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# Role of the cerebellum in implicit motor skill learning: a PET study

Michikazu Matsumura [a], Norihiro Sadato [b,e,f,*], Takanori Kochiyama [a], Satoshi Nakamura [b], Eiichi Naito [c], Ken-ichi Matsunami [c], Ryuta Kawashima [d], Hiroshi Fukuda [d], Yoshiharu Yonekura [b]

[a] *Faculty of Human Studies, Kyoto University, Kyoto, Japan*
[b] *Biomedical Imaging Research Center, Fukui University, Fukui, Japan*
[c] *Gifu University School of Medicine, Japan*
[d] *IDAC, Tohoku University, Sendai, Japan*
[e] *Department of Cerebral Research, National Institute for Physiological Sciences, Okazaki, Japan*
[f] *Japan Science and Technology Corporation (JST)/Research Institute of Science and Technology for Society (RISTEX), Kawaguchi, Japan*

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**Abstract**

To depict neural substrates of implicit motor learning, regional cerebral blood flow was measured using positron emission tomography (PET) in 13 volunteers in the rest condition and during performance of a unimanual two-ball rotation task. Subjects rotated two balls in a single hand; a slow rotation (0.5 Hz) was followed by two sessions requiring as rapid rotation as possible. The process was repeated four times by a single hand (Block 1) and then by the opposite hand (Block 2). One group of volunteers began with the right hand ($n = 7$), and the other with the left ($n = 6$). Performance was assessed by both quickness and efficiency of movements. The former was assessed with the maximum number of rotation per unit time, and the latter with the electromyographic activity under constant speed of the movement. Both showed learning transfer from the right hand to the left hand. Activation of cerebrum and cerebellum varied according to hand. Activation common to both hands occurred in the bilateral dorsal premotor cortex and parasagittal cerebellum, right inferior frontal gyms, left lateral cerebellum and thalamus, supplementary motor area, and cerebellar vermis. The left lateral cerebellum showed the most prominent activation on the first trial of the novel task, and hence may be related the early phase of learning, or "what to do" learning. Left parasagittal cerebellum activity diminished with training both in first and second blocks, correlating inversely with task performance. This region may therefore be involved in later learning or "how to do" learning. The activity of these regions was less prominent with prior training than without it. Thus the left cerebellar hemisphere may be related to learning transfer across hands.


*Keywords:* Positron emission tomography; Motor skill; Motor learning; Cerebellum; Cerebral blood flow; Learning transfer

## 1. Introduction

Motor skill learning is a complex behavioral process with many interrelated components. It is often assessed by measuring the accuracy or efficiency of movement that is targeted to a specific outcome [1,44]. When successive attempts to perform the movement result in the desired outcome, a motor skill has been acquired [28]. In compound and sequential movements, there are too many muscle actions whose temporal relationships are too rapid and their magnitudes too precise to plan consciously. Movement is thus largely automatic, controlled by a background subconscious mental subroutine. When learning new compound movements, one might be aware of a few muscles and joints, nonetheless, the unlearned novel movement is 'uncoordinated': muscles are not yet linked together in the correct combination, timing, or magnitude of activation. Thus, implicit motor learning can be defined as a class of motor learning that does not require conscious participation, instead, relates to a background subconscious mental subroutine, establishing the correct combination, timing, or magnitude of activation of the muscle [52].

In humans, neuronal mechanisms of motor learning have been studied using positron emission tomography (PET) or

* Corresponding author. Tel.: +81-564-55-7841; fax: +81-564-55-7786.
*E-mail address:* sadato@nips.ac.jp (N. Sadato).

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functional magnetic resonance imaging (fMRI) while a subject performs sequence learning [47,15,45,20,21,19], visual tracking [18], or maze tracing tasks [53]. As the effects of motor skill learning are not easily isolated from those of the physical behaviors required to perform the task, it is often difficult to assign task-related activation found in functional neuroimaging to either implicit motor learning or related cognitive processes. The purpose of the present study is to implement a motor task in order to isolate and describe the neural correlates of implicit motor learning.

First, in order to assess implicit motor learning, we chose a task that requires complex muscle coordination but no explicit cognitive contribution. The selected unimanual movement involves rotating two balls in the palm of either hand [23]. This complex, multipoint hand movement is considered a motor skill, as it requires smooth coordination of the fingers and palm, along with appropriate timing. The two-ball rotation task includes a sequential pattern of activation of the finger involved in correctly performing the task, whose temporal relationships are too rapid and their magnitudes too precise to plan consciously. Hence acquiring the two-ball rotation skill is, by definition mentioned above, implicit motor learning. This motor skill can be easily acquired and continuously improved during the timecourse of a PET experiment (approximately 2 h), but learning does not require any complex cognitive procedures such as the generation or memorization of a sequence, or the coordination of visual inputs with motor outputs. Our working hypothesis is that the brain regions participating in implicit motor learning show preferential activity during earlier learning phases, which then decreases as the movement is repeated and becomes more efficient.

Second, we attempted to address the hand effect on the learning process by examining both hands, starting with the training of one hand followed by the opposite hand. Our hypothesis was that the learning related areas irrespective of the trained hands are candidates for transferring the learning effect, if any.

We measured regional cerebral blood flow (rCBF) with PET and $^{15}O$ water as an index of neuronal activity [36] consecutively during learning of the motor skill, which was novel to all subjects. To exclude the speed-accuracy trade-off [9], and to eliminate a frequency-dependent change in neuronal activity [41,42], the task was performed at a slow (0.5 Hz), constant frequency with auditory pacing during PET scanning. Simultaneously, discharges on an electromyogram (EMG) were monitored to evaluate the degree of learning, assuming that the EMG indicates energy expenditure, and hence efficiency of the movement. After each PET scan with cued movements (paced rotation task sessions), subjects were asked to rotate the balls as quickly as they could for 1 min, which was repeated twice (quick rotation task sessions). The number of rotations per minute (rpm) during the quick rotation task session was used to measure the quickness of the movements. Total length of the training period was strictly controlled. A correlational change between quickness and smoothness, as well as between smoothness and rCBF, was explored. Finally, the regions with learning related activation irrespective of the trained hands were depicted, correlating the activity with the learning transfer.

## 2. Subjects and methods

We studied 13 normal male volunteers ($21.2 \pm 2.5$ years old, mean $\pm$ S.D.), all right-handed according to the Edinburgh inventory [31]. The protocol was approved by the Institutional Review Board, and all subjects gave their written informed consent for the study. A small plastic catheter was placed in the cubital vein of each subject's left arm for injection of the radioisotope. The subjects lay in a supine position with their eyes closed and patched and their heads were immobilized with an elastic band and sponge cushions. Each subject underwent 10 consecutive PET scans, with a 10-min interval between scans. A complete experimental session consisted of two rest scans and eight task scans.

### 2.1. Task

Subjects performed a unimanual two-ball rotation movement [23] (Fig. 1). Two stainless-steel balls, each 4 cm in diameter and weighing 120 g, were placed on the subjects' right and left palms. Performing with only one hand at a time, the subjects rotated the balls in a clockwise direction by the right hand and counter-clockwise by the left hand. One full rotation was achieved when the positions of the two balls were exchanged completely. None of the subjects had ever performed this task before.

