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The ipsilateral cerebellar hemisphere is overactive during hand movements in akinetic parkinsonian patients

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Summary

We compared the rCBF changes induced by the execution of a finger-to-thumb opposition motor task in the cerebellar hemispheres of 12 normal subjects, 12 parkinsonian patients whose medication had been withheld for at least 18 h and 16 parkinsonian patients on medication using single photon emission tomography and i.v. ^{133}*Xe. The normal subjects and parkinsonian patients on medication exhibited the same pattern of response, with a significant increase in rCBF in the contralateral primary motor cortex and in the supplementary motor areas. No significant rCBF change was detected in the cerebellum of these two groups; this finding was expected since our technique cannot detect cerebellar activation when the motor task is executed at a relatively low rate and small amplitude as it was in this study. The parkinsonian patients off medication exhibited a markedly different pattern of activation characterized by a significant overactivation in the ipsilateral cerebellar hemisphere and a significant underactivation in the supplementary motor areas. These results suggest that parkinsonian patients off medication may try to compensate for their basal ganglia–cortical loop's dysfunction using other motor pathways involving cerebellar relays.*

Keywords: Parkinson's disease, akinesia, cerebellum, SPECT, levodopa

Abbreviations: CM = canthomeatal lane; rCBF = regional cerebral blood flow; SPECT = single photon emission tomography; SMA = supplementary motor area; S1M1 = primary sensory motor area; UPDRS = Unified Parkinson's Disease Rating Scale

Introduction

In humans, it is possible to map the active brain areas involved in movements by measuring regional cerebral blood flow (rCBF) changes using single photon emission tomography (SPECT) (Sabatini *et al*., 1993) or PET (Fox *et al*., 1985; Colebatch *et al*., 1990; Deiber *et al*., 1991). This approach has been helpful to describe the functional plasticity of the human motor system after stroke recovery (Chollet *et al*., 1991; Weiller *et al*., 1992; Sabatini *et al*., 1994) and in amyotrophic lateral sclerosis (Kew *et al*., 1993). The reorganization of multiple motor or motor-related areas acting in parallel appears to constitute the central mechanism of brain plasticity when the pyramidal tract is lesioned (Weiller *et al*., 1995). Several studies have shown that the cerebellum is one of the brain areas which actively contributes to this phenomenon (Chollet *et al*., 1991; Weiller *et al*., 1992).

Parkinson's disease is a model of chronic dysfunction of the human extrapyramidal motor system. PET and SPECT studies have previously shown that the subcortical dopamine deficit of Parkinson's disease induces a functional deafferentation of the supplementary motor area of the cortex (SMA) (Playford *et al*., 1992; Rascol *et al*., 1992). This SMA deafferentation can be reversed by dopaminergic drugs like apomorphine (Jenkins *et al*., 1992; Rascol *et al*., 1992) and levodopa (Rascol *et al*., 1994). The hypothesis tested in this study is based on a model previously reported for patients with a pyramidal tract deficit, namely that a chronic lesion

of the extrapyramidal pathway may affect the function of a motor centre like the cerebellum acting in parallel. Motor activation of the ipsilateral cerebellar hemisphere can be measured in normal subjects with SPECT (Sabatini *et al*., 1993) and PET (Jenkins *et al*., 1994). Until now, few neuroimaging data have been produced on motor cerebellar function in Parkinson's disease because the usual position of the patients' head in the scanner does not allow a full view of the cerebellum. The aim of the present SPECT study was, therefore, to compare rCBF changes induced by a motor task in the cerebellar hemispheres of normal subjects and akinetic Parkinson's disease patients receiving on or off their medication.

Material and methods

Subjects

Forty subjects were included in this study: 28 Parkinson's disease patients and 12 normal control subjects. All patients were clinically diagnosed as having 'idiopathic' Parkinson's disease according to the UK Brain Bank diagnostic criteria (Gibbs and Lees, 1989). All patients had a positive and sustained response to dopaminergic treatments. Patients with clinical features suggestive of striatonigral degeneration (Fearnley and Lees, 1990), progressive supranuclear palsy (Daniel *et al*., 1995) or associated dementia were excluded.

