ABNORMALITIES OF NONVISUALLY-GUIDED EYE MOVEMENTS IN PARKINSON’S DISEASE

by TREVOR J. CRAWFORD, LESLIE HENDERSON and CHRISTOPHER KENNARD

(From the Department of Neurology, The London Hospital, London, and Department of Psychology, Hatfield Polytechnic, Hatfield, Herts, UK)

SUMMARY

Rapid eye movements (saccades) were examined in 7 patients with idiopathic Parkinson’s disease (PD) and a matched group of normal control subjects. The effect of instructional and stimulus conditions used to elicit saccades was examined using 3 experimental paradigms. Eye movements directly elicited by a novel peripheral target were unimpaired in patients with PD as compared with control subjects. Saccades to a remembered target location, however, were dysmetric in the PD group and showed a characteristic multistep pattern. The PD impairment was not caused by a loss of information on target location since their final eye position was close to the target at all eccentricities. Peak velocity, duration, and latency did not distinguish between PD patients and controls. These results support the view that for saccades which are not directly elicited by a visual target there is a neural pathway that can be distinguished from structures involved in the generation of visually elicited (or ‘reflexive’) saccades. The finding that in PD saccades to a remembered target are selectively impaired suggests that structures in the basal ganglia play a crucial role in this alternative pathway.

INTRODUCTION

In recent years there has been converging evidence regarding the role of the basal ganglia in motor behaviour. It has been shown from a number of perspectives that pathology of the basal ganglia leads to impairment in the control of movements, particularly in tasks with reduced visual or environmental information for eliciting or guiding movement.

It is known that the basal ganglia not only process visual information (e.g., Caan et al., 1984) but many cells in the caudate nucleus and globus pallidus are selective for movements that are executed in response to a visual stimulus (Aldridge et al., 1980). In recent animal neuropharmacological studies, Hikosaka and Wurtz (1985a, b) and Gelissen and Cools (1987) found that the substantia nigra, pars reticulata to superior colliculus pathway plays a crucial role in the generation of nonvisually-guided movements. In clinical studies of patients with Parkinson’s disease (PD) it has been shown that temporary deprivation of sight of the target during a manual tracking task severely compromises their performance. Once the target is restored performance improves substantially (Flowers, 1978; Cooke and Brown, 1979; Stern et al., 1983). These studies...
suggest that the extent to which a movement is visually guided (or utilizes external references) is one important dimension in the general organization of movement. However, there is no adequate model of the neural pathways involved in the control of different categories of limb movements. Recent eye movement research has begun to address this issue.

There are a number of different ways in which rapid eye movements (saccades) can be used to foveate a target. Human saccadic eye movements have therefore been studied with a number of different target paradigms in an attempt to elucidate the contribution of specific neural centres to the generation of different types of saccades. In the most commonly used saccadic paradigm, a saccade is triggered 'reflexively' to the onset of a peripheral target. Other paradigms require a more 'volitional' element in the saccade generation. For example, in the 'antisaccade' target paradigm saccades are required which are of the same amplitude but in a direction opposite to the target. In the 'remembered' target paradigm a saccade is summoned to the location where a target had previously been briefly present.

It is becoming evident from studies which have used these target paradigms that the extent to which cortical and midbrain oculomotor centres contribute to the control of saccadic eye movements depends crucially on the stimulus configuration and task specification used to elicit eye movements. Frontal lesions produce impairments of antitarget and remembered target saccades, while reflexive saccades are unimpaired (Guitton et al., 1985; Deng et al., 1986). In Huntington's disease, a disorder affecting the basal ganglia, there is an impairment both of remembered saccades and the ability to inhibit saccades in the presence of a distraction target (Leigh et al., 1983; Lasker et al., 1987).

In the other major clinical disorder of the basal ganglia, Parkinson's disease, a number of studies have reported an impairment in saccadic eye movements (DeJong and Melvill Jones, 1971; Melvill Jones and DeJong, 1971; Corin et al., 1972; Shibasaki et al., 1979; Teräväinen and Calne, 1980. White et al., 1983), but there are disagreements on the extent of the dysfunction. In mildly affected patients (Gibson et al., 1987) there is remarkably little evidence of any impairment in reflexive saccades. However, in certain other paradigms eye movement abnormalities may be more clearly identified. For example, Bronstein and Kennard (1985) found that patients with PD, when compared with normal subjects, are less able to anticipate a regular target step and make a predictive saccade. It may be that this particular difficulty is a manifestation of a more general impairment in generating nonvisually-driven saccadic eye movements. A recent study has shown that under some circumstances patients with PD can in fact produce anticipatory saccades; however, such saccades are considerably more hypometric than those of control subjects (Crawford et al., 1989). Moreover, Carl and Wurtz (1985) have presented a brief abstract reporting that in 3 hemiparkinsonian subjects saccadic velocities for remembered saccades were diminished, but only when directed contralateral to the impaired side.

