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Cerebral and cerebellar sensorimotor plasticity following motor imagery-based mental practice of a sequential movement

Michael G. Lacourse, PhD; Jessica A. Turner, PhD; Elizabeth Randolph-Orr, BFA; Steven L. Schandler, PhD; Michael J. Cohen, PhD

Neuromotor Rehabilitation Research Laboratory and Neuroimaging Research Laboratory, Department of Veterans Affairs Long Beach Healthcare System, Long Beach, CA; Department of Kinesiology and Physical Education, California State University, Long Beach, CA; Department of Psychiatry and Human Behavior, University of California, Irvine, CA; Chapman University, Orange, CA

Abstract—Motor behavior and sensorimotor activation of the cerebrum and cerebellum were measured before and after motor imagery-based mental practice (MP) and physical practice (PP) of a sequential motor task. Two-button-press sequences (A, B) were performed outside a magnetic resonance imaging scanner and at 2 Hz inside the scanner during a pretest. Participants (n = 39) completed PP, MP, or no practice (NP) of Sequence A for 1 week and were posttested. Sequence A performance improved 121%, 86%, and 4% for the PP, MP, and NP groups, respectively ($p < 0.05$), while Sequence B improved 56%, 40%, and 38% ($p > 0.05$). PP improvements were accompanied by increased striatal and decreased cerebellar activation, while MP improvements were accompanied by increased cerebellar, premotor, and striatal activation. The efficacy of MP for activating cerebral and cerebellar sensorimotor networks suggests that MP might be an effective substitute or complement to PP to activate compensatory networks for motor rehabilitation.

Key words: basal ganglia, cerebellum, fMRI, mental practice, motor imagery, motor learning, neurorehabilitation, sensorimotor, supplementary motor area, thalamus.

INTRODUCTION

A motor image is the mental representation of a previously executed movement [1], while motor imagery-based mental practice (MP) is a process whereby a motor image is evoked repeatedly to improve motor behavior [2,3]. For example, athletes use MP techniques to supplement PP and facilitate motor skill acquisition [4]. Motor images are likely embedded in a distributed functional network, including cerebral systems that affect motor performance

Abbreviations: BOLD = blood oxygen level dependent, CNS = central nervous system, CONTRA = contralateral, EMG = electromyographic, fMRI = functional magnetic resonance imaging, FOV = field of view, IPSI = ipsilateral, IRB = institutional review board, LSD = least significant difference, MNI = Montreal Neurologic Institute, M1 = primary motor cortex, MP = mental practice, MRI = magnetic resonance imaging, NP = no practice, PET = positron emission tomography, PMA = premotor area, PP = physical practice, RF = radio frequency, ROI = region of interest, SCI = spinal cord injury, SD = standard deviation, SMA = supplementary motor area, S1 = primary somatosensory area, SPM = statistical parametric map, SVC = small volume correction, TE = echo time, T1 = spin lattice relaxation time, TR = repetition time.

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Address all correspondence to Michael Lacourse, PhD; VA Long Beach Healthcare System, 5901 7th Street, 151J, Long Beach, CA 90822; 562-826-5885; fax: 562-961-8017; email: mlacourse@csulb.edu.

by controlling states of arousal, focusing attention, or priming various neuromuscular systems for movement [5]. Though less effective than physical practice (PP), MP does improve motor behavior [4].

MP has a potential clinical benefit for patients with central nervous system (CNS) trauma, such as spinal cord injury (SCI) or stroke [2,6]. The benefit would be to repetitively activate cerebral and cerebellar sensorimotor structures damaged by a stroke or deafferented/deefferented by a traumatic SCI without movement, thereby engaging damaged or compensatory sensorimotor networks to promote motor rehabilitation. Though evidence exists for an episodic cerebral/cerebellar response to motor imagery performance, the question remains whether chronic MP techniques effectively promote functional recovery from injury by priming the sensorimotor system for motor rehabilitation.