Parkinson's disease patients were included only if they suffered from an akinetic-rigid syndrome without a tremor, in order to avoid rCBF signals related to this involuntary movement. The 28 Parkinson's disease patients were divided in two separate groups: in the first group (12 patients off medication) levodopa and other antiparkinsonian drugs had been withheld for at least 18 h to allow the reappearance of the parkinsonian symptoms, and in the second group (16 patients on medication) levodopa and other antiparkinsonian drugs were not interrupted. No patient on medication suffered from dopa-induced dyskinesia that was scored >1 (mildly disabled) in Item 33 of the Unified Parkinson's Disease Rating Scale (UPDRS) (part IV: complications of therapy in the past week) (Fahn *et al*., 1987). The two Parkinson's disease patient groups (on and off medication) were carefully matched in order to avoid relevant demographic, clinical or therapeutic differences (*see* Table 1).

Informed consent was obtained from all patients and normal subjects, and the project was approved by the CCPPRB–Toulouse I ethical comittee.

Paradigm design

Two rCBF measurements were obtained on the same day for each subject with a 60 min interval between scans: one measurement was obtained during the execution of a motor task (movement of one hand) and the second while lying quietly (resting state). The chronological order of the two measurements was randomized across subjects. Motor task and resting states were balanced for visual and auditory stimuli and were performed under conditions of sensory deprivation.

The motor task, described previously (Rascol *et al*., 1992, 1994; Sabatini *et al*., 1993), consists of sequential finger-to-thumb opposition movements in turn lasting for the 4 min of the rCBF data acquisition period. Handedness was not considered in the data analysis because we have previously demonstrated that this motor task induces symmetrical rCBF changes when performed with the dominant or non-dominant hand (Sabatini *et al*., 1993). Both groups of Parkinson's disease patients were asked to perform the motor task with their most affected hand. In case of symmetrical bilateral impairment, they were asked to execute the task with their dominant hand. This last instruction was also given to the normal subjects. rCBF data were then analysed considering cortical and cerebellar regions of interest contralateral and ipsilateral to the hand which executed the movement.

The manner in which each subject performed the motor task was measured using video recordings of the hand movements. This procedure allowed quantification of the motor task frequency (number of fingers-to-thumb oppositions per minute) and amplitude (on a 0–3 subjective scale where 0 = no spacing between the thumb and the fingers and 3 = maximal opening amplitude between the thumb and the finger, i.e. 90°). All subjects practised the motor task until they were able to perform the movement with a stable amplitude and frequency. Special efforts were made to arrange the experiment so that the three groups executed the motor task in a quantitative similar way. For this purpose, the Parkinson's disease patients off medication (i.e. those who had the greatest difficulties in executing the motor task because of akinesia) were studied first. They were asked to execute the motor task 'as well as they could with the largest possible amplitude and the most regular moderate frequency'. The rCBF measurements were performed when the patients had found their best and most stable performance. The mean frequency and mean amplitude achieved by the Parkinson's disease patients off medication were then calculated (mean frequency = 43/min and mean amplitude = 1.5 on the 0–3 scale). The Parkinson's disease patients on medication and normal control subjects had the capacity to execute the motor task more rapidly and with a larger amplitude than the patients off medication; however, they were instructed to perform the motor task at the same frequency and amplitude as that achieved by the Parkinson's disease group which was off medication. The rCBF measurements were performed when they were able to execute the motor task with the appropriate required performance. At the end of the study, the video recordings of all the subjects' hand movements were analysed blind to compare the mean amplitude and frequency of the three groups. The absence or presence of movements in the other parts of the body was checked during the period of data acquisition.

rCBF measurement

The technique used to measure rCBF has been described previously (Sabatini *et al*., 1993). Briefly, rCBF was assessed

Table 1 *Demographic data and performance of the motor task in the three groups*

	Normal subjects (n = 12)	PD group off medication (n = 12)	PD group on medication (n = 16)	ANOVA
Age (years)	58±4	61±3	60±2	NS
PD duration (years)	–	6±1	8±1	NS
Levodopa dose (mg/day)	–	620±150	672±97	NS
UPDRS when off medication	–	26±4	22±3	NS
UPDRS when on medication	–	9±3	8±4	NS
Motor task frequency (per min)	36±2	43±6	41±5	NS
Motor task amplitude (0–3 scale)	1.7±0.1	1.4±0.2	1.9±0.2	NS

PD = Parkinson's disease; NS = not significant.