In the present investigation we compared reflexive saccades with saccades to remembered target locations in mild to moderately affected patients. We reasoned that
if the basal ganglia are particularly important in the processing of nonreflexive saccades in the absence of visual feedback, then parkinsonians should show abnormalities in the generation of saccades of this type. We therefore conducted a study of saccadic eye movements in PD under a number of visual target conditions. The nonvisually-guided task was similar to the remembered (REM) target task used in animal studies (Hikosaka and Wurtz, 1985a, b), while the visually-guided task used the standard procedure for eliciting reflexive saccades to random target steps. There was a possibility that any parkinsonian saccadic impairment in the REM task was due to an incidental property of the stimulus configuration in the REM task. In this task the peripheral target is exposed while the subject is still fixating a central target. Previous studies have shown that when 2 targets are displayed concurrently in a visual hemifield, a saccade is directed to an intermediate position between the 2 targets (i.e., towards the apparent 'centre of gravity'; see Findlay, 1982, and Findlay and Crawford, 1983). Although the 'centre of gravity' effect is usually demonstrated when both targets are presented to one side of the vertical meridian, it is possible that this mechanism could be operating in the REM task. We therefore included a control paradigm to examine this possibility by using a temporal target overlap (OLP) condition.

**MATERIAL AND METHODS**

**Subjects**

Seven PD patients (4 females, 3 males), mean age 61 (range 52—71) yrs, agreed to take part in this study. The control group consisted of 7 age-matched subjects (4 females, 3 males; mean age 63, range 53—72 yrs), none of whom had known neurological or visual impairment. No control subject was taking psychotropic medication. The parkinsonians were assessed on the Webster (1968), Hoehn and Yahr (1967) and the minimental state dementia scale. The clinical ratings of the PD patients are shown in Table 1. None of our patients showed signs of dementia and they were all receiving their normal medication (L-DOPA or bromocriptine) at the time of testing.

**Eye movement recording and target paradigms**

Eye movements were recorded by an infrared scleral reflection device (ACS EM130). The frequency range was flat to 80 Hz and the system was linear over ±15° with a resolution of 15 min arc. Eye position was differentiated electronically (3 dB point, 60 Hz) to obtain eye velocity. Peak velocity was therefore measured at the point of maximum analogue output during the saccade. The stimulus and eye movement data were recorded on a Mingograf chart recorder, which had a frequency response greater than 200 Hz,
and on analogue tape. Subjects were seated 150 cm from the target array. Nine green LED targets, each of which subtended 0.25°, were located at 3.75° intervals from the centre position out to +15° and −15° in the periphery. The target paradigms were controlled by an Apple II+ microcomputer. Targets were presented in a randomized and counterbalanced design such that each of the 8 targets was presented 6 times. The experiments were conducted in the dark. Head movements were restrained by a head support with an adjustable head band. Each subject was tested in three conditions: reflexive random (RAN), remembered target (REM), and temporal overlap (OLP) conditions. These trial formats are shown in fig. 1.

In the visually-guided RAN condition a trial commenced with the onset of the centre LED. After a period of 1 s this LED was turned off and replaced by 1 of the 8 peripheral target LEDs selected at random; 1 s later the target LED was turned off and the centre LED reappeared. The subjects were asked to move their eyes quickly and accurately to whichever peripheral LED came on.

The second visually-guided condition, OLP, was very similar to that of RAN (see fig. 1) with the addition that a temporal centre-peripheral target overlap was introduced. A trial commenced with the onset of a centre fixation LED as in the RAN condition. After 1 s, 1 of the 8 peripheral LEDs was illuminated for a period of 1 s. At the same time the central fixation LED remained on for a further 500 ms; 2 LEDs were thus visible for this period. As in the RAN condition, subjects were asked to move their eyes quickly and accurately to the peripheral target as soon as it appeared.

