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Saccadic Eye Movements in Parkinson’s Disease: I. Delayed Saccades

C.J. Lueck, S. Tanyeri, T.J. Crawford, L. Henderson, and C. Kennard

The Royal London Hospital, London, U.K.

The saccadic eye movements of nine patients with Parkinson’s disease were compared to those of nine age-matched controls in two paradigms generating volitional saccades. In both paradigms, subjects had to make delayed saccades to peripheral LED targets: a peripheral target appeared 700 msec before a buzzer sounded, the buzzer being the signal to make a saccade to the target. In the first paradigm ("centre-off"), the fixation target was extinguished simultaneously with buzzer onset. In the second ("centre-remain") it was not extinguished until 1000 msec later. The results showed that for outward saccades in both paradigms, there was no difference between Parkinsonian patients and controls, but saccadic latencies were significantly shorter in the "centre-remain" paradigm. The initial outward saccades were indistinguishable from the normal, reflex saccades of the same subjects. However, saccades returning to the centre (a type of remembered target saccade) were hypometric and showed multisteping. Both effects were more pronounced in patients with Parkinson’s disease. The significance of these findings in terms of current hypotheses about the nature of the Parkinsonian saccadic deficit is discussed.

The use of eye movement recording (oculography) to investigate motor abnormalities in Parkinson’s disease has been a subject of interest for over twenty years (Highstein, Cohen, & Mones, 1969; Von Noorden & Preziosi, 1966). Oculography is particularly suited to the study of movement dis-
orders such as Parkinson's disease for several reasons: the mechanical plant
has a constant moment of inertia, is limited in its degrees of freedom
of movement, and the accuracy of the various oculographic recording tech-
niques is extremely high. In addition, much more is known about the
normal neurophysiology of the initiation and control of eye movements
than is known about the control of limb movements (see Fuchs, Kaneko,

Most investigations of eye movements in Parkinson's disease have been
directed towards fast eye movements (saccades). Early studies suggested
that prolonged latency, hypometria, and multiple stepping were charac-
teristic features of the disease (Corin, Elizan, & Bender, 1972; Von
Noorden & Preziosi, 1966). These "characteristic" Parkinsonian features
are, however, seen only in certain types of saccade. For example, it was
shown as early as 1971 that saccades made to novel visual targets (reflex
saccades) were almost indistinguishable from those made by controls
(Melvill Jones & DeJong, 1971), whereas saccades made back and forth
between two constantly illuminated targets (volitional saccades) were
markedly abnormal in the patient group (DeJong & Melvill Jones, 1971).
For saccadic eye movements to be a useful tool in the study of Parkinson's
disease, therefore, it is important to know exactly which features of a
stimulus elicit the typical abnormalities.

This information has implications that potentially reach beyond the topic
of oculomotor control in Parkinson's disease. (1) It may have relevance to
Parkinsonian somatomotor abnormalities, the exact pathophysiology of
which is still far from clear. (2) There may be implications concerning the
normal mechanisms of saccadic control. A neuropsychological dissociation
of performance in two saccadic tasks suggests to us the possibility that
there is a degree of separability in the processing paths mediating perform-
ance of the tasks.¹

Types of Saccade

On the basis of neurophysiological and clinical studies, saccades have been
divided into three types: spontaneous, reflex, and voluntary (Pierrot-
Deseilligny, 1989; Tusa, 1988; Zee, 1984). Spontaneous saccades are those
made in the absence of an obvious stimulus, either internal or external.
Reflex saccades are those made immediately in response to the onset of
novel visual, auditory, or somatosensory stimuli. Voluntary saccades are
generally defined as those saccades made in response to an "internal"
stimulus, or to a prespecified command. They are generated in the absence
of a novel external target. On the basis of the various paradigms used to

¹A referee's vigorous comment at this juncture reminds us that such inferences are not
uncontroversial. It therefore seems worth emphasizing that here we assert no more than a
working hypothesis.
study them, voluntary saccades have, in turn, been subdivided into four major types: remembered and predictive saccades, antisaccades, and volitional saccades. A remembered saccade is one made to the remembered location of a recent visual target after it has disappeared, usually in response to the onset of an auditory cue. A predictive saccade is made in anticipation of a visual signal made predictable by its regularly repetitive nature. An antisaccade is a saccade made when following instructions to redirect fixation to a location equally distant from, but in the opposite direction to, the point at which a target light suddenly appears (i.e. the target's mirror image). Volitional saccades are those made either in the complete absence of a target, or to a constantly displayed target (i.e. there is no "novelty" of the target). These saccades occur in response to external commands such as "look up" or "look at that table", or they may be generated internally when searching for a target in an unchanging visual environment. Different types of saccade are thought to be mediated through slightly different cerebral pathways (for a review, see Zee, 1984; or Tusa, 1988).