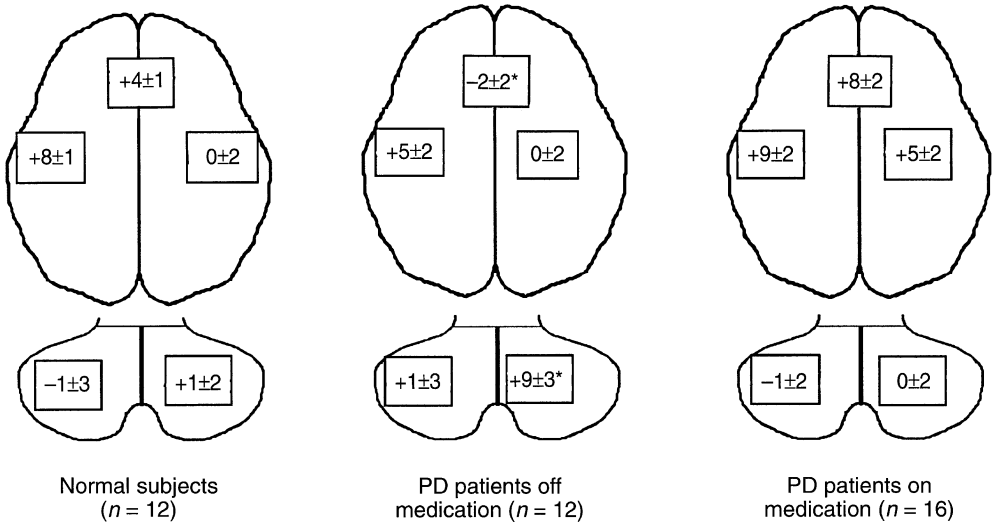

Fig. 1 Comparisons of percentage changes in rCBF (mean±SEM) induced by motor activation in the five regions of interest of the three groups of subjects. The hemisphere ipsilateral to the hand movement is drawn on the right. MANOVA: a group and region of interest interaction, $P < 0.05$; *post hoc* Fisher test: $^*P < 0.05$ for Parkinson's disease patients off medication versus normal subjects and $P < 0.01$ for Parkinson's disease patients off medication versus those on medication.

using SPECT (Tomomatic 64, Medimatic, Copenhagen, Denmark) and intravenous injection of Xenon (2220 MBq). The mean global flow was measured from data collected from three transverse slices simultaneously at 0, 4, and 8 cm above the canthomeatal plane (CM). The rCBF changes were studied in five regions of interest obtained from Slice 1 (CM+0) and Slice 3 (CM+8) (*see* Fig. 1). We determined the features of the five regions of interest (i.e. their shape, number of pixels and topography) by visual analysis of images of the tomographic slices, and by applying known functional anatomy of the motor system and data from an anatomical stereotaxic atlas (Talairach and Tournoux, 1988) Once these features had been determined, they were recorded in a Macintosh II microcomputer for image processing. The different regions of interest were then superimposed on each of the corresponding rCBF slices. This method of analysis allowed us to compare regions of interest with the same topography, shape and number of pixels in every subject. The features of each region of interest can be described as follows: each pixel measured 3.5×3.5 mm^2. In Slice 1 (CM+0), we drew two symmetrical and lateral 15-pixel regions of interest on each cerebellar hemisphere. The cerebellar regions of interest were parallel and separated from the vertical interhemisphere axis by 2 cm. Three regions of interest were drawn in Slice 3: one medial anterior region corresponding to the two SMA (12 pixels) and two symmetrical and lateral regions (16 pixels each) corresponding to the contralateral and ipsilateral primary sensory motor areas (contra- and ipsilateral S1M1). Finally the rCBF data were normalized for the five motor regions of interest using a global factor calculated from the global CBF of the three slices (rCBF at rest/rCBF during the motor task). The rCBF value for each region of interest collected during the motor task was multiplied by this factor to eliminate non-specific rCBF changes. Localization of the regions of interest on the SPECT scans were carried out blind. Considering the limited spatial resolution of our tomography system, the rCBF values in the cortical regions of interest may only represent the partial value of the specified anatomical regions. The arterial pCO_2 was continuously