### 2.2. Task performance

There were two types of tasks: a paced rotation and quick rotation. During paced rotation, the subjects rotated the balls at 0.5 Hz, acoustically paced by an electric metronome. During the quick rotation, the subjects rotated the balls as quickly as they could. Paced rotation was performed during rCBF measurement, and quick rotation was done between rCBF measurements. The time course of a complete ten-scan experimental session is illustrated in Fig. 1. Subjects in Group 1 ($n = 7$) performed first with the right hand and then with the left hand. The first (and last) PET scan was a rest scan. During the rest scan, the subject lay quietly and held two balls on each palm without any movements. A metronome beating at a steady rate of 0.5 Hz was introduced 30 s before injection of the isotope and continued for the duration of the rest scan. At the end of the scan, the experimenter removed the balls from the subject's palms. For the second PET scan, two balls were again placed on each palm 50 s before injection of the isotope. The paced rotation of the right hand started

20 s before injection of the isotope and continued for 100 s post-injection. The subject was instructed not to move the left hand, and the absence of movement was confirmed by EMG recording (R2-6). The paced rotation was followed by two quick rotations which started 1 min after the end of PET measurement. Each quick rotation lasted one minute, and was separated from the next by an interval of one minute. Finally, the experimenter removed the balls from the subject's palms. The subject then lay quietly until the next paced rotation session, and was asked not to perform any mental rehearsals of the task. This procedure was repeated for the third, fourth, and fifth PET scans. For the sixth, seventh, eighth, and ninth PET scans, the two-ball rotation task was performed by the left hand. Subjects in Group 2 ($n = 6$) followed an identical procedure, except that they began with the left hand and ended with the right (Fig. 1). There were therefore four distinct blocks of task data, recorded from members of Group 1 who began first with the right hand (First-Right) and followed with the left (Second-Left), and those of Group 2 who began first with the left hand (First-Left) and followed with the right (Second-Right).

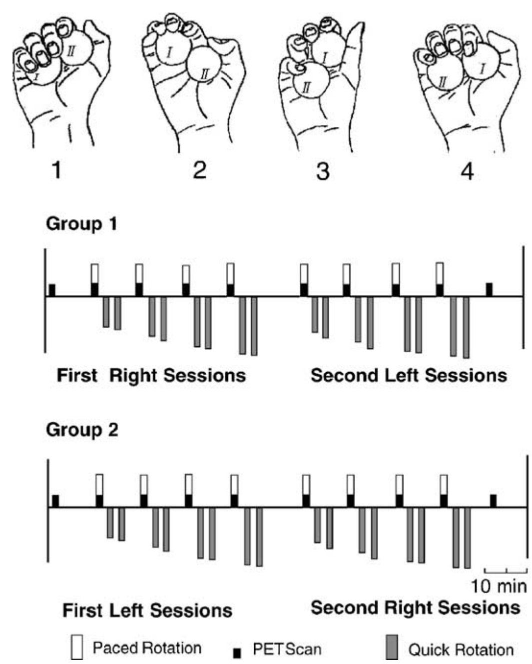


Fig. 1. (Top row) One run of the two-ball rotation movement with the right hand. The subject rotates the two balls around each other on the palm in a clockwise direction (Phases 1–4). At the end of one rotation, the positions of the balls are exchanged. (Lower rows) Time course of scanned training tasks. The first and last PET scans were performed without any movement (rest scans). The other eight PET scans were performed during paced rotation task sessions. After each PET scan, a quick rotation task session of 1 min in duration was repeated twice with a 1-min interval between sessions. Group 1 ($n = 7$, middle row) started with the right hand (First-Right sessions) followed by the left hand (Second-Left sessions), and Group 2 ($n = 6$, bottom row) started with the left hand (First-Left sessions) followed by the right hand (Second-Right sessions). Vertical bar height schematically represents number of rotations per minute.

### 2.3. EMG recording and behavioral monitor

Task performance was recorded on videotape throughout the experimental session. In addition, the EMG was recorded bipolarly from two different muscles, *m. extensor digitorum commtinis* and *m. flexor carpi ulnaris*, via surface electrodes on both hands. After 1000× amplification without any frequency masking, the EMG signals were digitally stored with a 16 bit, 1 kHz sampling rate through an AD converter and processed later (Acknowledge III software, BIOPAC systems, Santa Barbara, CA, USA). One of the experimenters counted the number of rotations throughout the experiment, and later verified the count on the video recordings. The number of rotations per minute (rpm) during the quick rotation sessions was used as an index of performance.

### 2.4. Positron emission tomography

The PET scans were performed with a General Electric Advance tomograph (GE, Milwaukee, WI, USA) with the interslice septa retracted. The physical characteristics of this scanner have been described in detail elsewhere [8,27]. The scanner acquires 35 slices with interslice spacing of 4.25 mm. In the 3-D mode, the scanner acquires oblique sinograms with a maximum cross-coincidence of ±11 rings. A 10-min transmission scan using two rotating $^{68}Ge/^{68}Ga$ sources was performed for attenuation correction. Images of CBF were obtained by summing the activity during the 60-s period following the first detection of an increase in cerebral radioactivity after the intravenous bolus injection of 10 mCi of $^{15}O$-labeled water [40]. The images were reconstructed with the Kinahan–Rogers reconstruction algorithm [25]. Harming filters were used, giving transaxial and axial resolutions of 6 and 10 mm (full-width at half-maximum; FWHM), respectively. The field of view and pixel size of the reconstructed images were 256 and 2 mm, respectively. No arterial blood sampling was performed, and thus the images collected were those of tissue activity. Tissue activity recorded by this method is nearly linearly related to rCBF [12,13].

### 2.5. Magnetic resonance imaging

For anatomical reference, a high-resolution whole-brain MRI was obtained for each subject. The MRIs were performed on a 1.5 T MR system (Horizon; GE, Milwaukee, WI, USA). A regular head coil and a conventional T1-weighted, spoiled GRASS volume sequence with a flip angle of 30°, echo time of 5 ms, repetition time of 33 ms, and field of view of 24 cm were used. A total of 124 transaxial images were obtained. Matrix size was 256×256, slice thickness was 1.5 mm, and pixel size was 0.937 mm × 0.937 mm. Each high-resolution image was normalized to the template T1-weighted image, which was already fitted to the standard stereotaxic space [51]. The high-resolution MRIs were used for anatomical localization of the activated areas in the cerebellum, which was performed according to the published atlas by Courchesne et al. [7] and Press et al. [34,35].

### 2.6. Performance data analysis

Across four session blocks (First-Right (FR), Second-Left (SL), Second-Right (SR), and First-Left (FL)), order effect and hand effect were evaluated statistically using two-way analysis of variance (ANOVA), in which the value of the rpm during a quick rotation was used as an independent variable (Fig. 2).

