



# Asymmetric influences of pointing on saccade latency in hemi-Parkinson's disease

Jocelyne Ventre-Dominey<sup>a,\*</sup>, Peter Ford Dominey<sup>b</sup>, Emmanuel Broussolle<sup>c</sup>

<sup>a</sup> INSERM-Unit 94, 16 avenue Doyen Lépine, 69500 Bron, France

<sup>b</sup> CNRS-Cognitive Sciences Institute, 69500 Bron, France

<sup>c</sup> Neurology Unit, Neurology Hospital, 69003 Lyon, France

Received 17 November 1999; received in revised form 10 July 2000; accepted 22 September 2000

## Abstract

The objective of this study was to investigate whether eye–hand coupling was preserved or not in PD. We studied predictive saccade performance during hand pointing in six Parkinson's disease (PD) patients with asymmetrical motor signs compared to nine age-matched healthy subjects. The motor responses (saccades and hand pointing) were elicited under open loop conditions (without vision of the hand), by a visual target stepping at a predictable location (10° right and left from the centre) and time. The subjects had to simultaneously move the eyes and point with the finger to the visual target alternating at one of three fixed frequencies (0.25, 0.5 and 1 Hz), for 30 cycles. This task was performed in two sessions balanced over the subjects: one session of ocular saccades only and another session of combined ocular saccades and manual pointing. In the PD group, motor performance was perturbed particularly in terms of increased latencies of hand movements. Interestingly, during pointing, associated predictive saccade disorders were tightly related to the defects of the pointing hand. Indeed, with respect to the latency of predictive saccades alone, the predictive saccade latency during hand pointing significantly decreased in the control group and in the PD group when using the non-affected hand. In contrast, for the PD group when using the affected hand, the saccade latency was increased from the latency values of predictive saccades induced without pointing. Moreover, in the control and in the PD groups, the correlation between eye and hand latencies was highly significant, suggesting an intact eye–hand coupling. No saccadic amplitude disorders were found in either condition. These results demonstrate that eye–hand coupling is preserved in PD, as revealed by the possible beneficial or adverse effects on the ocular saccades, respectively, of the less- or more-affected hand motor responses. This eye–hand coupling mechanism likely involves regions other than the nigro-striatal pathways affected in PD. © 2001 Elsevier Science Ltd. All rights reserved.

**Keywords:** Eye–hand coordination; Hand pointing; Ocular saccade; Parkinson's disease; Prediction

## 1. Introduction

When we reach towards objects in our visual surroundings, we often produce coordinated eye and hand movements, involving complex central eye–hand coupling processes [10,15,28,30,31]. These eye–hand coupling mechanisms likely integrate the command and the resulting position or motor signals from both systems to assist the adequate completion of the goal-directed movements. Recently, by studying the temporal aspects

of eye–hand coupling in humans, Neggers and Bekkering [18] demonstrated that during goal-directed hand pointing to a foveated target, saccades to new targets cannot be elicited until the reaching movement ends up. This saccadic inhibition to new targets during pointing is aimed to 'home in' the hand and the eye onto the fixated region. Neggers and Bekkering [18] suggested that such a 'homing in' mechanism might be tied to attention and likewise be responsible for some temporal features of eye–hand coordination.

Behavioural studies of eye–hand coordination in monkey demonstrated a role of the cerebellar dentate nucleus in eye–hand coupling during tracking tasks [27]. Likewise, electrophysiological unit recordings in primate have identified several additional sites integrat-

\* Corresponding author. Tel.: +33-4-72913410; fax: +33-4-72913401.

E-mail address: ventre-dominey@lyon151.inserm.fr (J. Ventre-Dominey).

ing eye and hand information, in the parietal cortex [2,20,22], in the supplementary eye field (SEF) [17], in the premotor area [4], and in the superior colliculus (SC) [32]. Interestingly, saccadic inhibition and fixation [16] and, more recently, hand-movement-related activity [21,33,34] have been demonstrated in monkey SC. Werner et al. [33] described collicular and underlying reticular neuron activity related to hand movements with onset and modulation patterns similar to those of muscle activity during reaching to visual targets. Moreover, the SC is directly linked to the SEF, where activity has been demonstrated to signal ocular movements specifically related to hand movements. These different observations suggest that oculo-manual coordination is subserved by a distributed neural network likely made up of possible different cortical regions, the midbrain and the cerebellum. The striatum is also known to constitute an important point of convergence for sensory and motor inputs of several cortico-striato-thalamo-cortical motor circuits [1] and is thus a potential candidate for such an interactive mechanism. Parkinson's disease (PD) is characterized by a degeneration of mesencephalic dopaminergic neurons that leads to a perturbation of striatal function and is thus a good model for the study of striatal dysfunction in humans. Indeed, both saccadic [26] and manual motor control [6] are impaired in PD, providing a suitable framework for the study of potential interactions. In view of the anatomical and physiological organisation of the basal ganglia, there thus remains an important question concerning the role of basal ganglia in eye–hand coordination.