recorded using a cutaneous electrode and a pCO_2 monitor (Kontron 634, Kontron, Basle, Switzerland). A small blood sample was withdrawn for determination of the packed cell volume. Systolic and diastolic blood pressure were measured at the moment of each rCBF measurement.

Statistical analysis

The rCBF values were compared between the resting state and the motor task state in the five regions of interest of each group using a paired Student's *t* test. A comparaison between the three groups of subjects, of the percentage changes in rCBF induced by the execution of the motor task in the five regions of interest, was performed using a multivariate analysis of variance (MANOVA). A *post hoc* univariate analysis (Duncan test) was examined following a significant *F* test. Significance was accepted when $P < 0.05$. Results are expressed as mean$\pm$SEM.

Results

There was no significant difference in the frequency and amplitude of the motor task between the three groups (Table 1). Five Parkinson's disease patients on medication exhibited mild bilateral dyskinetic movements during data acquisition. One Parkinson's disease patient off medication had some minor associated movements of the contralateral hand when executing the motor task. There was no significant difference between the mean global CBF of the three groups of subjects at rest or during the execution of the motor task. The normalization factor did not differ between the three groups. There was no difference in blood pressure or arterial pCO_2 between the three groups or within the same group from one scan to another. When the subjects were at rest, there were no differences in rCBF between the symmetrical regions of interest within each group, and there were no significant inter-group differences in rCBF when comparing the corresponding regions of interest in the three groups

When comparing rCBF data at rest and after activation in each group, the normal subjects and Parkinson's disease patients on medication exhibited the same patterns of rCBF activation. In these two groups, the execution of the hand movements induced a significant increase in rCBF in the contralateral S1M1 and in the SMA (*see* Table 2) but not in the ipsilateral S1M1 or in the cerebellar hemispheres. In contrast, the Parkinson's disease patients off medication showed a different pattern of activation; the motor task induced a significant rCBF activation in the contralateral S1M1 and in the ipsilateral cerebellar hemisphere while no significant signal was recorded in the three other regions of interest (*see* Table 2).

When we compared percentage changes in the rCBF in the five different regions of interest of the three different groups, the MANOVA showed a significant interaction between group and region of interest ($P < 0.05$). A *post hoc* univariate analysis (Duncan test) showed that the percentage change in ipsilateral cerebellar rCBF (ipsilateral to the hand movement) was significantly larger in the Parkinson's disease group off medication compared with the two other groups of subjects ($P < 0.02$). The percentage change in rCBF in the SMA was significantly smaller in the Parkinson's disease group off medication than in the two other groups ($P < 0.001$). There were no significant differences between the three groups in terms of percentage changes in rCBF in the contra- and ipsilateral S1M1 or in the contralateral cerebellar hemisphere.

Discussion

The main finding of our study was that the ipsilateral cerebellar hemisphere was overactive in Parkinson's disease patients who were off their medication when they performed a motor task. This abnormality was not observed in the Parkinson's disease patients who were on medication. We also confirm that the SMA is underactive in Parkinson's disease patients off medication and that normal SMA activity is restored by dopaminergic treatment. In the resting condition, no significant rCBF abnormality was observed in Parkinson's disease patients, either on or off medication.

