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Review

Imaging basal ganglia function

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In this review, the value of functional imaging for providing insight into the role of the basal ganglia in motor control is reviewed. Brain activation findings in normal subjects and Parkinson's disease patients are examined and evidence supporting the existence for functionally independent distributed basal ganglia-frontal loops is presented. It is argued that the basal ganglia probably act to focus and filter cortical output, optimising the running of motor programs.

Key words: Motor control; Parkinson's disease; positron emission tomography.

INTRODUCTION

While there have been considerable advances in our understanding of the pathophysiology of movement disorders, based on development of animal models of parkinsonism and chorea and observations of the functional effects of stereotactic surgery in tremor and Parkinson's disease (PD), rather less is known about the precise role that the basal ganglia play in motor control. Single unit electrical recordings have been obtained from the basal ganglia of lesioned and intact awake animals, both at rest and during performance of rewarded motor acts, and also from the pallidum and subthalamus of PD patients undergoing placement of electrical stimulators. Additionally, the behavioural problems of patients with PD, Huntington's disease (HD), and dystonia and the nature of their involuntary movements has been extensively documented. As a result of these observations it has been suggested that the basal ganglia may play a role in determining the force and velocity of movement (Hallett & Khoshbin, 1980; Anderson & Horak, 1985), preparing for movement (Schultz & Romo, 1988; Alexander & Crutcher, 1990; Kimura, 1990), selecting motor programs (Brotchie et al. 1991), enabling movements to become automatic (Brotchie et al. 1991), facilitating sequential movement (Marsden, 1987; Kimura, 1990; Brotchie et al. 1991), inhibiting unwanted movements (Penney & Young, 1983; Mink & Thach, 1991), alerting animals to the presence of novel or rewarding circumstances (Brown & Marsden, 1990; Ljungberg et al. 1992; Schultz, 1992), and mediating selective attention (Wichman & DeLong, 1999) and conditional learning and planning (Taylor et al. 1986; Gotham et al. 1988; Robbins et al. 1994). The basal ganglia, however, clearly do not act in isolation but are part of a system of parallel distributed corticosubcortical loops. At least 5 separate loops have been described (Alexander et al. 1990) and these loops link the basal ganglia via the ventral and dorsomedial thalamus to cortical premotor and prefrontal areas including dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), and anterior cingulate cortex (ACA). These loops are believed to be spatially segregated, based on the findings of anterograde and retrograde tracer experiments in nonhuman primates (Middleton, 1997). It has been proposed that the basal ganglia may act to 'bind' the functions of these segregated loops (Wichman & DeLong, 1999).

The striatum (caudate and putamen) receives input from all cortical areas and from the thalamus and substantia nigra pars compacta. It then sends projections to the internal segment of the globus pallidus (GPi) via direct and indirect pathways and it is known that there is considerable convergence present in these

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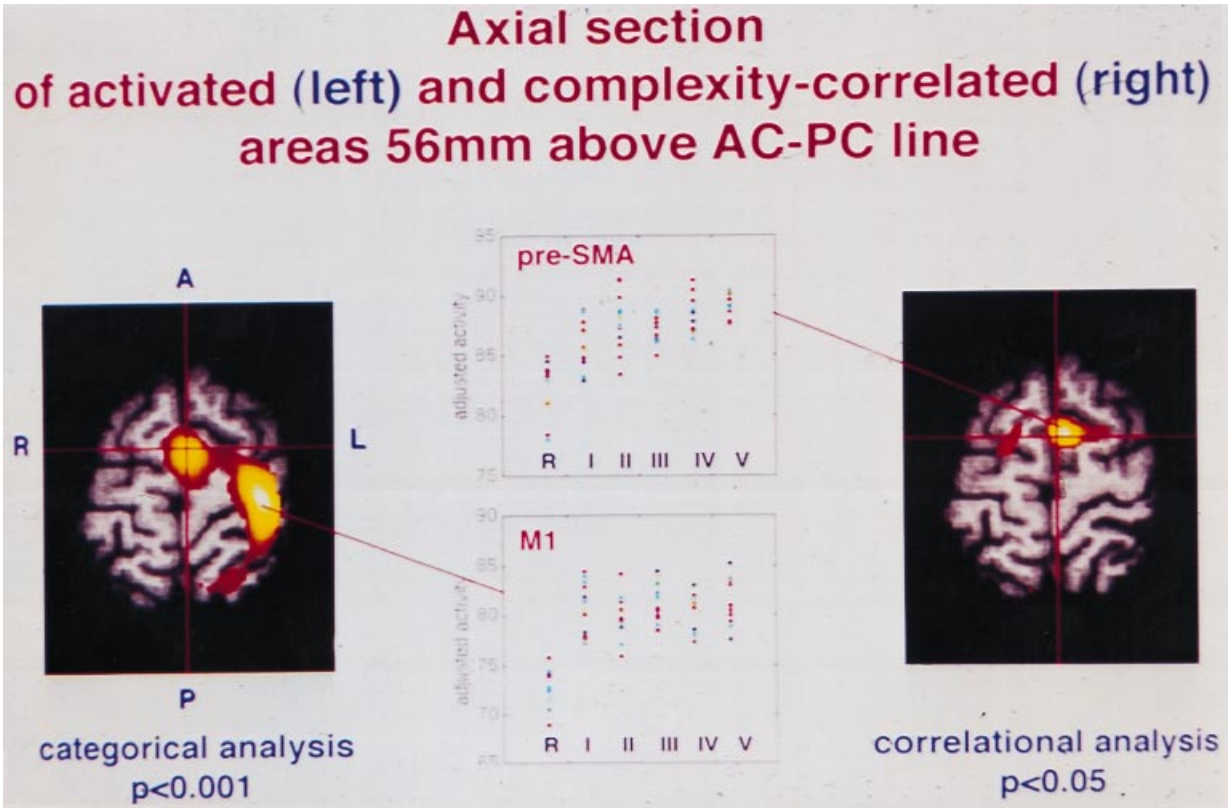

