Brain (1998), **121,** 1437–1449

A review of differences between basal ganglia and cerebellar control of movements as revealed by functional imaging studies

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Summary

The role of the basal ganglia and cerebellum in the control of movements is unclear. We summarize results from three groups of PET studies of regional CBF. The results show a double dissociation between (i) selection of movements, which induces differential effects in the basal ganglia but not the cerebellum, and (ii) sensory information processing, which involves the cerebellum but not the basal ganglia. The first set of studies concerned motor learning of a sequence of finger movements; there was a shift of activation in the anterior–posterior direction of the basal ganglia which paralleled changes in the motor areas of the frontal cortex. During new learning, the dorsolateral prefrontal cortex and striatum (caudate nucleus and anterior putamen) were activated. When subjects had to select movements, the premotor cortex and mid-putamen were activated. With automatic (overlearned) movements, the sensorimotor cortex and posterior putamen were activated. When subjects paid attention to overlearned actions, activation shifted back to the dorsolateral prefrontal cortex and striatum. The cerebellum was not activated when subjects made new decisions, attended to their actions or selected movements. These results demonstrate components of basal ganglia–(thalamo)-cortical loops in humans. According to earlier studies in animals we propose that the basal ganglia may be concerned with selecting movements or the selection of appropriate muscles to perform a movement selected by cortical areas (e.g. premotor cortex). Secondly, a visuomotor co-ordination task was examined. In the absence of visual control over arm movements, subjects were required to use a computer mouse to either generate new lines or to re-trace lines on a computer screen. The neocerebellum (hemispheres of the posterior lobe, cerebellar nuclei and cerebellar vermis), not the basal ganglia, was more engaged when lines were re-traced (compared with new line generation). Animal experiments have shown that error detection (deviation from given lines) and correction occurs during line re-tracing but not line generation. Our data suggest that the neocerebellum (not the basal ganglia) is involved in monitoring and optimizing movements using sensory (proprioceptive) feedback. Thirdly, the relative contribution of sensory information processing to the signal during active/passive execution of a motor task (flexion and extension of the elbow) was examined; it was found that 80–90% of the neocerebellar signal could be attributed to sensory information processing. The basal ganglia were not involved in sensory information processing. They may be concerned with movement/muscle selection (efferent motor component); the neocerebellum may be concerned with monitoring the outcome (afferent sensory component) and optimizing movements using sensory (feedback) information.

Keywords: basal ganglia; cerebellum; movement control

Abbreviations: BA = Brodmann area; rCBF= regional cerebral blood flow

Introduction

Lesions of the basal ganglia and cerebellum produce well-known motor deficits in animals and human subjects. However, the physiological role of these structures for the control of movements still remains unclear [for reviews concerning the basal ganglia see Brooks (1995), for the cerebellum see Bloedel (1992) and Thach *et al*. (1992)].

Animal experiments have shown that the basal ganglia represent a relay station within the so-called basal ganglia–

thalamocortical loops (for review see Alexander *et al*., 1990). There are at least five different, functionally and anatomically segregated loops. In primates, projections from dorsolateral prefrontal cortex ('dorsolateral prefrontal loop') terminate in the caudate nucleus which projects to the globus pallidus and substantia nigra. The globus pallidus and substantia nigra send projections to the thalamus which sends return projections to the dorsolateral prefrontal cortex (Alexander *et al*., 1990). Similarly, the primate sensorimotor motor circuit projects to the putamen which projects to the globus pallidus and substantia nigra. Both nuclei send return projections via the thalamus back to the lateral and medial premotor cortex as well as the primary motor cortex (Alexander *et al*., 1990).

Despite detailed anatomical knowledge, little is known about the physiological role of the basal ganglia in motor control (for reviews see Brooks, 1995; Mink and Thach, 1991*a*). It has been proposed that the basal ganglia control single modes of movement selectively (review in Mink and Thach, 1991*a*), e.g. ramp or closed-loop movements, ballistic or open-loop movements, self-paced movements, internally guided versus externally driven movements, etc. However, none of these hypotheses has been able to clarify the generic role of the basal ganglia in movement control.

It has been postulated that the cerebellum is preferentially involved in controlling (i) complex (as opposed to simple) movements (Thach *et al*., 1992); (ii) multi-joint (as opposed to single joint) movements; (iii) movements that require visuomotor co-ordination (Stein and Glickstein, 1992); or (iv) learned automatic movements (as opposed to untrained 'first time' movements) (Thach *et al*., 1992). The contradictory interpretations across many different studies suggest that some unrecognized aspect of the movements, which was not identified or examined, may have been controlled by the cerebellum.

In this paper, we present results from recent PET studies which examined the role of the basal ganglia and cerebellum in movement control. Most of the results have been published elsewhere (Passingham *et al*., 1995; Jueptner *et al*., 1996*a*, 1997*a–c*; Weiller *et al*., 1996). However, the summary of findings allows new conclusions about the basal ganglia and cerebellar role in movement control, which are not evident from the previous publications alone.

The main aim of the experiments was to compare the roles of the basal ganglia and cerebellum in the control of movements. The basic approach (analysis of task components) originated from our studies on motor learning; functional imaging studies have shown that almost all brain areas which are involved in motor control are also involved in motor learning (Grafton *et al*., 1992; Halsband and Freund, 1993; Jenkins *et al*., 1994). It seems unlikely that all brain areas are concerned with the same task. Therefore we analysed components of the motor learning task (like rehearsal, selection of movements and improvement of performance) to differentiate the roles that these brain areas play during motor learning. We found that cortical areas were activated when subjects made decisions (e.g. about what movement to perform next) or when they attended to their actions (Jueptner *et al*., 1997*b*). On the other hand, the basal ganglia and cerebellum were activated when subjects improved their performance (Jueptner *et al*., 1997*c*). In these studies, sensory cues were used to guide discrete (short-lasting) finger movements.

In the next study, we analysed the sensory guidance of continuous movements. Both the basal ganglia and cerebellum receive information from sensory, motor and association cortices. However, they differ in the areas from which they receive sensory, especially visual, information (Jueptner *et al*., 1996*a*). We found that the neocerebellum (but not the basal ganglia) was more active when movements were performed under sensory guidance. These results revealed that the neocerebellum, not the basal ganglia, relies on sensory (feedback) information to optimize movements.

