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Globus Pallidus and motor initiation: the bilateral effects of unilateral quisqualic acid-induced lesion on reaction times in monkeys

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Abstract The results of many experimental studies have shown that the globus pallidus (GP) is involved in the control of motor activities, particularly during motor execution. Whether or not the GP is involved in the initiation phase is still a matter of controversy, however. This question was investigated in the present study in *Papio papio* monkeys after GP lesion using a simple reaction time (RT) task, focusing particularly on the initiation phase. The monkeys were trained to perform this task, which consisted of raising their hand as quickly as possible in response to a visual signal. The RT and its premotor and motor components were measured. In addition, the distribution of the RTs was analyzed in order to assess the number of long latency responses. After making unilateral GP cell lesions by locally injecting small amounts of the excitatory amino acid quisqualic acid, a bilateral increase was observed in RT. This lengthening involved both the premotor and the motor phases of the RT when the task was performed with the contralateral limb and only the premotor phase when it was performed with the ipsilateral one. A significant increase was observed in the percentage of long latency responses recorded in the contralateral limb after the GP lesion but not in the ipsilateral one. Increases in the RT and in the percentage of long latency responses are thought to constitute two indices of the akinesia observed in our task involving speed constraints, which suggests that the GP may participate in motor initiation. A complete recovery of the RT was observed within one month, whereas the increase in the percentage of long latency responses persisted. These two indices of akinesia seemed therefore to result from an impairment involving both motor and nonmotor processes. These data suggest that the GP may be involved in the control of postural adjustment, motivation, and/or the control of the initial isometric part of movements. The time course of the recovery from the deficits observed after GP lesion shows the existence of mechanisms which seem to have been operative particularly in the case of impairments affecting motor processes.

Key words Globus pallidus · Reaction time
Premotor and motor phases · Long latency responses
Quisqualic acid lesion · Monkey

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Introduction

The globus pallidus (GP), together with the other structures belonging to the basal ganglia (BG), forms a functional group which participates in the regulation of motor activity. It has been established on the basis of both experimental (DeLong 1971) and clinical data (Martin 1967) that this nucleus is involved in movement control.

In primates, the GP consists of two segments, the external (GPe) and internal (GPi) segments, which are separated by the internal medullary lamella. The GP has been classified as one of the "motor" structures on the basis of anatomical data on its afferent and efferent projections: the GP receives striatal afferents, mainly arising from the putamen (Put), which is one of the targets of the corticostriatal fibers originating from the motor cortex (MI; Künzle 1975), the premotor cortex (PM) and the supplementary motor area (SMA; Künzle 1978). On the other hand, the GP gives off pallidal efferents via the ventroanterior (VA) and ventrolateral (VL) thalamus (Devito and Anderson 1982; Parent and Debellefeuille 1982, 1984) to the SMA (Percheron et al. 1986; Schell and Strick 1984; Tokonu et al. 1992) and to the MI (Nambu et al. 1988) from its internal segment, which is one of the main output points from the BG.

Experimental investigations have established that the GP plays a key role in the control of motor execution. After GP lesion, an increase in the movement time has been reported to occur (Beaubaton et al. 1981; Horak and Anderson 1984; Mink and Thach 1991c). Likewise, electrophysiological recordings have shown that a change in the activity of GP cells occurs during move-

ments: these changes have been correlated with changes in movement parameters such as direction, amplitude, and velocity (Georgopoulos et al. 1983). In other studies, after assessing pallidal activity in a variety of tasks, no consistent relationship was observed, however, between pallidal activity and the physical parameters of movement defined above (Brotchie et al. 1991; Mink and Thach 1991b). These results suggested that these movement parameters may not be under pallidal control.

The GP also seems to play an important role in postural control. Experimental GP lesions have been found to induce a flexed posture in the anterior contralateral limb (Beaubaton et al. 1981; DeLong and Coyle 1979; Hore and Vilis 1980; Mink and Thach 1991c) and a contraversive head deviation in the monkey (DeLong and Coyle 1979). Electrophysiological recordings have shown, moreover, that a sustained discharge occurs in most GP cells (DeLong 1971; Iansek and Porter 1980). One of the reasons for the continuous nature of this discharge may be that the activity of these neurons was coupled to that of postural muscles serving to support the trunk, neck, and head (Iansek and Porter 1980).

In electrophysiological studies, context-dependent responses to sensory stimuli that triggered motor responses have been recorded in neurons of the caudate (Rolls et al. 1983; Rolls and Williams 1987) and the putamen (Liles 1985; Rolls and Williams 1987). As the functional representation observed in the striatum is maintained in the GP (Delong et al. 1985) through striatopallidal connections with a specific topographical organization (Smith and Parent 1986; Hedreen and Delong 1991), it seems likely that this context-dependent activity may be reflected in the GP.

The existence of strong afferent inputs to the GP from the striatum, which is involved in movement initiation (Schultz and Romo 1988), suggests that the GP may be engaged in the neural processes underlying the initiation of movement. The experimental data relating to this question are contradictory, however. Some electrophysiological data seem to support the idea that the GP is involved in motor initiation: a change in the neuronal discharge was observed prior to the onset of electromyographic activity (EMG) in the cat (Neafsey et al. 1978) and monkey (Nambu et al. 1990). The results of three other electrophysiological studies suggested that the GP cannot initiate movement, since the activity of only a few GP units changed before the EMG and the bulk much later (Mitchell et al. 1987; Mink and Thach 1991b). Other data from studies involving experimental lesions in monkeys, showing that after pallidal lesion no change in the movement latency occurred in a reaching task (Horak and Anderson 1984) or in a tracking task (Mink and Thach 1991c), are not compatible with the idea that the GP may contribute to motor initiation.