Where? and When?

For the forthcoming argument it is important to be more specific about the exact nature of the stimuli in the above types of saccade. Two different types of information are required by the saccadic system in order to programme and initiate a saccade: "where?" (i.e. to what location in space should the eyes be redirected?) and "when?" (i.e. exactly when should this redirection take place?) (see Becker & Jürgens, 1979). The origins of these two types of information for the different varieties of saccade are shown in Table 1. In the case of reflex saccades, both where? and when?

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Origin of Where? and When? Signals for Different Types of Saccade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where?</td>
<td>Voluntary: remembered</td>
</tr>
<tr>
<td></td>
<td>Memory of target</td>
</tr>
<tr>
<td></td>
<td>Memory of target</td>
</tr>
<tr>
<td></td>
<td>Cognitive manipulation of novel target location</td>
</tr>
<tr>
<td></td>
<td>Stimulus already present/cognitive command</td>
</tr>
<tr>
<td>When?</td>
<td>Novel target itself</td>
</tr>
<tr>
<td></td>
<td>Buzzer</td>
</tr>
<tr>
<td></td>
<td>Internal representation of stimulus timing</td>
</tr>
<tr>
<td></td>
<td>Novel target itself</td>
</tr>
<tr>
<td></td>
<td>Verbal command/buzzer/internal timing cues</td>
</tr>
</tbody>
</table>
information are obviously provided directly by the perceived stimulus, whatever its modality. In the case of *remembered* and *predictive* saccades, the *where?* information is provided indirectly by a visual signal: the visual target has been extinguished before saccade initiation takes place, so the actual *where?* information needed for saccadic generation must be based on an internal representation of where the target was. The *when?* signal is often provided by a buzzer in the case of *remembered* saccades, and presumably by an internal model of the repetitive stimulus timing in *predictive* saccades. In *antisaccades*, the *where?* information is provided by an internal “cognitive” manipulation of the position of a novel visual target, whereas the *when?* cue is provided by the target onset itself. In the case of *volitional* saccades, *where?* information is provided by internal cognitive processes. It may be derived from visual cues already present (e.g. “look at that table”) but does not arise directly as the result of change in sensory input. *When?* information may be provided either by a non-visual command signal (e.g. a buzzer), or else timing may be generated internally (e.g. “look back and forth in your own time”).

**Previous Studies in Parkinson’s Disease**

Recent studies of the different types of eye movement have confirmed that in Parkinson’s disease, *reflex* saccades are essentially normal, provided only mild to moderately affected patients are studied (Crawford, Henderson, & Kennard, 1989a; Gibson, Pimlott, & Kennard, 1987; Lueck, Tanyeri, Crawford, Henderson, & Kennard, 1990; Tanyeri, Lueck, Crawford, & Kennard, 1989). Inclusion of more severely affected patients shows that *reflex* saccades can eventually become affected (White, Saint-Cyr, Tomlinson, & Sharpe, 1983), but in severe or longstanding Parkinson’s disease pathological changes are not confined to the basal ganglia (Halliday et al., 1990). The results of studies based on more severely affected patients cannot therefore be interpreted in terms of disease restricted to the basal ganglia.