In the middle section of fig. 1 the sequence of events in the REM condition is shown. The total duration of the centre LED from trial onset was 1500 ms, and after 800 ms a peripheral target was presented for 200 ms. Subjects were instructed to maintain fixation at the centre and not to move their eyes towards the peripheral LED until the centre LED went off 500 ms later. The offset of the centre LED, which occurred simultaneously with a 200 ms tone from a centrally presented tone generator, was the cue to make a saccade.
to the location where the target had appeared. Subjects received a block of practice trials to ensure that they fully understood the object of the test; 48 trials of each paradigm were presented.

Primary saccade data were digitized from the chart records by hand using a digitizing tablet on a Tektronix 4052 processor with a spatial resolution of 0.01 inch. Measurements of amplitude, peak velocity, duration, latency and accuracy were extracted from the data. The identification and rejection of movement artefacts introduced by blinks and head movement was achieved by visual inspection of each saccade.

Two measures of the accuracy of the primary saccade were calculated from the saccade gain (saccade amplitude/target amplitude) of each saccade. The mean gain provided a measure of constant error; that is, the overall tendency towards undershoot or overshoot of the target. A gain of unity therefore denotes perfect accuracy; gains below and above unity represent undershoot and overshoot, respectively. The SD of a subject's gain values within a condition expressed variable error: that is, the randomly varying component in the subject’s responses. Statistical analyses were performed using ANOVA and Student's t test.

RESULTS

Fig. 2 shows the distribution of saccade latencies in the REM task. It is evident that the proportion of saccades preceding the movement cue for a saccade (i.e., the offset of the fixation target) is no different for PD patients and controls. In both groups on approximately 30% of the trials, saccades occurred before the movement cue. These early saccades were analysed separately in the subsequent analyses.

There was a significant effect of the type of task on saccade latencies (F(2,24) = 12.46, P < 0.01). The group factor (PD vs Controls) was not significant, nor was there a significant group by task interaction, showing that the subject group factor was not differentially affected by the target condition. PD patients (t = 2.42, P < 0.05) and controls (t = 2.85, P < 0.05) produced longer saccade latencies in the REM task (fig. 3). Although PDs appear to have a faster mean reaction time in the REM task compared with the controls, this was not statistically significant (P(t) = 0.28).

Fig. 2. Histograms showing the distribution of saccadic latencies in the remembered (REM) target paradigm. A, PD patients; B, controls.
TABLE 2. MEAN SACCADIC GAIN (SACCADE AMPLITUDE/TARGET AMPLITUDE)

<table>
<thead>
<tr>
<th>PD patients</th>
<th>RAN*</th>
<th>OLP*</th>
<th>REM*</th>
<th>Early REM*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.15</td>
<td>1.16</td>
<td>1.19</td>
<td>0.88</td>
</tr>
<tr>
<td>2</td>
<td>0.94</td>
<td>0.92</td>
<td>0.67</td>
<td>0.79</td>
</tr>
<tr>
<td>3</td>
<td>0.97</td>
<td>0.98</td>
<td>0.75</td>
<td>0.90</td>
</tr>
<tr>
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<td>0.89</td>
<td>0.95</td>
<td>0.82</td>
<td>0.63</td>
</tr>
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<td>5</td>
<td>0.98</td>
<td>0.98</td>
<td>0.77</td>
<td>0.58</td>
</tr>
<tr>
<td>6</td>
<td>0.92</td>
<td>0.93</td>
<td>0.90</td>
<td>0.72</td>
</tr>
<tr>
<td>7</td>
<td>1.14</td>
<td>1.03</td>
<td>0.90</td>
<td>1.22</td>
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<tr>
<td>Mean</td>
<td>1.0</td>
<td>0.99</td>
<td>0.85</td>
<td>0.81</td>
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<table>
<thead>
<tr>
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<th>RAN*</th>
<th>OLP*</th>
<th>REM*</th>
<th>Early REM*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.92</td>
<td>0.96</td>
<td>0.91</td>
<td>0.87</td>
</tr>
<tr>
<td>2</td>
<td>0.99</td>
<td>0.89</td>
<td>0.86</td>
<td>0.81</td>
</tr>
<tr>
<td>3</td>
<td>0.83</td>
<td>0.86</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.03</td>
<td>0.89</td>
<td>0.85</td>
<td>1.05</td>
</tr>
<tr>
<td>5</td>
<td>0.84</td>
<td>0.81</td>
<td>0.98</td>
<td>0.97</td>
</tr>
<tr>
<td>6</td>
<td>0.92</td>
<td>0.92</td>
<td>0.88</td>
<td>0.83</td>
</tr>
<tr>
<td>7</td>
<td>1.10</td>
<td>1.14</td>
<td>0.89</td>
<td>1.07</td>
</tr>
<tr>
<td>Mean</td>
<td>0.95</td>
<td>0.92</td>
<td>0.91</td>
<td>0.93</td>
</tr>
</tbody>
</table>

* For explanation of abbreviations, see text.