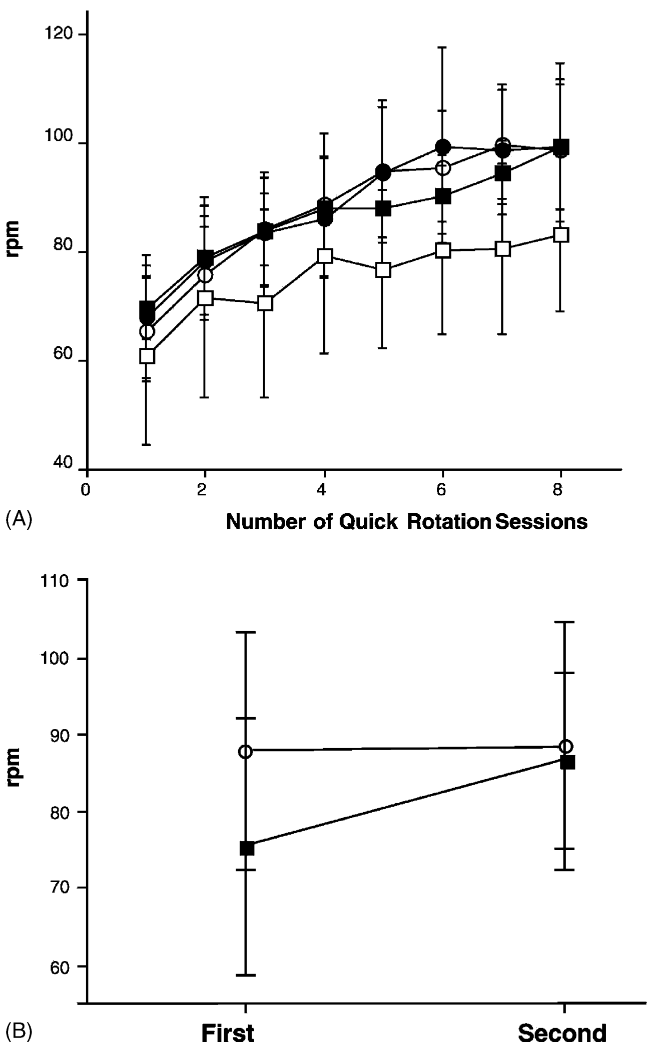


Fig. 2. (A) Learning effect measured in rotations per minute (rpm) during eight quick rotation sessions in the First-Right session block (open circles, $n = 7$), Second-Left (closed squares, $n = 7$), Second-Right (closed circles, $n = 6$), and First-Left (open squares, $n = 6$). (B) Interaction between hand effect and order effect for task performance, as measured during quick rotation sessions (in rpm). Right-hand performance (open circles) did not show any significant difference irrespective of the order of training, whereas left-hand performance (closed squares) was significantly better when the right hand was trained first than when the left hand was trained first.

### 2.7. EMG data analysis

The EMG recorded during the paced movements was analyzed as follows. The baseline fluctuation of the EMG was removed with a 25 Hz high-pass filter. The EMG recording was rectified and integrated for every 10-s throughout the task performance. A grand summation was also calculated for the 100 s of the task performance during the PET measurement, as an integrated EMG. The EMG recording of the hand muscle showing the clearest phasic activity patterns during the paced rotation sessions was selected to represent the task performance (Fig. 3). The EMG recording from *m. extensor digitorum communis* was used for the analysis throughout the individual subject's performance. As the levels of the recorded EMG varied among subjects, and as the investigation was concerned with the magnitude of the change independent of the absolute EMG values, the values of the integrated EMG were normalized to the first task segment of each paced rotation session of each subject. The correlation between the normalized EMG discharge during each paced rotation and the averaged rpm during the two consecutive quick rotations was evaluated by analysis of covariance (ANCOVA) with subject effect as a covariate of no interest. The averaged rpm of each subject was subtracted from the measured rpms of each subject to adjust the measured rpms so that the averaged value of each subject was centered to zero (adjusted rpms).

### 2.8. CBF data analysis

The data were analyzed with statistical parametric mapping (SPM96; from the Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc., Sherborn, MA, USA) [14,16,17]. The scans from each subject were realigned using the first image as a reference. After realignment, each image was transformed into a standard stereotaxic space [51] and filtered with a Gaussian kernel of 10 mm FWHM in the $x$, $y$, and $z$ axes.

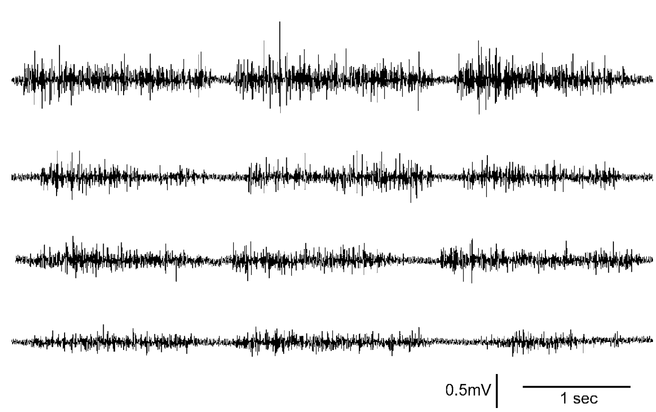


Fig. 3. Typical EMG recording of one subject from the right m. extensor digitorum communis during the first, second, third, and fourth (from top to bottom) sessions of the First-Right session block. The horizontal scale indicates 1 s and the vertical represents 0.5 mV.

### 2.8.1. Task-related activation

The following general linear model was then applied to evaluate the hand and order effect on the task-related activation. As Group 1 started the training from the right hand whereas Group 2 started with the left hand, two-group comparison enables the evaluation of the order effect. Global normalization was performed by means of proportional scaling [12]. The corresponding scans were ordered by study, by subject within study, and by condition within subject (Table 1). Subjects 1–7 are from Group 1, and 8–13 from Group 2. Conditions 1 and 10 are rest scans. Condition 2 was assigned to the first trial by the right hand, 3 to the second, 4 to the third and 5 to the fourth. Similarly, conditions 6–9 were assigned to left-hand trials; condition 6 to the first, 7 to the second, 8 to the third and 9 to the fourth. Hence, in Group 1, conditions 2–5 are assigned to First-Right, and 6–9 for Second-Left. In Group 2, conditions 2 to 5 are assigned to Second-Right, and 6–9 to First-Left (Table 1). Let $Y_{ijt}^{k}$ denote the rCBF at voxel $k$ for the $j$th condition of subject $i$ in group $t$ ($j = 1 \ldots 10$; $i = 1, \ldots, 13$; $t = 1, 2$).

$$Y_{ijt}^{k} = \alpha\varphi_{jt}^{k} + \gamma_{i}^{k} + \varepsilon_{ijt}^{k}$$

where $\alpha\varphi_{jt}^{k}$ is the interaction effect for condition $j$ of group $t$ (the condition-by-group effect), $\gamma_{i}^{k}$ is the subject effect, and $\varepsilon_{ijt}^{k}$ is an error term which is independent, normally distributed random variable with zero means. As this model fits separate condition effects for each study, this is a split plot design. To test hypotheses about regionally specific task effects and their interaction with hand and order effects, the estimates were compared using the linear contrasts summarized in Table 1. The task-related neuronal activities by right hand performance (main effect) were depicted with contrast (1). The resulting set of voxel values for contrast (1) constituted a statistical parametric map of the $t$-statistic SPM$\{t\}$. The SPM$\{t\}$ were transformed to the unit normal distribution (SPM$\{Z\}$). The threshold of SPM$\{Z\}$ was set at $Z > 3.09$. The resulting foci were characterized in terms of spatial extent ($k$) and peak height ($u$). The significance of each region was estimated using distributional approximation from the theory of Gaussian fields. This characterization is in terms of the probability that a region of the observed number of voxels could have occurred by chance [$P$($n$max $> k$)], giving the corrected $P$ values at cluster levels for multiple comparisons over the entire volume analyzed, or that the peak height observed could have occurred by chance [$P$(Zmax $> u$)] giving the corrected $P$ values at voxel levels. The statistical threshold was set at $P < 0.05$ [16,17]. The interaction effects of the prior training (order effects) on the main effect were assessed by contrasts (2) and (3). The task-related neuronal activities by right hand performance, irrespective of the order of the training, were depicted by eliminating the voxels that showed the interaction effects ($P < 0.05$, uncorrected) by contrast (2) or (3) from the areas depicted by contrast (1). Similarly, contrasts (4), (5) and (6) were tested to depict the regions activated by the left hand