In this study, we address this issue in PD patients in a repetitive pointing task where the subjects were instructed to naturally move the eyes and point with the finger, under open loop conditions (without vision of the hand), to a visual target alternating back and forth at one of three fixed frequencies. We will investigate the predictive saccade performance during pointing in order to determine in asymmetric PD patients the possible impact of the affected versus the non-affected hand on the oculomotor system.

## 2. Methods

### 2.1. Subjects

We measured simultaneous eye and hand performance in six right-handed PD patients (three males and three females, mean age:  $55 \pm 10$  years, mean disease duration:  $4.8 \pm 2.1$  years). All patients were chronically treated with levodopa plus a peripheral decarboxylase inhibitor (the mean levodopa dosage was  $322 \pm 200.1$  mg/day). Prior to the experiments, the patients' motor disability was assessed while on medication by using the Unified Parkinson's Disease Rating Scale (UPDRS) score [8], and the Hoehn and Yahr staging (Table 1). In all the patients, the akinetic-rigid syndrome was asymmetric: four patients had a predominant left and two patients a predominant right hemi-Parkinson syndrome.

A control group of nine healthy right-handed age-matched subjects (five males and four females; mean age =  $53.5 \pm 8.4$  years) was studied in the same experimental conditions for further statistical comparison with the PD group. The control subjects had no history of neurological or ophthalmological disorders. All the subjects gave informed consent to participate in this research study.

### 2.2. Task and apparatus

The subject was seated in a dark room in front of a set-up consisting of a computer screen, a mirror and a touch-sensitive screen, which were horizontally oriented and parallel to each other. Visual targets were displayed on the computer screen and reflected in the mirror. The subject looked at the mirror and pointed on the touch screen to the reflected virtual images of the visual targets. The visual target consisted of a small lit square subtending a  $2.2^\circ$  visual angle. Head movements were prevented by maintaining the subject's head on a chin rest. The subject had to track the visual targets in the 'open-loop' condition (without vision of the hand) by hand pointing and ocular saccades.

Table 1  
Clinical description of the six PD patients<sup>a</sup>

Patient no.	1	2	3	4	5	6
Sex	F	M	F	M	F	M
Age (years)	38	45	55	67	60	66
Duration of disease (years)	5	8	2	7	4	3
Hoehn and Yahr (0–5)	1.5	1.5	1.5	2	1.5	2
UPDRS motor score (max. = 108)	10	28	6	14	16	18
UPDRS lateralized motor score (max./side = 36)	R: 2; L: 6	R: 11; L: 6	R: 1; L: 4	R: 4; L: 6	R: 7; L: 2	R: 5; L: 7
Hemibody with predominant motor signs	L	R	L	L	R	L

<sup>a</sup> R = right; L = left; the motor score refers to items 18–31 of UPDRS and the lateralized motor score to items 20–26 of UPDRS.

Table 2

Mean movement latency in the different experimental conditions, in the control and PD groups<sup>a</sup>

	Saccade		Saccade (during pointing)			Hand pointing		
	Control	PD	Control	PD-AH	PD-NAH	Control	PD-AH	PD-NAH
0.25 Hz	–48	127	–280	169	100	558	1148	804
0.5 Hz	–147	158	–411	94	–340	300	889	402
1 Hz	–20	56	–121	188	27	269	625	535

<sup>a</sup> AH: affected hand; NAH: non-affected hand.

### 2.2.1. Hand-pointing recording

As soon as the subject pointed to the visual target, the analogue signal of the touch was recorded by the touch-sensitive screen (MicroTouch TM) and digitized at a sampling rate of 1 kHz. The time and position of the touch and the associated target were analysed off-line by an interactive software (Cortex, NIH, Bethesda, MD) on a PC.

### 2.2.2. Eye movement recording

Eye movements were recorded by d.c. electro-oculography (EOG). Cutaneous electrodes were placed on the outer canthi for horizontal eye movement recording and on the upper and lower ridges of the right eye for vertical eye movement recording. Vertical eye movements were recorded for blink rejection. The EOG signals were amplified and filtered with a low-pass analogue filter (40 Hz). The filtered EOG signals were then digitized at a sampling rate of 250 Hz and stored for off-line analysis by interactive software [7].

### 2.3. Behavioral paradigm

The predictive motor responses (30 cycles of saccades and pointing) were elicited by a visual target stepping at a predictable location (10° right and left from the centre) and at a predictable frequency (0.25, 0.5 or 1 Hz).

Each subject performed this predictive paradigm for each frequency in two sessions balanced over subjects: a session where only the saccades were tested and a second session where saccades and hand pointing were both tested in order to analyse the eye–hand interaction.