In the third study we analysed the relevance of sensory input for the cerebellar and basal ganglia control of movements (Weiller *et al*., 1996; Jueptner *et al*., 1997*a*). We were interested to see to what extent the cerebellar and basal ganglia signal was due to sensory information processing. Active and passive movements were compared. Passive movements were studied to separate the afferent sensory from the efferent motor component (see Weiller *et al*., 1996). The studies showed that passive movements did not elicit changes in regional CBF (rCBF) in the basal ganglia. However, the increase of cerebellar rCBF during passive movements was almost identical to that during active movements. These results suggested that the cerebellar signal seen during movement execution may represent processing of sensory feedback information.

Thus, our series of experiments revealed that both the basal ganglia and cerebellum were engaged when subjects improved their performance (see motor learning studies). The basal ganglia were differentially activated when subjects had to select movements. There was no activation in the basal ganglia when movements were optimized using sensory feedback (visuomotor co-ordination study). There was no activation of the basal ganglia when movements were performed passively. As passive movements separate the afferent sensory from the efferent motor component the results suggest that the basal ganglia are not concerned with monitoring the outcome of movements (afferent sensory component). The basal ganglia may be more concerned with the selection of the appropriate movements/muscles (efferent motor component).

During movement selection, there was no cerebellar activation. However, the neocerebellum was activated when movements were performed under sensory guidance (visuomotor co-ordination study). During passive movements, the cerebellar activation was almost identical to that during active movements. These results suggest that the neocerebellum may be more concerned with optimizing movements, by monitoring the outcome of movements (sensory information processing).

Material and methods

Subjects

The rCBF was analysed as an index of neuronal activity (Jueptner and Weiller, 1995). In each study a group of six healthy, right-handed volunteers was tested. None of them had a history of neurological or psychiatric disease; none of them took any medications. Approximately 30 min prior to scanning, subjects were acquainted with the task and performed eight to 10 test trials for each experimental condition. All subjects gave written informed consent prior to the examination. The study was approved by the Ethics Committee of the Hammersmith Hospital and by the University of Essen.

Experimental design

Motor learning studies

From the motor learning studies five different conditions were analysed.

(i) 'New sequence learning' involved learning a new sequence of keypresses. The sequence was eight moves long and was learned by trial and error; in many respects similar to a pianist learning a new piece. The movements were paced by a tone at a frequency of one tone every 3 s. Correct identification of a movement was rewarded by a high-pitched tone. Incorrect movements were followed by a low-pitched tone. The subject first tried to identify the first move in the sequence. At each pacing tone the subject tried one finger. This continued until the subject was given positive (high-pitched) feedback. The subject then tried to identify the second keypress by trial and error, then the third keypress, and so on until the subject had correctly identified the sequence of eight movements. The end of the sequence was signified by three short high-pitched tones. The subject then returned to the beginning of the same sequence and continued to perform the task in the same way. In each new learning condition, subjects were given new sequences. The sequences were identical for all subjects. When a subject had learned the sequence to criterion (no errors in one run through), a further new sequence was presented to continue the process of motor learning.

(ii) For the 'prelearned sequence' condition, subjects learned a standard sequence in the same way as described above, ~90 min prior to scanning. Subjects continued to perform the task until they made no errors; this was called the 'prelearned sequence'. After a rest period of 2 min, they continued to rehearse the same sequence for 3.5 min, then had another rest of 2 min. A total of 10 trials was completed, each consisting of 3.5 min of rehearsal and 2 min of rest. The automaticity of the motor task was assessed in the last trial. Subjects were asked to repeat five- or six-digit strings presented at a rate of once every 1 s. They had to repeat them immediately and in the same order. Immediately prior to scanning, subjects performed two further trials of the prelearned sequence, while lying on the scanner couch. This ensured that they were able to perform it in this situation. During scanning, the same prelearned sequence was used for all runs of this condition.

(iii) In the 'attention' condition, subjects performed the prelearned sequence. However, immediately prior to scanning, they were told to 'think of the next movement' once they finished the previous one. This meant that the subjects had to pay attention to the prelearned sequence. Again, the same standard prelearned sequence was used for all runs in this condition.

(iv) In the 'free selection' condition, subjects were told to press any key randomly, 'as if you were tossing a coin each time'. The movements were paced at a frequency of once every 3 s. Subjects were instructed not to repeat the same key twice. Prior to scanning, they practised this task for 2 min.

(v) In the 'repetitive' condition, the subjects were required to press a single key repetitively with their middle finger on each trial. Their four fingers rested on the keys as in the other conditions.

Each condition was repeated three times. A personal computer was used to generate trigger and feedback tones and to register the subjects' performance (Jueptner *et al*., 1997*b*, *c*).

Visuomotor co-ordination study

In the visuomotor co-ordination study, four different conditions were analysed.

(i) In the 'new line generation' condition (or 'drawing') the subjects had to draw straight lines on a computer screen by moving a mouse with their right hand (subjects were unable to see their moving hand). The movements were paced by one tone every 3 s. A red 1-cm diameter circle was used as a pointer instead of a standard mouse arrow. The starting point of each line was defined as the final position of the previous movement. As the pointer was moved, a straight continuous line was created. The subjects started by drawing a line after the pacing tone. They were allowed to draw a line in any direction. They were instructed to draw the lines slowly to ensure continuous movements for 3 s. After 3 s, the next pacing tone sounded, the screen was cleared and subjects had to choose another direction to draw. The subjects' performance was monitored by the computer which recorded the direction, distance, duration and velocity of the movement; these data were then used to generate the lines in the next three conditions (copying, watching and fixation). During each new run of the 'drawing' condition, the parameters were stored again.

(ii) In the line re-tracing condition ('copying'), the same set of lines were presented to the subjects. Every 3 s, a pacing tone sounded and the line appeared again on a blank screen. The subjects had to keep the pointer at the end of the line (retracing its original path) as it slowly contracted towards its first point. The direction and length of each line were derived from the immediately previous run of 'drawing'. At any moment, the velocity of line contraction was identical

to the velocity of movement when this line was generated in the immediately previous run of 'drawing' by the same subject. Thus, for each subject, the movements were matched in the two conditions. The target was defined as an area of 2 cm radius at the end of the line as it contracted.

