Motor Learning Produces Parallel Dynamic Functional Changes during the Execution and Imagination of Sequential Foot Movements

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The aim of the present positron emission tomography study was to measure the dynamic changes in cerebral activity before and after practice of an explicitly known sequence of foot movements when executed physically and to compare them to those elicited during motor imagery of the same movements. Nine healthy volunteers were scanned while performing both types of movement at an early phase of learning and after a 1-h training period of a sequence of dorsiflexions and plantarflexions with the left foot. These experimental conditions were compared directly, as well as to a perceptual control condition. Changes in regional cerebral blood flow associated with physical execution of the sequence early in the learning process were observed bilaterally in the dorsal premotor cortex and cerebellum, as well as in the left inferior parietal lobule. After training, however, most of these brain regions were no longer significantly activated, suggesting that they are critical for establishing the cognitive strategies and motor routines involved in executing sequential foot movements. By contrast, after practice, an increased level of activity was seen bilaterally in the medial orbitofrontal cortex and striatum, as well as in the left rostral portion of the anterior cingulate and a different region of the inferior parietal lobule, suggesting that these structures play an important role in the development of a long lasting representation of the sequence. Finally, as predicted, a similar pattern of dynamic changes was observed in both phases of learning during the motor imagery conditions. This last finding suggests that the cerebral plasticity occuring during the incremental acquisition of a motor sequence executed physically is reflected by the covert production of this skilled behavior using motor imagery.   © 2002 Elsevier Science (USA)

Key Words: positron emission tomography; explicit sequence learning; physical execution; motor imagery; foot movements; healthy subjects.

INTRODUCTION

Motor imagery (MI) refers to the dynamic process of simulating movements without their overt execution (Decety and Jeannerod, 1995; Decety, 1996; Decety and Grèzes, 1999). Over the past 20 years, there has been a growing interest in the study of this type of mental experience, as external correlates of this internal process have now been identified, and because several investigators have proposed that mental practice using MI could be used as a potential adjunct to neurological rehabilitation (Warner and McNeill, 1988; Decety, 1993b; Van Leeuwen and Inglis, 1998; Jackson *et al.,* 2001). Recently, various methodological approaches have been used to identify the existence of psychophysical and physiological similarities between imagined and physically executed movements (see Jackson *et al.,* 2001, for a review). For instance, the results of several brain imaging studies have demonstrated that the cortical and subcortical structures activated during the imagination of upper-limb movements share commonalities with those implicated in the execution of these movements (Jeannerod, 1994; Leonardo *et al.,* 1995; Stephan *et al.,* 1995; Roth *et al.,* 1996) (see Table 1). Most of these studies, however, have focused on the performance and imagination of movements during early acquisition of new skills. Thus, it is still unknown whether the anatomofunctional similarities found in these conditions can be observed in different phases of motor learning, and more specifically, whether the cerebral plasticity that occurs during learning of a new motor skill through physical practice is reflected by the changes in the neural structures activated during imagination of this skilled behavior.

Motor sequence learning refers to the increasing spatial and temporal accuracy of movements with practice (Willingham, 1998). Most functional brain imaging experiments exploring this type of learning have shown that physical practice produces changes in the overall pattern of cerebral structures involved during the execution of sequential movements of the fingers, hands, or arms (for example, see Doyon, 1997; Van Mier, 2000,

TABLE 1

Summary of the Results of Brain Imaging Studies in Healthy Subjects That Compared Physically Executed versus Imagined Upper-Limb Movements

Studies	Motor tasks	Motor-related activated regions										
		pF	pM	sma	Cg	SM	M1	S1	Ps	Pi	Ce	BG
SPECT												
Ingvar and Philipson (1977)	Clenching of hand	I	√				E		E	√		
Roland *et al.* (1980)	Finger-to-thumb	E	E	√		E	E	E				
Gelmers (1981)	Finger-to-thumb	I		√		E			√			
Decety *et al.* (1988)	Writing	√	√	√		E					√	
PET												
Stephan *et al.* (1995)	Joystick mvts.		√	√	√	E			√	√	E	
Jueptner *et al.* (1997a)	Joystick mvts.										√	
Seitz *et al.* (1997)	Writing		E	E	I		E	E	√	√	E	
Deiber *et al.* (1998)	Cued finger mvts.	I	E	√	√					√	E	
	Free finger mvts.	I	√	√	√		E			√	E	
fMRI												
Rao *et al.* (1993)	Finger mvts.		√	√			E	E				
Sanes *et al.* (1994)	Outlining a square		√	√	√		E	E	√			
Tyszka *et al.* (1994)	Finger-to-thumb			√	√							
Kim *et al.* (1995)	Finger-to-thumb		√	√			√		√			
Leonardo *et al.* (1995)	Finger-to-thumb		√			√			√			
Sabbah *et al.* (1995)	Finger mvts.			E		√						
Porro *et al.* (1996)	Finger-to-thumb		E				√	E				
Roth *et al.* (1996)	Finger-to-thumb		√	√			√	E				
Luft *et al.* (1998)	Finger-to-thumb		√				√	√			√	E
Lotze *et al.* (1999)	Clenching of hand		√	√	√		√	E			√	
Binkofski *et al.* (2000)	Outlining two circles		√	√	√	E			√			
Gerardin *et al.* (2000)	Finger mvts.	√	√	√			√	√	√	√	E	√
Porro *et al.* (2000)	Finger-to-thumb		√	√			√	E				
EEG												
Naito and Matsumara (1994)	Finger mvts.			√								
Beisteiner *et al.* (1995)	Joystick mvts.					√						
Cunnington *et al.* (1996)	Tapping board			√								
Green *et al.* (1997)	Finger mvts.	I	I				E					
MEG												
Lang *et al.* (1996)	Finger mvts.						√					
Schnitzler *et al.* (1997)	Finger mvts.						√					

Note. Abbreviations: mvts, movements; √, activated during both physically executed and imagined mvts; E, activated during physically executed mvts only; I, activated during imagined mvts only; BG, basal ganglia; Ce, cerebellum; Cg, cingulate cortex; M1, primary motor cortex; pF, prefrontal cortex; Pi, inferior parietal cortex; Ps, superior parietal cortex; pM, premotor cortex; S1, primary somatosensory cortex; SM, sensorimotor cortex; sma, supplementary motor area. Please note that for technical reasons or because of a priori hypotheses, most experiments cited in this table did not cover the whole brain. (Reproduced with permission from *Arch. Phys. Med. Rehabil.*)

for reviews). For instance, during the initial (fast) acquisition phase of this skill, significant activations have often been observed in the dorsal premotor cortex (Grafton *et al.,* 1995), inferior parietal cortex (Seitz and Roland, 1992; Grafton *et al.,* 1995), and cerebellum (Seitz and Roland, 1992; Rauch *et al.,* 1995). By contrast, once the motor routine is established and rehearsed with physical practice, it has been proposed that the striatum, in concert with other cortical and subcortical regions, may mediate the long-term representation of the motor program (see Doyon, 1997; Doyon and Ungerleider, 2002, for reviews).

The goal of the present PET study was thus to measure the dynamic changes in cerebral activity between early and more advanced learning phases of sequential foot movements performed physically, and to compare

them with the ones elicited during MI of the same sequence. To this end, we used a new learning paradigm that involves the acquisition of an explicitly known sequence of foot movements. We hypothesized that, during both the early and late phases of acquisition, the imagination of sequential foot movements would activate a network of structures similar to that observed when subjects performed the Foot-Sequence Task physically.