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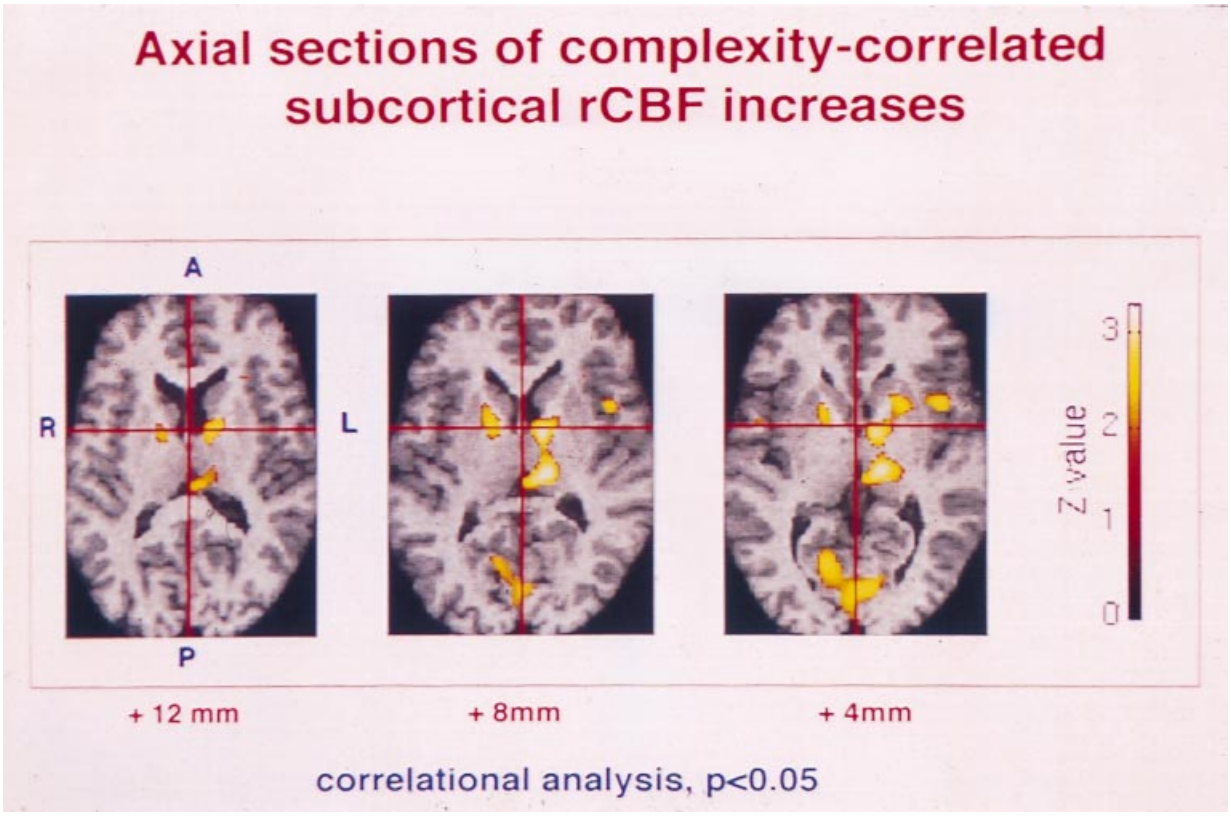

Fig. 1*a*, *b*. For legend see opposite.