One explanation for the potential effectiveness of MP for motor rehabilitation is that motor imagery and movement preparation similarly activate cerebral and cerebellar sensorimotor structures [1]. Neuroimaging experiments using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) show regional cerebral activity during executed movements in the supplementary motor area (SMA) [7–11], primary motor cortex (M1) [12–15], rolandic region [11], premotor area (PMA) [16–18], medial frontal cortex [19], cerebellum [16,18,20], and basal ganglia [21,22]. Likewise, motor imagery activates the SMA [10,11,14,18], M1 [15,23–26], PMA [9,15,27,28], superior parietal lobule [18,29], and cerebellum [14,22]. Efferent discharges produced during imagery may also activate descending motor pathways [1]. MP increases spinal reflex excitability at a level only slightly weaker than during movement [30,31], and corticospinal excitability is similar during imagery and movement [32,33]. Combined with evidence for similarities in movement timing and motor control laws [34,35] and similar autonomic response modulation [2], apparently, movement preparation and motor imagery engage similar functional brain systems [1]. A summary of sensorimotor system activation during movement and MP is presented in **Figure 1**.

PP of a movement sequence improves performance and induces short- and long-term functional plasticity of the brain, including M1 [36], SMA [37,38], PMA [17,37], posterior parietal area [17,37], prefrontal areas [37,38], and cerebellum [17,37,38]. Though MP also improves motor behavior [4,39], little evidence exists yet for accompanying cerebral and cerebellar plasticity.

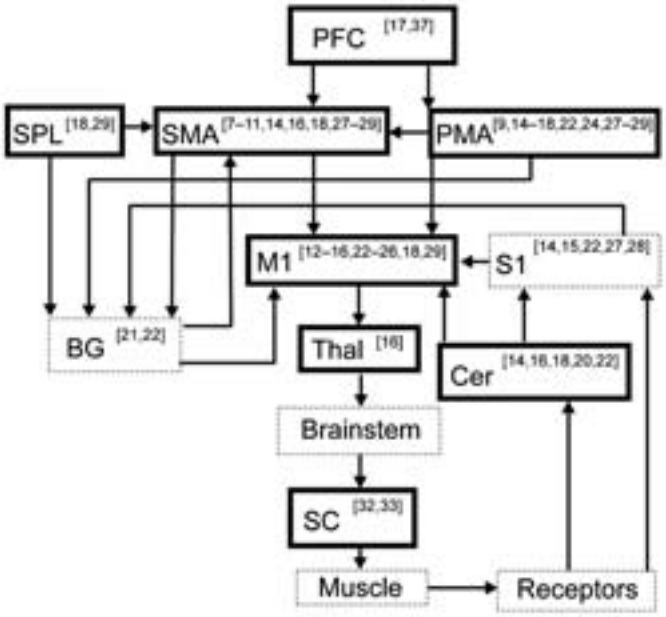

Figure 1.
Activation model for cerebral sensorimotor network during executed and imagined movements. Sensorimotor regions functionally activated during executed and imagined hand movements. Literature citations provided within each box can be found in reference section of main paper. Activated during executed and imagined movements - - - - -. Activated during executed movements only ——. PFC = prefrontal cortex, SPL = superior parietal lobule, SMA = supplementary motor area, PMA = premotor area, BG = basal ganglia, M1 = primary motor area, S1 = primary somatosensory area, Cer = cerebellum, Thal = thalamus, and SC = spinal cord.

Notable exceptions are Pascual-Leone et al. [40], who found similar modulation of M1 neural circuitry following MP and PP of a motor skill, and a recent study by Lafleur et al. [41], where PP produced parallel changes in cerebral activation during executed and imagined foot movements.

The effects of MP on motor behavior are well documented, and extensive literature can be found on functional sensorimotor plasticity related to PP [42]. Unknown is the pattern of cerebral and cerebellar functional plasticity accompanying MP-related motor learning. A better understanding of the mechanisms that accompany MP effects on motor behavior is important for developing rehabilitation strategies that effectively enhance motor recovery from CNS trauma.