Table 1
Layout of comparisons (R2–10)

| | Condition no. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Group 1: First-Right (FR) and Second-Left (SL) ($n = 7$) | | | | | | | | | | |
| Condition | Rest1 | FR1 | FR2 | FR3 | FR4 | SL1 | SL2 | SL3 | SL4 | Rest2 |
| Group 2: First-Left (FL) and Second-Right (SR) ($n = 6$) | | | | | | | | | | |
| Condition | Rest3 | SR1 | SR2 | SR3 | SR4 | FL1 | FL2 | FL3 | FL4 | Rest4 |
| (1) Effect of right-hand movement | (FR1 + FR2 + FR3 + FR4) − (Restl + Rest2) × 2 + [(SRI + SR2 + SR3 + SR4) − (Rest3 + Rest4) × 2] | | | | | | | | | |
| (3) Effect of prior training on the right (positive) | [(SRI + SR2 + SR3 + SR4) − (Rest3 + Rest4) × 2] − [(FR1 + FR2 + FR3 + FR4) − (Restl + Rest2) × 2] | | | | | | | | | |
| (3) Effect of prior training on the right (negative) | [(FR1 + FR2 + FR3 + FR4) − (Restl + Rest2) × 2] − [(SRI + SR2 + SR3 + SR4) − (Rest3 + Rest4) × 2] | | | | | | | | | |
| (4) Effect of left-hand movement | (FL1 + FL2 + FL3 + FL4) − (Rest3 + Rest4) × 2 + [(SL1 + SL2 + SL3 + SL4) − (Restl + Rest2) × 2] | | | | | | | | | |
| (5) Effect of prior training on the left (positive) | [(SL1 + SL2 + SL3 + SL4) − (Restl + Rest2) × 2] − [(FL1 + FL2 + FL3 + FL4) − (Rest3 + Rest4) × 2] | | | | | | | | | |
| (6) Effect of prior training on the left (negative) | [(FL1 + FL2 + FL3 + FL4) − (Rest3 + Rest4) × 2] − [(SL1 + SL2 + SL3 + SL4) − (Restl + Rest2) × 2] | | | | | | | | | |
| (7) Effect of hand movement | (FR1 + FR2 + FR3 + FR4) − (Restl + Rest2) × 2 + [(SRI + SR2 + SR3 + SR4) − (Rest3 + Rest4) × 2] + (FL1 + FL2 + FL3 + FL4) − (Rest3 + Rest4) × 2 + [(SL1 + SL2 + SL3 + SL4) − (Restl + Rest2) × 2] | | | | | | | | | |
| (8) Hand Effect (Right > Left) | (FR1 + FR2 + FR3 + FR4) − (Restl + Rest2) × 2 + [(SRI + SR2 + SR3 + SR4) − (Rest3 + Rest4) × 2] − [[(FL1 + FL2 + FL3 + FL4) − (Rest3 + Rest4) × 2] + [(SL1 + SL2 + SL3 + SL4) − (Restl + Rest2) × 2]] | | | | | | | | | |
| (9) Hand Effect (Left > Right) | [(FR1 + FR2 + FR3 + FR4) − (Restl + Rest2) × 2 + [(SRI + SR2 + SR3 + SR4) − (Rest3 + Rest4) × 2]] + (FL1 + FL2 + FL3 + FL4) − (Rest3 + Rest4) × 2 + [(SL1 + SL2 + SL3 + SL4) − (Restl + Rest2) × 2] | | | | | | | | | |

movement irrespective of the order of the training. To depict the regions that show the task-related activation irrespective of the hands, the same procedure was applied to the different combination of contrasts, namely, (7), (8), and (9) (Table 1), where contrast (7) is for task effect, and contrasts (8) and (9) are for hand × task interaction. As the task-related activation irrespective of the hands revealed asymmetric distribution in the left cerebellar hemisphere and the right inferior frontal gyrus, confirmation procedure for the asymmetry followed. First, each image was flipped over the mid-sagittal plane to generate a Flipped group. The interaction between group effect (Flipped group versus non-flipped Original group) and the task effect (Task–Rest) performed by either hand indicates the asymmetry of the neural substrates for the motor task. This interaction was evaluated on a pixel-by-pixel basis by two-group comparison with a split plot design using SPM96. As the regions of interest had been already known, uncorrected p values were reported for this particular procedure.

To identify brain regions with learning effect irrespective of the trained hands, we assumed that such areas must (1) be activated by both right hand and left hand training, (2) display a session effect during either training session block, and (3) display activity that covaried with performance. *Session effect*: Learning/time effect was assessed within right hand session blocks, and hence without rest conditions, asking if there is any difference among task conditions (R1, R2, R3, and R4), using the following general linear model. Let $Y_{ij}^k$ denote the rCBF at voxel $k$ for the $j$th trial of right hand performance within the FR or SR session blocks of subject $i$ ($j = 1 \ldots 4$; $i = 1, \ldots, 13$),

$$Y_{ij}^k = \varphi_j^k + \gamma_i^k + \varepsilon_{ij}^k$$

where $\varphi_j^k$ is the session effect, $\gamma_i^k$ is the subject effect, and $\varepsilon_{ij}^k$ is an error. Each session contains two samples, one from FR and another from SR. Note that the rest conditions were eliminated, and hence there are 52 scans. Four conditions and 13 subject blocks makes 17 parameters, having 16 degrees of freedom, giving 36 residual degree of freedom. To test the overall significance of the condition effect, $F_{3,36}$ were calculated voxel-by-voxel with a statistical threshold of $P < 0.001$, uncorrected for multiple comparisons. A similar calculation was performed for left hand session blocks.

### 2.9. Correlation with EMG discharge

Areas that showed both task-related activation irrespective of the hands, and session effects during either right or left hand performance, were examined for potential correlation with rCBF and performance (as measured by relative changes in EMG). To examine whether the rCBF in cortical areas correlated with normalized EMG discharge, the following model was utilized. Let $Y_{iqj}^k$ denote the rCBF at voxel $k$ for the $j$th measurement in session block $q$ of subject $i$ ($j = 1 \ldots 4$; $q = 1 \ldots 4$; $i = 1, \ldots, 13$),

$$Y_{iqj}^k = \xi^k (G_{iqj} - g \ldots) + \gamma_{iq}^k + \varepsilon_{iqj}^k$$

Session block 1 corresponds to First Right, 2 to Second Left, 3 to Second Right and 4 to First Left. $\xi^k$ is the regression effect on the normalized EMG, $g_{iqj}$ is the normalized EMG of subject $i$ in $j$th session of session block $q$, and $g \ldots$ is the mean of the normalized EMG over all sessions and subjects, $\gamma_{iq}^k$ is the subject-session-block interaction effect, and $\varepsilon_{iqj}^k$ is an error term. The corresponding scans were ordered by session block, by subject within session block, and by condition within subjects. A hypothesis was tested, asking whether the slope fitted for sessions across the session blocks is significantly different from 0.