(iii) In the third condition ('watching') the same sequence of lines was used as in the immediately previous runs of 'drawing'. The lines contracted as in 'copying'. After each pacing tone, the screen was cleared and a single line appeared on the screen. The pointer automatically moved in alignment with the end of the line as it contracted. The subjects followed the cursor with their eyes. No hand movements were made.

Each condition was repeated three times. A personal computer was used to generate trigger tones and to register the subjects' performance (Jueptner *et al*., 1996*a*).

Sensory movement control studies

From the sensory movement control studies one paradigm will be discussed here. Active and passive movements of the right elbow were compared with each other and to a resting condition.

(i) Active movements were performed with the subjects' arm fixed to the guide hinge. Elbow flexions were performed against gravity with the arm reaching a 90° (upright) position at the end of the flexion. Subjects were instructed to perform the movements at a constant velocity with one movement (flexion or extension) lasting 1 s. The movements were triggered by a metronome

(ii) In the passive movement condition, a motor was used to induce sequential flexions and extensions of the elbow resting in a guide hinge (amplitude of 90°). One movement of 90° amplitude (flexion or extension) was completed in 1 s as in the active movement condition. Subjects were instructed to relax their arms during this passive movement task. The metronome produced tones at a frequency of 1 Hz as in the other conditions. EMG recordings were taken to ensure that subjects did not produce voluntary muscle contractions.

(iii) In the baseline condition (rest) subjects kept their eyes closed. The metronome again produced tones at a frequency of 1 Hz to control for auditory input. No movements were executed. Each condition was repeated four times (Jueptner *et al*., 1997*a*).

Data acquisition

For each subject, 12 sequential rCBF scans were performed. Subjects lay in a supine position with eyes being closed in a darkened room (except for the visuomotor co-ordination study). The head position was maintained by use of a standard American football helmet (internally coated with air cell cushioning) or by an individually moulded Styropor head rest to minimize involuntary head movements during the scans.

Scans were performed using a CTI/Siemens ECAT 953B scanner (for the motor learning and visuomotor coodination studies) and a CTI ECAT 953–15 camera in the other studies (CTI, Knoxville, Tenn., USA). The ECAT 953B scanner covers an axial field of view of 10.5 cm. The CTI ECAT 953–15 camera covers 5.4 cm and was tilted to include the entire cerebellum. Radioactivity was administered as a bolus injection of $H_2{}^{15}O$ through a venous line in the left arm (injection time was 30 s for the ECAT 953B studies and 40–50 s for the ECAT 953–15 camera). Emission data were corrected for attenuation by the tissues of the head using a transmission scan, which was performed prior to the activation scans. During each scan, 3 ml of radiolabelled water was applied containing 20 mCi of ^{15}O. Dynamic PET scans were collected over a period of 90 s; the paradigm was started 20 s prior to data acquisition and continued for 2 min. Any increase in the amount of radioactivity in a specific region reflects an increase in rCBF (Mazziotta *et al*., 1985; Fox and Mintun, 1989) which in turn is coupled to synaptic neuronal activity (Jueptner and Weiller, 1995).

Data analysis

All calculations were performed on Sparc computers (SUN Microsystems, Mountain View, Calif., USA) using the interactive image display softeware ANALYZE (Biodynamic Research Unit, Mayo Clinic, Minn., USA) and SPM software for image analysis and matrix operations (SPM95, Functional Imaging Laboratory, Queens Square, London, UK) in the Matlab environment (Mathworks, Sherborn, Mass., USA).

The data were corrected for attenuation of the tissues of the head using a transmission scan. All scans were corrected for involuntary movement artefacts using realignment to the first corrected image (Woods *et al*., 1992; Friston *et al*., 1995). All images were transformed into the standard anatomical space (Talairach and Tournoux, 1988; Friston *et al*., 1995) and filtered with a low-pass Gaussian filter ($15 \times 15 \times 9$ mm in the *x*, *y*, *z* dimensions) to increase the signal-to-noise ratio (Friston *et al*., 1995).

Differences in global blood flow between subjects and conditions were removed by analysis of covariance (Friston *et al*., 1995). Pixel by pixel comparisons were performed to reveal significant differences in rCBF between conditions (i.e. $P < 0.05$, corrected for multiple comparisons). Results are displayed as statistical parametric maps showing the areas of significant increase in rCBF (Friston *et al*., 1995).

MRI scans were obtained and processed as described previously (Jueptner *et al*., 1995). The group MRI scans served as a template on to which the average PET data were superimposed for exact anatomical localization of activations.

Results

Task performance

During new learning of a sequence of finger movements, the error rate and reaction times decreased significantly, revealing a modification of motor behaviour ('motor learning'). No change of response times occurred during free selection of

movements, as during the performance of the prelearned and repetitive movement tasks. When subjects paid attention to the performance of a prelearned task, there was a slight (significant) increase in response times (Jueptner *et al*., 1997*b*, *c*).

In the visuomotor co-ordination study, no significant differences in task performance were observed between new line generation ('drawing') and line tracing ('copying'). More precisely, there was no difference in the total length of lines drawn, the total duration of hand/mouse movements or the average velocity of movement (Jueptner *et al*., 1996*a*).

During the studies of the sensory control of movements, EMG was used to record muscular activity in the active and passive movement conditions. During active movement, there was alternating activation of the biceps and triceps muscles (flexion and extension). During passive movements, no muscular activity could be recorded (Jueptner *et al*., 1997*a*).

Changes in rCBF

All results are presented as SPM{*t*} maps showing significant increases in rCBF at a threshold of $P < 0.05$ (corrected for multiple comparisons). The significant changes in rCBF were superimposed onto the stereotactically normalized group MRI. The peak co-ordinates in rCBF increases, and the relative rCBF values at these peaks, are given elsewhere (Jueptner *et al*., 1996*a*, 1997*a*–*c*). Table 1 gives a summary of brain areas activated during different motor learning and movement execution tasks.