This experiment specifically tested whether improvements in motor sequence performance and accompanying changes in cerebral and cerebellar activations are similar following motor imagery-based MP and PP. Changes in

fMRI signal intensity, location, or spatial extent in cerebral and cerebellar regions of interest (ROIs) (**Figure 1**) from pre- to posttest were considered indicators of functional plasticity. We hypothesized that PP would yield greater improvements in motor behavior than imagery practice and that cerebral and cerebellar plasticity would be similar following PP and motor imagery-based MP. The experimental design was modeled after Karni et al. [43].

METHODS

Participants

Thirty-nine male (n = 18) and female (n = 21) right-hand-dominant participants, mean ± standard deviation (SD) age = 23.3 ± 5.5 yr, completed the experiment after providing informed consent. All participants were current university students. The Long Beach Institutional Review Board (IRB) of the Department of Veterans Affairs Health Care System and the Long Beach IRB of the California State University approved the protocol in accordance with the Helsinki Declaration of 1975, as revised in 1983. Handedness was determined with the Edinburgh Inventory [44]. We estimated sample size using the tables and equations supplied by Cohen [45] and using the parameters: $\alpha = 0.05$, $\beta = 0.20$ (statistical power = 0.80), $u = 2$ (the number of treatment conditions), and $f = 0.35$. The estimated value for the effect size f was based on preliminary data from a fixed-effects analysis showing a large increase of signal magnitude in the primary motor area (i.e., local maxima of cluster located in the contralateral precentral gyrus) from pre- to posttest following 1 week of intensive PP. Based on these criteria, the required number of participants per treatment group was estimated to be 13. Exclusion criteria included history of seizures, mental illness, substance abuse during the past 12 months, any medical illness, alcoholism, or current use of a medication known to alter neurologic activity.

Motor Task

Participants performed a sequential button-press task with the right hand using a four-key response pad (Neuroscan, Inc.) during two test sessions and daily practice (PP group only). They performed two different, but similar, button-press sequences during each test session: Sequence A (4 1 3 2 4) and Sequence B (4 2 3 1 4), with numbers (1–4) representing digits, i.e., index (1), middle (2), ring (3), and little finger (4) (Karni et al. [43]). The sequences were performed both outside and inside a magnetic resonance imaging (MRI) scanner during the test sessions and outside the scanner during practice sessions. Inside the MRI scanner, rate of performance was controlled at 2 Hz and paced by a flashing gray circle displayed in the center of a screen presented through a pair of goggles. We used this specific procedure to control for rate-dependent effects on the blood oxygen level dependent (BOLD) signal that might be confounded with the learning-related effects that were being assessed in this experiment (Karni et al. [43]). Outside the MRI scanner, we assessed motor behavior during the test sessions by computing the mean number of completed sequences and errors during two 30 s epochs of Sequence A and B performances. Errors were defined as a missing button press (error of omission) or an incorrect button press (error of commission) during a sequence repetition. A completed sequence may have included one or more errors of omission or commission. Measuring maximal speed of button-press performance outside the scanner provided an index of practice-related improvement in motor behavior, while controlled speed of motor sequence performance inside the scanner allowed for an assessment of functional plasticity within specific cerebral and cerebellar ROIs.

Experimental Design

Participants were randomly assigned to one of three practice conditions following the pretest: (1) PP, (2) MP, or (3) no practice (NP). Each group included at least six males and six females. Participants completed 30 min of daily practice for 1 week and were then posttested. The resulting independent variables were practice group (PP, MP, NP), test (pre, post), and sequence (A, B). All participants practiced Sequence A, while Sequence B was unpracticed and used as a within-subject control condition. The dependent variables were brain activation and movement sequence performance. We measured brain activation inside the scanner by using BOLD fMRI, and measured movement performance outside the scanner by counting the number of completed sequences and errors during repetitive 30 s epochs of the button-press task.

Test Procedures

Participants were screened via telephone before the initial test session. The procedures were described, and the consent forms and Edinburgh Handedness Inventory were completed during the initial session. Before the initial test, the motor task was explained and two random sequences

were performed outside the scanner so the participant would be familiar with the button-press instrument. This procedure was followed by two repetitions of Sequences A and B. Outside the scanner, participants performed four 30 s epochs of the movement sequences with a 30 s inter-trial rest period. We held the order of sequence performance constant outside the scanner to standardize the measurement procedure—A, B, B, A. The instruction was to correctly perform the sequence as many times as possible for 30 s. After completing the test outside the scanner, participants were transported to the MRI center and prepared for testing inside the scanner. Inside the scanner, the test consisted of 30 s epochs of the motor sequence performance using the following schedule: A, B, B, A, A, B, B, A. We also held this order of sequence performance constant for all participants to standardize the measurement procedure. The participants performed these tests before (pretest) and after (posttest) the week of practice.