METHODS

Participants

Nine healthy right-handed subjects (4 women and 5 men, mean age = 58.3 years, SD = 6.0) participated in
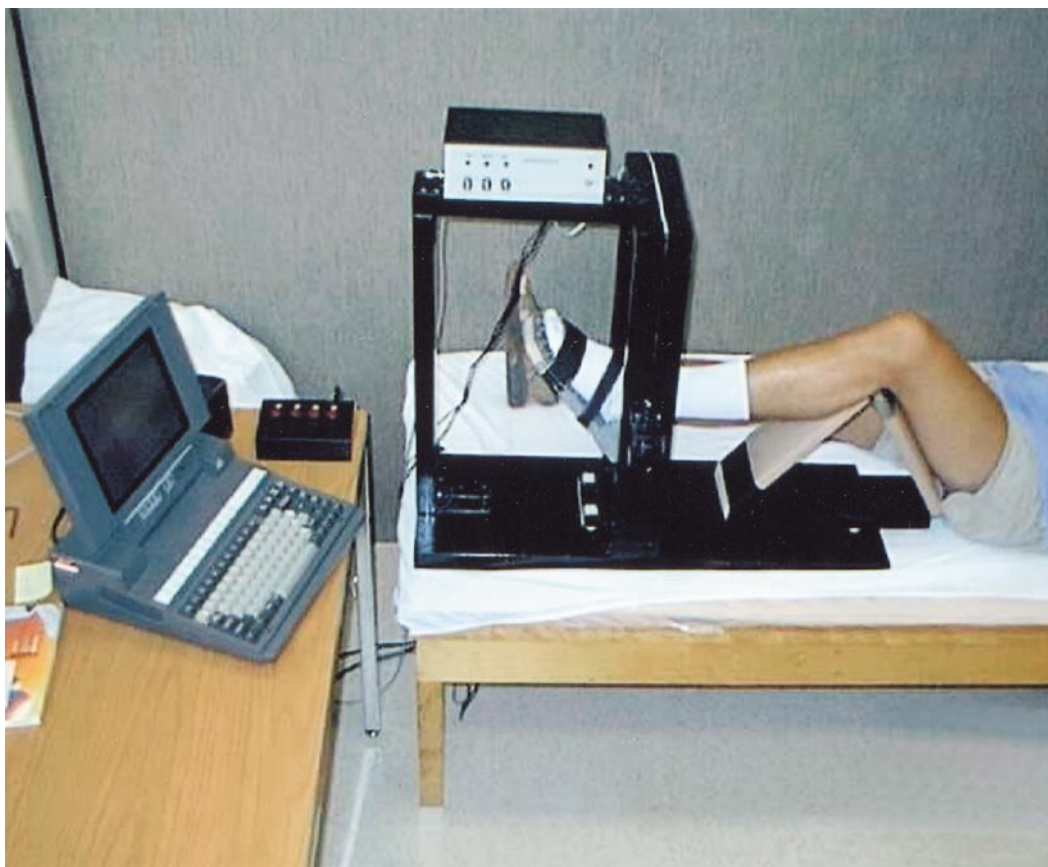
FIG. 1. The Foot-Sequence Task was adapted from the well known Serial Reaction Time Task. In this task, the participants are required to produce a dorsiflexion of the foot when they hear a high-pitched sound and a plantarflexion movement when they hear a low-pitched sound.

this experiment. In addition, all volunteers were right-footed, as assessed by a short home-made questionnaire based on a reliable measure of foot preference (Chapman *et al.,* 1987). The age range was deliberately chosen to provide matched control subjects for a group of patients with a stroke implicated in a separate study not reported here. The protocol was approved by the Ethics Committee of the Montreal Neurological Institute, and all subjects gave informed, written consent before participating.

Material

Foot-sequence task. We developed a new foot-sequence learning task based on the well known serial reaction time (SRT) task (Nissen and Bullemer, 1987). The apparatus consisted of a pedal (13 × 35 cm) mounted in a wooden frame (60 × 45 × 29 cm), which allowed free upward (dorsiflexion) and downward (plantarflexion) movements of the foot (Fig. 1). Subjects performed this task in a supine position, with their leg slightly raised and supported by pillows. The foot was secured to the pedal by two straps. The pedal was adjustable to align each volunteer's ankle rotation axis with the pivoting axle. A potentiometer on the pedal axis was adjusted by means of two tuning knobs to detect two different pedal angles (maximum dorsiflexion–maximum plantarflexion). We used the Microcomputer Experimental Laboratory programming package, running on a personal com-

FIG. 4. Merged PET-MRI sections illustrating increases of regional cerebral blood flow (rCBF) associated with the Execution and MI conditions, both before and after training on the Foot-Sequence Task. The images were averaged over the nine subjects and represent the four different experimental conditions (EE, Early Execution; EMI, Early Motor Imagery; LE, Late Execution; LMI, Late Motor Imagery) minus the Perceptual control condition. Each subtraction yielded focal changes in blood flow shown as *t* statistic images; the range is coded by the color scale (L, left; R, right). Areas of activation in the (A) cerebellar lobules, (B) dorsal premotor cortex, and (C) striatum.

FIG. 5. Merged PET-MRI sections illustrating the dynamic rCBF changes associated with physical learning of the Foot-Sequence Task for both the Execution and MI conditions. The images were averaged over the nine subjects and represent the Late minus Early phases of learning for the two different movement conditions. Conventions are as described in the legend of Fig. 4. (A) Significant rCBF changes in the medial orbitofrontal cortex (oF) and the rostral portion of the anterior cingulate (aC). (B) Areas of activation in the striatum (S) and the rostral portion of the anterior cingulate (aC).