In view of the above discrepancies among the data on the putative role of the GP in movement initiation, the aim of the present study was to analyze in conditioned monkeys the effects of selective unilateral lesions of pallidal neurons on the latency of a forelimb-raising movement using a reaction time task where the subjects had to trigger the movement as quickly as possible. This procedure, focusing particularly on the initiation phase of the movement, seemed to be appropriate for analyzing more specifically the contribution of the GP to the initiation processes. Some of the preliminary results of this study have previously been reported in abstract form (Alamy et al. 1990).

Materials and methods

The behavioral task

Two *Papio papio* monkeys (subjects P and T) were trained to perform a simple reaction time (RT) task. Briefly, the task consisted of raising one forelimb in response to a visual signal. The subject was placed in a cage facing a panel fitted with a platform, which served as the starting point of the motor response. The monkey spontaneously placed its muzzle in a mask attached to the top of the cage bars. By looking through the two eye-holes in the mask, it was able to see the panel. The motor sequence was triggered when the animal spontaneously placed its hand on the platform. After a preparatory period (PP) of variable length (400, 600, 800, or 1000 ms), a luminous signal was then switched on in the center of the panel. The subject was required to perform a nonaimed movement as quickly as possible before the luminous signal was switched off (maximum signal duration 250–300 ms during the training period and 1000 ms when the performances became stable). During the preoperative period (PREOP), the maximum signal duration (SD) was increased to 1000 ms both before and after the lesions, as the subjects were so severely handicapped after GP lesion that a longer SD was necessary for any movement to be observed. This change did not make any difference to the RT, as the regression analysis of the PREOP RT showed that there existed no significant trends in the RT values during the PREOP (with subject P, $F=0.024$ and $F=1.363$, $df=19$, $P>0.05$ in the two limbs; with subject T, $F=0.333$ and

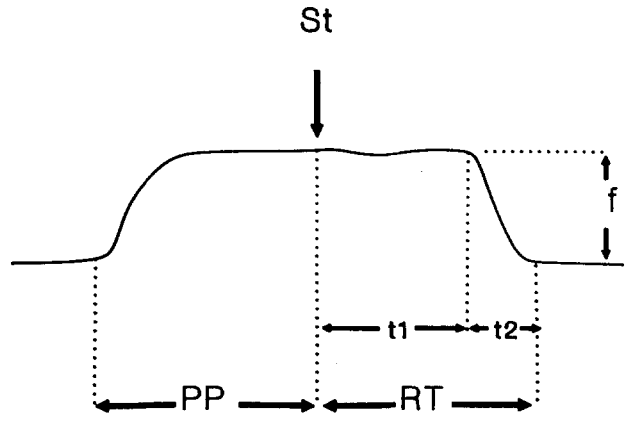

Fig. 1 Experimental procedure: the subject placed its hand on a starting platform, thus triggering the onset of a luminous signal (*St*) after a variable preparatory period (*PP*). The reaction time (*RT*) was the time elapsing between the onset of the luminous signal and the platform release. The strain gauge measurements of the amplitude (*f*) of any changes in the force exerted by the subject's hand during the RT showed the existence of two phases: the premotor phase (t_1), corresponding to the latency of the force change, and the motor phase (t_2), corresponding to the duration of this force change

$F = 0.673$, df = 19, $P > 0.05$). A liquid reward (fruit juice) was provided whenever the subject produced the correct motor response. The subjects underwent two daily series of 50 trials with each hand. The subjects' behavior (whether or not it seemed to result from the lesion) was also recorded during the daily sessions.

The RT was defined as the time elapsing between the signal onset (St) and the platform release. The RT values were recorded during each series of trials by means of a computer device. The RT could be decomposed into two phases on the basis of the changes in the force exerted by the subject's hand on the starting platform, which were measured by means of a system of strain gauges attached to the platform (Fig. 1). The following variables were therefore measured: the premotor phase t_1, corresponding to the force change latency period; the motor phase t_2, corresponding to the duration of the force change; the amplitude of the force change (f).

Statistical analysis

Once the subjects' RTs had become stable (after 6 months), 20 PREOP sequences of 50 trials were carried out with each hand. The distributions of the mean RT, t_1 and t_2 values, and those of the forces developed before and after the lesion were found to be normal. These mean values were therefore compared using Student's t-test. From the shape of the curve showing the changes in RT after GP lesion, the postoperative period could be seen to comprise three 15-day phases (PO1, PO2, and PO3) in subject P, and two 20-day phases (PO1 and PO2) in subject T. All the phases included 15 (in the case of subject P) or 20 (in the case of subject T) sequences of 50 trials with each hand. The means of the movement variables recorded in each of the phases were then compared with the PREOP means, using Student's t-test with a probability threshold of $P < 0.05$.

Lesion technique

The two animals were anesthetized with pentobarbital (Nembutal, 35 mg/kg i.v.) and their head fixed in a stereotaxic apparatus adapted for use with radiological methods. The GP was located using the stereotaxic coordinates given in the atlas by Davis and Huffman (1968). These coordinates were then corrected as follows:

1. Using a ventriculographic technique, consisting of injecting a radio-opaque substance into the lateral ventricles. This made it possible to detect the anterior and posterior commissures and hence to determine the position of the GP in relation to the commissures.

2. By performing electrophysiological recordings. With a unipolar steel electrode (0.7 mm in diameter), it was possible to record the spontaneous activity of the structures encountered along an oblique trajectory (the Put, the GPe, and the GPi) at an angle of 70° to the horizontal, and thus to avoid damaging the internal capsule. It is worthnoting that different trajectories were used for the electrophysiological recordings from those taken for neurotoxin injection purposes, so as to avoid causing any diffusion of the injected substance along the needle trace. The recordings were carried out either in more caudal planes (A12, A9) than the injection or more laterally than the injection planes.

The lesion was induced by unilaterally injecting 0.6 µl of quisqualic acid (QUIS) at a concentration of 0.18 M at four points on four anteroposterior planes (A15, A16, A17, A18). The injections were performed using a 2-µl Hamilton syringe implanted obliquely at an angle of 70° to the horizontal.