Even in cases where their *reflex* saccades are unimpaired, Parkinsonian patients still show distinct abnormalities in other types of saccade. For example, Parkinsonian *remembered* saccades exhibit greater hypometria and multisteping when compared to those of age-matched controls (Carl & Wurtz, 1985; Crawford et al., 1989a; Lueck et al., 1990). Similarly, Parkinsonian patients have a reduced tendency to make *predictive* saccades (Bronstein & Kennard, 1985), but when they do make them, the saccades are significantly hypometric (Crawford, Goodrich, Henderson, & Kennard, 1989b). In contrast, *antisaccades* have the same metrics in Parkinson’s disease as they do in normals (Lueck et al., 1990), although in both groups comparison with *reflex* saccades reveals reduction of amplitudes and velocities and prolongation of latencies.
In this paper the term "abnormal" will be reserved for any difference in saccadic metrics or dynamics that is observed when performance of patients is compared to that of controls, within a particular saccadic paradigm (e.g. "remembered saccades are abnormal in Parkinson's disease"). This serves to distinguish differences found between patients and controls from differences found between paradigms. For example, saccades made by normal subjects in a number of non-reflex paradigms are hypometric when compared to the reflex saccades made to novel visual targets. Non-reflex saccades exhibiting such hypometria include saccades to auditory targets (Zahn, Abel, & Dell'Osso, 1978; Zambarbieri, Schmid, Magenes, & Prablanc, 1982), those made in the dark (Becker & Fuchs, 1969), antisaccades (Lueck et al., 1990; Smit, van Gisbergen, & Cools, 1987), and predictive saccades (Bronstein & Kennard, 1987), but not, apparently, remembered saccades (Lueck et al., 1990; Ohtsuka, Sawa, & Takeda, 1989; Smit et al., 1987). In sum, differences in the metrics obtained for normal subjects suggest a disjunction between the pathways mediating reflex and remembered saccades, on one hand, and those mediating antisaccades and predictive saccades, on the other; whereas the pattern of selective impairment found early in Parkinson's disease suggests a disjunction between reflex saccades and antisaccades, which are normal, and remembered and predictive saccades, which are impaired. Taken together, these two sorts of dissociation (paradigmatic in normal subjects, selective neuropsychological impairment) imply that each of these four types of saccades may be served by a pathway that is in some respect distinctive.

The Novel Target Hypothesis

What is the fundamental difference in target conditions that determines whether a saccade will be normal or abnormal in Parkinsonian patients? The first hypothesis we shall consider asserts that Parkinsonian saccades are executed normally only if the saccade is directed towards a novel visual target.

In the remembered paradigm the saccade is generated after the disappearance of the target, whereas in the predictive paradigm the target has not yet appeared. The novel target hypothesis not only predicts Parkinsonian abnormality under such conditions of target absence, it also predicts abnormality if a visible target is present, provided that it is not novel.\(^2\) This prediction seems to be fulfilled by reports that volitional saccades made to constantly illuminated targets are hypometric and may be of reduced peak velocity in Parkinson's disease. This has been found in studies

\(^2\)An alternative way to express the requirements of the novel target hypothesis is in terms of the conjunction of where? and when? information in the same visible event.
using a buzzer to provide the when? signal (Shibasaki, Tsuji, & Kuroiwa, 1979). Even more marked effects have been reported in studies where the subject has to make saccades “in his own time”, i.e. without an external when? signal (Corin et al., 1972; DeJong & Melvill Jones, 1971; Teräväinen & Calne, 1980). However, a feature of these studies of volitional saccades is that the subjects have been required to generate an alternating sequence of saccades, usually at quite a high rate. It appears that, at least in the absence of a visible target, the ability to generate accurate sequences of saccades may depend on the integrity of the supplementary motor area (SMA) (Gaymard, Pierrot-Deseilligny, & Rivaud, 1990). This region is likely to be compromised in Parkinson’s disease, so it is necessary to ascertain whether a Parkinsonian abnormality continues to obtain in a discrete trial task, where only one saccadic excursion needs to be planned at a time.

Accordingly, the primary objective of this paper is to test the novel target hypothesis in a discrete trials format. In order to accomplish this we employ a “preview” manipulation in which the subject has been instructed not to respond to the arrival of the visual target but, instead, to delay the saccade until a buzzer sounds. A virtue of this arrangement is that it shares this preview feature with the remembered target paradigm, the present task differing only in the persistence of the target until after the delayed saccade has been executed.

Clearly, in executing an antisaccade, the subject cannot be said to direct a saccade towards a novel visual target. Consequently, the hypothesis would need to be considerably reformulated in order to accommodate the finding that antisaccades are normal in Parkinson’s disease. In contrast, the normality of Parkinsonian antisaccades is an unambiguous deduction from the alternative hypothesis, to which we now turn.