Focusing on the two cerebellar areas screened by these procedures, we applied three-way ANOVA with appropriate linear contrasts, incorporating session block order (first and second session blocks), hand (right and left), and the session (first, second, third and fourth in the session block). As each session of each session block contains one sample from each subject, this is a random effects model.

## 3. Results

### 3.1. Task performance

During the quick rotation task sessions, a gradual increase in rpm was observed within all session blocks. The rise was steeper during the earlier sessions, and more modest during the later sessions (Fig. 2A). In the First-Right and Second-Right blocks, the learning curves were almost saturated by the fifth quick-rotation session. The First-Left block showed a slower increase in rpm man the other blocks. Asymmetric skill acquisition was noted as an interaction between hand effect and order effect (Fig. 2B). The averaged (±S.D.) rpm was calculated from the rpm of the eight quick rotation sessions for each session block. Both hand effect and order effect were significant. Performance, measured by the averaged rpm, was significantly better by the right hand than by the left hand ($F_{1,204} = 12.0$, $P = 0.0007$). Performance was better in the second session block than in the first ($F_{1,204} = 8.2$, $P = 0.0046$). The interaction between hand effect and order effect was also significant ($F_{1,204} = 6.6$, $P = 0.011$). Right-hand performance did not show any difference irrespective of the order of training (first session, 87.9 ± 15.4 rpm; second session, 88.5 ± 16.0 rpm), whereas left-hand performance was better when the right hand was trained first (86.6 ± 11.3 rpm) than when the left hand was trained first (75.4 ± 16.6 rpm). There was no significant difference in the performance by the right and left hands in the second trials.

During the paced rotation sessions, EMG discharge during paced rotation gradually decreased as the session proceeded (Fig. 3). The general tendency toward this decrease throughout all rotation sessions is clearly demonstrated in Fig. 4A. The normalized EMG discharge during the paced

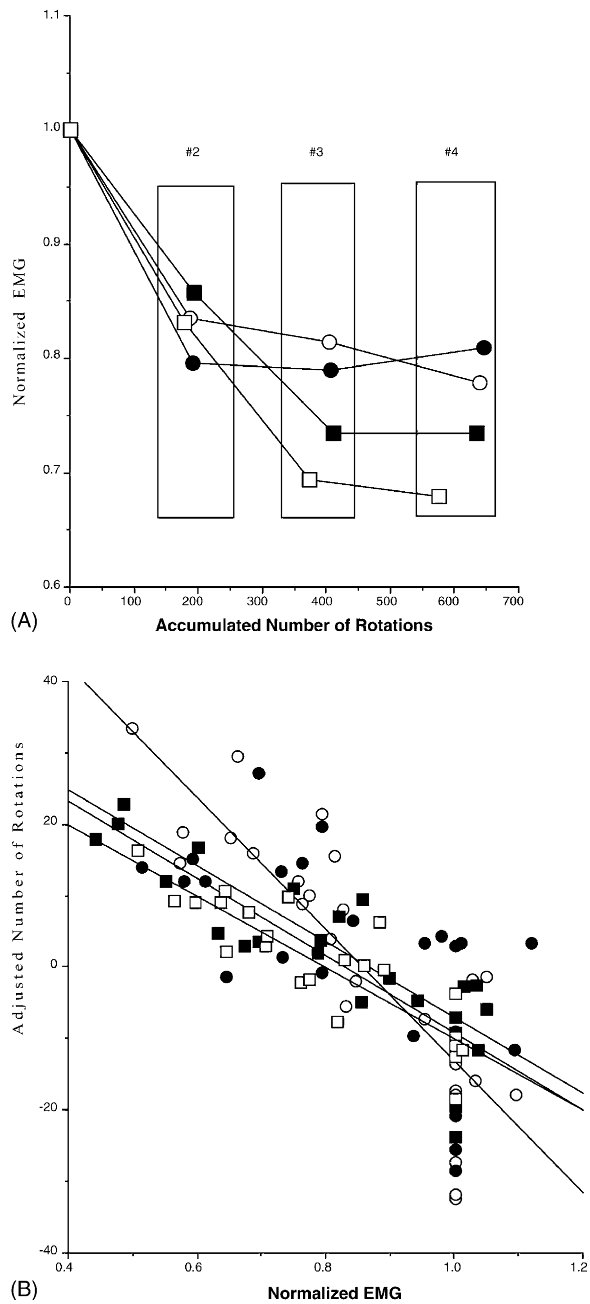


Fig. 4. (A) Normalized EMG discharge during paced rotation session plotted against accumulated number of rotations before the EMG recording session. Both EMG discharge and accumulated number of rotations were averaged within each session block: First-Right (open circles), Second-Left (closed squares), Second-Right (closed circles) and First-Left (open squares). (B) Normalized EMG discharge during paced rotation sessions plotted against the adjusted number of rotations during two consecutive quick rotation sessions immediately after the paced rotation session with regression lines fitted for each session block: First-Right (open circles), Second-Left (closed squares), Second-Right (closed circles) and First-Left (open squares). There was a significant negative correlation between EMG discharge and task performance in each session block without a significant difference among the blocks.

rotation sessions was negatively correlated with the adjusted rpm, obtained from two consecutive quick rotation sessions immediately after the paced rotation session, in each session block ($F_{1,77} = 72.2$, $P < 1.1 \times 10^{-12}$) (Fig. 4B). There was no significant difference between the slopes of the regression lines fitted for each session block ($F_{25,52} = 0.9446$, $P = 0.5491$). Typical individual data is also presented (Fig. 5).

### 3.2. Cortical activation

The rCBF measurements showed that the two-ball rotation task performed by the right hand, irrespective of the order of the session blocks, activated the left primary sensorimotor cortex (SM1), supplementary motor area (SMA), putamen, the right dorsal premotor cortex (PMd), inferior frontal gyrus (GFi) and postcentral gyrus, and the bilateral cerebellum. Cerebellar activation occurred mainly in the anterior quadrangular lobule of the cerebellum (Qua), extending caudally to the biventer (Bi) (Fig. 6). Performance by the left hand activated the right SM1, SMA, and postcentral gyrus, bilateral putamen, and cerebellum, mainly in the parasagittal portion of the hemisphere (Table 2, Fig. 6). Fig. 5 also shows that the activation in the left cerebellum by either hand extends laterally to the semilunar lobule of the posterior lobe (Se). Activation common to both hands, irrespective of the order of the trial, occurred in the bilateral PMd and Qua, right inferior frontal gyrus, left Se and thalamus, and SMA and cerebellar vermis. The right inferior frontal gyrus and left Se showed significantly asymmetric activation (Table 3).