Histology

At the end of the experiment, the monkeys were given an overdose of anesthesia and perfused with saline followed by 10% formalin. The brains were extracted and cut serially into 50-µm-thick coronal sections. The frontal slices were then labelled using the Klüver-Barrera method: after double-staining with luxol blue and cresyl violet, the cells and fibers were examined with a view to assessing the extent of the lesion and to checking whether the passing fibers were still intact by performing qualitative analyses on the staining. The lesions could easily be identified as those areas containing reactive gliosis and lacking neuronal cell bodies.

Results

Histology

The controls performed as described above confirmed that the lesion was restricted to the two segments of the GP in both monkeys, since neuronal destruction and glial proliferation were both observed exclusively in this structure. The extent of the lesion was assessed by making bilateral comparisons between the cell densities (Fig. 2). Microscopic comparisons on the bilateral cell densities in structures around the GP such as the Put and the thalamus revealed the existence of no noticeable asymmetry. A diagram of the lesion is given in Fig. 3, showing the site and the extent of the lesion. It was found to have damaged the dorsomedian part of the two pallidal segments in subjects P and T. Qualitative examination of the staining suggested that no great fiber loss had occurred, as the density of the passing fibers was the same on both the control and the injected sides.

In subject P, the lesion extended from A13 to A17 in the anteroposterior plane, encompassing both the external and internal segments of the GP and showing its maximum extent in plane A15 (Fig. 3A). In subject T, the lesion extended from A14 to A20, showing its maximum extent in plane A17 (Fig. 3B). The extent of the lesion was more rostral in subject T, whereas the dorsoventral extent seems to have been fairly similar in both subjects.

Behavioral observations

Subject P could perform the task as early as the 2nd day after surgery. It showed slight postural impairments involving the head, which was bent to the contralateral side, and the contralateral anterior limb, where the elbow was flexed and the fingers extended. When this subject was manipulating small pieces of food, the grasp was impaired. Subject P tended to make preferential use of the limb ipsilateral to the lesion. When this subject was observed performing the task after the GP lesion, the movements made with the arm contralateral to the lesion showed a loss of amplitude in comparison with both the ipsilateral arm and the animal's arm-raising performances prior to the pallidal lesion during the first postoperative period.

Subject T showed no postural deficits, but seemed to be suffering from an akinesia of the forelimb contralateral to the lesion, which was only obvious during the experiments. In this task-specific akinesia, which lasted for 6 days, the subject could not raise its contralateral limb when performing the behavioral task, but could