The Attentional Release Hypothesis

The original inspiration of the attentional release hypothesis is to be found in a suggestion by Posner (1980) that in normal subjects attention is “captured” in some way by the fixation stimulus, such that a saccade to a new location can be expedited by extinguishing the fixation stimulus. The capture assumption is consistent with the outcome of work using the “gap” paradigm, in which the fixation light is extinguished a short time before the target arrives to summon the saccade (Reulen, 1984; Saslow, 1967). Such a temporal gap has been reported to result in “express” saccades—reflex saccades that have unusually short latencies (Fischer, Boch, &
Ramsperger, 1984; Kalesnykas & Hallett, 1987; Mayfrank, Mobashery, Kimmig, & Fischer, 1986). In a considerable extension of this conception, Crawford et al. (1989b) suggested that in Parkinson’s disease “capture” might be abnormally strong, such that unless attention was released from the point of fixation by the arrival of a novel visual stimulus, the patient’s saccade would be hypometric.⁴

Attentional release could, in principle, be accomplished by two possible mechanisms. Either the disappearance of the fixation stimulus could allow release of attention (as in the original notion of capture), or, alternatively, a novel positive stimulus in the visual periphery could break fixation “capture” directly. Both mechanisms are potentially available in reflex and antisaccade paradigms, accounting for the observed lack of Parkinsonian abnormality.

The existing data suggest that fixation offset coincident with the when? signal must, by itself, be inadequate to permit generation of normal saccades, as this condition is met in the conventional remembered paradigm; yet such saccades are abnormal in Parkinson’s disease. Conversely, a novel visual stimulus must be sufficient, in itself, to provide adequate attentional release, as Crawford et al. (1989b) found that Parkinsonian patients who exhibited hypometric saccades in the remembered paradigm were able to generate normometric saccades in a reflex paradigm, even when the fixation stimulus persisted through saccade generation. The following experiment seeks to determine whether fixation offset can provide adequate attentional release when it is combined with a peripheral visual target that lacks novelty.⁵

In sum, our primary objective in the following experiment was to test the novel target hypothesis, within a discrete trials framework, using a previewed visual target that therefore lacked novelty. If Parkinsonian patients can achieve normal saccadic metrics in such a situation, then the novel target hypothesis must be abandoned and some other reason discovered for the hypometria found in previous studies of continuously alternating volitional saccades. Given a normometric outcome, an appealing solution would be to embrace, instead, the attentional release hypothesis, with the added proviso that fixation offset in combination with an already present visual target can provide adequate attentional release. In this case, Parkinsonian hypometria should be reinstated by having the

⁴To assist in distinguishing the original hypothesis from our extension of it, we refer to the former as “capture” and our extension as “attentional release”. Capture is a hypothesis about normal performance, largely directed towards latency effects. Attentional release, in contrast, attempts to explain the conditions where Parkinsonian patients are freed from their characteristic multiple-stepping hypometria.

⁵We could construe this mechanism in terms of fixation offset disinhibiting the attentional attractiveness of the persisting peripheral stimulus.
fixation stimulus persist. Therefore we included both these fixation conditions in our design.

Method

Subjects. The subject groups comprised nine patients with mild to moderate idiopathic Parkinson's disease and nine age-matched normal controls. All patients had taken part in a previous experiment (Lueck et al., 1990). The ages of the Parkinsonian patients ranged from 54 to 72 years (median 69 years); their clinical features, including disease duration—Hoehn-Yahr staging (Hoehn & Yahr, 1967)—are shown in Table 2. There was no clinical evidence of dementia in any of the patients. All patients except one (Patient 5) were receiving L-DOPA therapy and showed a good somatomotor response to this treatment. Patient 5 was not affected severely enough to have been started on L-DOPA. The time interval between last dose of L-DOPA and eye movement recording was standardized to 3–4 hr. It is noteworthy that in a previous paper (Lueck et al., 1990) these subjects