The mean gains were entered into a two-way ANOVA with groups (PD vs Controls) and target conditions (REM, OLP and REM) as factors. The main effect of conditions was significant (F(2,24) = 5.45, P < 0.05). Neither the group factor nor its interaction with conditions was significant. These data are displayed in Table 2, from which it can be seen that the effect of conditions takes the form of hypometric responses to the target in the REM condition. The overall difference between the RAN and REM conditions is reliable (t = 2.44, P < 0.05). Although the PD patients showed a tendency to greater undershoot in the REM condition, this did not reach significance.

Table 2 also shows in the REM condition the mean gain for saccades that preceded the movement cue (see fig. 2). These values show that our elimination of trials where there is a failure to inhibit early saccades is conservative. Interestingly enough, these early saccades are as hypometric overall as those that follow the cue and the tendency towards greater hypometria in the PD group is more marked.

The variable error component was also subjected to a two-way ANOVA. The effect of conditions was again significant (F(2,24) = 11.41, P < 0.01). While there was no overall effect of groups a significant interaction between group and conditions (F(2,24) = 4.87, P < 0.05) indicated that the inaccuracy evident in the REM condition was greater in the PD group. Whereas the difference between groups was not significant in the RAN condition, it was reliable in the REM condition (t = 1.86, P < 0.05). This selective effect of the REM task on the PD patients is shown in fig. 4. As with saccade gain, a separate analysis of the early saccades in the REM condition revealed the same pattern, with variable error greater in the PD early saccades (mean 0.33) than in the controls (mean 0.23).
Examination of the two error coefficients for the OLP condition shows clearly that we can reject the hypothesis that inaccuracy in the REM condition is simply due to the simultaneous presence of the 2 stimuli when the target location is specified. For neither type of error does the RAN condition differ significantly from the OLP.

The mean gains are shown for the two groups at each target eccentricity in Table 3. The tendency for PD patients to exhibit a greater impairment in saccade accuracy is not systematically qualified by target amplitude. It is particularly notable that the tendency towards a greater REM deficit is not confined to the larger target amplitudes.
TABLE 3. MEAN SACCADIC GAIN AT EACH TARGET AMPLITUDE

<table>
<thead>
<tr>
<th>Target amplitude (deg)</th>
<th>3.75</th>
<th>7.5</th>
<th>11.25</th>
<th>15.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAN*</td>
<td>1.07</td>
<td>0.99</td>
<td>0.97</td>
<td>0.88</td>
</tr>
<tr>
<td>REM</td>
<td>0.93</td>
<td>0.79</td>
<td>0.89</td>
<td>0.84</td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RAN</td>
<td>1.06</td>
<td>0.90</td>
<td>0.91</td>
<td>0.90</td>
</tr>
<tr>
<td>REM</td>
<td>0.95</td>
<td>0.86</td>
<td>0.95</td>
<td>0.88</td>
</tr>
</tbody>
</table>

* For explanation of abbreviations, see text.

Fig. 5 illustrates examples of parkinsonian saccades in the REM task. These examples show that inaccurate primary saccades frequently take the form of a markedly undershooting saccade followed by a sequence of multistepping saccades continuing in the same direction. One feature of note is the short latency of these secondary saccades. Intersaccadic intervals of less than 100 ms were found in 48% of the secondary saccades of this patient. Brief intersaccadic intervals have also been reported by Teräväinen and Calne (1980), who observed intervals as short as 20 ms. The short intersaccadic intervals of our patients were in the range of 50 to 100 ms.

A response on a given trial was classed as a multiple saccade if there were at least 3 components, or 2 components with the primary saccade less than half the amplitude.
of the final eye position. An ANOVA revealed a main effect of group with PD patients showing many more multiple saccades ($F(2,24) = 9.852, P < 0.01$). There was a significant main effect of task ($F(2,24) = 31.874, P < 0.01$), principally due to the increased incidence of multiple saccades in the REM condition. Furthermore, there was a reliable group by task interaction ($F(2,24) = 8.4089, P < 0.01$), which appeared to be due to the larger effect of the REM condition on the PD patients. The pairwise t test analyses of the incidence of multiple saccades showed that the PD patients produced far more of such saccades in the REM condition ($P < 0.001$). Although controls also generated more multiple saccades in this condition ($P < 0.05$), the effect was significantly larger in the PD patients ($P < 0.01$; see fig. 6).

