986) and 3 human MPTP-parkinsonian patients (Hotson et al., 1986) dopaminergic drugs improved several saccade parameters. In some idiopathic parkinsonian patients, saccade accuracy improved during 'on' phases or after chronic treatment (Gibson and Kennard, 1986; Gibson et al., 1987). Our results clearly confirm in a large group of patients that saccade accuracy is significantly improved by L-DOPA (Table 4). As was found by Gibson et al. (1987) we observed that saccade latencies tended to improve, but this change was not significant. We did not observe
alteration in saccade velocity after L-DOPA. This suggests that dopaminergic systems may not influence the different saccade parameters in the same way.

2. Alteration of saccade latency was more severe in the advanced stages of the disease. This can also be seen as an indirect argument in favour of a relationship between such ocular abnormalities and the general pathogenetic process of the disease. This correlation has already been mentioned by others (Corin et al., 1972; White et al., 1983b; Warabi et al., 1986). It is known that there is a correlation between the clinical severity of the disease and the severity of the dopaminergic cell degeneration (Marsden, 1982). The correlation between the intensity of saccade and motor impairment suggests a possible role for the dopaminergic deficit in the oculomotor syndrome. However, it is of course possible that with deterioration of the disease, other neurochemical deficiencies could account for more marked abnormalities of eye movement.

3. Very few data are available concerning oculomotor asymmetry in hemiparkinsonian patients (Carl and Wurtz, 1985; Gibson et al., 1987). In such patients the hand reaction time is reported to be slower on the neurologically more affected side (Yokochi et al., 1985). Shibasaki et al. (1979) looked for correlations between saccadic and limb parameters and showed a negative correlation between the maximal saccade velocity and the reaction time for the finger ipsilateral to the direction of the horizontal gaze; none was found with the contralateral finger. In the 20 hemiparkinsonian patients in this study, the difference between saccade latency directed towards the symptomatic hemibody and towards the unaffected side was at the limit of significance (P < 0.02). Thus it seems reasonable to suggest that asymmetric saccade abnormalities may be linked to the side of the disease. As the dopaminergic deficit is probably more severe in the striatum contralateral to the clinically affected side (Barolin et al., 1964; Perlmutter and Raichle, 1985; Martin et al., 1986), it is possible to hypothesize that part of the saccade abnormalities observed in hemiparkinsonians are related to this asymmetric dopaminergic deficit.

4. To our knowledge, very few attempts at correlation between saccade abnormalities and different cardinal symptoms of the extrapyramidal syndrome have been performed. It is often claimed that saccade abnormalities such as increased latency illustrate the akinetic component of the disease on eye movements. Teräväinen and Calne (1980a, b) noted that the presence of limb tremor was not a prerequisite for the occurrence of multiple step saccades. Warabi et al. (1986) observed that the oculomotor system was affected mainly at an advanced stage of bradykinesia. Gibson et al. (1987), comparing the latency of ocular saccades and of a 'hand saccadic test' found a significant correlation between them. Taken together, these results suggest that a link exists between ocular saccade abnormalities and limb movement parameters quantifying what is generally termed akinesia. In our 45 patients, however, no significant correlation was observed. A slight negative correlation (P < 0.05) with low r values was found between the akinesia score of the URSP and saccade latencies (r = −0.32) or saccade peak velocity performance (r = −0.34), but the use of a correction factor for multiple comparison showed that the caveat remains that these correlations were due to chance.

From these data we conclude that at least some components of saccadic eye movements
are probably under the control of the dopaminergic system. This control could be exerted in different ways.

1. It is unlikely that L-DOPA improved saccades through cognitive effects. As already mentioned, our population was selected in order to exclude demented patients; moreover, in another study, we looked for cognitive modifications induced by the L-DOPA test in parkinsonian patients and found no significant variation for several neuropsychological tests (Montastruc et al., 1987). However, some cognitive concomitants of dopamine system stimulation have been described by others (Mohr et al., 1987). In the same way, an effect of L-DOPA on the state of alertness should also be considered. In this study, it might have been expected to have led to opposite results since several patients, especially those never previously treated, complained of a tendency to drowsiness after L-DOPA ingestion.