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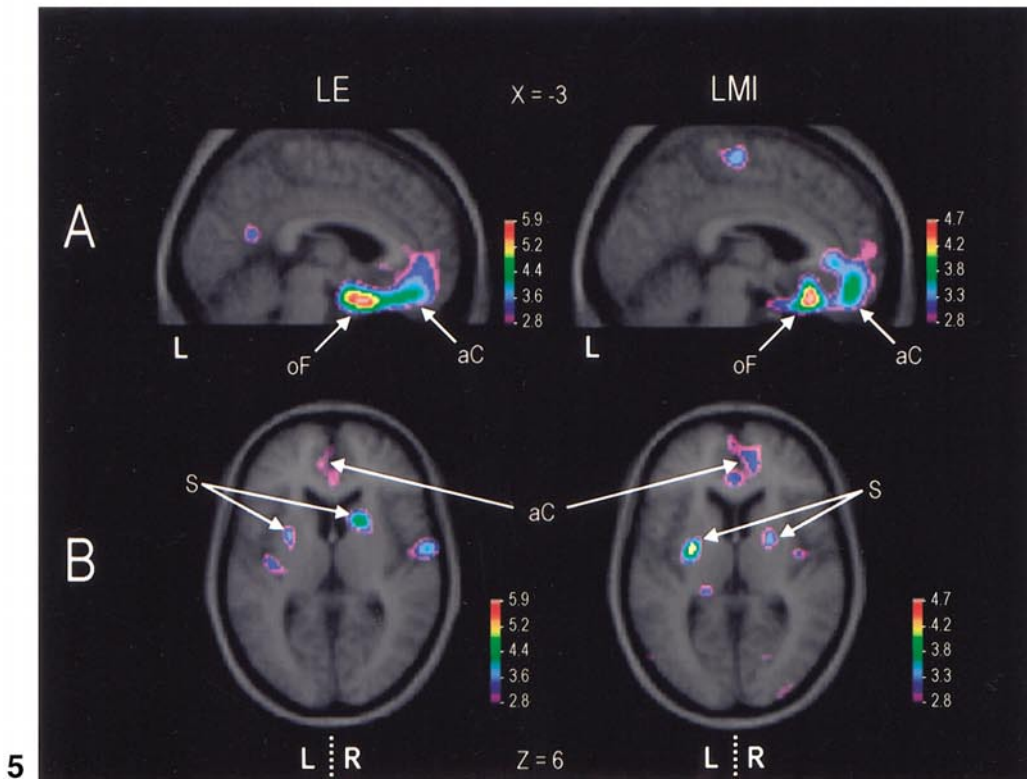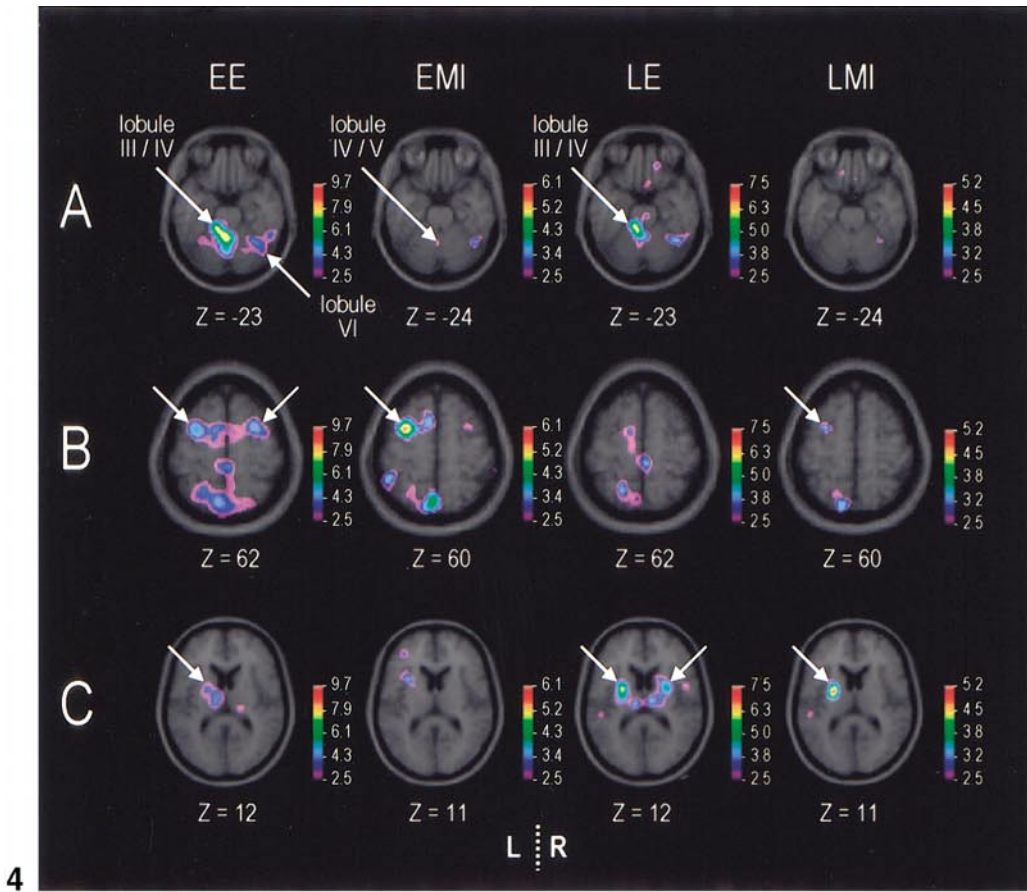
puter (Hewitt Rand; 386 Mhz), to produce two different auditory signals (200 ms in duration) through a speaker (Radio Shack; model 21-549-A). The participants were required to produce a dorsiflexion of the foot when they heard a high-pitched sound (2000 Hz) and a plantarflexion movement when they heard a low-pitched sound (100 Hz). For every foot movement, the response time (in ms) and response accuracy were transmitted to the computer by means of a relay box.

Electromyographic (EMG) recordings. A portable two-way electromyograph (Pathway MR-20; The Protheus Group) was used to obtain surface EMG recordings from the *tibialis anterior* and the *soleus,* to control for muscle activation during the Perceptual and MI conditions.

Procedure

Assessment of the subjects' imagery ability. Before the scanning session, each subject's motor imagery ability was evaluated using an adapted version of the Movement Imagery Questionnaire (MIQ) (Hall and Pongrac, 1983), called the Kinesthetic and Visual Imagery Questionnaire (KaVIQ). This test was chosen because it was adapted for older subjects and patients with locomotor deficits (Roy *et al.,* 1998). The participants were first required to execute a number of purposive movements, immediately followed by the motor imagery of the same movements using the first-person perspective (i.e., as if they were seeing and feeling themselves perform the movements from within). The subjects then rated their capacity to elicit mental images of the action on two different five-point scales (1 = high imagery; 5 = low imagery). The first scale referred to the clarity of the image, whereas the second evaluated the intensity at which they could feel themselves making the movement.

In addition to the KaVIQ, a home-made chronometric imagery measure (the Imaginary Tapping Index) was administered. In this test, subjects were asked to overtly and covertly tap their foot on the floor at a comfortable pace, while counting the number of taps until the experimenter told them to stop. Each trial was terminated after varying delays (10 s, 25 s, 45 s), and the presentation of these delays was randomized for each participant, such that they were unaware of when they should stop tapping. It was predicted that if the subjects adequately followed the instructions and were able to imagine themselves while tapping their foot: the number of taps produced should be similar in both physical and imagined conditions, and should correlate with increasing delays (see Decety and Michel, 1989; Decety and Lindgren, 1991; Decety, 1993a, for similar paradigms).

Foot-sequence task. Participants were asked to use the left foot when executing the Foot-Sequence Task. A trial began when one of the target sounds was heard

and ended when the subject's foot reached one of the two target positions (near-maximum dorsiflexion or near-maximum plantarflexion movements). The participants were instructed to move to the corresponding position as quickly as possible, while making as few errors as possible. After each trial, they were asked to return to a middle position, approximately half way between the maximum positions, in order to be ready to move in response to the upcoming target sound. The trials were presented with a fixed inter-stimulus interval of 2000 ms.

Before the PET session began, all subjects were given one block of 24 random trials in both physical and MI conditions, to become familiar with the presentation of the auditory stimuli and the apparatus itself. At the end of this familiarization period, participants completed one block of 36 trials during which stimuli were heard in a random order (Random condition) and were asked to execute plantarflexions and dorsiflexions accordingly. Following this block of trials, a predetermined 6-element sequence of dorsiflexions (D) and plantarflexions (P) (sequence = D-P-P-D-P-D) was explicitly taught to the volunteers. They were then asked to complete one block of 36 trials (i.e., six presentations of the six-element sequence) that was presented without any demarcation between the end of one sequence and the beginning of the next, such that the block appeared as a continuous series of trials. Blocks of practice were administered until the participants were able to correctly reproduce the sequence three times in a row without the auditory cues, indicating that they had acquired declarative knowledge of the sequence.