Practice Procedures

At the first practice session, we randomly assigned participants to an experimental condition (PP, MP, NP), and they completed five practice sessions during the week between the pre- and posttests. Practice consisted of 30 repetitions of alternating 30 s epochs of practice with 30 s epochs of rest. The total duration of daily practice was 30 min. An auditory tone was presented to cue the beginning of each epoch. The PP group was instructed to complete Sequence A at maximal speed while minimizing errors during each practice epoch. The MP group was instructed to imagine executing Sequence A at maximal speed while minimizing errors during practice, whereas the NP group was instructed to count backward for 30 s by a randomly selected odd number (e.g., 7), beginning with a randomly selected three-digit number (e.g., 973). Participants in the PP and MP groups were strongly encouraged to increase button-press speed during each practice session.

We used a four-step systematic motor imagery training protocol during the first practice session to standardize imagery training. In this protocol, participants—

1. Received motor imagery instruction, including relaxation and attentional focus techniques.
2. Performed motor imagery practice trials of contraction tasks not used in the experiment to become familiar with performing motor imagery training (e.g., lifting heavy objects).
3. Observed a visual model performing the experimental task.
4. Performed practice trials while the experimenter monitored electromyographic (EMG) activity and provided feedback (when necessary) to eliminate muscle activity during imagery practice trials.

MRI Acquisition

Imaging Apparatus

We used a 1.5 Tesla Eclipse scanner (Marconi Medical Systems, Inc., Cleveland, Ohio) with multislice echo-planar imaging capabilities and a receive-only head-coil to collect BOLD-fMRI data. MRI-compatible Silent Vision™ goggles and Silent Scan™ headphones from Avotec (Jensen Beach, Florida) were used for presenting stimulus and communicating with participants.

Imaging Methods

Participants were trained outside the scanner to perform the 2 Hz sequences without excess head movement. Inside the scanner, we fitted earplugs and headphones and minimized head motion by padding the head coil. A high-resolution axial full-brain anatomical image was acquired for each participant at the beginning of each session. The sequence used was spin lattice relaxation time (T1) relaxation-weighted three-dimensional (3-D) volume, RF (radio frequency energy) spoiled Fourier-acquired steady-state technique. The in-plane resolution was 0.94 × 0.94 mm, and the slice thickness was 2.5 mm.

The pulse sequence used for the functional scans was a gradient-echo echo-planar imaging sequence, with an echo time of 40 ms, repetition time of 3 s, 90° flip angle, and a fat-saturating prepulse. The acquisition matrix was 141 × 64, which was interpolated to a final matrix size of 128 × 128. The field of view (FOV) was 24 cm, leading to a final display pixel size of 1.88 × 1.88 mm^2. The slice thickness was 5 mm with no interslice gap. Slices for the whole brain were acquired in an interleaved order in the axial orientation. A total of 170 scans were acquired. A boxcar paradigm began with 10 acquisitions of rest (30 s), followed by 10 acquisitions while Sequence A was performed (30 s), rest, 10 of Sequence B (30 s), rest, 10 of B, rest, 10 of A, and rest. This paradigm was performed twice for a total of eight button-pressing epochs and nine rest epochs. The duration of the paradigm was 8 min and 30 s. During each scan, a flashing gray circle (~3° visual angle in diameter) was presented on the goggles at 2 Hz against a black background, with the word “REST” or “AAAA” or “BBBB” presented above it.

EMG During Practice

Technicians monitored EMG signals using a Neuroscan system (Neuroscan, Inc.) during motor imagery practice trials to determine whether muscle activation accompanied motor imagery performance. Technicians monitored the real-time EMG and signal and were trained to identify when activity during motor imagery epochs exceeded activity during rest. If the technicians observed EMG activity, they instructed the participants during the subsequent rest epoch to eliminate muscle contraction during imagery trials.