### 2.4. Data analysis

EOG velocity signals were automatically processed and used to detect the movement onset by our interactive software. In order to study the steady-state performance, the first five movements were eliminated from analysis. At each stimulus frequency, the following motor parameters were extracted:

1. The accuracy was measured by the amplitude of movements to the visual targets.

2. The latency was the the time elapsed between the displaced target onset, and the movement initiation.
3. The pointing effect (PE) on saccadic latency was calculated as the difference between saccadic latency in the condition of manual pointing (PS: pointing + saccade) versus the condition without manual pointing (S: saccade).

$$PE = PS \text{ latency} - S \text{ latency.}$$

In the PD group, the PE on latency was calculated separately for the affected hand and the non-affected hand. The more PE was decreasing and negative, the more reduced was the saccade latency during pointing, i.e. the greater the advantage of pointing on the saccades.

Statistical comparison was realized by a repeated-measures ANOVA and post-hoc analysis by planned comparisons. The dependent variables were the amplitude, latency and PE. The between-subject factor was the group (control, PD), and the within-subject factors, the target frequency (0.25, 0.5, 1) and the hand, in the control group (right hand and left hand), and in the PD group (affected hand, AH and non-affected hand, NAH).

The correlation between saccade and hand-pointing performance was analysed by a multiple regression analysis. To better quantify the eye–hand coupling over time, a cross-correlation between eye and hand performance was also computed trial by trial, in the control and in the PD group. The statistical significance was established at a 95% confidence interval. Statistical analysis was performed with the STATISTICA software package.

## 3. Results

### 3.1. Saccade only condition

The mean amplitude of saccades was normal at all stimulus frequencies [main group effect:  $F(1,16) = 2.9$ ,  $P > 0.05$ , group  $\times$  stimulus frequency interaction:  $F(2,32) = 0.7$ ,  $P > 0.05$ ]. The mean saccadic latency was not significantly different in the PD versus control group [main group effect:  $F(1,16) = 2$ ,  $P > 0.05$ ;

group × stimulus frequency interaction:  $F(2, 32) = 0.1, P > 0.05$ ] (Table 2 and Fig. 1).

### 3.2. Handpointing condition

#### 3.2.1. Pointing performance

The hand-pointing accuracy was not different between control and PD groups, with either hand (affected or not) for all stimulus frequencies [main group effect:  $F(1,14) = 0.3, P > 0.05$ ; group × hand interaction:  $F(2,28) = 1.18, P > 0.05$ ; group × stimulus frequency interaction:  $F(2,28) = 0.6, P > 0.05$ ]. In the PD group, the mean latency of hand pointing was significantly increased, independently of the stimulus frequency [main group effect:  $F(1,30) = 25, P < 0.001$ ; group × stimulus frequency interaction:  $F(2,60) = 1.8, P > 0.05$ ]. This effect was highly dependent on the pointing hand: affected or not [main hand effect in PD group:  $F(1, 4) = 17, P = 0.014$ ] (Table 2). This hand effect on latency was more pronounced for the lower frequencies, especially at 0.5 Hz, as revealed by planned comparisons ( $P < 0.05$ ). In the control group, the hand laterality (right hand versus left hand) had no effect on the pointing latency [hand effect in control group:  $F(1, 7) = 0.2, P > 0.05$ ].

#### 3.2.2. Saccade performance during pointing

As in the saccade only condition, the saccadic accuracy was normal [main group effect:  $F(1,10) = 0.001, P > 0.05$ ; group × hand interaction:  $F(1,10) = 0.35; P > 0.05$ ]. In contrast with the saccade only condition,

the mean saccadic latency during pointing was significantly increased in the PD group as compared to the normal group, independently of the stimulus frequency [main group effect:  $F(1,21) = 24.7, P < 0.0001$ ; group × stimulus frequency effect:  $F(2,42) = 1, P > 0.05$ ].

This saccade latency increase was strongly related to the hand used during pointing in PD group [main hand effect in PD group:  $F(1,5) = 21.1, P = 0.0058$ , hand × frequency interaction:  $F(2, 10) = 6.8, P = 0.013$ ]. As shown in Fig. 1 and Table 2, the saccade latency increased more when the affected hand was used during pointing than when the non-affected hand was used. This hand effect on saccade latency was maximal at the stimulus frequency of 0.5 Hz (planned comparison:  $P < 0.001$ ). In the control group, the mean latency of saccade during pointing was not significantly different between right and left hand [main hand effect in control group:  $F(1,7) = 4.1, P > 0.05$ ].

#### 3.2.3. Quantification of pointing effect (PE)

The more PE was decreasing and negative, the more reduced was the saccade latency during pointing, i.e. the greater the advantage of pointing on the saccades.