The possibility that a methodological artefact could account for the ipsilateral cerebellar overactivity, in the Parkinson's disease patients who were off medication, must be considered. We made certain that there were no significant differences in the way control subjects and Parkinson's disease patients, on or off medication, performed the motor task. We also checked that both groups of Parkinson's disease patients had similar demographic, symptomatic and therapeutic features. The limits of the spatial resolution of our tomograph cannot account for this result. SPECT studies of motor activation (Rascol *et al*., 1992, 1994; Sabatini *et al*., 1993) provide concordant results with comparable PET studies (Deiber *et al*., 1991; Jenkins *et al*., 1992; Playford *et al*., 1992). Our tomograph can measure a significant rCBF cerebellar activation in normal subjects performing a similar motor task to that used in this study (Sabatini *et al*., 1993). In the present protocol, however, no significant activation was recorded in the ipsilateral cerebellar hemisphere of the normal subjects because of the relatively low rate and small movement amplitude in the motor task which were matched to the limited motor skill of the Parkinson's disease patients who were off medication (Sabatini *et al*., 1993). The movement must be executed faster and with a larger amplitude to detect a significant cerebellar activation in normal subjects (Sabatini *et al*., 1993). Other observations support the relevance of our results. The cerebellar overactivation was only observed in the ipsilateral cerebellar hemisphere, in agreement with known cerebellar functional organization. Moreover, it was not observed in patients on medication. Cerebellar activation has probably been missed in previous PET studies because in such studies on Parkinson's disease patients, rCBF has been measured mainly in the motor cortex and basal ganglia. The cerebellum has only been partially imaged in PET studies

Table 2 *Mean rCBF values (ml/100g/min) in the five regions of interest at rest and during motor activation*

	rCBF (mean ± SEM in ml/100 g/min)					
	Normal subjects		PD group off medication		PD group on medication	
	Resting	Active	Resting	Active	Resting	Active
Ipsilateral cerebellum	65±2	65±2	72±3	78±4*	64±2	63±2
Contralateral cerebellum	65±2	65±2	72±3	72±3	64±3	63±2
Ipsilateral S1M1	58±3	58±2	60±3	60±3	53±2	56±2
Contralateral S1M1	58±2	63±2**	59±3	61±3*	55±2	59±3**
SMA	63±2	66±3*	64±4	62±4	59±3	64±3*

S1M1 = primary sensorimotor area; SMA = supplementary motor area. *$P < 0.01$ and **$P < 0.001$ (paired Student's t test, motor activation versus resting condition).

of Parkinson's disease patients, one single slice providing data of the upper cerebellum vermis.

If a technical bias cannot account for our results, then discussion of a possible pathophysiological mechanism is necessary. rCBF activation in cerebral sensorimotor areas such as the cerebellum reflects the synaptic activity related both to the efferent motor command and the afferent somatosensory feedback information. In a recent study, Jueptner *et al*. (1996) showed that passive movements activate identical parts of the cerebellar hemisphere to almost the same extent as the corresponding active movements, underlying the importance of the afferent somatosensory component in the cerebellar activation. There is, however, no evidence of excessive somatosensory input or sensitivity in Parkinson's disease patients and no overactivation has been observed in other sensorimotor areas like the sensorimotor cortex. Thus, we believe that our findings can be explained best by changes in the motor rather than in the somatosensory systems.

Cerebellar rCBF has been measured using PET in patients with parkinsonian tremor (Deiber *et al*., 1993). These authors showed that the cerebellum contributes to the generation of parkinsonian tremor. Similar conclusions have been reported in patients with essential tremor (Will *et al*., 1994). However, the design of Deiber *et al*'s (1993) study differed from ours in two important ways: (i) they studied Parkinson's disease patients in the resting condition, whereas we studied patients performing a motor task; (ii) they studied Parkinson's disease patients suffering from a severe resting tremor whereas we excluded such patients in order to avoid any tremor-related rCBF signals. In the resting condition, our Parkinson's disease patients who were off medication (without tremor) had slightly, but not significantly higher, mean cerebellar rCBF values than the patients on medication and the normal control subjects. This is in agreement with the absence of significant change in the cerebellar cortex glucose metabolism of MPTP-(1-methyl 4-phenyl 1,2,3,6-tetrahydropyridine-) treated monkeys (Schwartzman and Alexander, 1985). Deiber *et al*'s (1993) study and ours are thus different, but complementary. The cerebellum is probably involved in the genesis of parkinsonian resting tremor. It may play another role when akinetic Parkinson's disease patients execute a movement.