Components of motor learning

Brain areas involved in the learning of motor sequences (new minus prelearned). The comparison of new learning with the prelearned condition (Fig. 1) revealed significant activations in the dorsolateral prefrontal cortex [Brodmann areas (BA) 10, 9 and 46, bilaterally], anterior cingulate cortex (BA 24 and 32, bilaterally), lateral premotor cortex (BA 6, bilaterally), right parietal cortex (BA 7 and 40), insula (bilaterally), basal ganglia (striatum and globus pallidus, bilaterally) and thalamus (dorsomedial and ventro-anterior parts, bilaterally). Within the cerebellum there was more activation in the neocerebellar hemispheres of the posterior lobe (bilaterally), the cerebellar vermis of the posterior lobe (e.g. plane –32, Fig. 1) and the cerebellar nuclei. Since measurement in rCBF reflects synaptic activity (Jueptner and Weiller, 1995), the activation of the pontine nuclei in this comparison (e.g. plane –28, Fig. 1) probably reflects the activity of cortical afferents to the cerebellum.

Brain areas involved in improvement of performance (new sequence minus free selection). The comparison of the new learning condition with the free-selection task revealed significant activations in the right dorsolateral prefrontal cortex (BA 9 and 10), right anterior cingulate cortex (BA 32), right parietal cortex (BA 7 and 40), right insula and right caudate nucleus, most anterior putamen and globus pallidus (first row, Fig. 2). Within the cerebellum there was more activation in the neocerebellar hemispheres of the posterior lobes, the cerebellar nuclei, the cerebellar hemispheres and vermis of the anterior lobe. There was also more activation in the pontine nuclei probably reflecting the activity of cortical afferents to the cerebellum.

Brain areas involved in decision making and selection of movements (free selection minus repetition). The comparison of the free-selection condition with repetitive movements of the same finger revealed activations in the dorsolateral prefrontal cortex (BA 9, 10 and 46, bilaterally), anterior cingulate cortex (BA 24 and 32, bilaterally), lateral premotor cortex (BA 6, bilaterally) and parietal cortex (BA 7 and 40, bilaterally). In the mid-putamen (second row, Fig. 2) there was more activation during the free-selection condition than during repetitive movements of the same finger. There was no significant activation of the cerebellum in this comparison.

Brain areas involved in the performance of an overlearned motor task (prelearned minus baseline). The comparison of the prelearned condition with the baseline reference condition, in which no movements were performed (only presentation of tones by the computer) revealed activations in the left anterior cingulate cortex (BA 23 and 24), left lateral and medial premotor cortex (BA 6), left sensorimotor cortex, left parietal cortex (BA 7 and 40), left posterior putamen (third row, Fig. 2) and right neocerebellar hemisphere and nuclei.

Brain areas involved in the performance of repetitive finger movements (repetition minus baseline). The comparison of repetitive finger movements with the baseline reference condition, in which no movements were performed, revealed activations in the left anterior cingulate cortex (BA 23 and 24), left sensorimotor cortex, left posterior putamen (fourth row, Fig. 2) and right neocerebellar hemisphere.

Effects of attention to action (attention minus prelearned sequence). The comparison of attention to action with the prelearned condition revealed significant activations in the dorsolateral prefrontal cortex (left BA 10, BA 9 and 46, bilaterally) and in the anterior cingulate cortex (BA 24, bilaterally). There was a small activation of the right caudate nucleus. No significant activation was found in the cerebellum in this comparison.

Visuomotor co-ordination

New line generation versus control of eye movements (drawing minus watching). The comparison of these two conditions revealed significant activations in the right dorsolateral prefrontal cortex (BA

Table 1 *Overview of brain areas activated during different motor learning and movement execution tasks*

Brain areas	Comparisons									
	New sequence minus prelearned sequence	New sequence minus free selection	Free selection minus repetitive movements	Prelearned sequence minus baseline condition	Repetitive movements minus baseline condition	Attention (prelearned) minus prelearned sequence	Drawing lines minus eye movements	Copying lines minus eye movements	Active movements minus resting condition	Passive movements minus resting condition
Dorsolateral prefrontal cortex	++	+	+	–	–	+	(+)	–	–	–
Anterior cingulate cortex	++	+	+	+	+	+	+	+	+	–
Premotor cortex	++	–	++	+	–	–	++	++	–	–
Supplementary motor area	–	–	–	+	–	–	+	–	+	+
Sensorimotor cortex	–	–	–	+	+	–	++	++	++	++
Parietal cortex	++	+	++	+	–	–	++	++	+	+
Insula	++	+	–	–	–	–	+	–	–	–
Striatum	++	++	–	–	–	(+)	–	–	–	–
Mid-putamen	–	–	+	–	–	–	–	–	–	–
Posterior putamen	–	–	–	+	+	–	+	+	+	–
Globus pallidus	++	++	–	–	–	–	–	–	–	–
Neocerebellar hemisphere	++	++	–	+	+	–	++	++	++	++
Neocerebellar vermis	++	++	–	–	–	–	++	++	++	++
Cerebellar nuclei	++	++	–	+	–	–	++	++	++	++

Symbols used: ++ = strong activation; + = significant activation; (+) = activation at threshold level; – = no activation. In the sequence-learning studies, new sequence learning, performance of prelearned sequences, free selection of finger movements, repetitive movements of the middle finger, attention to action (prelearned sequence) and baseline condition (no movements, tones produced by computer) were compared with one another. In the visuomotor co-ordination study, drawing new lines (new line generation), copying given lines (line tracing) and eye movements alone (watching, with no hand/arm movements) were compared. In the sensory information processing, active/passive movements of the elbow were compared with rest (no movements).

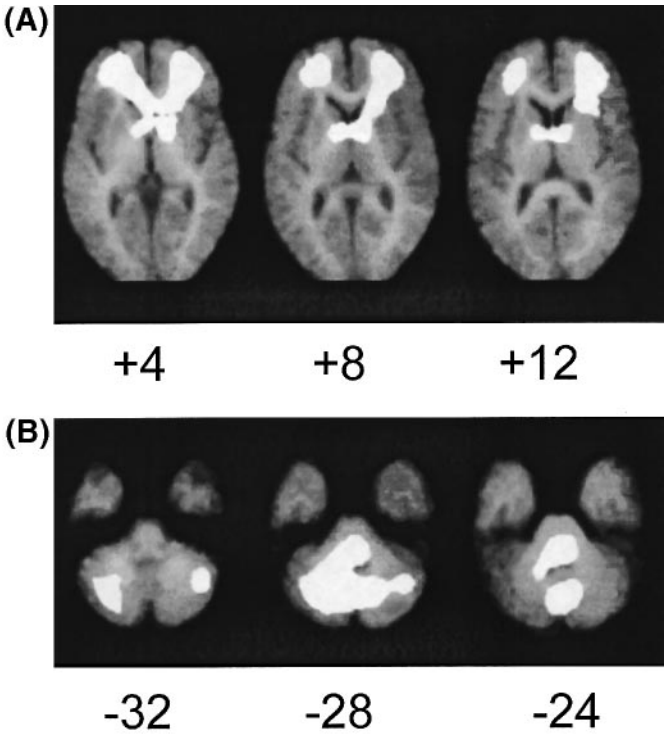

Fig. 1 SPM{*t*} maps of significant increases in rCBF superimposed onto a group MRI; white areas represent significant increases in rCBF in the 'new sequence learning' condition compared with the automatic performance of the prelearned sequence. (**A**) Activations in the basal ganglia. (**B**) Activations in the cerebellum. Numbers below the images indicate the level above (positive values) or below (negative values) the intercommissural plane (as defined by Talairach and Tournoux, 1988).