In the control group, as no significant difference between the two hands was found in the latency of saccades during pointing, we calculated PE by using the saccadic latency averaged between the two hands. As compared to saccades without pointing, saccade latencies during manual pointing become significantly reduced in the control group (mean PE = -243 ms) and, to a lesser extent, in the PD group with the non-af-

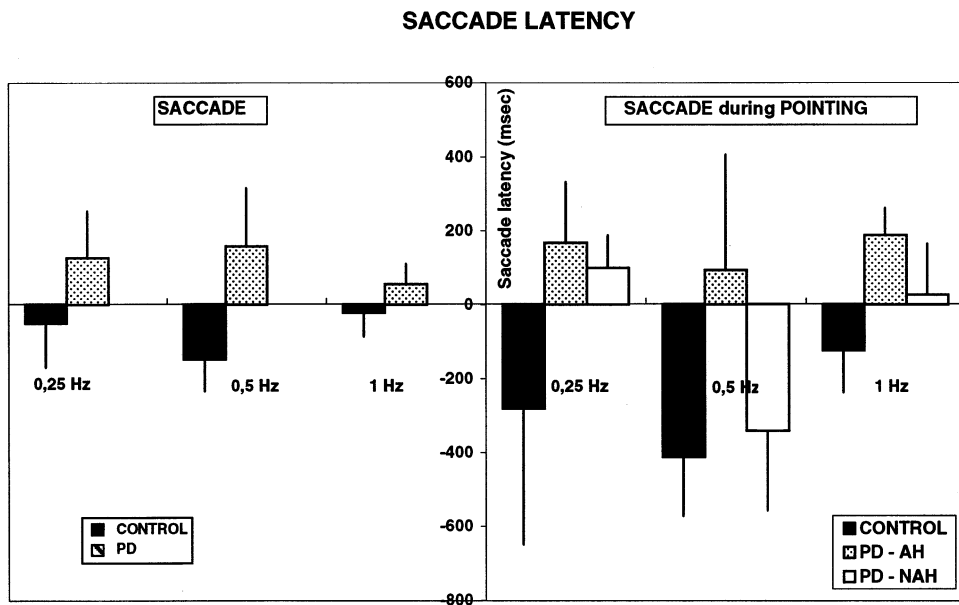


Fig. 1. Mean latency and standard deviations of predictive saccades with and without pointing in the control group and in the PD group, with the non-affected hand (NAH) and with the affected hand (AH). Predictive saccades latencies are presented in the two experimental conditions, saccades only and saccades during hand pointing, at the three stimulus frequencies (0.25, 0.5 and 1 Hz). As the effect of hand laterality on saccade latency was not significant in the control group, the latency in this group represents the average between the two hands. Bars: S.D.

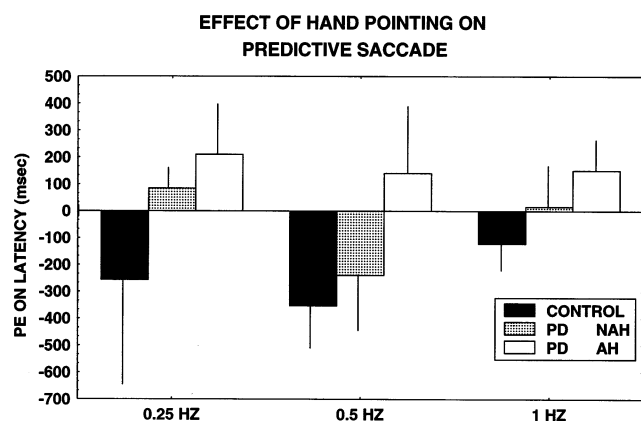


Fig. 2. Pointing effect (PE) on saccade latency measured as latency of saccade during manual pointing minus latency of saccade without pointing, at the three stimulus frequencies (0.25, 0.5 and 1 Hz), in the control group and in the PD group, with the non-affected hand (NAH) and with the affected hand (AH). Positive values of PE indicate the increased latency of saccades during pointing as compared to the saccades without pointing. As the effect of hand laterality on latency was not significant in the control group, the PE in this group represents the PE of latency averaged between the two hands. Bars: S.D.

affected hand (mean PE =  $-46$  ms) but were increased with the affected hand (mean PE =  $167$  ms). As shown in Fig. 2, this hand effect on latency measured by PE was significant, independent of the stimulus frequency [group  $\times$  hand interaction:  $F(1,9) = 28$ ,  $P < 0.001$ ; group  $\times$  hand  $\times$  frequency interaction:  $F(2, 18) = 3$ ,  $P = 0.07$ ].