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age (years)</th>
<th>Duration of Illness (months)</th>
<th>Hoehn-Yahr Staging</th>
<th>Current Medication (daily dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>72</td>
<td>8</td>
<td>II</td>
<td>L-DOPA 300 mg/Carbidopa 30 mg</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>204</td>
<td>III</td>
<td>L-DOPA 900 mg/Benserazide 225 mg Bromocriptine 70 mg Temazepam 10 mg</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>120</td>
<td>II</td>
<td>L-DOPA 1000 mg/Carbidopa 250 mg</td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>42</td>
<td>III</td>
<td>L-DOPA 1500 mg/Carbidopa 150 mg Methixine 15 mg Atenolol 100 mg Allopurinol 300 mg</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>10</td>
<td>II</td>
<td>Amiloride 5 mg Frusemide 40 mg Digoxin 0.125 mg</td>
</tr>
<tr>
<td>6</td>
<td>71</td>
<td>156</td>
<td>II</td>
<td>L-DOPA 1600 mg/Carbidopa 400 mg</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>18</td>
<td>II–III</td>
<td>L-DOPA 300 mg/Carbidopa 30 mg</td>
</tr>
<tr>
<td>8</td>
<td>70</td>
<td>78</td>
<td>II</td>
<td>L-DOPA 800 mg/Carbidopa 200 mg Temazepam 10 mg</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>126</td>
<td>III–IV</td>
<td>L-DOPA 1500 mg/Carbidopa 150 mg Temazepam 20 mg</td>
</tr>
</tbody>
</table>

The drugs linked by an oblique stroke are the two ingredients of a combined preparation.
were demonstrated to have normal reflex saccades but hypometric remembered saccades. They were therefore considered to be a representative sample of moderately impaired idiopathic Parkinsonian patients.

The ages of the controls ranged from 64 to 73 years (median 69 years). They were not taking any medication known to affect cerebral or oculomotor function. All subjects gave informed consent.

Apparatus. Eye movements were recorded using a magnetic scleral search coil (C-N-C Engineering, Seattle, Washington) (Collewijn, van der Mark, & Jansen, 1975; Robinson, 1963). Full details of this and methods for recording eye velocity and blinks have been given in Lueck et al. (1990) and will not be repeated here. In brief, eye position was electronically differentiated on-line, and both eye position and velocity were displayed on paper by a Mingograph chart recorder. The system had an overall bandwidth of 300 Hz and was linear to ±0.25% within the range of ±30°. Saccadic metrics were derived by digitization using a bit-pad accurate to ±0.05 cm. The overall accuracy of data analysis for timing, eye position, and velocity was therefore ±10 msec, ±15' arc, and ±10'/sec respectively. Blinks were recorded simultaneously using DC-electrooculography.

Subjects were seated comfortably in the dark in a chair with a firm head support, which minimized head movement. Stimulus presentation was controlled by a PDP 11/73 computer. The order of presentation of the two paradigms was counterbalanced across subjects. Precise details of the paradigms are as follows (see Figure 1):

Centre-off paradigm. A central red light-emitting diode (LED) was illuminated, and the subject was asked to look at it; 800 msec later a peripheral LED target was illuminated. This target could be one of four LEDs located horizontally at $\pm 7.5^\circ$ and $\pm 15^\circ$ from centre. Target presentation order was varied pseudo-randomly. Subjects were asked not to look at the peripheral target light until immediately after a buzzer sounded, a fixed interval of 700 msec after peripheral LED onset. The buzzer was a small tone generator located 20 cm behind the midpoint of the subject’s head. In this paradigm, the central LED was extinguished simultaneously with buzzer onset. The buzzer sounded for 200 msec, and then, 1000 msec after buzzer offset, the peripheral LED was also extinguished. The subject was told to return his/her gaze to the centre ready for the next trial, which commenced 1000 msec after peripheral light extinction. The exact timing of return to centre was not specified.

Centre-remain paradigm. This paradigm was identical in all respects to the centre-off one except for the fact that the central LED was not extinguished with buzzer onset. Subjects were again required to wait until after the buzzer had sounded to look at the peripheral light. The central LED was extinguished with the peripheral one, i.e. 1000 msec after buzzer offset.