Scanning conditions. Each subject underwent five PET scans within a single session that lasted approximately three hours. The order of presentation of the scanning conditions was pseudorandomized between participants (Fig. 2). Each scan lasted 60 s and was separated by an inter-scan period of approximately 10 min. Volunteers were required to begin each condition 10 s prior to the isotope injection. All the conditions were externally paced by auditory signals, at a constant rate of 0.5 Hz, so that the number of responses made during each scanning period (i.e., 36 trials per scan) was equal for each participant. The following five conditions were presented to each subject:

(1) Early Execution. In this condition, subjects were instructed to physically execute the same 6-element sequence of movements explicitly learned prior to the scanning session.

(2) Early MI. The participants were asked to imagine that they were performing the same sequence of movements in the first-person perspective. To insure that no movement or muscle contraction was produced during this condition, EMG activity was monitored during scanning and compared to the level of activity
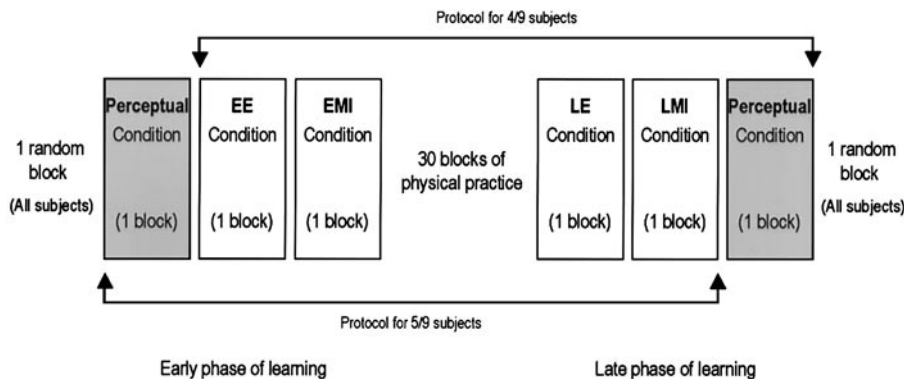
FIG. 2. Experimental design for the present study. First, prior to scanning, the participants were asked to complete one block of 36 trials during which high- and low-pitched sounds were heard in a random order. Immediately after this condition, each subject underwent five PET scans within a single session. After completing the Early Execution (EE) and Early Motor Imagery (EMI) scans in the early phase of learning, the participants were asked to practice the same sequence of movements for 30 blocks of 36 trials each. Both conditions were then administered in what is considered to be the late phase of learning (LE, LMI). The order of the scans was pseudorandomized between participants: The Perceptual condition was administered first for five subjects, while the remaining four completed this scan last. In addition, the Execution and MI sequence conditions were counterbalanced within each phase of learning. Finally, all participants completed an additional Random condition where no scanning took place.

observed during a one-minute baseline period obtained at rest before scanning.

(3) Late Execution. During the interscan period prior to this condition, subjects were asked to practice the sequence for 30 blocks of 36 trials each (i.e., 180 presentations of the sequence = 1080 trials). Sixty-second pauses separated each block, and 2-min pauses were introduced every five blocks of trials to prevent fatigue. Following this training period, participants were scanned again while they physically executed the sequence of movements.

(4) Late MI. In this scan, subjects were asked to imagine the same sequence of movements in the first-person perspective. Again, leg muscle activity was monitored to control for movement or contractions during the scan.

(5) Perceptual. In this condition, participants heard stimuli presented in random order, and were simply asked to pay close attention to the sounds. They were specifically instructed not to move or imagine moving their foot. This condition was either administered as the first or the last scan in the session, and the order of administration was counterbalanced within the group.

Finally, all participants completed an additional Random condition where no scanning took place. They were again instructed to execute movements of the left foot following a random presentation of auditory stimuli.

Postscan imagery measures. After each scan, subjects were given a series of questions to assess the quality of the motor imagery process (Malouin *et al.,* 1997). They were first instructed to judge the vividness and feelings of the mental images on a five-point scale. Furthermore, they were asked to rate at which level they were able to maintain the vividness of the images during the whole scan.

DATA ACQUISITION

PET scans were obtained with a CTI/Siemens HR+ 63-slice tomograph operating in a three-dimensional acquisition mode, at an intrinsic resolution of 4.2 × 4.2 × 4.0 mm. The field of view of the PET camera allowed visualization of the entire cortex and cerebellum. The relative distribution of CBF was measured during each 60 s scan with the water bolus H_2O^{15} methodology (Raichle *et al.,* 1983) without arterial sampling (Fox and Raichle, 1984). Subjects received approximately 10 mCi of ^{15}O-labeled H_2O per scan. For each subject, a high-resolution MRI study was also acquired using a Philips Gyroscan 1.5T with a T1-weighted fast field echo sequence giving 160 sagittal images with 1 mm^3 voxels and a TR of 19 ms, a TE of 10 ms and a flip angle of 30°.

DATA ANALYSIS

The MR images were resliced so as to be coregistered with the PET data (Evans *et al.,* 1991). An orthogonal coordinate frame was then established based on the anterior-posterior commissure line as defined in the MRI volume (Evans *et al.,* 1992). These coordinates were used to apply a trilinear resampling of each pair of MRI and PET data sets into a standardized stereotaxic coordinate system (Talairach and Tournoux, 1988) by means of an automated feature-matching algorithm (Collins *et al.,* 1994). To overcome residual anatomical variability persisting after stereotaxic standardization, the PET images were reconstructed with a 14-mm Hanning filter and then normalized for global CBF and averaged across subjects within each scanning condition. The mean state-dependent change (CBF) image volume was obtained (Fox *et al.,* 1985)

and converted to a t statistic volume by dividing each voxel by the mean standard deviation in normalized CBF for all intra-cerebral voxels (Worsley *et al.,* 1992).

Individual MR images were subjected to the same averaging procedure, such that composite stereotaxic image volumes, sampled at approximately 1.5 mm in each dimension, were obtained for both t statistic and MRI volumes. Anatomical and functional images were merged to allow direct localization on the MR images of t statistic peaks identified by an automatic peak-detection algorithm.

The significance of a given CBF activation was assessed by application of an intensity threshold to the t statistic images (Worsley *et al.,* 1992). This threshold, based on 3-D Gaussian random field theory, predicts the likelihood of obtaining a false-positive in an extended 3-D field. For an exploratory search involving all peaks within the gray matter volume of 600 cm^3, the threshold for reporting a peak as significant was set at $t \geq 4.2$, according to the method described previously by Worsley and collaborators (1996). Correcting for multiple comparisons, a t value of 4.2 corresponds to an uncorrected probability of $P < 0.0004$ (two-tailed) and yields a false-positive rate of only 0.07 in 218 resolution elements (each of which has dimensions $14 \times 14 \times 14$ mm), which approximates the volume of gray matter scanned. The threshold for peaks located in cerebral structures for which *a priori* hypotheses had been formulated was determined using a region-base method to measure significance levels (Worsley *et al.,* 1996).

RESULTS

Imagery Ability

Kinesthetic and visual imagery questionnaire. The mean rating of the subjects in the visual [2.7/5.0 (SD = 1.1) of 5.0] and kinesthetic [3.1/5.0 (SD = 0.8)] conditions of this test suggest that they were respectively able to produce a "moderately clear image" and experienced a "moderately intense sensation" when imagining the different movements. Thus, as a group, the participants included in this study were capable of producing relatively good mental images, both visually and kinesthetically.