In many cases these multiple saccades succeeded in carrying the eye close to the target position. Thus despite the hypometria of the primary saccade, the secondary saccades enable the eye to reach the correct target position. Fig. 7 shows the mean final eye positions in relation to the target eccentricities. In the REM condition there was no reliable difference between the PD and control groups in final eye position. The mean final eye positions of both PD patients and controls lay slightly beyond the target, with the exception of the controls at $15^\circ$, where the mean was $14.6^\circ$. The parkinsonian selective abnormality with REM targets is therefore not due to a selective loss of spatial information about the target position.

Since it is well known that saccadic velocity is an increasing function of amplitude a best-fit curve of the form $Y = A + B \times \log(X)$, where $A$ and $B$ are coefficients (the intercept and slope) and $X$ and $Y$ represent amplitude and velocity, respectively, was calculated individually for each subject for both the RAN and REM conditions. Saccadic velocities at 3 amplitudes were then extracted from these curves ($5^\circ$, $10^\circ$ and $15^\circ$) and the velocities subjected to a three-way ANOVA (Group $\times$ Task $\times$ Amplitude). These data are shown in Table 4. There was a significant effect of saccade amplitude ($F(2,24) = 331.3, P = 0.01$), confirming that saccade velocity increased with amplitude. There
was also a significant effect of task \((F = 4.72, P < 0.05)\) on saccade velocities but no interaction with saccade amplitude or subject group. This effect of the saccade task and the absence of an interaction with the group factor showed that the lower velocities in the REM task applied both to PD patients and the controls.

**DISCUSSION**

The results of this study show that patients with PD have a specific impairment in the generation of saccades to remembered targets. The parameters which most clearly revealed this deficit were the accuracy of the primary saccade and the incidence of multiple

**TABLE 4. MEAN VELOCITIES (DEG/s) AND SDs (IN BRACKETS) IN REM AND RAN TASKS**

<table>
<thead>
<tr>
<th>Saccade amplitude (deg)</th>
<th>RAN*</th>
<th>REM*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>PD patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>235</td>
<td>330</td>
</tr>
<tr>
<td>(21)</td>
<td>(29)</td>
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<td>246</td>
<td>340</td>
<td>395</td>
</tr>
<tr>
<td>(35)</td>
<td>(31)</td>
<td>(30)</td>
</tr>
</tbody>
</table>

* For explanation of abbreviations, see text.
saccades. Interestingly, in other saccadic tasks which show a parkinsonian deficit, dysmetria is also a major feature (DeJong and Melvill Jones, 1971; Teräväinen and Calne, 1980). Patients with Huntington’s disease also similarly generate inaccurate saccades to remembered targets (Lasker et al., 1987). Moreover, the nature of this deficit is comparable to that found in ballistic limb aiming movements in both human (Flowers, 1978; Hallett and Khoshbin, 1980) and animal (Caan and Stein, 1979) studies.

One possible interpretation of this parkinsonian selective deficit in the REM condition is that the increased inaccuracy stems from a decay of spatial information (i.e., defective memory) about the target location; this would yield a false estimation of target amplitude. We believe that this hypothesis can be rejected on the grounds that the corrective saccades in PD following the initial saccadic error resulted in the final eye position approximating to that of the target position and do not differ from the final eye position of the controls.

Another account of the deficit found in the REM condition which can be rejected is that the hypometric primary saccade is due to the simultaneous appearance of a target and fixation stimulus (e.g., the ‘centre of gravity’ effect). This characteristic is shared by the OLP task in which no deficit was found in either group.

In the present study the REM paradigm produced effects on both saccadic velocity and latency, which showed no consistent difference between PD patients and controls. Our findings that normal subjects, as well as PD patients, show overall reduced velocities in REM saccades, is consistent with recent results (Smit et al., 1987) using a similar paradigm in normal subjects. Whether time-based measures such as latency and peak velocity are found to be abnormal in PD may depend on other factors such as patient selection and experimental conditions.