It has been reported from previous clinical observations that cerebellar lesions may improve hypertony in Parkinson's disease patients. For example, surgical dentatectomy as well as cerebellar infarction have been noted to reduce or abolish ipsilateral rigidity in Parkinson's disease patients (Toth, 1961; Rivest *et al*., 1990). There is no clear explanation for this benefit but a reduction in the activity of the spinal stretch reflex due to the cerebellar lesion has been proposed. This does not imply, however, that a cerebellar overactivity could contribute to the genesis of parkinsonian rigidity. In fact, the normality of cerebellar rCBF, in the resting condition, in the Parkinson's disease patients who were off medication does not support such an hypothesis.

Thus, abnormal somatosensory inputs, and parkinsonian tremor and rigidity, are unlikely to explain our results. Akinesia is a more attractive explanation because the cerebellar overactivity was present only in dynamic conditions when akinetic Parkinson's disease patients who were off medication were asked to perform the motor task. Our results could then be interpreted as if Parkinson's disease patients tried to compensate for the failure of the basal ganglia motor loop by employing alternative motor pathways, involving, for example, the cerebellum. In a very recent PET study, Samuel *et al*. (1996) observed a similar phenomenon in the premotor and parietal cortex of Parkinson's disease patients. They suggested, as we do, that the deafferentation of the striato-mesial frontal projections in Parkinson's disease leads to compensatory overactivity of other motor-related cerebral areas during sequential finger movements. These authors could not measure rCBF accurately in the cerebellum with the PET scanner they used. Conversely, we could not easily differentiate the primary and premotor cortex according to the spatial resolution of our tomograph, but we easily measured rCBF changes in the cerebellum. It is probable that both studies show the same phenomenon at two different levels, involving the functional adaptation of the cerebello-parietal association cortex loop and premotor cortex to the defect of the basal ganglia loop.

Anatomically, the basal ganglia and the cerebellar loops are known to have distinct afferent and efferent pathways and different motor functions with little, or no, overlap in the primate. The SMA is dominated by thalamic inputs from

the subnucleus VLo which receives its major inputs from the basal ganglia, stressing the importance of the pallido-thalamo-SMA connections (Tanji, 1994). Conversely, the thalamic subnucleus VPLo is known to receive major inputs from the cerebellar nuclei and to send efferents to the primary motor cortex. There is, however, evidences of overlap between the two systems. Several authors have shown that, in the monkey, the SMA, rather than being exclusively connected with the basal ganglia, appears to be organized in a way rather similar to inferior Area 6, with one sector receiving cerebellar afferents and one sector related to the basal ganglia (Wiesendanger and Wiesendanger, 1985; Matelli *et al*., 1989; Tanji, 1994). The primary motor cortex and the SMA are recipients of transthalamic inputs from pallidum, thalamus and cerebellar nuclei, thus supporting the concept that a mixed subcortical input consisting of weighted contributions from cerebellum, basal ganglia, substantia nigra and spinothalamic tract is directed to each functional component of the motor cortex (Rouiller *et al*., 1994). Additional anatomical convergence exists both in the intralaminar nuclear complex of the thalamus (Jones, 1985) and in the magnocellular division of the red nucleus (Kennedy 1990).