9 and 46), left anterior cingulate cortex (BA 24), right supplementary motor area (medial BA 6), lateral premotor cortex (BA 6, bilaterally), sensorimotor cortex (bilaterally), parietal cortex (BA 7 and 40, bilaterally), right temporal cortex (BA 37), left insula, left posterior putamen, neocerebellar hemispheres, cerebellar nuclei and vermis of the posterior lobe.

Line tracing versus control of eye movements (copying–watching). The comparison of these two conditions revealed significant activations in the anterior cingulate cortex (BA 23 and 24, bilaterally), right lateral premotor cortex (BA 6), sensorimotor cortex (bilaterally), parietal cortex (BA 7 and 40, bilaterally), temporal cortex (BA 37, bilaterally), left posterior putamen, neocerebellar hemispheres, cerebellar nuclei and vermis of the posterior lobe.

Line tracing versus new line generation (copying minus drawing). The direct comparison of these two conditions revealed small activations in the parietal cortex (BA 7, bilaterally) and a massive activation of the neocerebellar hemispheres, cerebellar nuclei and vermis of the posterior lobe. There was no activation of the basal ganglia in this comparison.

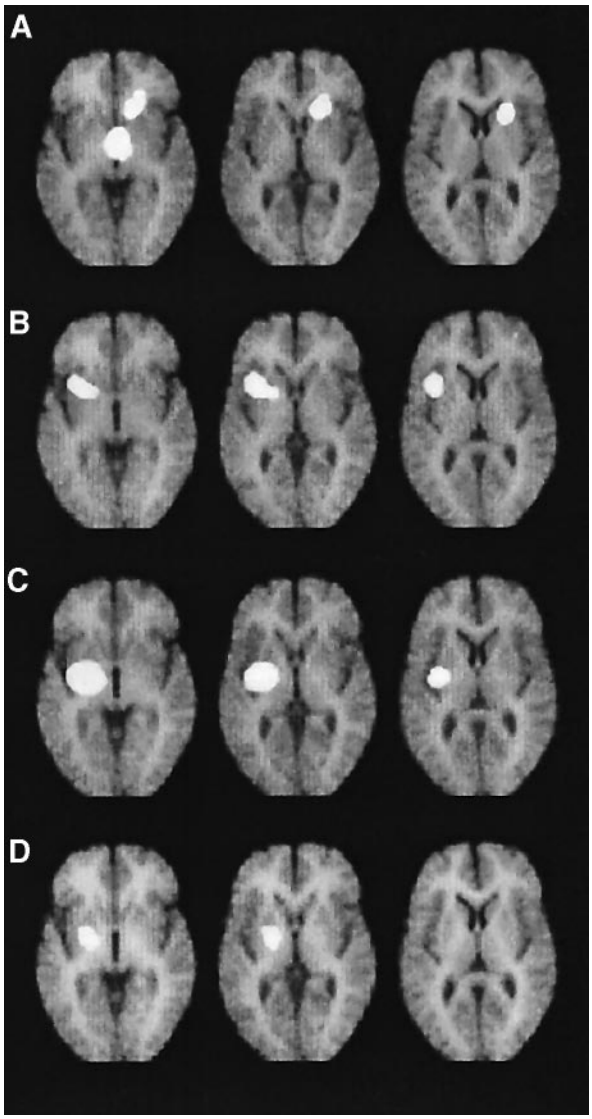

Fig. 2 SPM{*t*} maps of significant increases in rCBF at the level of the basal ganglia superimposed onto a group MRI; the white areas represent significant increases in rCBF. (**A**) New learning of a sequence of finger movements is compared with freely selected finger movements. (**B**) Freely selected finger movements compared with repetitive movements of the middle finger at the same frequency. (**C**) The automatic performance of a prelearned sequence of finger movements is compared with the baseline condition in which no movements were performed; tones were produced by the computer to control for auditory input. (**D**) Comparison of repetitive movements of the middle finger with the baseline condition in which no movements were performed. The images correspond to planes 0, +4 and +8 mm above the intercommissural plane (as defined by Talairach and Tournoux, 1988).

Sensory control of movements

Active movements of the right elbow (active movements minus rest). The comparison of these two

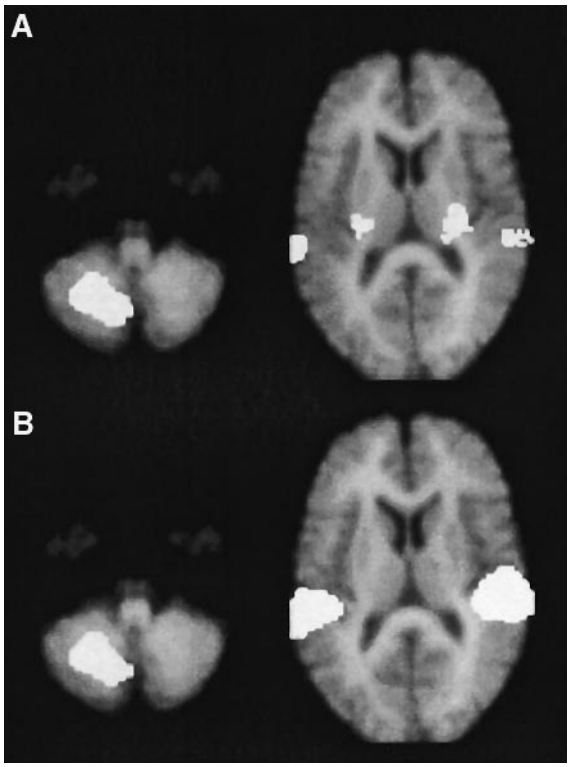

Fig. 3 SPM{*t*} maps of significant increases in rCBF superimposed onto a group MRI; the white areas represent significant increases in rCBF in the movement conditions compared with rest. (**A**) Activations during active movement of the elbow compared with rest in the cerebellum and basal ganglia. (**B**) Activations during passive movement of the elbow compared with rest in the cerebellum and basal ganglia.

conditions revealed significant activations in the anterior cingulate cortex (BA 24 and 32, bilaterally), left supplementary motor area (BA 6), left sensorimotor cortex, parietal cortex (BA 40, bilaterally), posterior putamen (bilaterally), neocerebellar hemispheres (bilaterally), cerebellar nuclei (bilaterally) and cerebellar vermis (Fig. 3).