Imaginary tapping index. Due to uncontrollable time constraints, this test could not be administered to one of our subjects. Thus, the analyses were performed based on the results of eight instead of nine subjects. As measured by paired t tests with a Bonferroni correction for multiple comparisons, the scores of the remaining participants revealed that the number of taps for each interval did not differ in both physical and imagined conditions [10 s: $t(7) = -1.96$, n.s.; 25 s: $t(7) = -2.32$, n.s.; 45 s: $t(7) = -2.20$, n.s.]. Furthermore, significant positive correlations were observed in both overt ($r = 0.798$, $P < 0.01$) and covert ($r = 0.804$,

TABLE 2

Average Surface EMG Recordings Observed in the *Tibialis Anterior* and the *Soleus* Muscles during the Perceptual and MI Scans, as well as during the One-Minute Baseline Levels Obtained at Rest Immediately before Scanning

Muscle	Condition or Scan	Average EMG value $\pm$ SD
Tibialis anterior	Baseline	8.47 ± 3.60 μV
	Perceptual	8.51 ± 3.57 μV
	Baseline	8.28 ± 3.45 μV
	Early MI	8.34 ± 3.39 μV
	Baseline	8.97 ± 3.96 μV
	Late MI	8.93 ± 3.73 μV
Soleus	Baseline	4.87 ± 3.21 μV
	Perceptual	5.07 ± 3.12 μV
	Baseline	4.86 ± 3.10 μV
	Early MI	5.11 ± 3.20 μV
	Baseline	4.69 ± 2.65 μV
	Late MI	4.99 ± 2.65 μV

$P < 0.01$) conditions between the different durations and the subjects' evaluation of the number of taps performed. Therefore, the results of this imagery index also suggest that subjects were able to generate adequate mental images of actions.

Postscan imagery measures. When subjects were asked to rate the clarity of the visual component of their actions after both Early and Late MI, they reported a mean score of 2.9/5.0 (SD = 0.9), which corresponds to the evaluation of a "moderately clear" image. Furthermore, the mean rating reported for the kinesthetic component of MI was 3.7/5.0 (SD = 0.6), suggesting that subjects "vaguely" sensed their foot moving. This last score shows that during scanning, subjects were able to imagine the movements, although they experienced more difficulty with the kinesthetic aspect of MI than when they completed the KaVIQ at the beginning of the experiment.

EMG Recordings

During scanning in the Perceptual and MI conditions, visual monitoring of the subjects' movements and of the electromyographic data did not reveal any noticeable movement of the left foot. Table 2 shows the average surface EMG recordings observed in the *tibialis anterior* and the *soleus* muscles during the Perceptual and MI scans, as well as during the 1-min baseline levels obtained at rest immediately before scanning. Paired t tests with a Bonferroni correction for multiple comparisons confirmed that the EMG recordings showed no change in muscle activity during scans compared to baseline levels. In addition, no difference in EMG activity was observed between the MI conditions before and after physical practice. These findings indicate that the pattern of cerebral activations observed
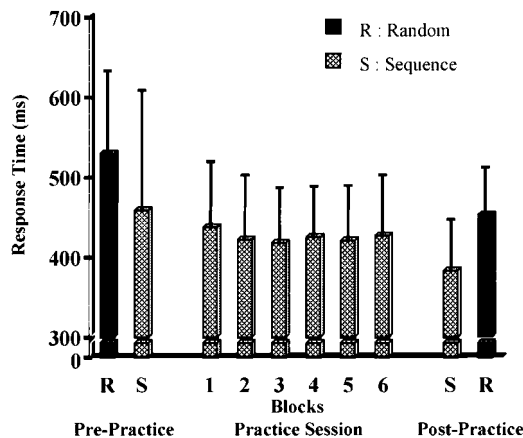
FIG. 3. Mean RT data of the nine subjects in both Random and Sequence conditions before, during, and after physical practice of the Foot-Sequence Task. Statistical analysis revealed a significant decrease in RT between the Random condition before practice and the Sequence condition after training. More importantly, switching from the Sequence to the Random condition following the practice sessions produced a significant increase in RT, suggesting that the improvement in performance was due to specific learning of the sequence.

in the MI conditions cannot be attributed to movements or muscle contractions.

Performance Measures

The accuracy and the response time (RT) were recorded for each trial on the Foot-Sequence Task. However, as a minimal number of errors were made throughout the different conditions (less than 7%), this variable could not be used as a reflection of learning. Thus, RT constituted the behavioral variable of interest, which was averaged over blocks of 36 trials for the two Sequence conditions that were performed in the scanner, as well as for the two Random conditions completed before and after scanning. During the training session, however, the data were averaged over five blocks of 36 trials.

Figure 3 illustrates the mean RT data of the nine subjects in both Sequence and Random conditions before, during and after physical practice of the Foot-Sequence Task. The critical alpha level was set at 0.05. An ANOVA for repeated measures conducted on the mean RT over the six blocks of trials during the practice sessions did not reveal any significant difference in performance. However, paired *t* tests corrected for multiple comparisons yielded a significant decrease in RT between the Random condition before practice [529.6 ± 104.2 ms (mean $\pm$ SD)] and the Sequence condition after training (383.1 ± 64.3 ms) [$t(8) = 5.62, P < 0.01$]. More importantly, the comparison between the Sequence and Random conditions following the practice sessions showed a significant increase of 69.6 ms in RT [$t(8) = -4.43, P < 0.01$]. This finding concurs with those of many experiments that used different versions

of the SRT Task (e.g., Grafton *et al.,* 1995; Rauch *et al.,* 1995; Doyon *et al.,* 1996; Hazeltine *et al.,* 1997; Honda *et al.,* 1998), and suggests that the improvement in performance seen after training is due to specific learning of the sequence *per se* (and not solely to the unspecific general ability to perform the movements).

Blood Flow

Tables 3 and 4 report statistically significant relative cerebral blood flow changes for each of the planned subtractions that were conducted, together with the exact stereotaxic coordinates based on the brain atlas developed by Talairach and Tournoux (1988). Because the latter atlas does not entail the precision required to localize specific regions within the cerebellum, the more detailed 3-D atlas of the human cerebellum developed by Schmahmann and collaborators (1999, 2000) was used to identify the cerebellar regions that were activated in this study. It should be noted that for comparison purposes, brain regions located within a volume of 1 cm^3 from one another were considered to be the same area of activation.

Overt and covert performance of sequential foot movements. We first compared the Perceptual control with the four sequence conditions to determine whether overt and covert performance of a motor sequence with the lower limb produce activations in similar brain regions (Table 3). Subtraction of the Perceptual condition from both the Early Execution and MI conditions revealed similar activations in the left precuneus and left anterior cerebellum (lobule III/IV/V) (Fig. 4A). Common changes in rCBF were also found bilaterally in the dorsal premotor cortex (Fig. 4B) and inferior parietal lobule, although activations in the right hemisphere did not reach significance in the MI condition. Several brain regions, however, were only associated with either the Execution or MI conditions. Early execution produced exclusive activations in the left thalamus and striatum (Fig. 4C), in the foot area of the right primary motor cortex, right middle temporal gyrus, right superior parietal lobule, and right posterior cerebellum (lobule VI) (Fig. 4A), as well as bilaterally in the SMA. By contrast, a unique change in rCBF in the Early MI condition was only observed in the left pre-SMA.