2. Some studies have demonstrated that the latency of visual evoked potentials was longer (about 20 ms) in parkinsonian patients (Bodis-Wollner and Yahr, 1978). Moreover, several results have suggested that L-DOPA improves Ganzfeld electroretinographic findings (Jaffe et al., 1987), pattern electroretinograms (Nightingale et al., 1986) and visual evoked potentials (Bodis-Wollner and Yahr, 1978; Gawel et al., 1981; Nightingale et al., 1986; Onofrj et al., 1986). These findings may explain part of the latency alterations but are insufficient to account for the velocity and amplitude abnormalities.

3. Electrophysiological and lesion experiments have clearly demonstrated that the cortical frontal eye field is involved in the control of saccadic eye movements (Schiller et al., 1979; Goldberg and Bushnell, 1981). This area receives a dopaminergic innervation through the mesocorticolimbic pathway which is known to be impaired in Parkinson's disease (Javoy-Agid and Agid, 1980). Such a deficit at the cortical level could explain part of the genesis of the parkinsonian saccadic abnormalities and their improvement by L-DOPA.

4. Finally, as already mentioned by others (White et al., 1983b; Bronstein and Kennard, 1985), attention must be drawn to the recent experimental electrophysiological data which link the basal ganglia to the saccadic oculomotor system (for review, see Wurtz and Hikosaka, 1986). Cells of the substantia nigra pars reticulata modify their firing rate in relation to saccades towards a remembered target (Hikosaka and Wurtz, 1983) or towards a visual stimulus (Joseph and Boussaoud, 1985). This structure constitutes one of the main outputs of the basal ganglia. It is likely that the direct pathway which links this nucleus to the superior colliculus is GABAergic (Boussaoud and Joseph, 1985; Hikosaka and Wurtz, 1985). No clear GABAergic deficit has been reported in Parkinson's disease (Agid and Javoy-Agid, 1985; Kish et al., 1987). On the contrary, the degeneration of the dopaminergic nigrostriatal pathways is the most characteristic neurochemical abnormality of this disease. To understand saccadic abnormalities in parkinsonian patients, it is thus possible to suggest an influence of the nigrostriatal dopaminergic pathway on a relay of the general cerebral oculomotor loop underlying saccadic mechanisms. As reviewed by Alexander et al. (1986), the cortical areas involved in saccadic generation project to caudate nucleus. The caudate projects in turn to the pallidum and substantia nigra pars reticulata. Electrophysiological data correlate saccadic mechanisms to the
caudate (Hikosaka and Sakamoto, 1986), and it is therefore reasonable to hypothesize that this nucleus probably relays relevant information for the saccadic oculomotor loop. The deficit of saccades could then be due to a modification of the caudate relay after degeneration of its dopaminergic input.

**Smooth pursuit**

Qualitative abnormalities of smooth pursuit such as saccadic, cogwheel or stepwise movements have been described in parkinsonism for several years (Highstein et al., 1969; Corin et al., 1972; Shibasaki et al., 1979; Teräväinen and Calne, 1980a, b). We only know of two quantitative studies, both on relatively small numbers of patients (White et al., 1983b; Gibson et al., 1987). Both reported that smooth pursuit gain was reduced in Parkinson's disease. Our results clearly confirm in a large population of parkinsonian patients that smooth pursuit velocity is reduced. Severely affected patients showed worse pursuit than milder ones. Shibasaki et al. (1979) and White et al. (1983b) also noted that the more severe patients had poorer pursuit values. No correlation was found between smooth pursuit and akinesia, tremor, rigidity or instability. This was also observed by Shibasaki et al. (1979), although Gibson et al. (1987) reported a significant correlation between eye and limb smooth pursuit gain.