Some authors have already proposed that patients with Parkinson's disease might use alternative pathways, e.g. via the cerebellum, to compensate the loss of basal ganglia (Glickstein and Stein, 1991; Marsden and Obeso, 1994). It is known that movements driven by external stimuli employ different cortical routes from those driven by internal decisions, the former using lateral frontal areas while the latter use those more medial (Goldberg, 1985; Passingham *et al*., 1989). Visual feedback may improve the motor performance in Parkinson's disease patients. Visual input may have access to the motor cortex without traversing the basal ganglia, using pontine nuclei and cerebellar relays. This visuo-motor pathway, relaying through the cerebellum, could explain why the motor performance of Parkinson's disease patients is improved when operating under visual control (Glickstein and Stein, 1991). In our experiment, however, subjects were asked to keep their eyes closed when moving the hand and the experiment was conducted under sensory deprivation conditions. Therefore, it is difficult to advocate an involvement of such visuocerebellar pathways to explain the cerebellar overactivation observed in the present protocol.

PET studies have shown that the cerebellum is activated when normal subjects are learning a motor task (Jenkins *et al*., 1994). Brooks (1995) suggested that, according to PET data, the cerebellum could be involved in motor skill acquisition or in promoting automaticity of movements, while the basal ganglia could instead facililate a required movement by monitoring and optimizing the pattern of muscular activity. The normal subjects and Parkinson's disease patients in the present study were trained to execute the motor task in advance and there is an attenuation of activation of the cerebellum as subjects become more practised (Seitz *et al*., 1990; Friston *et al*., 1992; Jenkins *et al*., 1994). This previous training may be important in explaining our results. It is clear that the 'motor states' of the three cohorts of the present study were not identical. The Parkinson's disease patients on medication and the control subjects had to be asked to slow down their natural performance, in order to mimic the best that could be achieved by the patients who were off medication. Thus, a different approach to the motor task may have influenced the levels of cerebellar activation seen in these three groups. Subjects in the three groups were all taught the task prior to SPECT and we checked that all groups performed the opposition task automatically, even while distracted. Thus, it is unlikely that the Parkinson's disease patients off medication, although having greater motor difficulties than the two other groups, were still learning to master the task during SPECT. Thus, we do not believe that they required a greater level of cerebellar activation simply because they, unlike the other two groups, might still be acquiring the skill (Frith *et al*., 1996).

Finally, it is conceivable that neurochemical abnormalities in the cerebellum of Parkinson's disease patients may also explain an abnormal function of this structure in Parkinson's disease. The cerebellar overactivity was not observed in the group of Parkinson's disease patients receiving a dopaminergic treatment. This observation suggests that the central dopaminergic deficit is related to this abnormality. Dopaminergic projections to the cerebellum appear to be quite scarce and no major decrease in cerebellar dopamine content has been reported in Parkinson's disease (Agid *et al*., 1989). There is then little evidence for a direct role of a dopaminergic deficit within the cerebellum in Parkinson's disease. It is more likely that what we observed is the functional consequence of a distant dopaminergic deficit within the basal ganglia or motor cortex. However, Pifl *et al* (1991) showed that dopamine concentrations were significantly reduced in the cerebellar cortex and dentate nucleus of MPTP-treated monkeys. Moreover, noradrenaline and serotonin markers are also known to be reduced in the cerebellum of MPTP-treated monkeys and Parkinson's disease patients (Agid *et al*., 1989; Pifl *et al*., 1991). Such abnormalities can provide additional causes of a cerebellar dysfunction and a primary cerebellar dysfunction cannot be totally ruled out.

In conclusion, the results presented here suggest that cerebellar function is affected by the basal ganglia deficit in Parkinson's disease. We suggest that this finding should be investigated further using PET and functional MRI neuroimaging techniques in humans, and electrophysiological neuronal recordings in the primate MPTP model of Parkinson's disease. Our data support the hypothesis that in Parkinson's disease patients suffering from a chronic impairment of the basal ganglia motor function, as in stroke and ALS (amyotrophic lateral sclerosis) patients, the deficit of one motor pathway is being compensated for by the use of another. This observation in the cerebellum is concordant with similar findings in the parietal and premotor cortices of Parkinson's disease patients (Samuel *et al*., 1996). However, the effectiveness of this adaptative strategy remains unclear

since, as already pointed out, lesions likely to involve the cerebello-thalamo-cortical pathways do not seem to have a major adverse effect upon movement in Parkinson's disease (Marsden and Obeso, 1994).

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