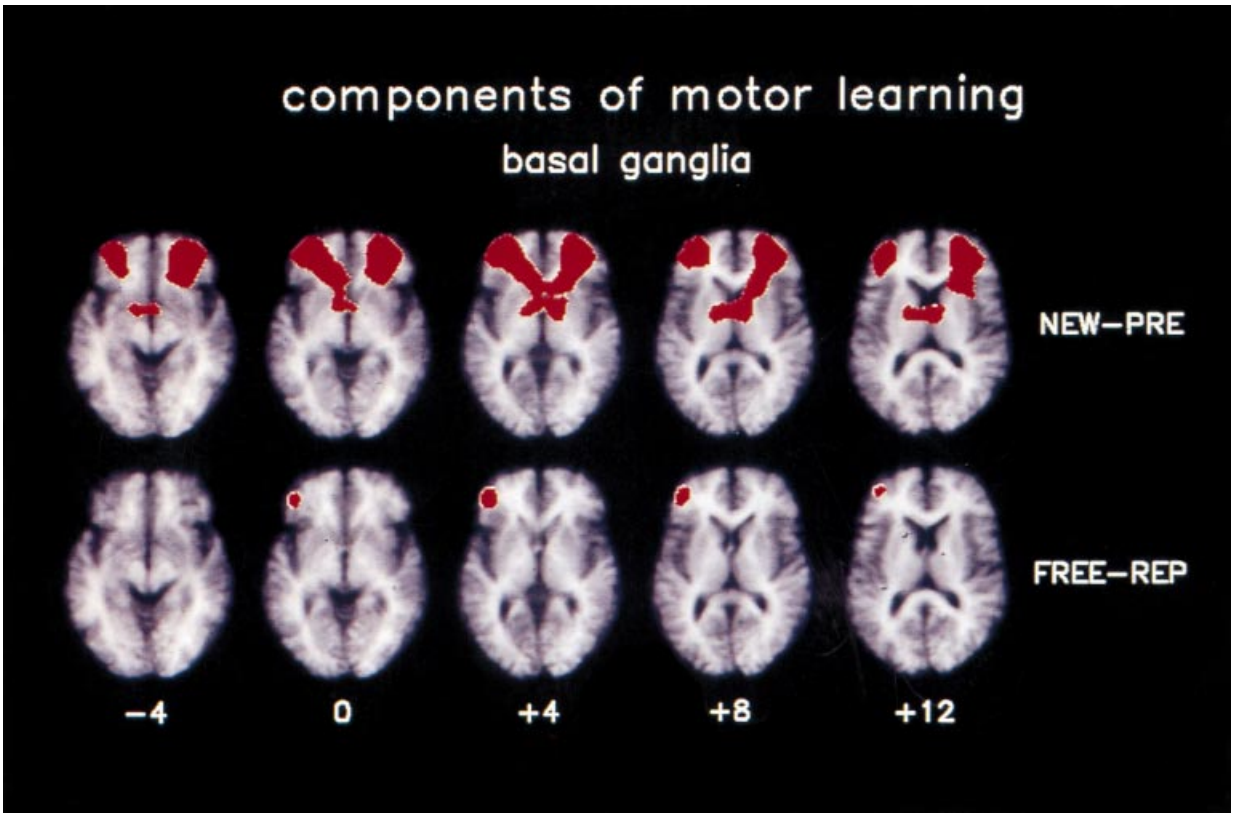

Fig. 2. Areas of relatively increased cortical and subcortical activation in normal subjects overlayed on an MRI template (*a*) when learning a novel sequence of finger movements by trial and error movements is compared with performance of prelearned sequential finger movements and (*b*) when free selection of finger movements is compared with repetitive finger movements. Novel sequence learning activates the caudate–prefrontal loop. (Courtesy of M. Jueptner.)

connections (Penney & Young, 1986; Parent, 1996). The internal segment of the globus pallidus (GPi) and substantia nigra pars reticulata (SNr) are the major output relays of the basal ganglia. The posteroventral GPi projects to arcuate premotor cortex and primary motor cortex via the thalamus while the posterodorsal GPi projects to the supplementary motor area (SMA) and anterodorsal GPi to dorsal prefrontal cortex (DPFC) (Middleton & Strick, 1997). The subthalamic nucleus (STN) receives input from both the frontal cortex and the external pallidum (GPe) and sends efferent projections back to GPe and to GPi. It also communicates with the pedunculopontine nuclei which are thought to control gait and posture.

Positron emission tomography (PET), single photon emission tomography (SPECT) and magnetic resonance imaging (MRI) all provide a means of studying changes in regional cerebral blood flow (rCBF) in man in vivo under activating conditions. The majority of activation studies examining basal ganglia function have involved $H_2^{15}O$ PET so this review will concentrate on this modality. The functional resolution of state of the art PET cameras is 4 mm and this is adequate to enable blood flow changes in the putamen, pallidum, and head of caudate to be independently monitored.

ACTIVATION STUDIES IN NORMAL SUBJECTS

Setting the basic parameters of movement

One approach for determining whether specific brain areas have a role in mediating a function is to examine whether they show correlated levels of blood flow when that function is performed at different intensities. It has been suggested that the basal ganglia have a role in controlling the force and velocity of movements based in part on the observation that patients with Parkinson's disease have bradykinesia and take longer to achieve full power during actions.

Fig. 1*a*, *b*. Areas of significantly increased cortical and subcortical activation in normal subjects overlayed on an MRI template where increases in rCBF correlate with sequence complexity. Rostral SMA, putamen, pallidum, thalamus, and cerebellum show correlated activation but not sensorimotor cortex. (Courtesy of H. Boecker.)

Two PET activation studies have addressed this question: Jenkins et al. (1997*a*) measured rCBF when paced joystick movements were performed in freely chosen directions at frequencies increasing from once every 5 s to once every second. Sensorimotor cortex and cerebellar blood flow increased in parallel with frequency of movement over this 0.2–1 Hz range while dorsal prefrontal and lentiform nucleus blood flow remained at a constant level of activation. Dettmers et al. (1995) demonstrated that sensorimotor cortex rCBF rises when increasing levels of force are used to press a morse key. When 50% of maximal force is exerted the rCBF response plateaus. The putamen was also activated by finger presses, however, levels of rCBF remained stable between 10% and 50% of maximal force. The findings of these 2 studies therefore indicate that, while sensorimotor cortex and cerebellum play a primary role in determining basic movement parameters, the putamen has some other modulatory role. Single unit recordings from putamen in awake nonhuman primates support this conclusion; neuronal firing rates were principally determined by moving to particular targets rather than the force or velocity of movement applied (Alexander & Delong, 1985).

Volitional versus cued action

Jueptner et al. (1996) examined brain activation during performance of a task where subjects had to freely draw a series of connected straight lines, changing direction every 3 s, on a computer screen using a mouse. The sequence of lines was then played back to the subject who had to trace over the lines as they appeared using the mouse. Finally, as a control condition, the subject simply watched the lines appearing on the screen. Free line drawing but not tracing of lines, activated dorsal prefrontal cortex, an area known to play a role in movement selection (Frith et al. 1991). In contrast, the cerebellum was most active during the tracing condition which primarily involved visual tracking. The putamen was activated to a similar extent during both free line drawing and line tracing suggesting that its role was to facilitate the drawing movements per se irrespective of whether they were volitional or cued.

Sequence generation

The basal ganglia do not act in isolation but rather as relays in parallel distributed cortical–subcortical loops. Given this, it is helpful to understand the function of these loops when attempting to understand the role of the basal ganglia. One approach for determining loop function is to look for activation in components which is correlated with particular dimensions of paradigms during their performance.