After practice in the late learning phase, comparisons of both Executed and MI conditions with the Perceptual control condition produced similar activations in the left precuneus, left striatum (Fig. 4C), and in adjacent regions of the left inferior parietal lobule. Again, unique activations were also observed in both Executed and MI conditions. Execution of the sequence in this learning phase elicited changes in activity in the left SMA, left superior parietal lobule, left anterior cerebellum (lobule III/IV) (Fig. 4A), right primary motor cortex, right striatum (Fig. 4C), as well as in the

TABLE 3

Comparison of the Four Experimental Conditions with the Perceptual Condition

Brain region	Stereotaxic coordinate			
	x	y	z	t Statistic
Early Execution minus Perceptual				
Left hemisphere				
Dorsal premotor cortex	−28	−1	57	5.72
Supplementary motor area	−4	−13	68	4.55
Inferior parietal lobule	−43	−40	50	5.50
Precuneus	−8	−69	56	5.42
Thalamus	−8	−23	2	4.37
Striatum	−21	−2	11	3.83
Cerebellum (lobule III/IV)	−4	−49	−18	9.67
Right hemisphere				
Dorsal premotor cortex	27	3	63	4.84
Supplementary motor area	9	−1	57	3.48
Primary motor cortex	1	−35	68	5.08
Middle temporal gyrus	58	−38	−12	4.50
Inferior parietal lobule	35	−64	45	3.76
Superior parietal lobule	24	−66	54	4.01
Cerebellum (lobule VI)	32	−56	−23	4.16
Perceptual minus Early Execution				
Left hemisphere				
Precuneus	−7	−62	14	4.26
Right hemisphere				
Insula	42	12	−14	5.01
Early MI minus Perceptual				
Left hemisphere				
Dorsal premotor cortex	−28	1	56	6.13
Presupplementary motor area	−7	5	65	3.90
Inferior parietal lobule	−42	−44	50	5.66
Inferior parietal lobule	−52	−37	21	5.00
Precuneus	−3	−66	57	4.91
Cerebellum (lobule IV/V)	−1	−57	−20	3.93
Late Execution minus Perceptual				
Left hemisphere				
Supplementary motor area	−7	−14	68	3.48
Inferior parietal lobule	−47	−32	23	4.82
Superior parietal lobule	−19	−56	63	3.94
Precuneus	−7	−69	54	4.42
Thalamus	−9	−19	9	4.17
Striatum	−26	−2	9	6.29
Cerebellum (lobule III/IV)	−4	−47	−14	7.54
Right hemisphere				
Primary motor cortex	3	−35	68	4.77
Thalamus	9	−14	11	3.99
Striatum	27	1	12	4.81
Late MI minus Perceptual				
Left hemisphere				
Dorsal premotor cortex	−28	1	57	3.52
Presupplementary motor area	−8	15	50	3.23
Inferior parietal lobule	−39	−38	44	3.61
Inferior parietal lobule	−52	−35	18	3.40
Precuneus	−13	−71	54	4.26
Striatum	−24	−4	8	5.16

Note. Activation foci in this and other tables represent peaks of statistically significant increases in normalized CBF (see text). The stereotaxic coordinates are expressed in mm. The *x* coordinate corresponds to the medial-lateral distance relative to the midline (positive = right hemisphere), the *y* coordinate represents the anterior-posterior distance relative to the anterior commissure (positive = anterior), and the *z* coordinate corresponds to the superior-inferior distance relative to the anterior commissure-posterior commissure line (positive = superior).

TABLE 4

Comparison of the Execution and MI Conditions in the Late and Early Phases of Practice

Brain region	Stereotaxic coordinate			
	x	y	z	t Statistic
Late Execution minus Early Execution				
Left hemisphere				
Rostral anterior cingulate	−7	46	0	3.58
Medial orbitofrontal cortex	−4	10	−24	5.94
Inferior parietal lobule	−40	−25	21	3.58
Striatum	−27	3	3	3.82
Right hemisphere				
Medial orbitofrontal cortex	3	36	−21	4.98
Striatum	19	12	5	4.77
Early Execution minus Late Execution				
Left hemisphere				
Dorsal premotor cortex	−27	3	62	3.84
Inferior parietal lobule	−55	−42	44	3.42
Cerebellum (lobule IV/V)	−1	−54	−21	3.69
Right hemisphere				
Dorsal premotor cortex	20	10	65	4.50
Cerebellum (lobule VI/Cr I)	8	−85	−20	4.97
Cerebellum (lobule VI/Cr I)	38	−73	−24	3.83
Late MI minus Early MI				
Left hemisphere				
Medial orbitofrontal cortex	−3	24	−21	4.70
Striatum	−28	−7	9	4.45
Right hemisphere				
Rostral anterior cingulate	1	37	0	3.52
Striatum	23	5	−2	3.29
Early MI minus Late MI				
Left hemisphere				
Inferior parietal lobule	−52	−45	33	3.63
Cerebellum (lobule VI)	−24	−59	−20	3.84

thalamus bilaterally. By contrast, activations in the MI condition were found exclusively in the left dorsal premotor cortex (Fig. 4B) and pre-SMA, although the latter region only approached significance.

As we hypothesized that the pattern of cerebral activations observed during MI of sequential foot movements would resemble that seen in the physical execution condition, we tested this assumption directly. To do so, the MI condition was subtracted from the Execution condition, both before and after physical practice of the sequence. During the early learning phase, significant activations related to the Execution condition were found in the left SMA ($x = −1$, $y = −18$, $z = 66$; $t = 6.05$) and left anterior cerebellum (lobule IV) ($x = −8$, $y = −45$, $z = −15$; $t = 9.81$), as well as in the right medial primary motor cortex ($x = 3$, $y = −33$, $z = 66$; $t = 7.23$). The reverse subtraction did not reveal any significant peak of activation. Finally, activations related to the Late Execution condition were again observed in the left anterior cerebellum (lobule III) ($x = −11$, $y = −38$, $z = −18$; $t = 9.57$) and the right

primary motor cortex ($x = 7$, $y = -38$, $z = 66$; $t = 7.66$), but not in the left SMA. Once more, no significant peak was detected when activity from the Executed condition was subtracted from that in the MI condition.

Dynamic cerebral changes associated with Execution and MI of sequential foot movements following practice. To identify the brain areas specifically associated with learning per se, the Early Execution condition was subtracted from the Late Execution condition (Table 4). Significant peaks of activation were found in the left rostral portion of the anterior cingulate (Figs. 5A and 5B) and left inferior parietal lobule, as well as bilaterally in the medial orbitofrontal cortex (Fig. 5A) and striatum (Fig. 5B). The inverse comparison (Early–Late) produced differences in blood flow in the left inferior parietal lobule, left anterior cerebellum (lobule IV/V), right posterior cerebellum (lobule VI/Cr I), and in the dorsal premotor cortex bilaterally.

The main purpose of this study was to determine whether the changes in rCBF observed between the Early and Late phases of learning in the MI condition parallel those seen in the Execution condition. To this end, a comparison between the two different phases of learning in the MI condition was carried out (Table 4). Similarly to the Executed condition, subtracting the Early from the Late MI condition produced significant changes of activity in the left medial orbitofrontal cortex (Fig. 5A) and in the striatum bilaterally (Fig. 5B). In addition, rCBF differences were observed in the right rostral portion of the anterior cingulate (Figs. 5A and 5B) for the MI condition only. Finally, in accord with the results obtained when the Late Execution conditions was subtracted form the Early Execution condition, peaks of activation were also found in the left inferior parietal lobule and cerebellum, although this activation was located more laterally to the one observed during actual movements.