Passive movements of the right elbow (passive movements minus rest). The comparison of these two conditions revealed significant activations in the left supplementary motor (BA 6), left sensorimotor cortex, parietal cortex (SII, bilaterally), neocerebellar hemispheres (bilaterally), cerebellar nuclei (bilaterally) and cerebellar vermis (Fig. 3).

Direct comparison of active and passive movements (active minus passive movements). The direct comparison of these two conditions revealed significant activations in the left anterior cingulate cortex (BA 24 and 32), left supplementary motor (BA 6), posterior putamen (bilaterally), right neocerebellar hemisphere and cerebellar nuclei.

Discussion

The basal ganglia and cerebellum, and motor learning

The main aim of the experiments was to compare the roles of the basal ganglia and cerebellum in the control of movements. The basic approach (analysis of task components) originated from our studies on motor learning; functional imaging studies have shown that almost all brain areas which are involved in motor control are also involved in motor learning (Grafton *et al*., 1992; Halsband and Freund, 1993; Jenkins *et al*., 1994). It seems unlikely that all these brain areas are concerned with the same task. Therefore, we analysed components of the motor learning task to differentiate the roles that these brain areas play for motor learning.

Brain areas involved in the learning of new motor sequences

The comparison of a 'new learning' condition with the automatic performance of a well-trained and thus automatic task (new learning minus prelearned condition) revealed activations in the striatum, globus pallidus, neocerebellar hemispheres, cerebellar nuclei bilaterally and the cerebellar vermis (Jueptner *et al*., 1997*b*). As both conditions required subjects to perform sequences of finger movements, the observed increases in rCBF cannot be related to movement execution. They must be related to some of the components involved in motor learning (Jueptner *et al*., 1997*b*). This finding contradicts previous reports which attributed pure motor executive functions to the basal ganglia (for review, see Brooks, 1995).

Brain areas involved in improvement of performance

Learning new sequences required subjects to perform many different (mental) operations like making new decisions (about which finger to move next), to control and remember the outcome of a movement (whether it was correct or not), to rehearse mentally the sequence learned so far, to attend to what they were doing (attention to action) and to improve motor performance. In order to analyse the improvement of motor performance, new learning was compared with a condition which was similar in many of the components of motor learning: the free-selection task. This task required subjects to make new decisions (about which finger to move next), to control and remember a movement ('don't repeat the same key twice') and to attend to what they were doing. However, during the free-selection condition, motor performance did not change over time (Jueptner *et al*., 1997*c*). Thus, the comparison of new learning with this free-selection condition revealed the brain areas concerned with improvement of motor performance. Again, the striatum, globus pallidus, neocerebellar hemispheres, pars intermedia

and the cerebellar nuclei on both sides were more active during new learning. As in the previous comparison (new minus prelearned sequence), activation of the dorsolateral prefrontal cortex was paralleled by an activation in the striatum. Again these results support the view that the basal ganglia and cerebellum are specifically concerned with improvement of motor performance (motor learning).

Brain areas involved in decision making and selection of movements

Previous PET experiments have shown that the dorsolateral prefrontal cortex is activated when subjects make decisions, e.g. when subjects decide between directions in which to move a joystick (Deiber *et al*., 1991; Playford *et al*., 1992), decide in which direction to draw a line (Jueptner *et al*., 1996*a*), decide which finger to move (Frith *et al*., 1991; Jueptner *et al*., 1997*c*), decide when to move a finger (Jahanshahi *et al*., 1995) or decide not to move (fixation of a static target compared with pursuit eye movements; Jueptner *et al*., 1996*a*). In previous studies, we have shown that prefrontal cortex is active during new learning which requires subjects to make new decisions. It is no longer active during the performance of a prelearned task or performance of a simple repetitive task which does not require practice. Prefrontal activation is re-established when subjects attend to what they are doing (attention minus prelearned sequence; Jueptner *et al*., 1997*b*, *c*).

The lateral premotor cortex was activated during new learning (compared with prelearned sequences), in the free selection of movements (compared with repetitive movements) and during performance of a prelearned sequence (Jenkins *et al*., 1994; Jueptner *et al*., 1997*c*). All of these tasks require subjects to select movements in the presence or absence of a significant dorsolateral prefrontal cortex activation. These findings confirm earlier reports by Deiber *et al*. (1991) and Colebatch *et al*. (1991) who demonstrated that premotor cortex is active when subjects select movements.

Changes in rCBF observed in frontal motor areas were paralleled by similar changes at the level of the basal ganglia; during new learning of motor sequences we found activation of the striatum and globus pallidus (new minus prelearned sequences, new sequences minus free selection). During free selection of movements, the activation was confined to the anterior putamen (free selection minus baseline, free selection minus repetition). The pattern was different for the prelearned task. Here we found activation that lies more posteriorly in putamen (prelearned sequences minus baseline). Similarly the activation for the repetitive task also lies more posteriorly (repetition minus baseline). These results are in accordance with anatomical data from animal experiments (e.g. Alexander *et al*., 1990) and demonstrate for the first time, that, within the basal ganglia, components of the basal ganglia–thalamocortical loops can be visualized in humans.

Our data show that once a motor task has become automatic, the prefrontal loop of the motor system is no longer engaged; the executive parts of the motor system (motor loop) take over and allow the prefrontal cortex to be engaged in another task. Neuropsychologists call this situation a dual performance task. Shaffer (1975) demonstrated that a skilled typist is able to type accurately while holding a conversation. The results summarized here may provide the neurophysiological explanation for this phenomenon; highly overtrained tasks (like writing) may be performed by the executive parts of the motor system, leaving the prefontal loop free to be engaged in another task (holding a conversation).