### 3.2.4. Saccade and pointing latency correlation

To better establish the eye–hand coupling performance, we analysed the correlation between eye and hand pointing latencies in PD and control groups, at the stimulus frequency of 0.5 Hz where the hand effect on latency was maximal. Multiple regression analysis demonstrated a significant correlation of saccade and hand-pointing latencies in the control group ( $r = 0.96$ ,  $P < 0.001$ ) and in the PD group, more with the non-affected (NA) hand ( $r = 0.68$ ,  $P < 0.001$ ) than with the affected (A) hand ( $r = 0.47$ ,  $P < 0.01$ ). A steady pattern of well-correlated eye and hand latencies over time is presented in Fig. 3 both in the control group and in the PD group with the non-affected hand only. In contrast, in the PD group with the affected hand, even though the eye and hand are still well correlated, the pattern of eye–hand latencies becomes highly variable. To better quantify the eye–hand correlation changes over time, a eye–hand latencies cross-correlation was computed over the 30 trials, using lags of 0 to  $\pm 15$ , in the control group and in the PD group, independently for the affected and for the non-affected hand. In the control group, and in the PD group with the non-affected hand, the cross-correlation was similar with the highest

level of correlation, respectively  $r = 0.93$  and  $r = 0.7$ , with a 0 inter-trial lag, followed by a progressive decrease of the nevertheless significant correlation as the inter-trials lags increased (Fig. 4). In contrast, in the PD group with the affected hand, the eye–hand correlation was significant at  $r > 0.3$  only for the narrow intertrials lags (0–2 inter-trials lags), then sharply varied with increasing lags. Interestingly, when computed trial by trial, i.e. with 0 inter trial lags, the cross-correlation between eye and hand latencies was similar at  $r$  close to 0.5 when comparing the non-affected and the affected hand of the PD group.

## 4. Discussion

In the current study, we investigated, in hemi-Parkinson's patients, the interaction between the eye- and hand-motor systems in a repetitive tracking task where eye and hand both track the same visual target. Our findings in the PD group demonstrate a strong asymmetric influence of pointing on saccade latency. In the control group, the saccadic performance improved while the subject was pointing with either hand. Interestingly, in the PD group, eye- and hand-motor performance were also tightly coupled. Thus, the saccade latency improved when pointing with the non-affected hand and was impaired when pointing with the affected hand, reflecting in saccade performance, the asymmetrical deficits of hand pointing. Our results thus suggest that, in hemi-PD patients, information related to hand motion significantly influences coordinated eye movements.

In our study, as in related studies conducted in normal subjects [12,13,24], it has been shown that eye–

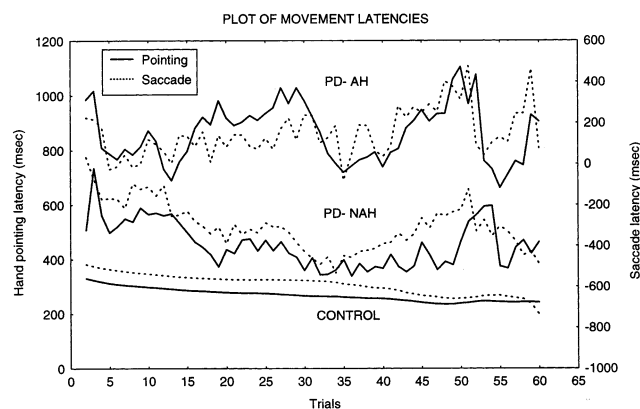


Fig. 3. Pattern of predictive saccade and hand movement latencies over the 30 trials (i.e. 60 right and left movements), in Control group and in PD group, with the non-affected (NAH) and the affected (AH) hand. Note the difference of a steady eye–hand latency pattern in the control group and, to a less extent, in the PD group with the non-affected hand (NAH) pointing and inversely the unsteady pattern in the PD group with the affected hand (AH) pointing.