Analysis. All outward primary saccades were analysed first. Factors analysed included saccade latency, saccade gain (amplitude of primary saccade divided by target amplitude, expressed as a percentage), and peak velocity of saccades at 10°, derived from a linear regression between the peak velocity and the logarithm of the amplitude. Such a graph yields an approximately straight line across the range of the saccadic amplitudes generated by this study and allows an estimate of peak velocity to be made on the basis of all saccades, while remaining independent of the effects of differing saccade amplitudes.

Primary saccades were divided into those that occurred before the buzzer onset ("errors") and those occurring after its onset. Errors were discarded before analysis (error rate varied across subjects from 0 to 15%). Any saccade occurring within 50 msec either side of a blink was also discarded (a maximum of a further 1% of saccades were discarded in this way).

During the course of analysis, it became apparent that there appeared to be a marked difference between the returns to centre of the Parkinsonian patients and those of control subjects. Accordingly, returns to centre were analysed post hoc in a way analogous to primary "outward" saccades, but latency was measured from peripheral light offset. The total number of saccades required to return to centre was also measured. "Return" saccades were discarded if they occurred within 50 msec of a blink, but otherwise all saccades were included in analysis.
Each of the saccadic measures was subjected to a $2 \times 2$ analysis of variance with group as a between-subjects factor, and paradigm as a within-subject factor. A product-moment correlation coefficient was determined for the latencies of outward and return saccades. This was also done for gain. Regression lines were calculated for gain on latency for both groups to exclude the possibility of a speed-accuracy trade-off.

Results

The results of the analysis of the different metrics and dynamics for all saccades are displayed in Table 3.

"Outward" Saccades. For outward saccades, the only significant effect to emerge from the analyses of variance was a reliable prolongation of latency in the centre-off paradigm, $F(1, 16) = 11.37, p < 0.01$. In particular, none of the measures distinguished statistically between groups, and none of the Group $\times$ Paradigm interactions was significant.

"Return" Saccades. There was a markedly significant difference between the gains of the two groups, $F(1, 16) = 10.22, p < 0.01$. Parkinsonian patients showed greater evidence of multistepping than did controls when returning to centre, though this just failed to reach significance.

<table>
<thead>
<tr>
<th>TABLE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccadic Metrics in Patients and Controls</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Latency (ms)</th>
<th>Gain (%)</th>
<th>Peak Velocity at 10° (°/sec)</th>
<th>Steps to Return to Centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-O</td>
<td>C-R</td>
<td>C-O</td>
<td>C-R</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>Outward saccades</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>300</td>
<td>260</td>
<td>91</td>
</tr>
<tr>
<td>(81)</td>
<td>(77)</td>
<td>(10)</td>
<td>(12)</td>
</tr>
<tr>
<td>Controls</td>
<td>290</td>
<td>270</td>
<td>92</td>
</tr>
<tr>
<td>(84)</td>
<td>(71)</td>
<td>(6)</td>
<td>(7)</td>
</tr>
<tr>
<td><strong>Return saccades</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>460</td>
<td>270</td>
<td>62</td>
</tr>
<tr>
<td>(426)</td>
<td>(387)</td>
<td>(18)</td>
<td>(19)</td>
</tr>
<tr>
<td>Controls</td>
<td>620</td>
<td>450</td>
<td>75</td>
</tr>
<tr>
<td>(410)</td>
<td>(481)</td>
<td>(14)</td>
<td>(12)</td>
</tr>
</tbody>
</table>

Mean Latency and Peak Velocity results given to nearest 10 msec and 10°s$^{-1}$, respectively. Standard deviations in parentheses under each entry.

C-O: Centre-off paradigm; C-R: Centre-remain paradigm.
The main effect of paradigm was significant, centre-remain return saccades showing the larger gain, $F(1, 16) = 5.04, p < 0.05$, together with a smaller degree of multisteping, $F(1, 16) = 13.25, p < 0.01$. Latencies were also significantly longer in the centre-off paradigm, $F(1, 16) = 5.28, p < 0.05$.

Comparison of “Outward” and “Return” Saccades. Product-moment correlation coefficients between outward and return saccades for latency failed to reveal any significant correlation in either paradigm. The same was true of gain. Regression of gain on latency using data from both paradigms suggested that there was a slight reduction of gain with increasing latency for both Parkinsonian patients and normals, but the effect was slight, the slope being of the order of $-0.01$ msec$^{-1}$ (where gain is expressed in percent).