Interestingly, the prefrontal loop, i.e. the dorsolateral prefrontal cortex and the striatum, is re-engaged when subjects attend to the performance of an automatic (overlearned) task (att–pre). This result confirms and extends findings reported by Raichle *et al*. (1994). These authors reported a decrease in the activation of the prefrontal cortex as subjects repeatedly supplied the same verbs in response to a list of nouns. They also showed that the activation of the prefrontal cortex increased again when a new task was given; the subjects were provided with a new list of nouns. In our experiment, subjects performed the same task in both conditions. However, when subjects paid attention to the performance of a prelearned (and thus automatic) sequence the activation of the dorsolateral prefrontal cortex reoccurred. This shift of activation back to prefrontal cortex was accompanied by a shift of the activation within the basal ganglia, i.e. from the posterior putamen back to the striatum (caudate nucleus and anterior putamen). Again this result confirms the existence of basal ganglia–thalamocortical loops in human subjects.

Mink and Thach (1991*a*) recorded the discharge of single neurons in the globus pallidus of the rhesus monkey. They used five different motor tasks to test whether pallidal discharge was exclusively related to one mode of movement. The movement tasks differed in terms of movement velocity (fast versus slow movements), mode of movement (ramp and sinusoidal movements) and sensory guidance (visually guided versus internally guided). Mink and Thach (1991*a*) found that no single task engaged all pallidal neurons to the exclusion of others and they suggested that pallidal discharge was used for purposes other than initiating and controlling any one movement task. Inactivation of the globus pallidus (Mink and Thach, 1991*c*) led to coactivation of wrist flexors and extensors, and to slowness of all movements. The authors concluded that pallidal neurons play little or no role in the voluntary initiation of movements. They suggested that the role of the basal ganglia is to switch off maintained motor activities that would otherwise interfere with voluntary movement commands. In other words, the basal ganglia may help to select the appropriate muscles for movement commands generated elsewhere.

In our motor learning studies, activation of the basal ganglia paralleled changes of activation in cortical motor areas. According to Mink and Thach (1991*a*, *c*), these activations may reflect the process of selection of appropriate

muscles for movement commands generated in cortical motor areas.

Visuomotor co-ordination study: line tracing and new line generation

As both the basal ganglia and cerebellum were involved in improvement of performance (motor learning studies), we tried to differentiate the roles of these two subcortical structures further. In the motor learning studies, sensory cues had been used to guide discrete (i.e. short-lasting) finger movements. In the following study we analysed the sensory guidance of continuous movements. Both the basal ganglia and cerebellum receive information from sensory, motor and association cortices. However, they differ in the areas from which they receive sensory, especially visual, information.

The cerebellum receives visual inputs via the pons from the dorsal visual system, including area V5 and parietal area 7 (Ungerleider *et al*., 1984; Schmahmann and Pandya, 1991). Inputs from the temporal lobe originate mainly in the superior temporal sulcus (Schmahmann and Pandya, 1989, 1991). On the other hand, the striatum receives input from the parietal cortex and inferior temporal cortex (Selemon and Goldman-Rakic, 1985; Saint-Cyr *et al*., 1990).

Somatosensory (proprioceptive) information from muscle spindles and tendon receptors is conveyed to the cerebellum via the climbing and mossy fibre systems; these afferents provide the cerebellum with information about joint position, direction and velocity of movements (Murphy *et al*., 1973; Bauswein *et al*., 1983; Kolb *et al*., 1987; Berretta *et al*., 1991; Bosco and Poppele, 1993; Grill *et al*., 1994). The basal ganglia receive proprioceptive information mainly via the primary somatosensory cortex (Crutcher and DeLong, 1984; Alexander, 1987; Connor and Abbs, 1990; Flaherty and Graybiel, 1993; Wichmann *et al*., 1994).

The visuomotor co-ordination study served to test to what extent the cerebellum and basal ganglia differ in their specialization for the sensory guidance of movements.

During line tracing and new line generation, the actual movements being performed were identical in terms of direction, distance, duration and velocity of movement. Subjects generated their own controls during line generation and the identical parameters were used for the line re-tracing condition. Therefore, differences in rCBF between these two tasks (Jueptner *et al*., 1996*a*) cannot be attributed to different movements being performed.

There was, however, a fundamental difference between the two tasks. When subjects generated new lines, they were free to choose any direction, thus there could be no errors. During line re-tracing, errors (i.e. deviations of the pointer from the moving end of retracting line) were bound to occur. Animal experiments have shown that line re-tracing tasks are performed discontinuously, with execution of movements alternating with control of movement outcome (Miall *et al*., 1987; Stein and Glickstein, 1992). In the present experiment, line re-tracing required subjects to monitor their movements continuously, and to detect and correct errors.

The comparison of line re-tracing with new line generation revealed small significant activations in the anterior cingulate and inferior parietal cortex, and a massive activation of the neocerebellar hemispheres, neocerebellar vermis and cerebellar nuclei bilaterally, but no signal in the basal ganglia. Activation of the anterior cingulate cortex (BA 24) is probably due to the attention demanded by the line re-tracing task (Corbetta *et al*., 1990; Pardo *et al*., 1990; Devinsky and Luciano, 1993). There was also more activity in the inferior parietal cortex (BA 7 and 39). Projections from parietal cortex to the cerebellum convey the information about location and motion which is essential for the visual guidance of movements (Stein and Glickstein, 1992). There was also more activation in the cerebellar nuclei, cerebellar vermis and adjacent hemispheres of the pars intermedia and neocerebellar cortex bilaterally. This result strongly suggests that the neocerebellum was involved in monitoring the outcome of movements, i.e. in the detection and correction of errors which occur during line re-tracing. In other words, the cerebellum makes use of sensory information (visual information about target position, proprioceptive information about arm position) to optimize movements (minimize errors, i.e. deviations of the pointer from the target).

Within the basal ganglia, there was no difference between the two conditions. In both tasks (when compared with the resting condition), there was a massive activation of the sensorimotor cortex which was paralleled by an activation of the posterior putamen. Again these results confirm our previous findings, that an activation of the cortical areas of the motor loops also involves the motor loop equivalent of the basal ganglia, i.e. the posterior putamen.