Within the areas of task-related activation common to both hands, left Se showed the significant session effect during right hand performance whereas the left Qua close to the dentate nucleus showed the session effect during left hand performance (Table 4). These areas showed positive correlation with averaged EMG discharge across all sessions of FR, SR, FL, and SL (Table 4). The most lateral portion of the left Se (−26, −58, −34) in Talairach's coordinates, showed significant order effect ($F_{1,88} = 11.918$, $P = 0.0009$) and session effect ($F_{1,88} = 4.309$, $P = 0.007$) without

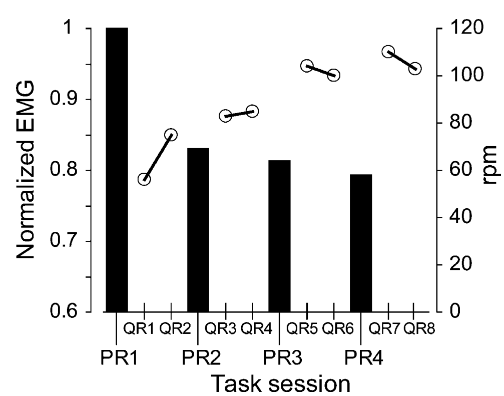


Fig. 5. Representative individual data of performance by means of normalized EMG discharge (closed bar) during paced rotation (PR) and number of rotation per min (open circle) during quick rotation (QR).

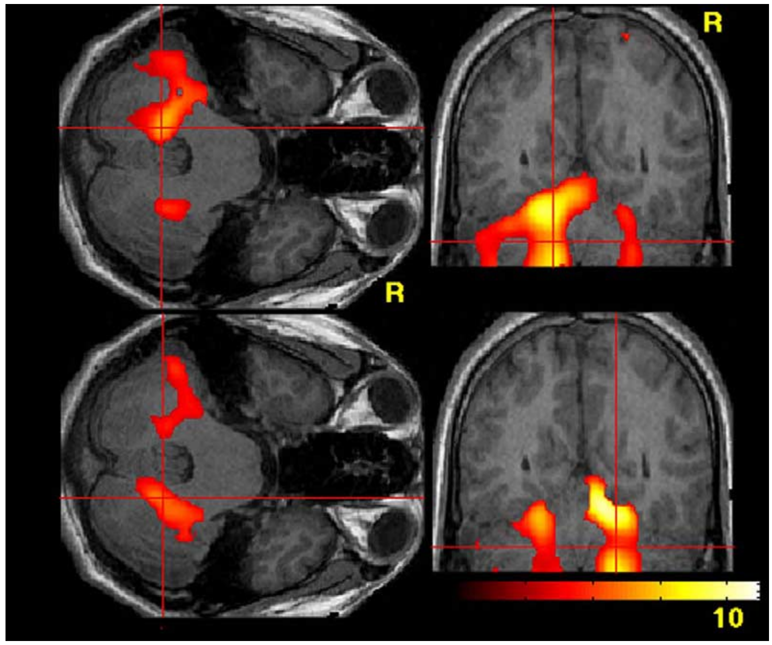


Fig. 6. (Top row) Comparisons of adjusted mean rCBF between the two-ball rotation task by the left hand and the rest condition irrespective of the order of the training, superimposed on the subject's anatomically normalized MRI. Red lines indicate the projections of each section that cross in the anterior quadrangular lobule of the anterior lobe of the left cerebellum at Talairach's coordinate of $x = -16$ mm, $y = -60$ mm, and $z = -38$ mm. The pixels show levels of statistical significance at $P < 0.05$ with a correction for multiple comparisons. (Bottom row) Activation by the two-ball rotation task with the right hand compared with the rest condition, irrespective of prior training. Red lines are crossed at Talairach's coordinates of $x = 16$ mm, $y = -60$ mm, and $z = -38$ mm. Irrespective of the hand, the lateral portion of the cerebellar hemisphere was activated, shown in the axial view.

significant hand effect. This area also showed significant order × session effect ($F_{3,88} = 4.70$, $P = 0.0043$), whereas order × session × hand effect ($F_{3,88} = 0.38$, $P = 0.767$) or hand × session effect ($F_{3,88} = 2.338$, $P = 0.092$) were not significant. Namely, the left Se in the first session blocks revealed greater session effect than that in the second blocks without a significant hand effect (Fig. 7). The activation of the first task set (s1) of the first session blocks

Table 2
Activation by the two-ball rotation task (contrasts 1 and 4 in Table 1, $n = 13$)

| Area | | Coordinates | | | $Z$ | %ΔCBF | Voxel-level |
|---|---|---|---|---|---|---|---|
| | | $x$ | $y$ | $z$ | | | Corrected $P$ |
| Right hand movement* | | | | | | | |
| SMI | Left | −40 | −20 | 58 | 8.84 | 28.3 | <0.01 |
| SMA | Left | −2 | −4 | 54 | 7.12 | 9.4 | <0.01 |
| Qua | Right | 12 | −54 | −18 | 8.28 | 12.8 | <0.01 |
| | Left | −22 | −56 | −22 | 6.88 | 7.3 | <0.01 |
| GFi | Right | 60 | 6 | 28 | 6.06 | 6.6 | <0.01 |
| Putamen | Left | −26 | −16 | 8 | 5.82 | 6.2 | <0.01 |
| Left hand movement+ | | | | | | | |
| GPoC | Right | 46 | −28 | 56 | 8.83 | 25.6 | <0.01 |
| SMI | Right | 36 | −18 | 66 | 8.51 | 26.1 | <0.01 |
| SMA | Right | 2 | −4 | 56 | 7.65 | 11.1 | <0.01 |
| Qua | Left | −18 | −52 | −20 | 8.51 | 15.7 | <0.01 |
| | Right | 24 | −52 | −28 | 6.84 | 8.0 | <0.01 |
| Putamen | Right | 30 | −14 | 6 | 5.65 | 5.5 | <0.01 |
| | Left | −22 | 4 | 6 | 5.17 | 5.2 | <0.01 |

*Using contrast (1) in Table 1. Effect of the order of the trial was eliminated by excluding areas defined by contrasts (2) and (3) with statistical threshold of $P < 0.05$, uncorrected for multiple comparisons. +Using contrast (4) in Table 1. Effect of the order of the trial was eliminated by excluding areas defined by contrast (5) and (6) with statistical threshold of $P < 0.05$, uncorrected for multiple comparisons. GFi, inferior frontal gyms; PMd, dorsal premotor cortex; Qua, quadrangular lobule of the anterior lobe of the cerebellum; SMI, primary sensonmotor area; SMA, supplementary motor area.

Table 3
Activation by the two-ball rotation task common to both hands, irrespective of the order of the trial ($n = 13$)

| Cluster size | Area | | Coordinates | | | $Z$ | %ΔCBF | Voxel-level | |
|---|---|---|---|---|---|---|---|---|---|
| | | | $x$ | $y$ | $z$ | | RH | LH | Corrected $P$ |
| 992 | SMA | | −2 | −2 | 54 | 7.41 | 9.1 | 9.4 | <0.01 |
| | PMd | Left | −22 | −8 | 62 | 6.83 | 10.8 | 9.0 | <0.01 |
| | | Right | 18 | −4 | 66 | 5.11 | 6.3 | 8.2 | <0.01 |
| 1696 | Qua | Left | −24 | −64 | −22 | 7.00 | 5.6 | 6.5 | <0.01 |
| | Se* | Left | −50 | −52 | −40 | 5.28 | 5.5 | 5.2 | <0.01 |
| 363 | Qua | Right | 26 | −54 | −34 | 6.65 | 7.3 | 6.1 | <0.01 |
| 270 | Cerebellar vermis | Right | 0 | −60 | −12 | 6.61 | 6.0 | 6.3 | <0.01 |
| 597 | Thalamus | Left | 22 | 2 | 6 | 5.69 | 5.0 | 5.4 | <0.01 |
| 406 | GFi+ | Right | 60 | 6 | 28 | 6.87 | 6.6 | 7.4 | <0.01 |

Using contrast (7) in Table 1. Hand effect was eliminated by excluding areas defined by contrasts (8) and (9) with statistical threshold of $P < 0.05$, uncorrected for multiple comparisons. RH, right hand sessions; LH, left hand sessions. GFi, inferior frontal gyrus; PMd, dorsal premotor cortex; Qua, quadrangular lobule of the anterior lobe of the cerebellum; SMA, supplementary motor area, Se; semilunar lobule of the posterior lobe of the cerebellum. *+Asymmetric activation ($z = 2.22$, $P = 0.039$, and $^{+}z = 4.02$, $P < 0.001$, corrected multiple comparisons for three locations).