In 22 patients a single dose of L-DOPA failed to improve maximal smooth pursuit velocity (Table 4). The published data on this aspect are conflicting. In parkinsonian patients, Highstein et al. (1969) reported that after 5–6 weeks of L-DOPA treatment, 5 patients had fewer saccades during smooth pursuit movements. This has also recently been observed after chronic treatment in one MPTP (Hotson et al., 1986) and 8 idiopathic parkinsonian patients (Gibson et al., 1987). However, in 8 other patients, Sharpe et al. (1987) did not observe any change in smooth pursuit gain between 'off' and 'on' periods. There is virtually no information about the existence of a dopaminergic influence on smooth pursuit in animals. In 3 monkeys, haloperidol (a dopamine antagonist) induced disrupted smooth pursuit, characterized by eye fixation accompanied by some saccadic eye movements (Ando et al., 1986). Several abnormalities of smooth pursuit have also been described in men treated with neuroleptic drugs (Holzman et al., 1973; Matsue et al., 1986) but the value of these results is still debated since schizophrenia and affective disorders might in themselves influence eye tracking function (Lipton et al., 1983). Our results, at first sight, do not support any role for L-DOPA on smooth pursuit movement. Nevertheless, the statistical analysis must be discussed further. Adjustments for multiple comparisons are strict and the statistical power of the test may have been insufficient to detect any difference. Among the 12 comparisons which were performed in the analysis of the oculomotor results in the L-DOPA test and before using the Holm method, only 2 differences (namely saccade accuracy and 40 deg/s smooth pursuit peak velocity) were significant according to the Mann-Whitney U test with an alpha of 0.01. It appears that the maximal probability that such a situation occurs by random chance alone is very low, below 0.004 \(P = 1 - (1-\alpha)^n \alpha (1-\alpha)^{n-1}\), where \(\alpha\) is the arbitrary value used to protect against false positive results and \(n\) the number of independent comparisons. We thus consider that it is probably excessive to
exclude completely an effect of L-DOPA on smooth pursuit in parkinsonian patients.

Little is known about the anatomical pathways underlying smooth pursuit. It is even more difficult than for saccades to hypothesize at which level a dopaminergic control, if it does exist, could occur. The basal ganglia are not cited as putative relays for smooth pursuit pathways. The cerebellar flocculus and the parietal cortex are two brain areas which play an important role in such movement. The dopaminergic innervation of the cerebellum is extremely slight (Simon et al., 1979) but this area contains dopaminergic receptors (Bouthenet et al., 1987). To our knowledge no dopaminergic deficit has been described in parkinsonian cerebellum. An impairment of the dopaminergic control of cortical processes of smooth pursuit would then be the more likely possibility.

**Optokinetic nystagmus**

We admit that the field of the optokinetic stimulus used in this experiment was too small to test all aspects of an optokinetic response. However, it must be emphasized that during stimulation all controls experienced a circular vection sensation totally irrelevant to a simple smooth pursuit mechanism. We then explored only one partial aspect of OKN, that which is observed in animals with foveal vision and which probably uses cortical pathways considered to be common with those of smooth pursuit (Baloh et al., 1982; Waespe and Henn, 1987).

We did not find any reports giving quantitative OKN data in parkinsonian patients. Two publications included some comments about OKN in such patients; both reported intact horizontal OKN in most patients (Corin et al., 1972; Shibasaki et al., 1979). This absence of deficiency in OKN seems rather surprising since smooth pursuit is impaired in Parkinson's disease. The present results in fact suggest that the 'cortical' pathways of OKN are not spared in the disease since maximal and mean OKN velocities of 'stare OKN' were significantly reduced in the patients. The abnormalities described in the present experiment can then be attributed to the pursuit system defect. On the other hand, this protocol cannot provide information about other aspects of OKN, especially those involving 'subcortical' mechanisms.