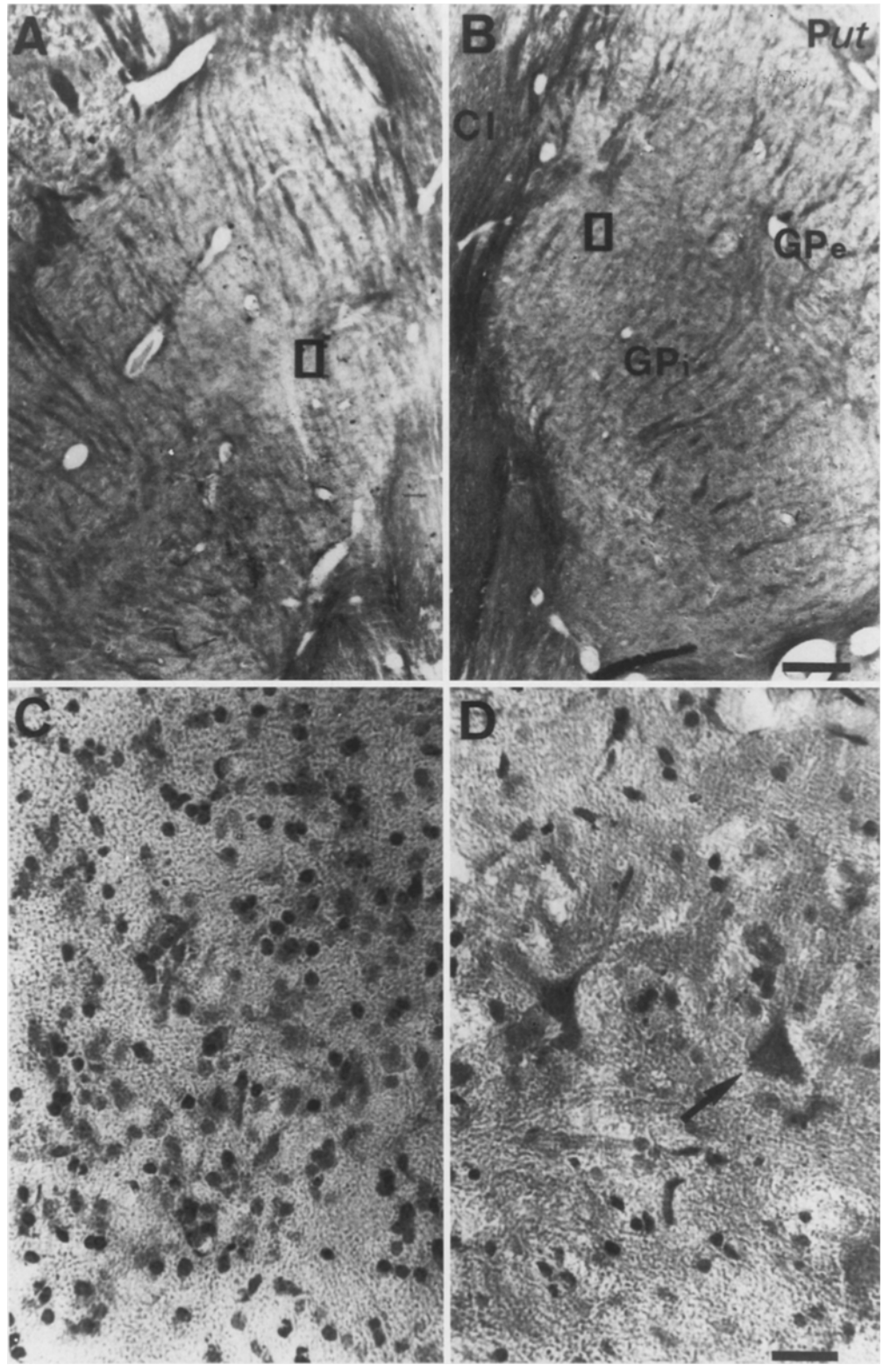

Fig. 2A–D The effect of quisqualic acid (Quis) injection on neurons of the internal segment of the globus pallidus (*GPi*). **A** The side ipsilateral to the Quis injection; **B** The side contralateral to the injection, which served as a control. The area in the *square* (**A**) has been enlarged in **C** on the side ipsilateral to the injection and in **D** on the control side. The frontal slices were labelled using double-staining with luxol blue and cresyl violet. The *arrow* in **D** shows a pallidal cell. *Scale bars* **A,B** 660 μm, **C,D** 33 μm. (*GPe* external segment of globus pallidus, *CI* capsula interna, *Put* putamen)

use this limb to grasp and eat food. This animal showed a preferential use of the ipsilateral forelimb, and its grasp was impaired. As the akinesia began to subside in the early postoperative period (the first postoperative period did not include the first 6 days, but began on day 7), the movements performed by the arm contralateral to the lesion showed a loss of amplitude in comparison with both the ipsilateral arm and the animal's arm-raising performances prior to the pallidal lesion.

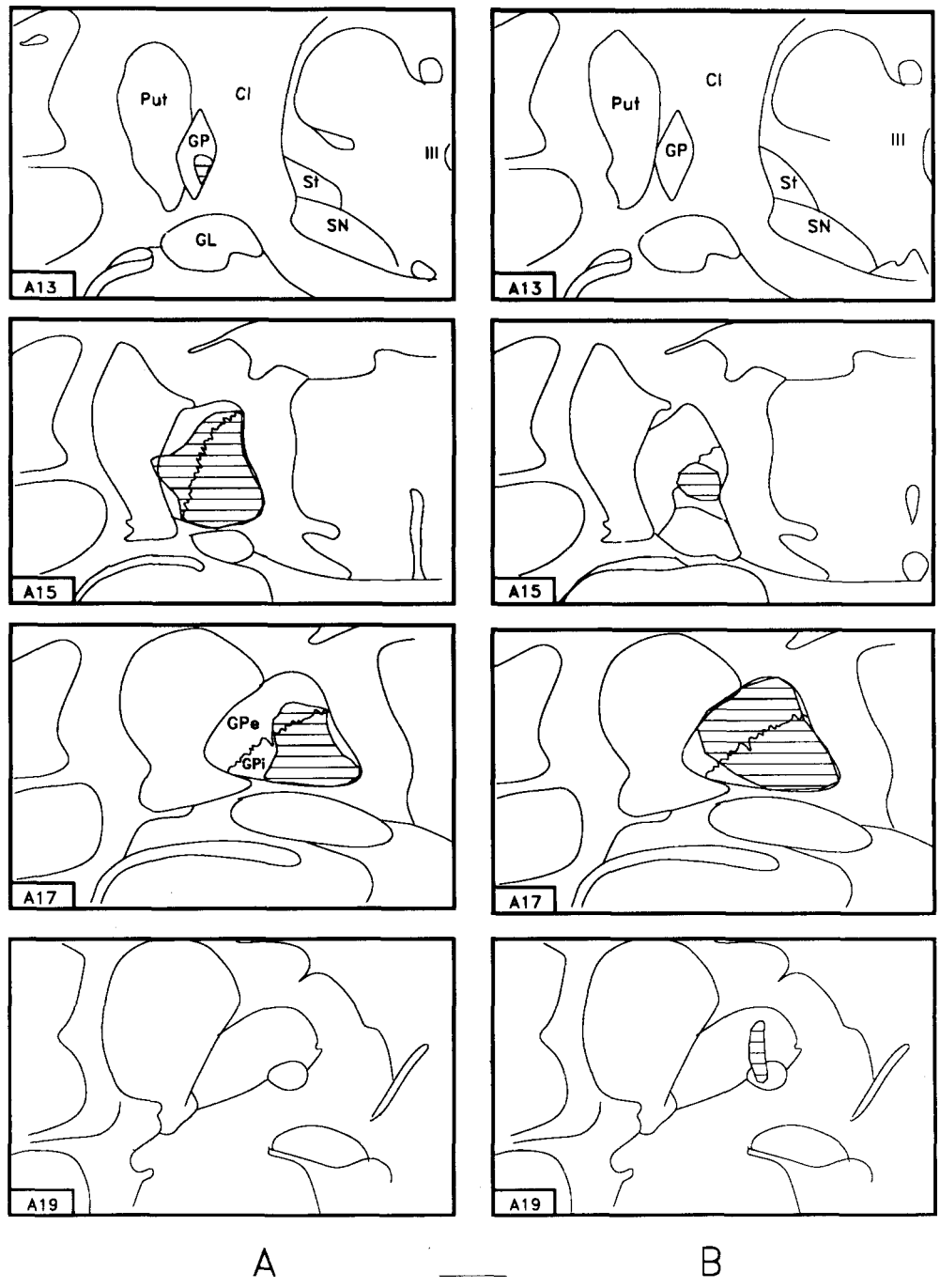

Fig. 3 Histological reconstruction in four frontal planes of the effect of unilateral quisqualic acid injection in the globus pallidus (*GP*) in subject P (**A**) and T (**B**). *Shading* indicates areas of cell body loss as defined under microscopy in four frontal sections, A13, A15, A17, A19. *Scale bar* 5 mm. (*GL* nucleus geniculati lateralis, *GPe* external segment of globus pallidus, *GPi* internal segment of globus pallidus, *CI* capsula interna, *Put* putamen, *St* nucleus subthalamicus, *SN* substantia nigra, *III* ventriculus tertius)