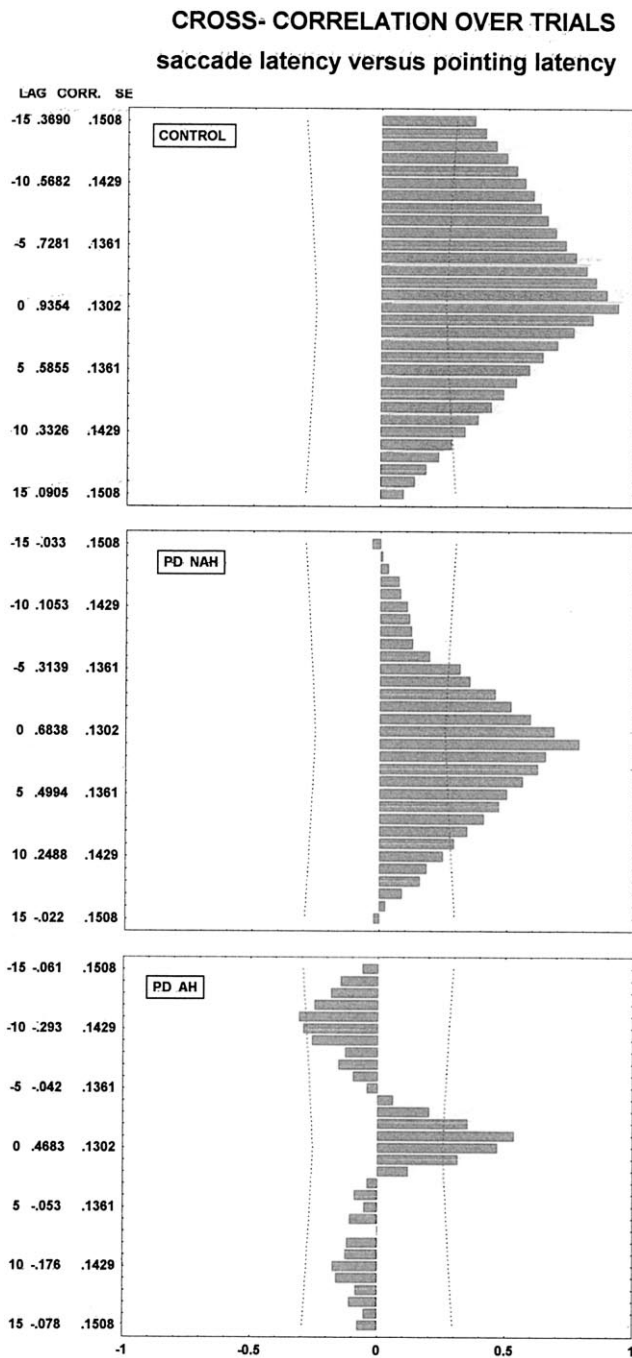


Fig. 4. Cross-correlation of eye and hand latencies over trials measured with lags of 0 to  $\pm 15$  inter-trial lags. In the control group and in the PD group with the non-affected hand (NAH), the correlation is significant at lag 0 and diminishes gradually with increasing lags. In contrast, in the PD group with the affected hand (AH), the significant eye–hand latencies correlation for lag 0 falls off sharply and becomes negative for longer lags. Abscissae: correlation coefficient. Ordinates: inter-trial lag, correlation factors (Corr.) and their standard error (S.E.) as a function of the inter-trial lags.

hand coordination could yield an improvement in motor performance. Interestingly, such a positive effect of pointing on oculomotor performance could be observed in our PD patients, only when the non-affected hand

was used. Moreover, even though the effect of hand pointing on ocular performance in PD diverged for the two hands, affected versus non-affected, we found that the degree of eye–hand coupling was maintained for both hands used (revealed by significant eye–hand latency correlations). Interestingly, a consequence of the somato-motor disorders observed in PD was displayed in the variability and the irregularity of the correlated eye–hand latency pattern. This variability in the eye–hand latencies, related to the affected hand result from a difficulty to maintain a steady pattern of motor latencies as we previously observed in predictive saccades in PD [26] independently of eye–hand coupling. Such a hand dependency observed in saccades during pointing argues in favour of preserved eye–hand coordination processing in Parkinson’s disease. Through this eye–hand coupling mechanism, information related to hand motion has a significant impact on the performance of simultaneous eye movements. More specifically, the output of the impaired hand-motor system adversely affects the output of the eye-motor system, in PD patients. Similar results have been reported in cerebellar patients [5,25], who presented the same adverse reciprocal interaction between the two motor systems in a visuo-motor tracking task with the eyes or the hand or with combined eye–hand movements. After cerebellar lesions, the eye and hand movements were affected with an increase in latency that was amplified when the subjects were tracking with both eye and hand, as compared with tracking with the eyes or the hand in isolation. The negative influence of the hand on the ocular output observed in two different central nervous system pathologies, PD and cerebellar hemispheric stroke, suggests that the mechanism involved in eye–hand coordination may take place in structures other than basal ganglia and cerebellar hemispheres.

While the existence of positive interaction between eye and hand has been largely described in normal subjects in visually guided tracking or reaching tasks [3,12,13,15,24,28–31], the motor information used in this eye–hand coupling, either the efferent copy or the proprioceptive inputs, still remains uncertain. Previous studies [10,28–31] have described the sources of signals, motor command and afferent information, underlying eye–hand coordination in tasks of smooth pursuit. Mather and Lackner [15] suggested that, as the ocular pursuit gain increased during passive hand movements, the corollary discharge was not the main factor of the pursuit enhancement during eye–hand tracking. Moreover, the experimental manipulation of motor afferences by arm vibration influences eye movement performance as well as eye–hand coupling [14,23]. When the arm is deafferented either by brachial ischaemic block in normal subjects [9] or in patients with acute peripheral neuropathy [29], the subjects are unable to produce smooth ocular pursuit by tracking