DISCUSSION

The overall objective of the present PET study was to measure the dynamic changes in cerebral activity associated with both early and more advanced learning phases of an explicitly known sequence of movements executed physically and to compare them to those elicited during MI of the same sequence. Taken together, the results support our original hypothesis, and suggest that overt and covert sequential movements of the lower-limb are mediated by partially overlapping brain regions. More importantly, our data reveal that the cerebral plasticity that occurs following physical practice of a motor skill is also reflected in the neural substrate mediating motor imagery of the same skill.

Overt versus Covert Performance of Sequential Foot Movements

To determine if executed and imagined sequential movements of the lower-limb were mediated by similar neural substrates, we compared the pattern of rCBF changes obtained when the Perceptual control was subtracted from the Early Execution and Early MI conditions. As expected, similar brain areas known to be associated with the performance of motor tasks were activated by both conditions. In accord with data from previous studies looking at upper-limb movements, overlapping peaks of activity were observed bilaterally in the dorsal premotor cortex (Rao *et al.,* 1993; Luft *et al.,* 1998), as well as in the ipsilateral (left) precuneus (Stephan *et al.,* 1995). Furthermore, significant activations were also found in the medial regions of the frontal lobes during both executed and imagined movements. Indeed, physical performance of sequential movements of the left foot was associated with bilateral activations in the SMA-proper, whereas MI of the same movements produced differences in rCBF in the left pre-SMA. The latter finding is of particular interest, as it concurs with other imaging studies that revealed activations in more anterior regions of the medial wall during covert movements when compared to overt movements (Tyszka *et al.,* 1994; Stephan *et al.,* 1995; Roth *et al.,* 1996; Gerardin *et al.,* 2000).

Another common peak of activity was also observed medially in the ipsilateral anterior cerebellum in both overt and covert conditions. This finding is consistent with those from recent studies, which have also reported an increase in activity in the ipsilateral anterior cerebellum during executed and imagined movements of the upper-limbs (Jueptner *et al.,* 1997a; Luft *et al.,* 1998; Lotze *et al.,* 1999). It is interesting to note that our peaks of rCBF activity in the anterior cerebellum were located rostrally with respect to the previously reported sites of activation. This discrepancy may be explained by the somatotopic map of the anterior cerebellum, which shows a more anterior and medial site of activation for foot movements when compared to movements of the hand (Nitschke *et al.,* 1996).

We found additional evidence of similar brain structures mediating overt and covert sequential foot movements when the Perceptual control was subtracted from the Late Execution and Late MI conditions. Indeed, after practice, similar peaks of activation were observed in the left inferior parietal lobule, left precuneus and left striatum in both the Execution and MI conditions. Thus, the results of this comparison, together with the findings reported above for the early phase of the acquisition process, suggest that overt and covert sequential movements of the lower-limb generally share a common neural substrate.

However, when the Execution and MI conditions were compared directly during both phases of the ac-

quisition process, we found brain areas that were exclusively involved in the physical performance of sequential movements of the foot. In the early phase of learning, these regions comprised the left SMA, the left anterior cerebellum and the right primary motor cortex (in the expected site for the control of foot movements), which concurs with findings from prior PET studies (Stephan *et al.,* 1995; Seitz *et al.,* 1997; Jueptner *et al.,* 1997a; Deiber *et al.,* 1998). In the more advanced acquisition phase, the left anterior cerebellum and the right primary motor cortex were again only activated when the movements were produced. This pattern of results suggests that the SMA, the anterior cerebellum and the primary motor cortex are less involved during MI, and that these structures are particularly important for the physical execution of movements. Based on the results of recent experiments using EEG (Beisteiner *et al.,* 1995), MEG (Lang *et al.,* 1996; Schnitzler *et al.,* 1997), and fMRI (Leonardo *et al.,* 1995; Sabbah *et al.,* 1995; Porro *et al.,* 1996; Roth *et al.,* 1996; Luft *et al.,* 1998; Lotze *et al.,* 1999), however, we cannot rule out the possibility that the primary motor cortex is activated during covert activities. Indeed, these studies have demonstrated that the activity in the primary motor cortex is enhanced during MI, but to a lesser degree than when movements are actually performed (about 30%). Therefore, the PET technique used in the present study may not have had the sensitivity necessary to detect weak signals in the primary motor cortex during the MI of sequential foot movements. Although still conjectural at this stage, this hypothesis could also apply to other structures, such as the SMA and the anterior cerebellum.

Physical Learning of Sequential Foot Movements

To determine the brain regions mediating the learning of a sequence of foot movements, we compared the level of blood flow activity associated with the Early Execution condition to that obtained later in the acquisition process. When examining the brain areas that were specifically involved at the beginning of learning, the results revealed significant peaks of activation in the left inferior parietal lobule, left medial anterior cerebellum (lobule IV/V), right posterior cerebellum (lobule VI/Crus I) (both medially and laterally), as well as in the dorsal premotor cortex bilaterally. This pattern of results concurs with findings from previous imaging experiments using the SRT Task with an explicitly known sequence, as blood flow changes during the initial phase of learning have been reported in the inferior parietal cortex (Grafton *et al.,* 1995; Rauch *et al.,* 1995; Honda *et al.,* 1998; Doyon *et al.,* in press), cerebellum (Rauch *et al.,* 1995; Doyon *et al.,* in press), and premotor cortex (Grafton *et al.,* 1995; Hazeltine *et al.,* 1997; Honda *et al.,* 1998; Doyon *et al.,* in press). Finally, numerous experiments with neurological pop-

ulations have demonstrated that patients with cerebellar lesions (Pascual-Leone *et al.,* 1993; Molinari *et al.,* 1997; Gomez-Beldarrain *et al.,* 1998) can show an impaired performance on the SRT Task at the beginning of the acquisition process, suggesting that this structure is involved in early sequence learning (see Doyon and Ungerleider, 2002, for a review).

In summary, the present findings show that the dorsal premotor cortex, inferior parietal lobule, and the cerebellum are involved in the fast learning phase. These results are in accord with previous studies that examined the neural substrate mediating upper-limb sequential movements, and suggest that these structures form a cortico-cerebellar network, which is critical for establishing the cognitive strategies and motor routines involved in executing a sequence of foot movements (see Doyon and Ungerleider, 2002, for a review).

Once the motor program supporting the motor sequence has been established and rehearsed through physical practice, however, the brain regions involved in producing the sequence are quite different. In fact, when the Early Execution condition was subtracted from the Late Execution condition, the pattern of cerebral blood flow changes comprised the left rostral portion of the anterior cingulate and left inferior parietal lobule, as well as the medial orbitofrontal cortex and striatum bilaterally. More specifically, the striatal peaks were located in both putamen, with a more extensive region of activation in the right hemisphere that extended into the caudate nucleus. Similar activations in the putamen have been reported in previous brain imaging studies that explored the neural substrate mediating advanced phases of implicit sequence learning using the SRT Task (Grafton *et al.,* 1995; Doyon *et al.,* 1996). This brain region has also been shown to be activated after physical practice of a sequence of finger-to-thumb opposition movements (Seitz *et al.,* 1990; Seitz and Roland, 1992) and a sequence of key presses learned previously by trial and error (Jenkins *et al.,* 1994; Jueptner *et al.,* 1997b). Furthermore, Miyachi and collaborators (1997) also found that the caudal portion of the basal ganglia of non-human primates was critical for the storage and/or retrieval of the repeating pattern of movements after extensive practice of a sequence learned by trial and error. Finally, these data are further substantiated by studies looking at the performance of patients suffering from Parkinson's disease, who demonstrated an impairment in learning a visuomotor sequence in the advanced phase of the acquisition process (Doyon *et al.,* 1997, 1998).