It has been proposed that the basal ganglia play an important role in mediating sequential limb movement. It is well recognised that, while patients with Parkinson's disease can perform single finger movements efficiently, attempts to perform repetitive or sequences of finger movements result in a rapid fall in amplitude and often motor arrest. Boecker et al. (1998) examined brain activation when normal subjects carried out varying sequences of finger–thumb opposition movements. The sequences ranged from 4 to 8 moves in length and were overlearned before scanning so that they could be performed automatically. Individual finger–thumb opposition movements were paced at a regular frequency of 1 Hz. Performance of finger movements compared with rest activated contralateral motor cortex, lateral and medial premotor areas and underlying anterior cingulate cortex, parietal cortex, thalamus, putamen and pallidum, and the cerebellum. Activation-induced blood flow changes that correlated with sequence complexity were seen in the rostral supplementary motor area (SMA), anterior putamen and pallidum, thalamus, and cerebellum but not in the lateral premotor cortex, caudal SMA, or primary motor cortex (see Fig. 1*a*, *b*). These findings therefore support the notion that a rostral SMA-putamen loop facilitates performance of learned patterns of movement while the motor cortex and caudal SMA are important for precise control of individual movements. Procedural learning can occur both explicitly and implicitly. Explicit learning is defined as acquisition of knowledge or skill when the subject is aware that the learning process is taking place, while implicit learning refers to the acquisition of knowledge or skill without awareness. Jenkins et al. (1997*b*) used a serial reaction time task (SRTT) performed unimanually to investigate the functional anatomy of implicit sequence learning. Normal volunteers were required to press keys with the fingers of the right hand rapidly in response to a visual stimulus which changed position on a screen every 1.25 s. Implicit learning, as judged by decreasing response times, occurred during covert presentation of a repeating 12-element sequence. The response times increased on presentation of a random sequence. Implicit learning was positively correlated with rCBF increases in contralateral motor and premotor cortex, and in the putamen bilaterally. It would seem, therefore, that the premotor-putamen loop not only facilitates learned

sequential movement, but also mediates the unconscious acquisition of skilled patterns of movement. Grafton et al. (1995*a*) used a 6 item covert sequence of arm reaching movements with a distractor verbal task to prevent the development of explicit knowledge during the implicit learning condition. These workers also reported rCBF increases during implicit learning in contralateral (left) primary sensorimotor cortex (SMC), supplementary motor area (SMA), and bilateral putamen.

Jueptner et al. (1997) contrasted levels of basal ganglia activation during the learning of novel sequences of finger movements with those seen during automatic movement. Subjects pressed on a keypad with 4 keys using the fingers of the right hand and their finger movements were paced at 3 s intervals by a tone. The novel condition involved learning a sequence of keypresses, 8 moves long, by trial and error with auditory feedback from a computer. The prelearned condition consisted of performing a sequence of 8 keypresses previously learnt until automatic. These workers found that dorsal prefrontal cortex (DLPFC) and caudate were only activated during novel sequence learning, suggesting a primary involvement of this loop with both motor decision making and working memory (see Fig. 2). The lentiform nucleus was similarly activated whether sequences of finger movements were being learnt by trial and error or being performed automatically.

Problem solving

The Tower of London (TOL) task examines a subject's ability to solve problems. The paradigm comprises moving coloured spheres situated in 3 wells on a computer screen until they match a specified arrangement (Morris et al. 1988). Spheres must be supported either by the well or another sphere and cannot be moved if another sphere is situated above. The complexity of the task depends on the minimum number of moves required to solve the problem. Addressing the TOL task engages numerous mental activities: trial and error of different strategies (planning), visual imagery, and working memory. The solution to the task can be indicated by touching the start and finish placement of spheres on the computer screen or simply indicating the number of moves required to solve the problem. Both approaches require mental rehearsal while the first approach also requires the appropriate arm movements to be selected, executed, and sequenced.

$H_2^{15}O$ PET studies have shown that the TOL task activates DLPFC, premotor areas, the anterior cingulate area, posterior parietal cortex, and the basal ganglia (Baker et al. 1996; Owen et al. 1996). A problem with these studies is that they both involve a categorical subtraction of a visually cued control condition, in one case also involving arm movement, from the condition of solving the problem. Free choice arm movement activates DLPFC and SMA relative to visually cued arm movement and this may have confounded the findings of both the above studies.

Dagher et al. (1997) approached the problem by searching for brain areas where levels of activation were correlated with the complexity of the problem. The solution was indicated by touching the start and finish position of the spheres on the computer screen with the right index finger. The TOL task activated left sensorimotor cortex, bilateral premotor, dorsal prefrontal, inferolateral and superior parietal areas, and rostral anterior cingulate compared with viewing a blank computer screen at rest (see Fig. 3). Areas where levels of activation correlated with problem complexity included medial and dorsolateral prefrontal cortex, rostral anterior cingulate, the precuneus and lateral parietal cortex, and right head of caudate nucleus. Areas where levels of activation correlated with numbers of arm movements included the left motor cortex and anterior putamen, caudal SMA and cingulate. These findings, therefore, again reveal dissociated function of caudate–prefrontal and putamen–premotor loops. The former is intimately involved in problem solving while the latter plays a role in execution of sequential limb movements.

Imagination of movement

Two studies have examined regional cerebral activation when performance of joystick movements with the right arm in freely chosen directions are imagined. Subjects were instructed to imagine moving each time an auditory tone sounded at 3 s intervals (Ceballos-Baumann et al. 1994*a*; Brooks et al. 1997). In both studies, imagination of limb movement led to significant activation of bilateral dorsolateral prefrontal cortex, SMA and lateral premotor cortex, and the contralateral lentiform nucleus. Sensorimotor cortex activation was not identified. The finding of basal ganglia activation associated with imagination of movement confirms that these structures play a role in facilitating movement selection and preparation.

Rewarded movement

In real life motor actions are usually performed with a view to gaining some form of reward or gratification.