their hand in total darkness, even though they are able to trigger a short latency smooth pursuit during active arm movements. In the context of oculo-manual interaction, Vercher et al. [29] concluded that the hand motor command is important for initiation of eye movements and that the arm proprioception might enhance and sustain ocular performance in terms of gain, phase and accuracy. This somato-motor feedback, either from the motor command or from the proprioceptive afferences, onto the oculo-motor system might rely on neural structures other than the basal ganglia. Indeed, the neural correlate of eye–hand interaction is recorded in several structures, including the parietal cortex [2,20,22], the premotor cortex [4], the supplementary eye field (SEF) [17] and the superior colliculus [32]. Recent electrophysiological studies in monkeys describe populations of gaze–reach neurons in the deep layers of SC and underlying reticular formation [33,34]. Moreover, these SC gaze-related reach neurons would code for arm movements in a gaze-centred framework; they can reflect either the corollary discharge involved in eye–hand coordination or the motor command, or part of it, thus involving SC and underlying reticular formation in the eye–hand motor programming [21,33]. If the SC represents one of the major centres of eye–hand interaction, there should exist gaze–reach descending activity from cortical areas to this part of the midbrain. In the cerebral cortex, among others, there are at least two frontal fields related to eye movements activity and directly connected to SC, the FEF and the SEF. Whereas the functional anatomy of FEF–SC connections is well established in oculomotor behaviour, it has only been more recently that the task-related signals flowing from the FEF to SC have been identified and described as a continuous multistage system yielding oculomotor cognitive processing [19]. However, as mainly saccade-related signals are integrated in FEF, this cortical area alone, even with its SC connections, cannot explain the eye–hand interaction activity observed in SC and studied in the current work. Interestingly, by confronting neuronal activity in the two oculomotor areas, FEF versus SEF, Mushiake et al. [17] demonstrated that while the FEF is mainly active with saccades independently of their co-execution with arm movements, the SEF activity signals whether a motor task is to be oculomotor only or a coupled eye–hand motor task. As the SEF, like the FEF, is directly connected to the SC [11], we can hypothesize that part of the eye–hand coordination takes place through the SEF–SC sub-system, either as part of the oculo- and somato-motor system command or as a parallel process subtending the eye–hand interaction through corollary discharge or proprioceptive inputs.

Gauthier et al. [10] developed a general model of the interaction between the two sensorimotor systems that might involve a specialized neural centre controlling the

oculo-manual coordination. This coordination centre would be activated through sensory and motor inputs coming from different sensory–motor systems involved in conjugated tasks. These observations and our results suggest that oculo-manual coordination mechanisms are likely subserved by neural networks connecting different cortical regions, possibly the direct pathway from SEF to the midbrain, independently of the striatum.

## 5. Conclusion

This study demonstrates that in asymmetrically affected PD patients performing a repetitive eye–hand pointing task without vision of the hand, a tight coordination exists between the oculo and somato-motor systems, with possible beneficial or adverse influence of the hand responses on the ocular saccades. In PD, the eye–hand coupling mechanism is intact, as reflected by the adverse influence of the affected hand and the opposite positive influence of the non-affected hand on saccade performance during pointing. Based on our data, we suggest that the hand-position signals, likely the efferent copy, can modulate the oculomotor command triggered by the stimulus, through a sensory–motor coordination mechanism. This eye–hand coordination mechanism might involve either other intact regions of the striatum or nervous structures other than the basal ganglia, such as the frontal cortex–SC system.

## Acknowledgements

The work was carried out at INSERM, 16 Avenue Doyen Lépine, 69500 Bron, France

## References

- [1] Alexander GE, Crutcher MD. Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *Trends in Neurosciences* 1990;13:266–71.
- [2] Andersen RA, Essick GK, Siegel RM. The encoding of spatial location by posterior parietal neurons. *Science* 1985;230:456–8.
- [3] Bekkering H, Adam JJ, van der Aarssen A, Kingma H, Whiting HTA. Interference between saccadic eye and goal-directed hand movements. *Experimental Brain Research* 1995;106:475–84.
- [4] Boussaoud D, Joffrais C, Bremmer F. Eye position effects on the neuronal activity of dorsal premotor cortex in the macaque monkey. *Journal of Neurophysiology* 1998;80:1132–50.
- [5] Brown SH, Kessler KR, Hefter H, Cooke J, Freund HJ. Role of the cerebellum in visuomotor coordination. I. Delayed eye and arm initiation in patients with mild cerebellar ataxia. *Experimental Brain Research* 1993;94:478–88.
- [6] Crawford TJ, Goodrich S, Henderson L, Kennard C. Predictive responses in Parkinson's disease: manual keypresses and saccadic eye movements to regular stimulus events. *Journal of Neurology, Neurosurgery and Psychiatry* 1989;52:1033–42.