DISCUSSION

The results show that for “outward” volitional saccades, there were no detectable differences between patients and controls. Moreover, performance was identical in both centre-off and centre-remain paradigms, except with regard to latency, which was, surprisingly, shorter in the centre-remain condition. In both groups and in both fixation light conditions the gains of outward saccades were similar to the gains of the comparable reflex saccades (as reported in Lueck et al. [1990]: 89.3 ± 5.3 for patients, and 90.2 ± 5.4 for controls).

For “return” saccades, however, the Parkinsonian gain was much lower than that of controls. This is not entirely surprising, because return saccades under these conditions are essentially a type of remembered target saccade (i.e. the return is executed after the fixation light has been extinguished). Both groups showed larger gains and shorter latencies of centre-remain returns than those of centre-off returns. As in the centre-remain condition the central fixation point has been visible much more recently when the return saccade is generated, this implies that the paradigmatic dissociation between reflex and remembered saccades may not be sharply categorical but may, rather, depend on target recency.

These findings have significant implications in two major areas. (1) There are implications concerning the generation of saccades in normal human subjects. (2) They relate to the question posed in the introduction concerning the cause of the Parkinsonian abnormality. These two areas will be dealt with in turn.
Implications Concerning Normal Saccade Generation

Previous studies of saccadic performance have shown that reflex saccades differ in their metrics and dynamics from antisaccades as well as remembered and predictive saccades (e.g. Smit et al., 1987). This provides a working hypothesis that the pathways by means of which reflex and non-reflex saccades are produced differ to some extent. Within the various non-reflex paradigms, the pathway mediating antisaccades must, in turn, be distinguished from the pathways serving remembered and predictive saccades, as of these only antisaccades are spared (Lueck et al., 1990). Similarly, the current study shows that volitional outward saccades, executed in a discrete trials situation, are also normal in Parkinson’s disease. Therefore they, too, must be distinguished from remembered and predictive saccades.

Volitional return saccades, on the other hand, may well be mediated through the same pathways as remembered and predictive saccades, because they demonstrate a definite Parkinsonian deficit. It is worth pointing out that while these saccades are designated “volitional return” saccades, this simply provides a reminder of the paradigm used to elicit them. They are, in fact, a species of remembered saccade, as they are made to the location of the central fixation light after it has been extinguished. Indeed, the only differences between the volitional return and remembered tasks are that in the return task no externally imposed when? signal is provided. Moreover, the task is represented to the subject as an incidental one, required merely in the service of outward saccades.

The fact that the normal group failed to show a prolongation of latency in the centre-remain paradigm contrasts with several of the previous studies of overlap paradigms in which a prolongation of latency has been found (e.g. Reulen, 1984; Saslow, 1967), but it is consistent with the findings of Crawford et al. (1989a). A possible explanation of this is that because of the age matching requirement our normal subjects are considerably older than those typically used in saccadic experiments. Elderly subjects tend to have longer saccadic latencies even under optimum stimulus conditions and may be less sensitive to an overlap manipulation that retards saccade initiation in younger subjects.

Implications Concerning the Parkinsonian Defect

The Novel Target Hypothesis. The failure to find Parkinsonian abnormality in volitional outward saccades, taken in conjunction with the fact that these same patients had exhibited abnormal hypometria in a previous
study of remembered saccades and in the present return saccades, seems to provide incontrovertible evidence against the novel target hypothesis.

The Attentional Release Hypothesis. The failure to find any impairment of the patients' performance of outward saccades consequent on persistence of the fixation stimulus (centre-remain) and the failure to detect a Parkinson-control difference in the centre-remain condition refutes the attentional release hypothesis, at least in its present form. Obviously the fate of this hypothesis as an account of Parkinsonian hypometria leaves unscathed the original "capture" hypothesis concerning the role of the fixation stimulus in normal saccadic performance.