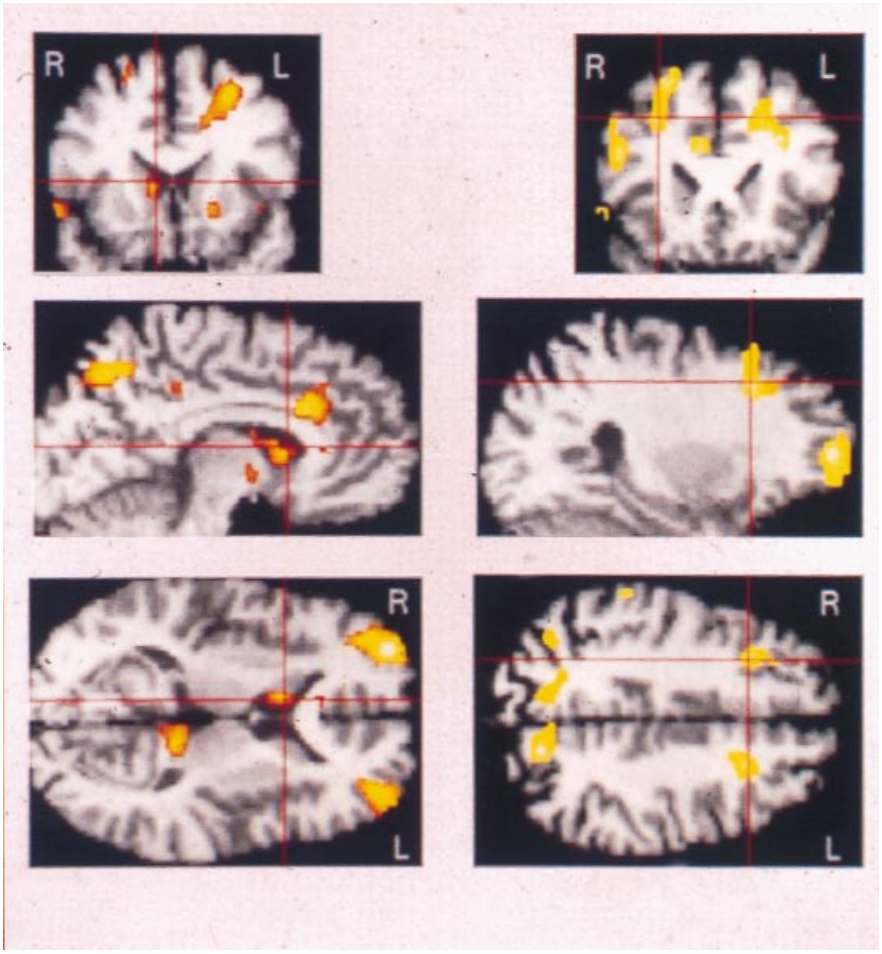

Fig. 3. Areas of significantly increased cortical and subcortical activation in normal subjects overlayed on an MRI template where increases in rCBF correlate with complexity of the Tower of London task. Prefrontal, caudate, cingulate, posterior parietal and precuneus show correlated activation. (Courtesy of A. Dagher.)

In contrast, most brain activation studies reported to date have not involved a level of reward yoked to the task other than the subject experiencing a feeling of satisfaction if their performance has been satisfactory. Lawrence & Brooks (1999) performed an $H_2^{15}O$ PET activation study where financial recompense for participation was linked to success. In this study subjects performed a computerised spatial search task, having to locate either valueless tokens or coins of varying denomination hidden in boxes on the screen. Each time a token/coin was found the box containing it was changed. Subjects were told that for a given array of boxes the coin would not be hidden in the same box twice so they were able to develop search strategies. All subjects had 12 rCBF measurements, 3 scans with no reward and 3 scans each at low, medium, and high levels of reward. This task was highly activating and brain areas that showed correlated levels of activation with the level of financial reward achieved were ventral and dorsal prefrontal cortex, temporal pole, nucleus accumbens, and substantia nigra. These findings are in line with studies by Schulz et al. (1993) who have demonstrated selective firing of nigral dopaminergic and ventral striatial neurons to the presence of reward-predicting stimuli.

PARKINSON'S DISEASE

Brain activation when unmedicated

The primary pathological deficit in Parkinson's disease is degeneration of the substantia nigra with loss of its dopaminergic projections to the caudate and putamen. A lesser involvement of mesencephalic dopaminergic projections to frontal areas occurs and the Lewy body pathology can also directly target cortex, 20% of patients going on to develop a dementing illness. A number of studies have examined basal ganglia blood flow changes associated with performance of motor tasks in patients with PD. Playford et al. (1992) demonstrated that when normal