The suggestion that the impaired accuracy of parkinsonian saccades to a remembered target is a selective deficit requires the following qualifications. First, the finding that conventional RAN saccades are of normal accuracy in PD may hold only for relatively mildly impaired or stably medicated patients. In advanced disease where the underlying pathology is less circumscribed, it may be more difficult to detect selective deficits. Secondly, the reliance of PD patients on a target that directly elicits the saccade is not confined to random steps since we have also shown impaired accuracy for predictive saccades in PD (Crawford et al., 1989; see also DeJong and Melvill Jones, 1971; White et al., 1983).

We now turn to consider, in a wider context, the source of this selective difficulty. Two factors may be relevant to the interpretation of this deficit. First, in a wide range of tasks PD patients perform better when visual feedback can be used to control their motor output (see Flowers, 1978; Cooke and Brown, 1979; Stern et al., 1983). A simple example of this phenomenon was highlighted by Hore et al. (1977), commenting on Martin’s (1967) clinical observations: ‘In one test for motor defects, patients were asked to reach out with their arm at shoulder height and touch alternately the tips of the examiner’s two forefingers which were held about a foot apart. With their eyes open the patients continued to perform well for several minutes . . . but if after the first movements he closes his eyes, the hand almost immediately falls away and the movement peters out.’ It is likely, therefore, that absence of on-line visual information may be
of particular significance in the REM deficit. Secondly, an alternative interpretation relates to the possibility that parkinsonian difficulties may be magnified when saccades have to be internally or voluntarily (as opposed to reflexively) elicited. Highteain et al. (1969) found that patients produced more multistep saccades when voluntary saccades triggered on verbal command, were compared to visually-directed saccades (see also Melvill Jones and DeJong, 1971). The extent to which the deficit will be manifested may, therefore, depend critically on whether external stimuli are available to elicit the response or whether the response is internally generated.

In an attempt to provide a schematic neural model of saccadic systems, Zee (1984) has drawn attention to two types of saccades and their supranuclear neural correlates. What may be called type A saccades are those quasireflexive saccades which are generated to the onset of a 'new' target in the peripheral environment. Type B saccades can be described as voluntary saccades elicited to internal cues or symbolic external target cues. Type A saccades are thought to be largely the prerogative of superior colliculus function, while the frontal eye fields feature in the control of type B saccades. Consistent with this scheme was the finding that although frontal lesions lead to abnormalities in directing antisaccades in man (Guitton et al., 1985) and REM saccades in monkeys (Deng et al., 1986) reflexive saccades are relatively unimpaired. Recent neurophysiological studies in the monkey by Hikosaka and Wurtz (1983) have demonstrated that some neurons in the substantia nigra, pars reticulata and caudate nucleus (Hikosaka and Sakamoto, 1986) alter their firing rate in response to saccades to remembered targets, but not to reflexive saccades. Furthermore, neuropharmacological inhibition of substantia nigra, pars reticulata-collicular pathways led to a reduction in saccadic velocities and amplitudes specifically to remembered targets (Hikosaka and Wurtz, 1985a, b).

The pathology of PD primarily involves a degeneration of the dopaminergic neurons in the substantia nigra, pars compacta. There are two projections of these neurons which might account for abnormalities in saccadic eye movements. The major projection is to the striatum, and dopamine deficiency at this site may lead to an abnormality of the inhibitory outflow, via the substantia nigra, pars reticulata, occurring prior to a remembered saccade. This would result in impaired disinhibition of the superior colliculus. Alternatively, a pathway from the substantia nigra, pars compacta to the superior colliculus, presumed to be dopaminergic, has recently been described in man (Johnson et al., 1987). As there are no data concerning the activity of this pathway in animals in relation to saccades it can only be surmised that its degeneration and the resulting lack of dopamine in the superior colliculus would result in abnormal saccades.

It is interesting to compare the saccadic deficit in another disease, Huntington's disease, in which there is a degeneration in the basal ganglia. Pathologically this condition differs from PD in that the nigrostriatal pathway is intact, but there is degeneration of neurons in the substantia nigra, pars reticulata and output neurons in the striatum (Gebbink, 1968). This would result in a reduction in the normal inhibitory outflow of the striatum to the superior colliculus. Although hypometric saccades in the REM paradigm have been found in this condition (Lasker et al., 1988) but not in the RAN paradigm, there is an important difference between the two pathologies. In PD there is no deficit in
the ability to suppress a reflexive saccade to the target in the REM paradigm, whereas in Huntington's disease frequent reflexive saccades were observed (Lasker et al., 1987).

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