Discrete Trials Versus Continuous Alternation. The contrast between the present failure to find a Parkinsonian abnormality in a discrete trials version of the volitional task and previous findings of abnormal hypometria in continuous-alternation volitional tasks (DeJong & Melvill Jones, 1971; Shibasaki et al., 1979) suggests that this variable is a crucial one for the determination of Parkinsonian abnormality. Webster (1968) showed that there was a marked Parkinsonian deficit during repeated activity in a manual tapping task, and a similar effect may apply to the oculomotor system. In support of this, it has been shown in monkeys that the change in firing rate of substantia nigra neurons that reduce their firing rate during remembered saccades is smaller if the animal makes remembered saccades at too high a frequency (Hikosaka & Wurtz, 1983).

It is thus possible that any paradigm which requires that saccades be made too rapidly may show a deficit in Parkinson's disease. As the current study was performed as a series of widely spaced discrete trials, this may explain the failure to replicate the results of DeJong and Melvill Jones (1971) and of Shibasaki et al. (1979) in that the Parkinsonian deficit was not here manifest for outward saccades. The effect of frequent repetitive activity is further discussed in the following paper (Lueck et al., Saccadic Eye Movements in Parkinson's Disease: II, this issue).

4In fact, the exact nature of the Shibasaki et al. (1979) experimental paradigm is not completely clear. In testing voluntary saccades, five lights were illuminated at 0° and ±26° to the right, left, up, and down, and subjects were told which light to look at. In their subsequent "reaction time" experiment (the one considered here as an example of volitional saccades), latency was measured from a buzzer that indicated when to make a saccade, presumably to one of the five targets used in the voluntary paradigm. There is no suggestion in the text that the target lights were turned on or off, and so we conclude that the lines labelled "T" in their Figures 2 and 3 refer to buzzer timing and not to actual changes in target position. Thus it is assumed that in their experiment two lights were effectively constantly illuminated, and a repeated buzzer signalled the timing of back-and-forth volitional saccades.
Abnormal Volitional Return Saccades

With respect to the saccades returning to centre, the first difficulty concerns the precise identification of the stimulus. Subjects were told to return to the centre before the next trial, but the exact timing was never specified. Thus, the return was a volitional event (when? information being provided by cognitive processes). The vast majority of saccades were made at some point after peripheral LED offset but were not obviously “triggered” by this offset, as their latencies (measured from this offset) were very long, with a large variance.

The hypometria exhibited by the patients under these circumstances demonstrates that the abnormality of their saccades to a remembered target may be revealed in an incidental task, that is not presented as a primary focus of the investigation.

Towards a New Hypothesis Concerning Parkinsonian Abnormality

With the collapse of the novel target and the attentional release hypotheses, it is time to take stock of what we have been able to determine so far. As this study suggests that continuously alternating saccades may be abnormal in Parkinson’s disease for reasons unrelated to the stimulus conditions, we shall, for present purposes, confine our attention to results obtained in the discrete trials framework. What seems at a purely empirical level to distinguish the paradigms in which the Parkinsonian abnormality is exhibited is the absence of a visual target at the time when the saccade is generated. This is most clearly evident from a comparison of performance in the closely matched remembered and outward volitional paradigms. Both commence with the arrival of a visual target, to which the subject has been instructed not to generate a reflex saccade. After a brief delay, a buzzer summons the saccade and simultaneously the fixation light is extinguished (centre-off variant). The only difference is that in the remembered target paradigm the target disappears just before the buzzer sounds, whereas in our volitional outward paradigm the target remains visible until after saccade initiation. This momentary lack of target visibility, in the former case, is sufficient to cause the patient’s abnormal hypometria.

To this demonstration, the normality of Parkinsonian antisaccades allows us to add the premise that performance will be spared even if the target information is not directly available in the visual signal but requires a cognitive transformation. However, as we have already remarked, the different metrics of antisaccades and reflex saccades in normal subjects may be a token of differences in the pathways serving production of these two types of saccade, so that more than one pathway may be spared in our patients.
The hypothesis at which we have finally arrived may therefore be called the "target availability" hypothesis. It asserts that the metrics of Parkinsonian saccades will be normal, in a discrete trials test, provided that target information is available in a visual signal present at the time the saccade is being generated. This formulation is entirely consistent with the existing evidence, but its virtue clearly lies in its provision of a parsimonious summary of the conditions under which the patients' saccades will be normal rather than its provision of a satisfying explanation of why this should be so.

REFERENCES


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