In addition to an increase of activity in the basal ganglia, the present findings suggest that the left rostral portion of the anterior cingulate is also involved in the advanced learning phase of sequential foot movements. This concurs with the results of Doyon and collaborators (1996) who used a similar paradigm with

the upper-extremity in a PET study. In the latter experiment and the present one, the activation peak was located in a region referred to as the rostral-ventral limbic division of the anterior cingulate cortex (Devinsky *et al.,* 1995; Bush *et al.,* 2000), which is located more anteriorly and ventrally with respect to the cingulate motor area (Shima *et al.,* 1991; Picard and Strick, 1996). Therefore, the increase in activation in this brain region was unlikely motor-related, although its exact role during the advanced stage of learning is unclear. Some investigators have suggested that the rostral portion of the anterior cingulate cortex is involved in episodic memory (Andreasen *et al.,* 1999) and in the retrieval of stimulus-response associations that were previously acquired (Vandenberghe *et al.,* 1999). Based on these hypotheses, one possible interpretation of our finding is that during the advanced phase of learning, the activity in this region was related to the explicit retrieval of the learned sequence of stimulus-response associations between the auditory stimuli and the foot movements.

Another brain region significantly activated during the advanced phase of learning was the inferior parietal lobule. The latter activation was located in a slightly more anterior and inferior region than the one found in the early phase of learning. Such a finding is in agreement with other imaging studies that reported experience-dependent activity in this area after physical training of a sequence of key presses that was learned by trial and error (Jenkins *et al.,* 1994; Jueptner *et al.,* 1997b) or practice of an explicitly known sequence of movements (Grafton *et al.,* 1995; Doyon *et al.,* in press).

Finally, our study revealed significant differences in rCBF in the medial regions of the orbitofrontal cortex of both hemispheres during the advanced phase of learning. The latter finding contradicts those from other studies, which suggest that the medial orbitofrontal cortex may be more involved during the initial phase of learning, when there is insufficient information available to choose the correct course of action (Elliott *et al.,* 1997, 1999, 2000). Additional evidence for a role of this structure in early learning comes from Savage and collaborators (2001) who suggested that it recruits effective strategies in novel situations. To our knowledge, no functional brain imaging experiment has shown activations in this region in the advanced learning phase of a motor sequential task. This unexpected finding may pertain to differences in memory systems, as we chose to test learning of a fully explicit sequence of movements from the beginning of the experiment. At present, however, this remains a working hypothesis awaiting further experimentation.

Taken together, our results suggest that the rostral portion of the anterior cingulate, medial orbitofrontal cortex, inferior parietal lobe, and the striatum are part of a neural substrate that allows for the explicit retrieval of cognitive strategies and of learned motor routines involved during the skilled performance of sequential foot movements. Surprisingly, at this stage of the acquisition process, the present study did not reveal any increase of activity in the primary motor region (Karni *et al.,* 1995; Pascual-Leone *et al.,* 1995; Kleim *et al.,* 1998). This might be due to the fact that the primary motor cortex is likely involved when subjects have been overtrained on a motor task, when performance becomes fully automatic (Karni *et al.,* 1995, 1998; Doyon, 1997).

It is noteworthy that the brain regions associated with learning sequential movements of the left foot were predominantly located in the ipsilateral (left) hemisphere, even though the motoric components of the task were subtracted out by comparing the rCBF activity in the two learning phases directly. Although unexpected, the reasons or this lateralization effect may be manifold. First, this pattern of findings may be related to the left hemisphere dominance in motor control and motor sequence learning. Support for this hypothesis comes from recent studies in patients with lateralized hemispheric damage, and from transcranial magnetic stimulation (TMS) studies in healthy volunteers, which have demonstrated the dominant role of the left hemisphere in rapid response selection and in shifting the focus of motor attention from one movement in a sequence to the next (Winstein and Pohl, 1995; Rushworth *et al.,* 1997, 1998; Schluter *et al.,* 1998, 2001). Second, the predominance of left hemisphere activations in this task may be due to the fact that movements were executed using the nondominant limb and that the neural representation of such movements may be less lateralized than those performed with the dominant one. The latter interpretation is consistent with findings from previous studies, which reported ipsilateral activations in left motor regions when subjects executed finger movements with the non-dominant hand, but not with the dominant (right) hand (Kawashima *et al.,* 1993; Kim *et al.,* 1993; Ziemann and Hallett, 2001). Finally, this left hemispheric dominance in activations could also be related to the nature of the foot sequence task, which depends less on spatial processing than the conventional SRT Task (e.g., Doyon *et al.,* 1996; Hazeltine *et al.,* 1997; Honda *et al.,* 1998).

Dynamic Cerebral Changes Associated with MI of a Foot Sequence

The main purpose of this experiment was to determine whether the pattern of cerebral blood flow changes observed in the Late Execution condition was reflected in the neural substrate elicited during MI. To do so, the Late MI condition was compared to the same condition performed at the early phase of learning. The resulting pattern of activations was then compared

with the one found when the same subtraction was performed between the Execution conditions. As expected, when sequential movements of the foot were imagined after physical practice, significant differences in blood flow were detected medially in the rostral portion of the anterior cingulate and medial orbitofrontal cortex, as well as in the striatum in both hemispheres. These findings are of particular interest, as they suggest that both MI and physical execution of movements share a common neural substrate, even after cerebral plasticity has occurred due to physical practice.

Conclusions

In the present study, we explored the pattern of dynamic changes in cerebral activity associated with both early and more advanced learning phases of sequential foot movements when executed physically and compared them to those elicited during MI of the same skill. Three main conclusions can be drawn from this experiment. First, overt and covert sequential movements of the foot share a common neural substrate, as was previously shown for upper-limb movements. Second, the pattern of rCBF changes we observed during the acquisition of lower-limb movements is similar to that obtained in previous studies that explored the neural network implicated in learning sequential upper-limb movements. Thus, in accord with prior brain imaging studies and the model proposed by Doyon and collaborators (1996, 2002), our data suggest that a corticocerebellar network is critical for establishing the cognitive strategies and motor routines involved in executing a sequence of movements of the foot. Once this motor program has been established and rehearsed with physical practice, however, the brain regions involved in acquiring a sequence of movements constitute a frontostriatal circuit, which allows for the explicit retrieval and long term conservation of the representation of cognitive strategies and learned motor routines. Finally, our findings demonstrate, for the first time, that the cerebral plasticity occurring during the incremental acquisition of an explicit motor sequence executed physically is also reflected in the brain regions mediating MI of this skilled behavior. Taken together, the results of this study constitute additional evidence that physical execution and motor imagery share a common neural substrate, and extend this relationship further to different levels of performance on a motor skill learning task. We believe our findings will help investigators understand how the cerebral mechanisms involved during executed and imagined movements interact after physical practice. Additional research is necessary, however, to determine if similar interactions can be observed when mental practice using motor imagery is used to rehearse a movement.

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