EMG signals were acquired with a sampling rate of 5 kHz and bandpass-filtered at 30 and 500 Hz, with a 60 Hz notch filter. The dorsal surfaces of the right hand (bony area) and of the right forearm were abraded and wiped with Omni™ Skin Prep before Ag-AgCl electrodes were filled with Sigma™ Electrode Crème and attached. The participant executed the motor task with his or her right hand to localize the area of muscle contraction via palpation. No postprocessing of the EMG signal was performed.

Data Analysis

Motor Behavior

Completed sequences and errors were counted offline for the two 30 s epochs of Sequences A and B performed outside of the MRI scanner during the pre- and posttests. The mean of the two epochs was computed for each participant and used for subsequent analyses. The mean and SD of the change in completed sequences (%) and number of errors was computed for each practice group.

Imaging and Statistical Analysis Methods

We performed image and statistical analyses in three steps. In step 1, images from the functional scans were reconstructed and spatially preprocessed. In step 2, we estimated a separate statistical parametric map (SPM) using a fixed effects analysis for each participant's pre- and posttest. A multisubject conjunction analysis was then performed across participants in each practice condition to create a "common" SPM for the pre- and posttests independently. In step 3, we estimated pre- versus posttest contrast SPMs for each participant and performed a multisubject conjunction analysis again to estimate the regions of increased and decreased activation that were common among each practice group. We performed image and statistical analyses using SPM99 (Wellcome Department of Cognitive Neurology, Queen's College, London) and MATLAB (Mathworks, Inc., Natick, Massachusetts).

In step 1 (image analysis), the first two images (i.e., 6 s) of the series were removed from further analysis because the tissue was not yet saturated. We realigned the remaining images to the third image using a trilinear interpolation algorithm, creating a realigned series of images and a mean image. We then coregistered the mean image to the participant's T1-weighted high-resolution anatomical scan, spatially normalized and transformed into a standard stereotaxic space (template provided by the Montreal Neurologic Institute [MNI]) to facilitate intersubject averaging and conventional reporting [46–48]. Finally, an 8 mm full width at half maximum Gaussian kernel was used for spatial smoothing.

In step 2, we performed a voxelwise statistical analysis using the general linear model and the theory of Gaussian fields to yield separate functional activation maps for each participant during the pre- and posttests [49,50]. Cross-correlations were computed between the signal intensity time curve and the hemodynamic response function (HRF) convolved boxcar activation waveform for each voxel over the whole brain. We performed a conjunction analysis across the 13 participants in each practice group and for each test to determine the "common" voxelwise activation versus baseline contrast maps [51]. The statistical threshold was set at $p < 0.001$ (uncorrected) and the degrees of freedom were 13 and 1,079. We used the map and associated *p*-values to determine the common activation foci for the participants within each practice condition. Finally, we performed a cluster-level analysis for ROIs (**Figure 1**) to determine the number of activated voxels in the ROI. The three measures of cortical activity for ROIs were therefore magnitude (i.e., *z*-value), location (i.e., *x*, *y*, *z* coordinates), and extent (i.e., number of activated voxels in an ROI).

In step 3, we computed pre- versus posttest statistical contrast maps within each participant and performed a conjunction analysis across participants in each practice group to localize changes in signal intensity between the pre- and posttests. This analysis differs from the step 2 analysis by a subtraction of activations across tests and by further localization of signal changes that occurred as a result of practice. The ROIs were the same as those used in step 2. We performed contrasts to assess both increases and decreases in the signal intensity. The four specific

voxelwise contrasts were $A_{pre} > A_{post}$ (i.e., decreased activation), $A_{post} > A_{pre}$ (i.e., increased activation), $B_{pre} > B_{post}$, and $B_{post} > B_{pre}$. Statistical tests used the small volume correction (SVC) option in SPM99 with a $p < 0.001$ (uncorrected) threshold *t*-statistic of 3.09 and an extent threshold of five voxels.