- [7] Darlot C, Denise P, Droulez J, et al. Eye movements induced by off-vertical axis rotation (OVAR) at small angle of tilt. *Experimental Brain Research* 1988;73:91–105.
- [8] Fahn S, Elton RL. (and the members of the UPDRS (Development Committee Unified Parkinson's Disease Rating Scale) In: Fahn S, Marsden CD, Calne D, Goldstein M, editors. *Recent developments in Parkinson's disease*. Florham Park, Macmillan, 1987:152–63.
- [9] Gauthier GM, Hofferer JM. Eye tracking of self-moved targets in the absence of vision. *Experimental Brain Research* 1976;26:121–39.
- [10] Gauthier GM, Vercher JL, Ivaldi FM, Marchetti E. Oculo-manual tracking of visual targets: control learning, coordination control and coordination model. *Experimental Brain Research* 1988;73:127–37.
- [11] Huerta MF, Kaas JH. Supplementary eye field as defined by intracortical microstimulation: connection in macaques. *Journal of Comparative Neurology* 1990;293:299–330.
- [12] Koken PW, Erkelens CJ. Influences of hand movements on eye movements in tracking tasks in man. *Experimental Brain Research* 1992;88:657–64.
- [13] Leist A, Freund HJ, Cohen B. Comparative characteristics of predictive eye–hand tracking. *Human Neurobiology* 1987;6:19–26.
- [14] Martin BJ, Roll JP, di Renzo N. The interaction of hand vibration with oculomanual coordination in pursuit tracking. *Aviation Space and Environmental Medicine* 1991;62:145–52.
- [15] Mather JA, Lackner JR. The influence of efferent, proprioceptive, and timing factors on the accuracy of eye–hand tracking. *Experimental Brain Research* 1981;43:406–12.
- [16] Munoz DP, Wurtz RH. Fixation cells in monkey superior colliculus. II. Reversible activation and inactivation. *Journal of Neurophysiology* 1993;70:576–89.
- [17] Mushiake H, Fujii N, Tanji J. Visually guided saccade versus eye–hand reach: contrasting neuronal activity in the cortical supplementary and frontal eye fields. *Journal of Neurophysiology* 1996;75:2187–91.
- [18] Neggers SFW, Bekkering H. Ocular gaze is anchored to the target of an ongoing pointing movement. *Journal of Neurophysiology* 2000;83:639–51.
- [19] Sommer MA, Wurtz RH. Composition and topographic organization of signals sent from the frontal eye field to the superior colliculus. *Journal of Neurophysiology* 2000;83:1979–2001.
- [20] Snyder LH, Batista AP, Andersen RA. Coding of intention in the posterior parietal cortex. *Nature* 1997;386:167–70.
- [21] Stuphorn V, Bauswein E, Hoffmann KP. Neurons in the primate superior colliculus coding for arm movements in gaze-related coordinates. *Journal of Neurophysiology* 2000;83:1283–99.
- [22] Taira M, Mine S, Georgopoulos AP, Murata A, Sakata H. Parietal cortex neurons of the monkey related to the visual guidance of hand movement. *Experimental Brain Research* 1990;83:29–36.
- [23] Tardy-Gervet MF, Gilhodes JC, Roll JP. Induction of illusory limb movement as a means of studying sensorimotor interactions in the eye–arm system. *Brain Behavioral Evolution* 1989;33:165–70.
- [24] van Donkelaar P. Eye–hand interactions during goal-directed pointing movements. *Neuroreport* 1997;8:2139–42.
- [25] van Donkelaar P, Lee RG. Interactions between the eye and hand motor systems: disruptions due to cerebellar dysfunction. *Journal of Neurophysiology* 1994;72:1674–85.
- [26] Ventre J, Zee DS, Papageorgiou H, Reich S. Abnormalities of predictive saccades in hemi-Parkinson's disease. *Brain* 1992;115:1147–65.
- [27] Vercher JL, Gauthier GM. Cerebellar involvement in the coordination control of the oculomanual tracking system: effects of cerebellar dentate nucleus lesion. *Experimental Brain Research* 1988;73:155–66.
- [28] Vercher JL, Gauthier GM. Oculo-manual coordination control: ocular and manual tracking of visual targets with delayed visual feedback of the hand motion. *Experimental Brain Research* 1992;90:599–609.
- [29] Vercher JL, Gauthier GM, Guedon O, Blouin J, Cole J, Lamarre Y. Self-moved target eye tracking in control and deafferented subjects: roles of arm motor command and proprioception in arm–eye coordination. *Journal of Neurophysiology* 1996;76:1133–44.
- [30] Vercher JL, Magenes G, Prablanc C, Gauthier GM. Eye–head–hand coordination in pointing at visual targets: spatial and temporal analysis. *Experimental Brain Research* 1994;99:507–23.
- [31] Vercher JL, Quaccia D, Gauthier GM. Oculo-manual coordination control: respective role of visual and non-visual information in ocular tracking of self-moved targets. *Experimental Brain Research* 1995;103:311–22.
- [32] Werner W. Neurons in the primate superior colliculus are active before and during arm movements to visual targets. *European Journal of Neurosciences* 1993;5:335–40.
- [33] Werner W, Dannenberg S, Hoffmann KP. Arm-movement-related neurons in the primate superior colliculus and underlying reticular formation: comparison of neuronal activity with EMGs of muscles of the shoulder, arm and trunk during reaching. *Experimental Brain Research* 1997;115:191–205.
- [34] Werner W, Hoffmann KP, Dannenberg S. Anatomical distribution of arm-movement-related neurons in the primate superior colliculus and underlying reticular formation in comparison with visual and saccadic cells. *Experimental Brain Research* 1997;115:206–16.