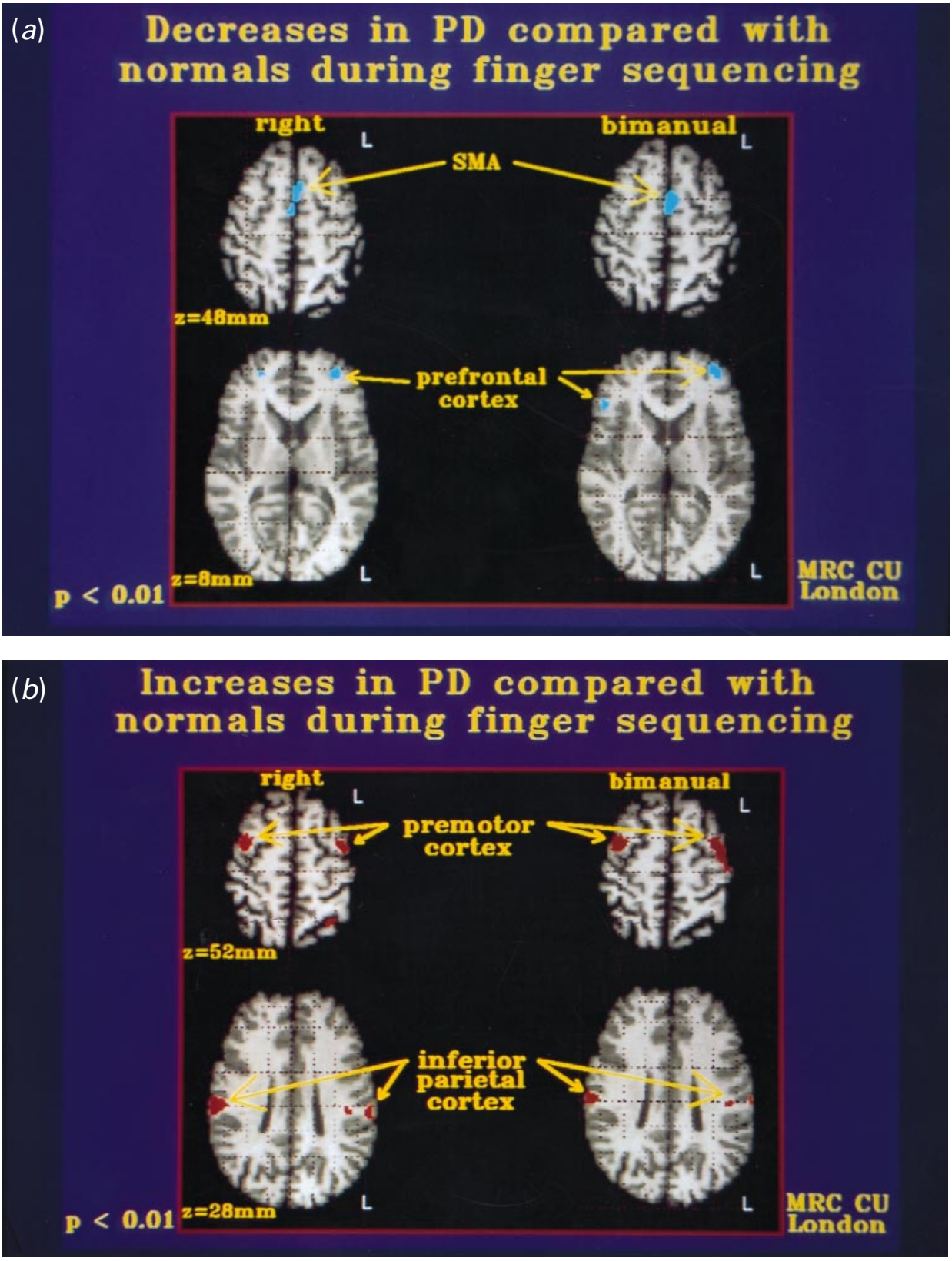

Fig. 4*a*, *b*. Areas of significantly increased and decreased cortical activation in PD compared with normal overlayed on an MRI template during performance of sequential finger movements. Rostral SMA and dorsal prefrontal cortex underfunction while lateral premotor and parietal areas are overactive in PD. (Courtesy of M. Samuel.)

subjects move a joystick in freely chosen directions paced by a tone every 3 s there is activation of right dorsolateral prefrontal and bilateral lateral premotor cortex, the supplementary motor area and contralateral motor cortex and lentiform nucleus. When PD patients were studied after stopping their medication for 12 h they were all able to perform the task but took 15–20% longer to respond to the buzzer and complete the selected joystick movements. The patients showed attenuated increases of contralateral lentiform nucleus, rostral SMA, anterior cingulate, and dorsolateral prefrontal rCBF compared with age matched controls. There was no significant difference in levels of contralateral sensorimotor and lateral premotor activation. Subsequently, Jahanshahi et al. (1995) investigated the activation deficits in PD associated with repetitive self-paced extension of the right index finger at a frequency ranging 0.2–1 Hz. Again, although PD patients successfully performed the paradigm, they showed significant impairment of contralateral striatal, SMA, anterior cingulate, and DLPFC compared with controls. Brooks et al. (1997) examined cerebral activation in PD during imagined performance of joystick movements with the right arm in freely chosen directions. Again, there was a failure to activate prefrontal and mesial premotor cortex while lateral premotor and parietal areas activated normally. These findings are all in line with the akinesia of PD patients arising from underfunctioning of their basal ganglia–frontal loops.

Impairment of SMA and DLPFC function in PD is postulated to be a consequence of excessive inhibitory output from GPi, the main output relay of the basal ganglia, secondary to the loss of striatal dopamine. The GPi sends inhibitory GABAergic projections to ventral thalamus which in turn sends excitatory projections to SMA, arcuate premotor, and dorsal prefrontal areas. SMA is thought to play a primary role in preparing volitional actions (Thaler & Passingham, 1989) while DPFC mediates their selection (Frith et al. 1991). An inability to activate SMA and DLPFC normally in PD may explain the difficulties that these patients experience when preparing and planning volitional movements or performing sequences of actions. While the SMA and DLPFC receive a major subcortical input from the basal ganglia, the lateral parietal and premotor areas are targeted by cerebellar projections. If SMA and dorsal prefrontal activation is impaired in PD, it might be predicted that these akinetic patients would adapt by making greater use of cerebellar-lateral parietal-lateral premotor connections. Two sets of workers have now demonstrated overactivity of this circuit in PD when patients perform sequential finger movements with one or both hands (Samuel et al. 1997*a*; Catalan et al. 1999) (see Fig. 4). The lateral parietal and premotor areas are thought to preferentially facilitate instructed rather than freely chosen movements (Thaler & Passingham, 1989). The ability of PD patients to overactivate these lateral cortical areas may explain why they are better able to perform visually cued as opposed to freely chosen actions.

Dagher et al. (1998) examined regional cerebral activation in PD patients performing the Tower of London task described in the previous section. The patients were able to perform the task satisfactorily, although they solved fewer problems in the allotted time. When levels of activation were correlated with problem complexity it became evident that the PD patients were deactivating rather than activating prefrontal and anterior cingulate cortex as solutions became harder. Along with this aberrant deactivation, PD patients showed positively correlated activation in medial temporal areas. This structure is normally required for short and long term recall rather than working memory and decision making. Recruitment of temporal cortex for problem solving is another example of switching to the use of non-basal ganglia dependent areas by PD patients to overcome their deficits. Owen et al. (1998) also studied PD patients performing the TOL task. A categorical comparison of problem solving and visual working memory with visually cued touching of spheres showed selective deactivation of right globus pallidus in PD. The authors concluded that dopamine deficiency in this condition is associated with abnormal basal ganglia outflow disrupting frontostriatal circuitry.