Effects of pallidal lesion on the percentage of long latency responses

The mean RTs recorded during the PREOP varied between 130 and 250 ms in subject P and between 200 and 310 ms in subject T. Figure 4 gives a random sample of the RT distribution in the two subjects during the PREOP and the first postoperative period in both the ipsilateral and the contralateral forelimb with respect to the lesion. After the GP lesion, the distribution of the RTs in the sequences recorded during all of the examined postoperative period (PO1, PO2, and PO3) differed from that of the prelesion RTs: a larger number of trials can be seen to lie outside this range of distribution (RT > 400 ms in the case of subject P and RT > 600 ms in that of subject T). These trials were called long latency responses to the visual stimulus. There was no upper limit to the long latency responses, as in our experiments the subject had to release the platform at the end of each trial to initiate the subsequent trial. The percentage of long latency responses can be taken to provide an index to the degree of akinesia resulting from the lesion.

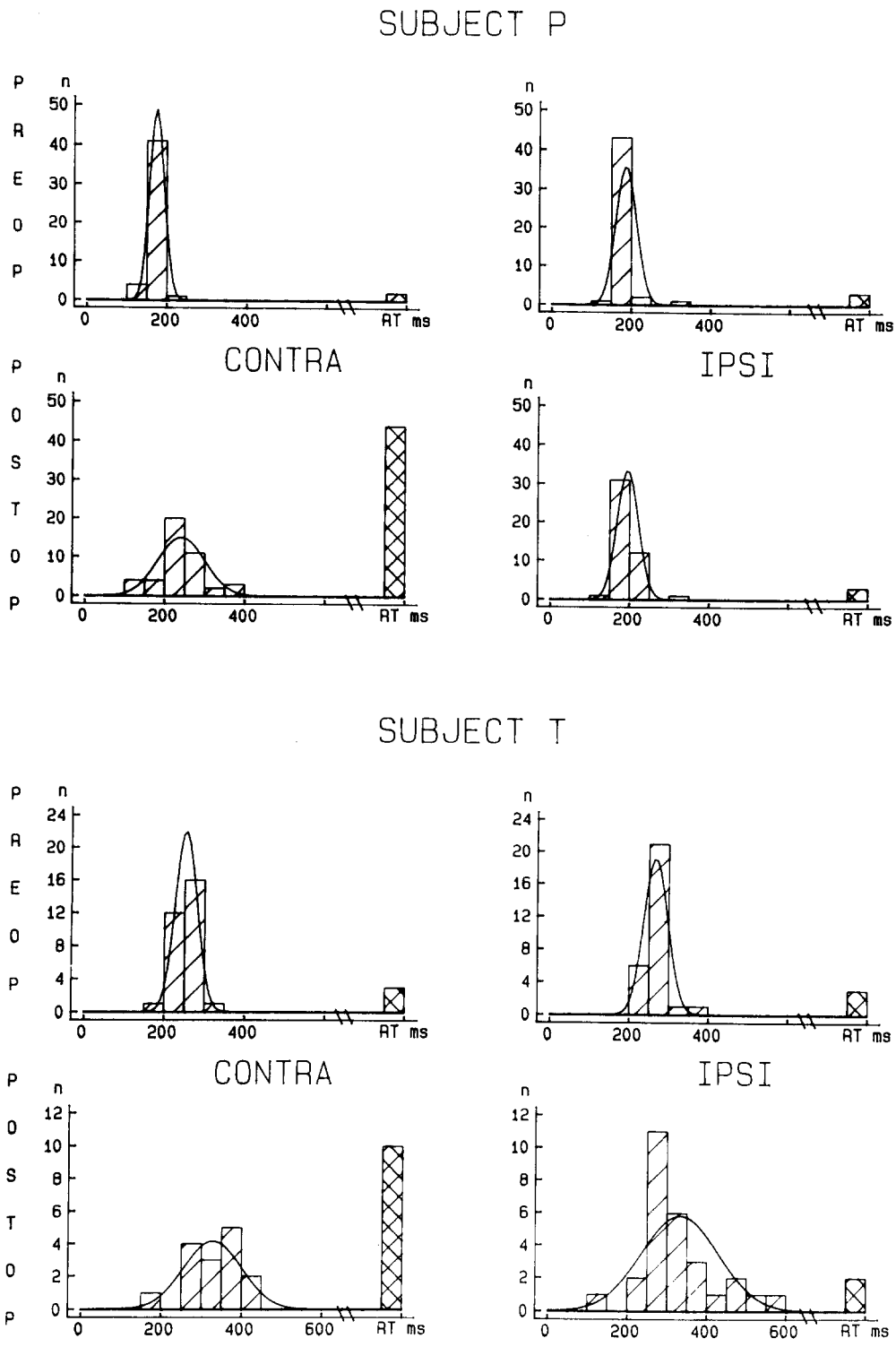

Fig. 4 Distribution of the reaction times in one sample trial performed by subjects P and T before (*PREOP*) and during the first postoperative period (*POSTOP*) after globus pallidus lesion in contralateral (*CONTRA*) and ipsilateral (*IPSI*) limbs. Any reaction times (*RTs*) that did not fit the first distribution (RT > 400 in subject P, RT > 600 in subject T) were taken to constitute long latency responses to the visual stimulus, and were rearranged in the *crosshatched blocks* on the *right* of each distribution curve

Contralateral limb

After the pallidal lesion, a statistically significant increase in the percentage of long latency responses occurred in both subjects. In subject P, the percentage of long latency responses, which was $6 \pm 5\%$ prior to surgery, increased significantly after the lesion in the three postoperative periods. This percentage reached $46 \pm 20\%$ ($t = 6.2$, $P < 0.05$) during PO1, $49 \pm 6\%$ during PO2 ($t = 14.7$, $P < 0.05$), and $41 \pm 10\%$ ($t = 9.79$, $P < 0.05$) during PO3.