Sensory control of movements: active and passive movements

The performance of the motor task not only required subjects to plan, prepare and initiate a movement (efferent motor component), but also to monitor how the movement was actually performed (afferent sensory component). Passive movements may be used to separate the afferent sensory from the efferent motor component of a voluntary movement (Weiller *et al*., 1996). Having found (in the visuomotor co-ordination study) that the cerebellum uses sensory information to optimize movements, we were interested to analyse the relative contribution of sensory afferents (through touch and proprioception) to the cerebellar signal seen during movement execution.

Passive movements lead to activation of muscle spindle afferents (primary muscle spindle afferents/group Ia fibres and secondary muscle spindle afferents/group II fibres) and cutaneous receptors (for reviews, see Ito, 1984; Rothwell, 1994). Animal experiments have shown that these afferents inform the cerebellum about many aspects of movement

execution, e.g. joint position, and direction and velocity of movements (Ishikawa *et al*., 1972*a*, *b*; Bauswein *et al*., 1983; Ito, 1984; Berretta *et al*., 1991; Bosco and Poppele, 1993; Rothwell, 1994). It has been shown that the cerebellum uses this proprioceptive feedback to optimize movements (Ito, 1984; Stein and Glickstein, 1992; Thach *et al*., 1992). In humans there has been a rather limited number of studies concerned with cerebellar sensory processing (Ivry and Keele, 1989; Grill *et al*., 1994; Jueptner *et al*., 1995; Jueptner *et al*., 1996*a*, *b*). While these data suggest that the cerebellum is involved in processing sensory information they do not reveal the functional relevance of this process.

In our previous studies we have shown that passive movements induce increases in rCBF in the same parts of the human neocerebellar hemisphere as active movements (Jueptner *et al*., 1997*a*). The local activation (percentage increase in rCBF at a specified location; see Table 1) and spatial extent of activation (size of activation as determied by the number of significant voxels) due to passive movements was almost identical to the active movements. This finding contradicts many previous reports which have postulated that the neocerebellar hemispheres are mainly concerned with movement planning. It has been shown, for example, that cooling or inactivation of the dentate nucleus leads to an increase in reaction time (for further reviews, see Thach *et al*., 1992; Mink and Thach, 1991*c*; Rothwell, 1994). However, movement planning only leads to a small increase in rCBF in a restricted area of the ipsilateral neocerebellar hemisphere (Jueptner *et al*., 1997*a*).

Our results from the analysis of passive movements suggest that neocerebellar activity is almost entirely driven by sensory systems (Jueptner *et al*., 1997*a*). This seems to be in strong contradiction to a wide range of clinical (lesion) studies in humans as well as animal experiments. At the beginning of this century, Holmes (1917) stated 'I have, however, examined every modality of sensation in many cases but have never found disturbances of any form, nor have I detected any evidence that would point unequivocally to any alteration of it'. Many single unit recording studies in animals have shown that the discharge of cells in the dentate nucleus is not higher during visually guided (i.e. sensory driven) movements than in self-paced rapid alternating movements (e.g. Thach *et al*., 1993). One explanation for this seemingly strong contradiction might be that cerebellar input is driven by sensory systems, but that cerebellar output is not. This hypothesis is favoured by the fact that passive sensory stimuli *per se* do not activate the dentate nucleus unless the animal moves in response (Strick, 1983). The sensory 'analysis' is easily demonstrated in the cerebellar cortex of animals and humans, e.g. during passive movements (Bauswein *et al*., 1983; Kolb *et al*., 1987) but it does not necessarily lead to changes of the cerebellar (output) nuclei. This means that the cerebellum might act as a 'sensory filter', 'comparator' or 'detector' (Eccles *et al*., 1972; Horne and Butler, 1995) analysing sensory informations (e.g. from muscle spindles) in order to optimize movements (see motor learning studies and visuomotor co-ordination task reported in this paper). However, recent studies have shown that the human cerebellum (including the cerebellar nuclei) may indeed be involved in processing sensory information (Ivry and Diener, 1991; Diener *et al*., 1993; Grill *et al*., 1994). Our own study of the effects of passive movements (in the absence of motor activity, i.e. with a silent EMG) on cerebellar activity has shown that passive movements lead to activation of the cerebellar nuclei (Jueptner *et al*., 1997*a*). Using functional MRI, Gao *et al*. (1996) demonstrated activation of the dentate nucleus during passive and active sensory tasks. These authors concluded that 'A new alternative hypothesis is that the lateral cerebellum is not activated by the control of movement *per se*, but is strongly engaged during the acquisition and discrimination of sensory information'.

On the other hand, the basal ganglia were only engaged during active movements. Again, we found an activation of the sensorimotor cortex which was paralleled by an activation of the posterior putamen (as in prelearned sequence minus baseline, repetition minus baseline, drawing minus watching and copying minus watching comparisons; for summary see Table 1). However, there was no activation in the posterior putamen during passive movements. Therefore, it seems unlikely that the activity of the basal ganglia is related to sensory information processing.

Conclusion

Both the basal ganglia and cerebellum were engaged when subjects improved their performance (motor learning studies). The basal ganglia were differentially activated when subjects had to select movements. There was no activation in the basal ganglia when movements were optimized using sensory feedback (visuomotor co-ordination study). There was no activation of the basal ganglia when passive movements were examined. As passive movements separate the afferent sensory from the efferent motor component the results suggest that the basal ganglia are not concerned with monitoring the outcome of movements (afferent sensory component). According to suggestions by Mink and Thach (1991*a*–*c*) the basal ganglia may be more concerned with the selection of the appropriate movements/muscles (efferent motor component). During movement selection, there was no cerebellar activation. However, the neocerebellum was activated when movements were performed under sensory guidance (visuomotor co-ordination study). During passive movements, the cerebellar activation was almost identical to active movement performance. These results suggest that the neocerebellum may be more concerned with optimizing movements by monitoring the outcome of movements (sensory information processing).

Acknowledgements

The original studies were supported by the Wellcome Trust, the Deutsche Forschungsgemeinschaft, grant Di-327/5–2, the

Kuratorium ZNS and, in part, by a grant from the European Union, Biomed1-project CT94/1261 concerted action.

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Received September 2, 1997. Revised January 15, 1998.
Accepted March 4, 1998