Localizing ROIs

ROI volumes were defined with a two-step process. In step 1, we determined "seed" MNI coordinates for ROI by computing the mean and SD of the coordinates reported for that ROI in a random sample of studies published in the journal *NeuroImage* (i.e., a form of meta-analysis). Only studies using hand-movement tasks were selected, and Tailarach and Tourneaux coordinates were converted to MNI coordinates for this analysis. We labeled the mean the center of the ROI, while we used the SDs of the published coordinates to define the dimensions of a "box" volume (i.e., 1 SD in each of the three dimensions). In step 2, the anatomical locations of the seed coordinates and box volumes were confirmed through a comparison with the anatomical regions of the MNI single-subject brain found in SPM99 [52]. Based on the model presented in **Figure 1**, the cortical ROIs were the prefrontal cortex, posterior parietal lobe, SMA, PMA, M1, and S1 (the primary somatosensory area). The subcortical ROIs were the thalamus, putamen, caudate, and cerebellum.

RESULTS

Motor Behavior

The mean increase (%) in the number of completed Sequences A and B from pre- to posttest for the three practice groups is presented in **Table 1**. The difference between the practice groups in mean increase (%) was statistically significant for the practiced Sequence A [$F(2, 36) = 10.90$; $p < 0.05$; $\omega^2 = 0.34$]. A post hoc Least Significant Difference (LSD) test revealed that all practice groups were significantly different from one another for Sequence A ($p < 0.05$), with the PP group achieving the greatest increase in completed sequences (mean = 121%), followed by the MP (mean = 86%), and NP (mean = 46%) groups, respectively. The effect size index *d* for MP versus NP of Sequence A was 0.79. No differences were found between the practice groups in the mean increase (%) for the unpracticed Sequence B [$F(2, 36) = 2.82$; $p > 0.05$; $\omega^2 = 0.08$]. Within each practice condition (i.e., the within-subject control condition), the increase in number of completed Sequence A's was significantly greater than the increase in Sequence B's for the PP group [$F(1, 12) = 29.20$; $p < 0.05$; $\varepsilon^2 = 0.71$] and MP group [$F(1, 12) = 17.40$; $p < 0.05$; $\varepsilon^2 = 0.59$], but not for the NP group ($p > 0.05$).

The mean change in the number of errors between the pretest and posttest for the three practice groups is presented in **Table 1**. No significant differences were found in the number of errors between the pretest and posttest for any of the practice groups for Sequences A and B ($p > 0.05$).

EMG Activity During Practice

Technicians monitored online EMG activity to determine whether muscle activation accompanied MP. Thirteen participants completed 5 days of practice with 30 practice epochs each day for a total of 1,950 epochs of MP in this experiment. EMG activity during MP greater than resting EMG was observed for all participants during at least one of the initial epochs on the first practice day. This behavior was immediately extinguished through feedback from the technician. No further incidents of EMG activation were reported during MP after the first day of practice.

Conjunction Analysis of Pre- and Posttest Activation

The conjunction analysis for each practice group during the pre- and posttests is displayed in **Figure 2(a)** to **(l)**.

Table 1.
Mean increase (%) in number of completed Sequences A and B from pre- to posttest for three practice groups: no-practice (NP), mental practice (MP), and physical practice (PP).

Practice Condition	Practiced Sequence A (Mean ± SD)		Unpracticed Sequence B (Mean ± SD)	
	Completed Sequences (%)	Errors (Number)	Completed Sequences (%)	Errors (Number)
NP	46 ± 5.3	–0.4 ± 0.5	38 ± 5.6	0.0 ± 0.7
MP	86 ± 13.1	0.9 ± 0.4	40 ± 5.3	0.6 ± 0.7
PP	121 ± 18.3	–0.5 ± 0.5	56 ± 5.8	2.4 ± 1.7