In subject T, the percentage of long latency responses, which was $8 \pm 5\%$ prior to surgery, increased significantly after the lesion in PO1 and PO2. This increase reached $44 \pm 25\%$ ($t = 4.19$, $P < 0.05$) during PO1 and $22 \pm 13\%$ ($t = 2.95$, $P < 0.05$) during PO2.

Table 1 Reaction times (*RT*) recorded during preoperative (*PREOP*) and postoperative (*POSTOP*) periods *PO*1–3 in ipsilateral (*IPSI*) and contralateral (*CONTRA*) limbs in the two subjects T and P. Values are mean ± SD

Subject	Operant arm	POSTOP RT (ms)	POSTOP RT (ms)
	CONTRA	195 ± 13	PO1 263 ± 37* PO2 225 ± 25* PO3 203 ± 8
P	IPSI	183 ± 12	PO1 192 ± 26* PO2 180 ± 6 PO3 180 ± 6
	CONTRA	279 ± 18	PO1 324 ± 44* PO2 280 ± 32
T	IPSI	270 ± 13	PO1 305 ± 26* PO2 281 ± 19

*Significant difference from the preoperative values at $P < 0.05$

Ipsilateral limb

After the lesion, no significant changes were observed in the percentage of long latency responses in either subject P or T. The percentage of long latency responses in subject P was 7 ± 8% during PREOP, 6 ± 6% ($t = 0.07$) during PO1 and 12 ± 3% ($t = 0.07$) during PO3. The percentage of long latency responses in subject T was 11 ± 5% prior to surgery 13 ± 9% ($t = 0.08$) during PO1 and 12 ± 3% ($t = 1.3$) during PO2.

Effects of pallidal lesion on reaction time

The effects of GP lesion on the RTs (the long latency RTs were excluded from the RT means) of subjects P and T can be seen from Table 1 in the case of both the contralateral and ipsilateral hands with respect to the lesion. A bilateral lengthening of the RT and an increase in the standard deviation were observed.

Contralateral limb

In subject P, the RT increased by 34% during PO1. This is a statistically significant increase ($t = 10.88$, $P < 0.05$). During PO2, the increase amounted to 15%, which was still statistically different from the PREOP values ($t = 5.46$, $P < 0.05$). A recovery was observed during PO3, when the RT increase dropped to 4% ($t = 2.56$).

In subject T, a 16% increase in the RT was recorded during PO1, which was statistically significant ($t = 2.87$, $P < 0.05$). The RT was recovered during the PO2 since the 1% RT increase was not statistically different from the PREOP value ($t = 0.04$).

Ipsilateral limb

In the two subjects, a significant increase in the RTs was recorded during PO1: the increase amounted to 6% in subject P ($t = 3.18$, $P < 0.05$), and to 13% in subject T ($t = 4.16$, $P < 0.05$). The RTs recorded in subject P during PO2 ($t = 0.7$) and during PO3 ($t = 0.45$) were no longer statistically different from PREOP. The RTs recorded in subject T during PO2 were not significantly different from the PREOP values ($t = 1.4$).

Effects of pallidal lesion on RT components and on the amplitude of the force change

The premotor phase (t_1) and the motor phase (t_2) were measured only during PO1. The lesion had differential effects between the two forelimbs on these two variables.

Contralateral limb

Comparisons between the t_1 values recorded before and after GP lesion showed that the values increased after the lesion in subjects P and T (Table 2). This increase was statistically significant in both subject P ($t = 10.84$, $P < 0.05$) and subject T ($t = 5.48$, $P < 0.05$). A significant increase in the duration of t_2 was observed in both subject P ($t = 7.6$, $P < 0.05$) and subject T ($t = 10.9$, $P < 0.05$; Table 2). The strain gauge data also show that the change in the force level recorded at the start of the

Table 2 Effects of globus pallidus lesion on the two phases t_1 and t_2 in the contralateral (*CONTRA*) and ipsilateral (*IPSI*) limbs in subjects P and T during postoperative period 1 (*PO*1). Mean values from 20 trials ± SD

Subject	Operant arm	t_1 (ms)		t_2 (ms)	
		PREOP	PO1	PREOP	PO1
P	CONTRA	164 ± 13	222 ± 18*	43 ± 10	83 ± 19*
	IPSI	155 ± 152	17 ± 14*	44 ± 9	40 ± 8
T	CONTRA	201 ± 10	232 ± 22*	65 ± 9	117 ± 19*
	IPSI	206 ± 17	273 ± 33*	48 ± 10	55 ± 8

*Significant difference from the preoperative values (*PREOP*) at $P < 0.05$

Table 3 Changes in the force (*f*) exerted by the hand on the platform (starting point of the motor sequence) after globus pallidus lesion during postoperative period 1 (*PO*1) in ipsilateral (*IPSI*) and contralateral (*CONTRA*) limbs in the two subjects T and P. Mean values from 20 trials ± SD

Subject	Operant arm	*f* (g)	
		PREOP	PO1
P	CONTRA	302 ± 42	266 ± 54*
	IPSI	509 ± 128	557 ± 80
T	CONTRA	825 ± 225	303 ± 64*
	IPSI	811 ± 97	748 ± 79

*Significant difference from the preoperative values (*PREOP*) at $P < 0.05$

motor sequence decreased by 12% with subject P ($t=6.3$, $P<0.05$) and 63% ($t=19$, $P<0.05$) with subject T (Table 3).

Ipsilateral limb

Comparisons between the t_1 values recorded before and after GP lesion showed that the values increased after the lesion in subjects P and T (Table 2). This increase was statistically significant in both subject P ($t=17.7$, $P<0.05$) and subject T ($t=5.94$, $P<0.05$). In the case of the t_2 values, no significant change was found to occur on the ipsilateral side after the lesion in either subject *P* ($t=1.7$) or subject T ($t=1.33$; Table 2). The strain gauge recordings do not show the existence of any change in the force exerted by the limb ipsilateral to the lesion in either subject *P* ($t=0.05$) or T ($t=0.36$; Table 3).