**Horizontal vestibulo-ocular reflex**

Clinical exploration of VOR has provided conflicting data. Generally, no spontaneous nystagmus has been observed in Parkinson's disease (Shibasaki et al., 1979; Shimizu et al., 1981; Stamboulis et al., 1981; White et al., 1983a). Nevertheless, in 36 patients Reichert et al. (1982) recorded spontaneous nystagmus in 14%. We did not observe horizontal nystagmus.

**VOR gain in darkness**

In this study the gain of the VOR was similar in controls and patients. Such results lead to the conclusion that the basic three neuron reflex is intact in Parkinson's disease. Some other authors have also reached the same conclusion. Teräväinen and Calne (1980a, b) suggested that the VOR gain in their patients was normal but they did not monitor
the exact position of the chair; their opinion was thus not demonstrated objectively. Likewise, Shimizu et al. (1981) reported that the gaze of their patients was very stable during head movements, offering the hypothesis that the VOR was adequate. These remarks are in agreement with the present data and with the fact that no peripheral vestibular damage or morphological changes in the brainstem VOR arc have been reported in Parkinson's disease.

White et al. (1983a), on the other hand, observed a decreased VOR gain in advanced cases although not in mild ones. Our results do not confirm this. Two comments may help to explain this difference. First, out of the 6 severely affected patients of White et al., 4 had received anticholinergic drugs. Such medications have been shown to reduce vestibular nystagmus significantly (Pyykkö et al., 1984, 1985). Our patients were free of such treatment. Secondly, White et al. (1988a) measured the VOR gain at 5 frequencies of head motion (from 0.3 to 3.0 Hz), whereas we only measured it at a single low frequency.

Visual vestibular interaction

Thirteen of our patients, generally the more severely affected, could not totally suppress their VOR by fixation. The ability to decrease the VOR gain by fixation is impaired in some parkinsonians, as has already been observed by others (Halmagyi and Gresty, 1979; Teräväinen and Calne, 1980b). White et al. (1983a) also reported impaired visual suppression of the VOR. However, they found that their severely affected patients were not only less able to decrease the gain but paradoxically increased it. We did not observe such a phenomenon. Our data can be explained by the existence of a relationship between smooth pursuit and VOR suppression (Sharpe and Lo, 1981). We were not able to demonstrate a significant correlation between the impairment of smooth pursuit and the alteration of the VOR gain suppression since we did not measure pursuit and VOR suppression at the same target or chair velocities, frequencies and amplitudes.

Voluntary control of the VOR

Controls and patients suppressed VOR gain less effectively by voluntary control (imaginary moving target) than by visual fixation. The patients performed significantly less well than controls. This was previously noted by White et al. (1983a), but in only 7 patients. As did White et al., we observed in our patients that mildly affected subjects were able to exert a voluntary (nonvisual) control over the VOR. However, although the mean VOR gain after imaginary suppression was higher in our more severely affected patients (group B), the difference was not significant. McKinley and Peterson (1985) suggested that voluntary control of the VOR does not use the smooth pursuit pathways. Some authors believe that spatial disorientation is an early symptom of Parkinson's diseases (Hovestadt et al., 1987); it is then possible that this deficit may explain the abnormal voluntary suppression of VOR gain (White et al., 1983a). However, one must be cautious before accepting this hypothesis since the idea of a generalized visuospatial deficit in Parkinson's disease has been challenged (Brown and Marsden, 1986).
A cerebral cortical loop has been proposed to control the VOR (Sharpe and Lo, 1981). An alteration in this loop could explain the ineffective control of VOR. However, it is not possible to confirm the existence of dopaminergic control of the VOR since the L-DOPA test remained negative in all situations explored. The neuropharmacology of vestibular function is poorly known (Zee, 1985). Its relationships with dopaminergic systems are virtually unexplored. In monkeys, Keller and Smith (1983) observed that depletion of catecholamines with 6-hydroxydopamine inhibited the adaptative responses that normally act to adjust the amplitude of the VOR. Nevertheless, this adaptation is a long-term mechanism, different from those that we studied.

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