Table 4
The areas with task-related activation common to both hands, session effect during task performance, and positive correlation with averaged EMG discharge during the two-ball rotation task

| Area | Side | Coordinates | | | Task-related activation* $Z$ score | | Session effect** $P$ value | | Correlation with EMG+ $Z$ score |
|---|---|---|---|---|---|---|---|---|---|
| | | $x$ | $y$ | $z$ | RH | LH | RH | LH | |
| Se | Left | −50 | −62 | −38 | 3.37 | 3.88 | 0.001 | >0.1 | 3.67 |
| | Left | −40 | −48 | −36 | 4.46 | 5.41 | <0.001 | 0.088 | 4.01 |
| | Left | −42 | −48 | −32 | 4.48 | 5.76 | 0.001 | >0.1 | 4.12 |
| Qua | Left | −26 | −58 | −34 | 3.80 | 4.96 | >0.1 | 0.001 | 3.30 |

Qua: quadrangular lobule of the anterior lobe of the cerebellum, Se: semilunar lobule of the posterior lobe of the cerebellum. RH: right hand sessions (FR and SR), LH: left hand sessions (FL and SL). *Task related activation irrespective of the hands using contrasts (7), (8), and (9) with the same statistical threshold as in Table 3. **$F$ test was applied to RH and LH separately by calculating $F_{3,36}$ without correction for multiple comparisons. +Averaged EMG amplitudes were fitted to all sessions of FR, SR, FL, and SL.

was significantly higher than that of the first task set of the second session blocks ($P = 0.0001$). The left Qua showed a significant order effect ($F_{1,88} = 9.452$, $P = 0.0028$) and session effect ($F_{1,88} = 5.726$, $P = 0.0013$) without significant hand × session effect ($F_{3,88} = 1.641$, $P = 0.199$) or hand effect ($F_{3,88} = 1.847$, $P = 0.201$). Namely, the left Qua showed gradual decrease in its activity as learning proceeded in the first and second session blocks, irrespective of trained hands. The activity was less prominent with prior training than without it.

## 4. Discussion

### 4.1. Task performance

In the present study, changes in motor performance were gauged by speed and energy expenditure. As the subject practised, movements that were initially slow and stiff became faster and more relaxed [29,33]. Efficiency of movements can be measured by acceleration transition [44] where the largest muscular discharge occurs [6]. Hence, a decrease in EMG discharge indicates decreased energy expenditure, characterizing more efficient movement.

Atkeson [2] specifies two general processes required in motor learning: the specification of an internal model, and its correction with feedback [28,52]. In the present paced rotation task, the former may correspond to identification of the combination, timing, and magnitude of muscle activation required to accomplish a multijoint hand movement. The latter was to coordinate the movement of two balls while minimizing the energy lost as the two balls collided or were pushed together. Thus, interaction torques between the two balls reflected the subject's skill. Repetition of the movement allowed sensory feedback to modify the model and thereby improve task efficiency (i.e., minimize interaction torques). As task performance improved, the muscle energy required to counterbalance these torques in turn decreased, along with the associated EMG discharge.

During the paced rotation task, the frequency of the movements was kept constant; therefore, a decrease in EMG discharge directly reflected skill learning. EMG discharge during the paced rotation task was in turn negatively correlated with the rpm during the consecutive quick rotation

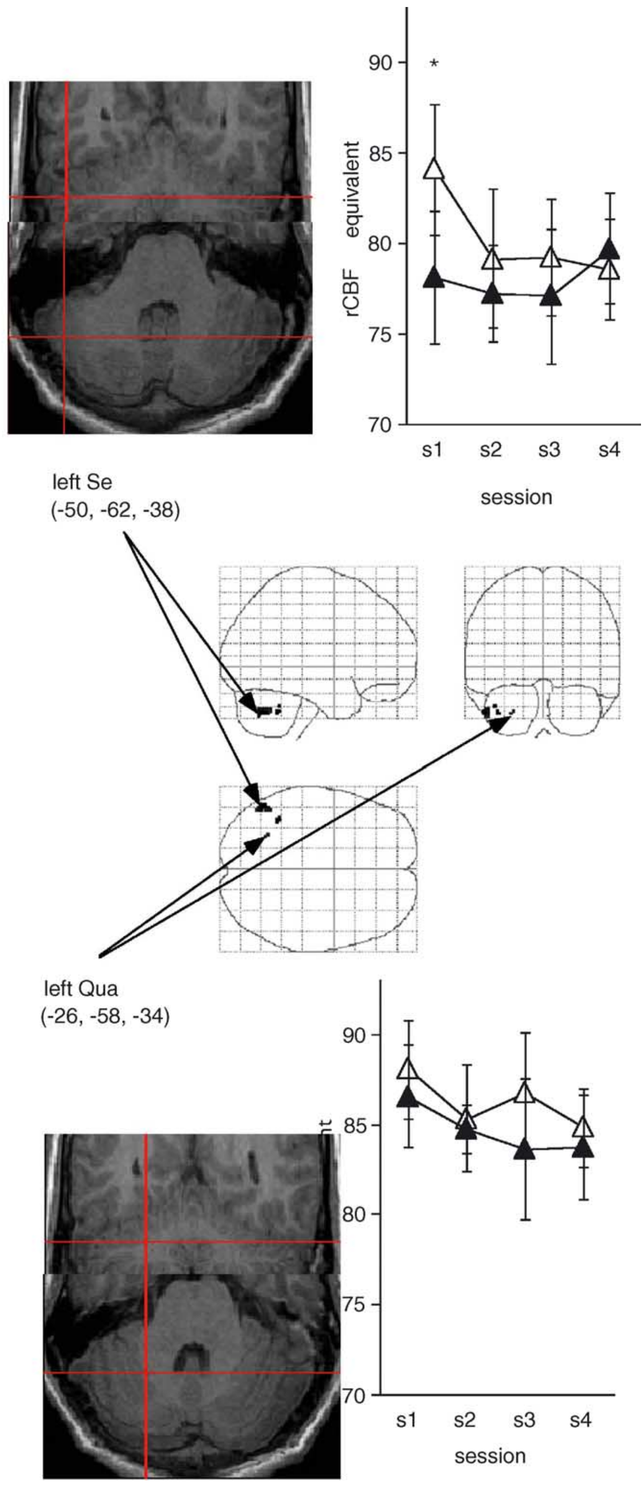


Fig. 7. The areas with task-related activation common to both hands, session effect during task performance, and positive correlation with averaged EMG discharge during the two-ball rotation task are shown in the orthogonal “line-of-sight” projection (middle figure). The location of the left Se (upper left figure) is specified by coronal (upper window) and transaxial (lower window) sections of the subject’s anatomically normalized MRI. The redlines are crossed at (−50, −62, −38) of Talairach’s coordinates. The averaged adjusted rCBF, assuming the global CBF is 50, are plotted against the number of sessions executed with either left or right hand (top right figure). Open triangles are for the first session blocks (First-Left and First-Right) and closed triangles for the second session blocks (Second-Left and Second-Right). Error bars indicate the standard deviation. The activity of the first task session is significantly higher when there is no prior training, compared to when there is prior training with the left hand (*, $P = 0.0001$). The location and the plot of the neural activity of the left Qua (−26, −58, −34) are shown in the same format (lower figures). Activity was significantly higher in the first session block than in the second ($P = 0.0028$).