Discussion

The aim of the present study was to analyze the effects of unilateral neurotoxic GP lesion on the initiation phase of a simple RT task performed by monkeys, where the task involved triggering the limb movement as quickly as possible in response to a visual signal. By introducing this speed constraint, we were able to focus our investigations on the control of the movement initiation phase.

Unilateral GP lesions affecting the two pallidal segments in trained monkeys resulted in a bilateral increase in RT. Furthermore, the GP lesion was followed by an increase in the percentage of long latency responses in the contralateral forelimb and a decrease in the force exerted by the subject's hand at the starting point of the motor response.

Choice of the neurotoxic acid

In order to perform a specific GP lesion, QUIS, an excitatory amino acid with excitotoxic properties, was used. QUIS has a much lower neurotoxic potency than either kainic acid (KA; Schwarcz et al. 1978), the most widely used excitatory amino acid for GP lesions (Horak and Anderson 1984; Mink and Thach 1991c), or ibotenic acid (IBO; Dunnett et al. 1991). Although KA is highly destructive to neuronal perikarya, it can cause a significant amount of damage to passing axons (Mason and Fibiger 1979). In addition, the neurons in various brain regions appeared differentially sensitive to KA (Köhler and Schwarcz 1983; Peterson and Moore 1980) and KA injections have often resulted in neuronal degeneration far from the site of infusion (Köhler and Schwarcz 1983; Zaczek et al. 1980). QUIS produces greater and more restricted destruction than IBO and less signs of nonspecific damage (Robbins et al. 1989a,b). We therefore chose QUIS because it has less nonspecific neuroanatomical effects than KA or IBO (Dunnett et al. 1987).

Akinesia after pallidal lesion

The present data show that both the RT and the percentage of long latency responses increased after the GP lesion. The deficits were particularly conspicuous in the limb contralateral to the lesion. A lengthening of the RT or no occurrence of the movement have been taken by Hallet (1990) to be signs of akinesia in humans. The RT deficits and the increase in the percentage of long latency responses observed in our study after GP lesion are two such signs that argue in favor of the idea that the GP may be involved in the control of motor initiation.

Our findings are in line with electrophysiological data suggesting that the GP may be involved in the control of the motor initiation phase of movements (Nambu et al. 1990; Neafsey et al. 1978). These data showed that the activity of the pallidal cells underwent a change prior to the onset of the movement, particularly prior to the first change in the EMG pattern in the cat in 30% of the GP cells and 50% of entopeduncular neurons (Neafsey et al. 1978) and in more than one third of the neurons located in the posterior ventrolateral portion of the two segments of the GP in the monkey (Nambu et al. 1990).

On the other hand, our results are also in agreement with pharmacological data showing that the impairment of the GABAergic transmission in the GP resulted in an akinetic state and a loss of spontaneous movements in rats (Pycock et al. 1976). These findings again support the idea that the GP may contribute to controlling the motor initiation phase of movements.

The BG are actually thought to be components of multiple, parallel, segregated circuits involving specific BG, thalamic and cortical areas (Alexander et al. 1986; Alexander and Crutcher 1990). The GP has a privileged location, since it relays BG outputs to the cortical motor areas via the thalamus. These parallel circuits may regulate some aspects of movement such as movement initiation. This hypothesis is consistent with the results of electrophysiological studies on the structures constituting these circuits, which show that the striatum (Schultz and Romo 1988), the VA and VL thalamic nuclei (Neafsey et al. 1978), and the SMA (Wiesendanger 1986) all participate in the initiation processes. Authors using RT procedures have, moreover, reported that the RT increased after experimental lesion of the Put in the monkey (Beaubaton et al. 1980), the striatum in the rat (Amalric and Koob 1987; Carli et al. 1985) and the thalamic VL nucleus in the cat (Bénita et al. 1979), as well as in human subjects with cortical lesions including the SMA (Vuillon-Cacciuttolo et al. 1988), which suggests that these structures may also be involved in movement initiation.

Our results do not, however, fit those obtained in previous studies in a reaching task (Amato et al. 1978, Horak and Anderson 1984) or in a tracking task (Mink and

Thach 1991c). These studies reported that no increase in the RT occurred after a GP lesion induced by injecting KA (Horak and Anderson 1984, Mink and Thach 1991c) or by electrolytic lesion (Amato et al. 1978). This discrepancy may be due to the fact that, since our task was visually triggered but not visually guided, the visual cue was the cue to move. Moreover, our subjects were required to trigger their movements as quickly as possible. This paradigm would reduce the use made by the subjects of visual cues. Since visual afferents come into play in the early stages of motor initiation (Conti and Beaubaton 1976; Prablanc et al. 1979), and as visual feedback is known to improve subjects' performances after pallidal lesion (Alamy et al. 1991; Hore et al. 1977) the effects of GP lesion may have been more obvious in our task, which was designed to reduce the use of visual information. Moreover, Mink and Thach (1991a) have reported that, in the ventrolateral part of the two segments of the GP, a higher proportion of neurons discharged during a ballistic movement corresponding to a visual open-loop movement, than during a visual closed-loop movement.

The bilateral increase in the RT observed after GP lesion suggests that the motor initiation was bilaterally controlled. This is in agreement with the results of electrophysiological studies in which a substantial proportion of the movement-related neurons were found to be related to both contralateral and ipsilateral movements (DeLong 1971; Iansek and Porter 1980). This bilateral relationship to movement of pallidal neurons is also consistent with the available anatomical data, as the GP projects bilaterally to the pedunculopontine nucleus (Carpenter 1981).