Regional cerebral activation in PD patients while performing a financially rewarded task has also been examined by Goerendt et al. (1999) using a similar spatial searching task to the one described previously. These workers were able to show that when levels of activation were correlated with reward obtained, PD patients failed to activate orbitofrontal and basal ganglia areas normally but instead recruited posterior parietal cortex, an area required for accurate location of objects in space.

The effects of dopaminergic stimulation

In order to see whether striatal-frontal association area projections could be functionally reafferented in PD the combined dopamine D1 and D2 site agonist, apomorphine was administered subcutaneously while patients performed paced joystick movements in freely chosen directions (Jenkins et al. 1992; Brooks et al.

1993). Reversal of akinesia was associated with a significant increase in both SMA and dorsolateral prefrontal cortex blood flow, implicating these areas in the initiation of volitional movements. Separate studies with ^{133}Xe SPECT (Rascol et al. 1992, 1994) have also demonstrated improvement in SMA flow when PD patients are successfully treated either with apomorphine or levodopa.

To determine whether the impaired movement related premotor and prefrontal activation in PD improves as a result of striatal fetal dopaminergic cell implantation, 4 patients who received bilateral human fetal mesencephalic transplants into caudate and putamen have been studied with $H_2^{15}O$ PET at baseline and over 2 y following surgery (Piccini et al. 1998). The $H_2^{15}O$ PET activation studies comprised of 12 measurements of rCBF, 6 at rest and 6 while performing paced joystick movements every 4 s in freely selected directions using the right hand. Activation-induced increases in SMA rCBF during arm movement increased by 5% 7 mo and by 10% by 19 mo postsurgery. Clinical improvement on the Unified Parkinson's Disease Rating Scale (UPDRS) paralleled the restoration of levels of frontal activation. These findings suggest that clinical improvement and restoration of cortical function after implantation of fetal dopaminergic cells requires maturation of these cells and possibly reafferentation of striatocortical loops.

Functional effects of stereotactic lesioning

Over the last decade, there has been a resurgence of interest in posteroventral medial pallidotomy as a treatment for PD. Medial pallidotomy has now been shown in several series to dramatically reduce or abolish levodopa-induced abnormal involuntary movements in chronically treated PD patients and to improve their 'off' bradykinesia, tremor, rigidity and gait by 30–40% as assessed with the UPDRS. More recently, high frequency electrical pallidal stimulation has also been reported to provide similar clinical benefits. The mechanisms underlying these functional responses, however, are still unclear.

The rationale underlying pallidotomy is that the loss of striatal dopamine in PD leads to reduced inhibition of the GPi by both the direct and indirect striatal pathways. This results in an excessive inhibitory output from GPi to the ventral thalamus and in turn its excitatory projections to SMA and prefrontal cortex. Intraoperative single-cell recordings in PD patients have confirmed the presence of abnormal burst firing of the GPM at rest at an increased level. It is therefore argued that by lesioning the motor GPi this excessive inhibition is removed so facilitating volitional and sequential movements in PD. This lesioning can be achieved by stereotactic thermocoagulation or high frequency electrical stimulation.

A PET activation study from our unit reported significantly increased activation of SMA, lateral premotor cortex, and dorsal prefrontal cortex in a single PD case while off medication after undergoing unilateral pallidotomy (Ceballos-Baumann et al. 1994*b*). This patient was studied while performing paced joystick movements in freely selected directions and postoperatively showed an improvement in both response time and the number of completed joystick movements. This study was subsequently extended to involve a group of 6 PD patients (Samuel et al. 1997*b*). As a group, these patients showed significant improvements in dyskinesia score (75%), 'off' contralateral wrist rigidity (83%) and contralateral bradykinesia (56%) when assessed with the UPDRS after pallidotomy. There were significant associated increases in levels of SMA and right DLPFC activation on joystick movement (Fig. 5). A second PET activation pallidotomy study involved 6 PD patients who were scanned off medication at rest and then while reaching at 3 s intervals out to grasp different lighted targets arranged in a row (Grafton et al. 1995*b*). Pallidotomy resulted in no overall improvement in disability in this cohort but the motor task was associated with increased levels of caudal SMA and ventral lateral premotor activation after surgery. Despite the lack of clinical improvement, levels of SMA and lateral premotor activation before and after pallidotomy correlated with levels of performance in this patient group. As this was an externally cued reaching task it was not designed to activate prefrontal areas.

There have been 2 PET reports on the effects of high freqency electrical pallidal stimulation on regional brain function. In the first study levels of resting rCBF were measured with the stimulator switched off, switched on at a subeffective intensity, and switched on at a clinically effective intensity (Davis et al. 1997). Effective posteroventral GPi stimulation improved contralateral bradykinesia and rigidity in 8 of the 9 PD patients when they were assessed off medication and this was associated with increased resting SMA and putamen/external pallidal rCBF. Stimulation of the GPi at a lower intensity did not lead to clinical improvement or increase SMA rCBF. The authors concluded that decreased akinesia in PD following pallidal stimulation resulted from