task. This indicates that the rpm, or variable of speed, of the quick rotation task is also an appropriate measure for skill learning in the present experiment.

### 4.2. Neural substrates for implicit motor learning

Irrespective of training, constant activation was observed in certain areas of the motor cortex, as described in a previous study using the same task [23]. On the other hand, changes in activation patterns corresponding to motor skill acquisition were limited to the cerebellum.

#### 4.2.1. No correlational change in M1

As measured by PET technology, the effects of motor skill learning in the primary motor cortex [22] can be divided into an early phase (up to 30 min) and a late phase (in the range of weeks). In a complete experimental session, which included 40 min of training, no significant change in rCBF of M1 was observed when the rate of movements in the trained and untrained conditions were kept the same [20,15]. This is compatible with a study by Karni et al. [24], who employed a similar task and found no change in M1 activation during the initial phase of learning up to 30 min. However, after several weeks of training, Karni et al. observed a significant increase in the extent of M1 activation. The authors speculated that fast learning involves processes that select and establish an optimal routine or plan for the performance of the given task, and that slow learning (mediated by the M1 region) may reflect the ongoing long-term modification of basic motor modules.

#### 4.2.2. Cerebellum

With respect to its role in motor control, the cerebellum is functionally divided into medial, intermediate, and lateral sagittal zones [4]. The lateral zone may play a role in composing compound movements from single constituents, such as the coordination of simultaneous motion at multiple joints, and its functional impairment is characterized by decomposition of those compound movements [5]. The intermediate zone receives inputs chiefly from receptors in muscles, joints, and skin, and secondarily from the motor and somesthetic areas of the cerebral cortex via the cortico-pontocerebellar system. Because the intermediate zone receives signals from regions in which voluntary movements are planned, as well as from the peripheral effectors that execute them, it has been proposed to serve as a “comparator” in the execution of movement [50]. Neuroimaging studies have shown that unilateral hand movement tasks that lack learning components activate the ipsilateral intermediate zone [11,48,43], supporting the notion that the ipsilateral intermediate zone is involved with the execution of motion. Impairment of the intermediate zone causes agonist and antagonist muscle discharge to become variable, producing unstable movements [5].

*4.2.2.1. Lateral cerebellum.* As the subject learned the present task, EMG discharge and rCBF in the cerebellum both decreased; this correlation is consistent with the hypothesis that the lateral cerebellum is involved with motor feedback and learning [32]. Using a visuomotor task that necessitated detection and correction of visuomotor errors, Flament et al. [10] reported a decrease in cerebellar activation during learning. A recent fMRI study showed that the lateral cerebellum is involved in on-line motor adjustment to unpredictable sensory stimuli, whereas the anterior lobe is involved in motor execution [43]. Hence, the lateral cerebellum might participate in on-line motor adjustment to the desired "motor plan" issued in the cerebral association motor areas, generating the internal model to provide feedforward control [24]. Once the model is established, neural activities of the lateral cerebellum diminish due to a decreasing requirement for movement-by-movement internal monitoring, somatosensory feedback, or both.

Our findings suggest a left-sided prevalence of cerebellum for implicit motor learning. In particular, during task performance the left lateral cerebellum and the right inferior frontal gyms close to the ventral portion of the premotor cortex were asymmetrically activated irrespective of the hand used or the order of training. This asymmetry may be explained by a corticopontocerebellar connection; the dorsal lateral cerebral convexity provides the majority of the pontine efferents [46]. Our findings provide support for previous studies suggesting that the left cerebellum may actively reference the right inferior frontal gyrus when coordinating hand movements. Using a maze-tracing task performed by either hand, van Mier et al. [53] found that the left lateral cerebellum and the right cerebral hemisphere showed practice-related activation, suggesting functional connection between them. Molinari et al. [30] showed that patients with left lateral cerebellar lesions performed worse on a serial reaction time task than patients with right cerebellar lesions. In a non-human primate study, Rizzolatti et al. [37–39] found that the neurons in the ventrorostral part of area 6 discharged selectively during goal-related hand movements. They suggested that different types of goal-related neurons form a vocabulary of simple motor acts localized in the ventral portion of area 6.

It is noteworthy that, while the left lateral cerebellum was consistently active during task performance, activity was highest when the two-ball rotation task was performed for the first time, irrespective of hands. This finding suggests that the left lateral cerebellum may be related to the early phase learning, or "what to do," learning.

*4.2.2.2. Parasagittal cerebellum.* The present study showed that a unimanual two-ball rotation task activated the Qua corresponding to the Larsel lobules IV and V, extending caudally to the Bi, Larsel lobule VIII [26], presumably corresponding to the intermediate zone. This finding is consistent with those of a human PET study [11] and animal experiments [49]. The persistent activation of the intermediate zone through the FR and FL session blocks indicates that it is important in the execution of movement. This is consistent with the existing hypothesis mat a major role of the cerebellum is to provide feedforward signals for generating muscle torques at a joint in order to adjust for interaction torques generated by other joints [3]. Winstein et al. [54] showed that the anterior lobe was activated during a unimanual visual tracking task in which demand for the coordination of rapid reversal was high. Together, these findings suggest that the anterior lobe is important in the execution of smooth ball rotation in the present experiment.

Regardless of the hand used, neuronal activity of the left Qua close to the dentate nucleus decreased with improved task performance (as gauged by a decrease in EMG measurements). A plausible interpretation of this result is that decreased activation in the left parasagittal cerebellum corresponds to task learning for either hand, in addition to the execution of left hand movement. Thus, the left Qua activity is related to the continuous improvement of the performance with feedback, and hence "how to do" learning. Across all situations, this area showed larger activities in the first session block than the second (order effect). And hence the left Qua may also be related to learning transfer. The relationship between asymmetry of the learning transfer and left lateralized learning related cerebellar activation needs to be explored by future investigations.

In summary, during performance of the implicit motor learning tasks, the learning related activity was confined to the left lateral and parasagittal cerebellum irrespective of the hand used. The left lateral cerebellum showed the prominent activation on the first trial of the novel task, and hence may be related to the early phase of learning, or "what to do" learning. The left parasagittal cerebellum showed gradual decrease in activity as learning proceeded, and hence represents the later phase of learning, or "how to do" learning. Left lateralized learning related activity in the cerebellum may be related to the asymmetric learning transfer from right hand to the left hand.

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