The increase in the percentage of long latency responses was observed only in the contralateral limb. The increase in the percentage of long latency responses and the lengthening of the RT as signs of akinesia therefore seem to reflect impairments involving two different processes. The lengthening of the RT may have resulted from a defective motor process, while the increase in the percentage of long latency responses may have been due to an impairment affecting nonmotor processes such as motivational or attentional. No data have yet been published showing the involvement of the GP in the control of attentional processes. There exist electrophysiological data supporting the idea that motivational deficits occur after GP lesion, since the firing patterns of some neurons among the pallidal population did not depend on the subjects' performances (Nishino et al. 1985). These responses were similar to those observed in the caudate nucleus (Nishino et al. 1984). It has been suggested that these neurons may carry the internal motivational components to motor acts (Nishino et al. 1985).

Effects of the GP lesion on the control of posture

In our experiments, the subjects showed a transient tendency to flex the forelimb contralateral to the lesion. Other authors have also observed a flexed posture in human patients with pallidal lesions (Martin 1967) and in animals with experimental lesions (Beaubaton et al. 1981). The fact that the flexion was not very pronounced in our two subjects may be attributable to the small extent and/or to the unilateral nature of the lesion. Electrophysiological recordings have shown that a sustained discharge is produced by pallidal cells in GPe and GPi (DeLong 1971; Iansek and Porter 1980). The reason for this continuous discharge may be that this activity is linked to the activation of postural muscles in the trunk, neck and limbs (Iansek and Porter 1980) . This study provides further support for the hypothesis that the GP may be involved in postural maintenance.

The bilateral increase in the RT observed in our monkeys after pallidal lesion suggests that the GP may participate in the postural adjustments that occur prior to the onset of the movements. It is likely that any impairment to the anticipatory postural adjustments will therefore be reflected in the RTs. There exists anatomical evidence that the GP is involved in postural adjustments, since, on the one hand, the GP gives off bilateral efferent projections to the pedunculopontinospinal pathway (Carpenter 1981), and, on the other hand, the GP projects via the thalamus to the SMA (Schell and Strick 1984; Tokonu et al. 1992), which is known to be involved in the regulation of posture (Massion and Viallet 1990).

Effects of the GP lesion on the control of the isometric part of the movement

The RT was defined as the time elapsing between the onset of the visual signal and the subject's response, consisting here of releasing the platform. It includes a premotor and a motor phase. The onset of the initial burst in the EMG began prior to and continued into the motor phase.

The present results show that a lengthening of the motor phase occurred after pallidal lesion. This lengthening may be attributable to a change in the initial EMG burst. Horak and Anderson (1984) have reported that the amplitude of the initial burst decreased after GP lesion performed by locally injecting KA. Other authors have observed changes in the GP cellular activity in 50% of the GPe cells and 53% of the GPi neurons during the motor phase in monkeys trained to perform a tracking movement (Mitchell et al. 1987). Our finding that the motor phase, corresponding to the isometric part of the movement, was impaired after pallidal lesion, supports the idea that the GP may be involved in the control of motor execution.

Since the characteristics of the initial EMG burst are known to define those of a forthcoming movement, such as the velocity and the amplitude (Mustard and Lee 1987), a change in the pattern of this burst may indeed have been responsible for the slowing down of movements observed in monkeys after GP lesion in both

pointing (Alamy et al. 1991; Beaubaton et al. 1981) and reaching tasks (Horak and Anderson 1984).

A decrease in the amplitude of the initial EMG burst after GP lesion has also been found to occur in human parkinsonian patients (Hallet and Khoshbin 1980) as well as after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) treatment in the monkey (Doudet et al. 1990). This decrease in the EMG amplitude might be partly responsible for the bradykinesia observed. Pallidal bradykinesia is therefore similar to the EMG pattern observed in parkinsonian patients as well as in the MPTP model of Parkinson's disease. In addition, electrophysiological data have indicated that in an MPTP animal model of Parkinson's disease a change occurred both in the spontaneous activity of the GP (Filion 1979) and in the response of pallidal neurons to striatal stimulation in monkeys (Filion et al. 1989). A common pathway may therefore be involved in the expression of pallidal or nigral bradykinesia: the striatopallidothalamocortical pathway.

The lateness of the movement onset observed in the contralateral limb of our two subjects after the lesion may also be partly attributable to the decrease in the force exerted at the onset of the motor sequence and the slowness of the platform release observed under our experimental conditions. Electrophysiological data have, moreover, suggested that the GP might participate in force control, since the patterns of GP activity were linked to the isometric force exerted between two fingers in the monkey (Allum et al. 1983).

Since the increase in the motor phase and the decrease in the force exerted at the onset of the motor sequence were restricted to the contralateral limb, it can be concluded that deficits linked to the motor execution, as opposed to motor initiation impairments, are to be observed particularly in the contralateral limb after GP lesion. These data suggest that the GP may exert a differential control on the initiation and execution phases.

The time-course of functional recovery

The data obtained in the present study show that a complete recovery of the deficits observed in the RT occurred within the last postoperative period, whereas the increase in the percentage of long latency responses persisted. Thus we can suppose that in the last postoperative period, the initiatory mechanism became functional but was not always activated.

A possible explanation for the functional recovery observed in our study after unilateral GP lesion may be that compensatory activities took place in either the intact part of the GP or the contralateral GP, since electrophysiological data have shown that a substantial proportion of the movement-related neurons in the GP was related to both contralateral and ipsilateral movements (DeLong 1971; Iansek and Porter 1980). These mechanisms seem to have brought about recovery only in the case of those impairments which may affect motor processes.

In conclusion, the results of these lesion experiments shed some light on the role played by the GP in motor initiation. GP lesion induces akinesia, which may result from an impaired postural adjustment, a decrease in motivation, and/or a slowness in the initial isometric part of the movement. The animals recovered from the motor deficits after unilateral GP lesion, while the non-motor impairments persisted.

The results presented here were obtained in the case of GP lesions involving the two pallidal segments. Since there exist anatomical, electrophysiological, and neurochemical differences between the GPe and GPi (Alexander and Crutcher 1990), it might be worth to investigating the effects of applying selective lesioning to one segment. The question as to whether the GPe and GPi may play different roles in the control of motor activity certainly requires further investigation.

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