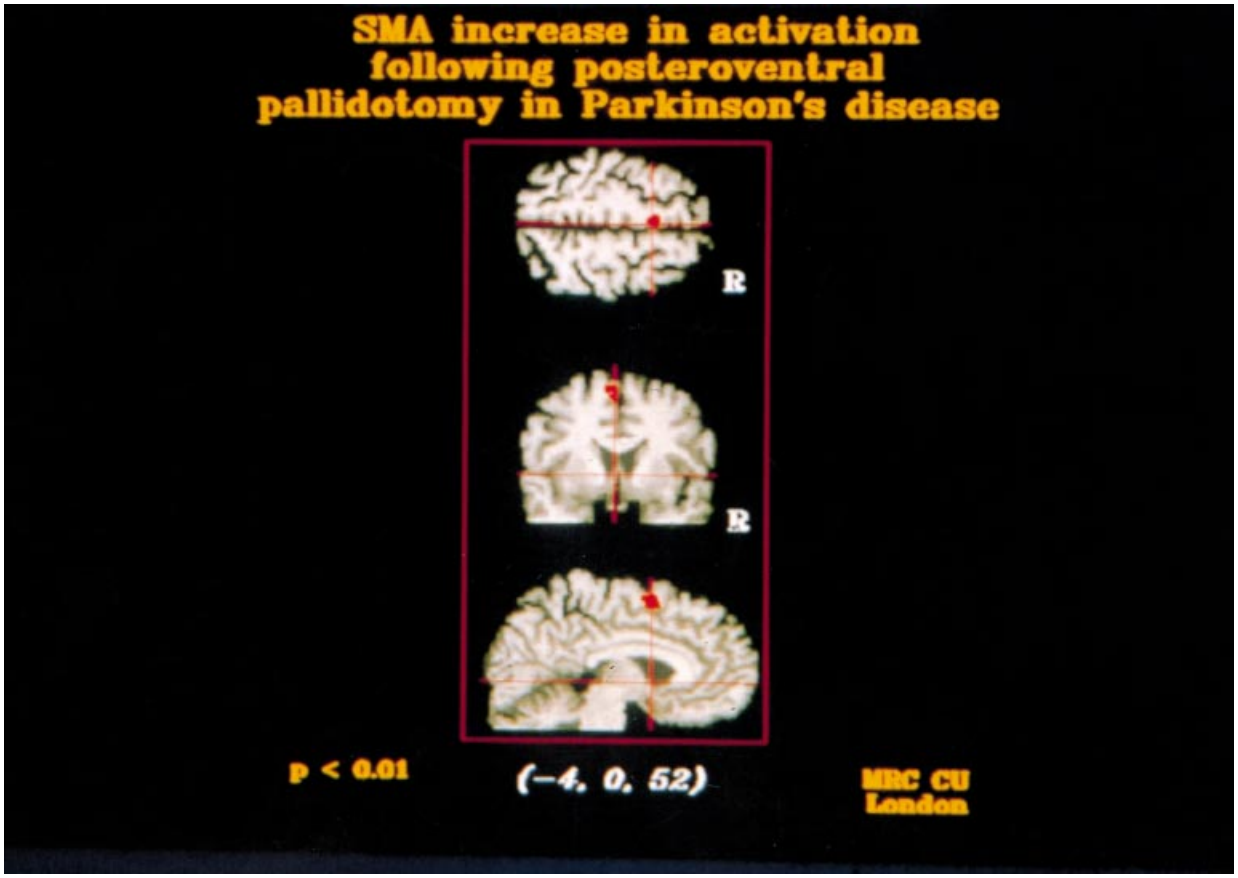

Fig. 5. The location of significantly increased SMA activation in PD overlayed on MRI during performance of joystick movements in freely chosen directions before and after posteroventral pallidotomy. (Courtesy of M. Samuel.)

increased SMA activation although their study was strictly performed under resting rather than activating conditions. The second PET study measured changes in rCBF associated with moving a joystick in freely chosen directions in 6 PD patients while off medication with the GPi stimulator switched off and then again when the stimulator was switched on (Limousin et al. 1997). In this study clinically effective GPi stimulation did not lead to any significant changes in levels of SMA or DLPFC activation.

There have been 2 reports of $H_2^{15}O$ PET activation findings in PD patients before and after STN stimulation (Ceballos-Baumann et al. 1997; Limousin et al. 1997). Levels of rCBF were measured in patients with PD when off medication during performance of paced joystick movements in freely selected directions. Both studies reported relative increases in activation of rostral SMA lateral premotor, and dorsolateral prefrontal cortex during movement when the STN stimulator was switched on.

To summarise, pallidotomy, and pallidal and subthalamic stimulation can all act to increase levels of SMA and dorsal prefrontal activation in PD along with resolution of bradykinesia, adding further support to the suggestion that these cortical areas play a primary role in planning and preparing actions.

CONCLUSIONS

The above activation studies suggest that the basal ganglia are activated whenever movements are performed, planned, or imagined. Levels of activation appear to be independent of the frequency or force of movement in the ranges tested. The caudate-prefrontal loop mediates novel sequence learning, problem solving, and movement selection while the putamen-premotor loop facilitates automatic sequential patterns of limb movement and implicit acquisition of motor skills. A nigral-nucleus accumbens-prefrontal loop appears to subserve motor responses to rewarding stimuli.

A role for the basal ganglia that is compatible with these activation findings has been suggested by Connolly & Burns, 1993*a*, *b*). They propose that when a motor decision is made by higher centres the basal ganglia facilitate the required movement by focusing the pattern of muscular activity used to reach the goal state, whether the movement be self-initiated or cued. Once a motor program has been so optimised it can

then be relayed to the primary motor cortex for execution and also to the cerebellum to enable it to become automatic. This suggested role for the basal ganglia would explain their activation during imagination of movement and their lack of involvement in determining the basic parameters of movement.

If, as we have postulated, the basal ganglia are involved in focusing motor programs once they have been selected, it is at first sight surprising that removal of their output in PD should result in improvement rather than further disability. It may be that, once optimised by the basal ganglia, a motor program is dumped elsewhere (e.g. the cerebellum) and its future automatic running does not require pallidal output. As a consequence, as long as PD patients perform previously learned as opposed to novel movements, pallidotomy would act to beneficially alleviate rigidity without impairing automatic running of motor programs.

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