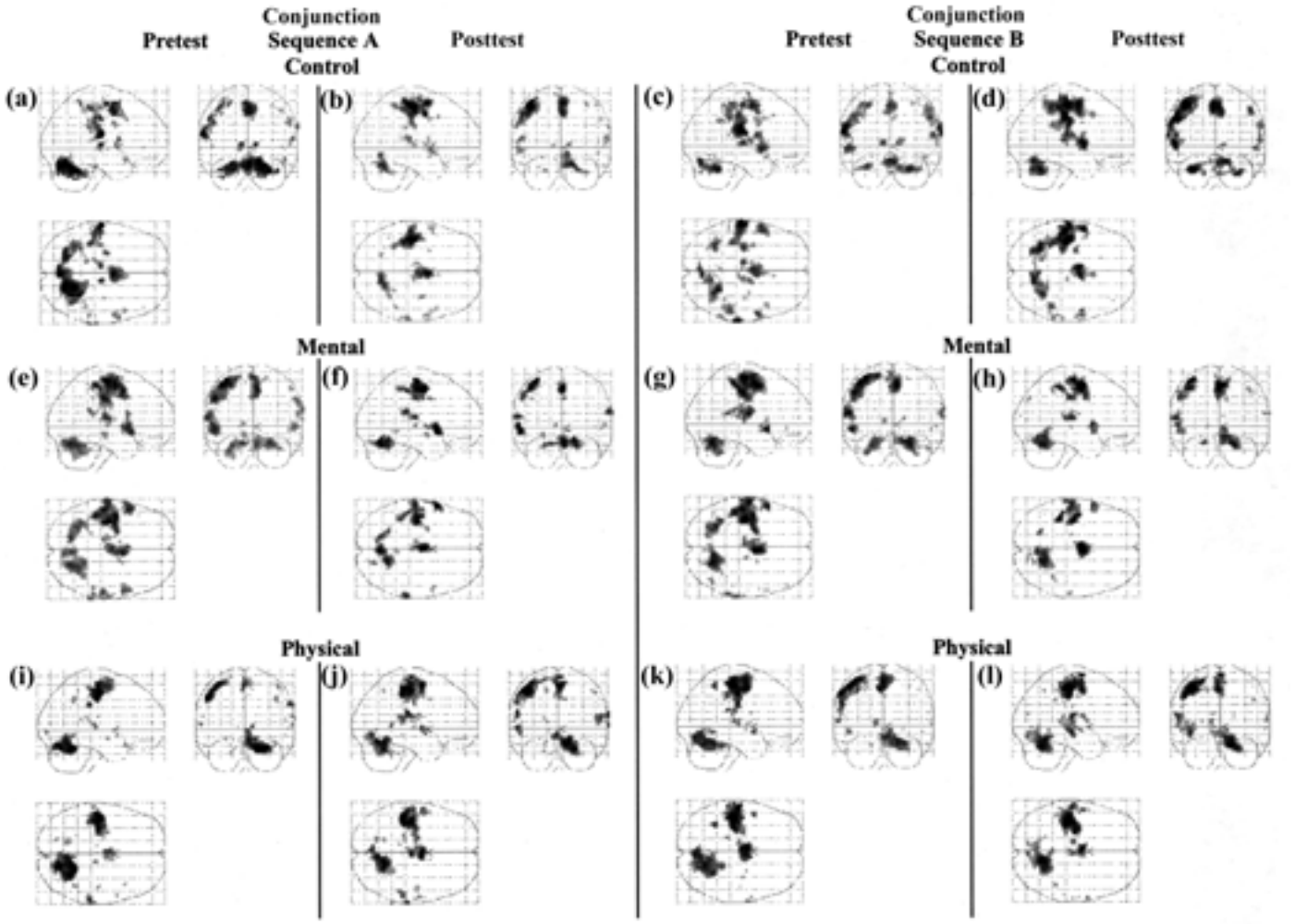

Figure 2.
(a)–(l): Glass brains displaying significantly activated voxels ($p < 0.001$; uncorrected) in regions of interest (ROIs) from a conjunction analysis (n = 13; degrees of freedom = 1,079) performed on the participants in each of three practice groups (no practice, mental practice, and physical practice) for Sequences A and B during pretest and posttest. **Note:** Significantly activated voxels in non-ROIs are deleted from glass brains.

The SPMs indicate those areas significantly activated by the motor task relative to the rest condition. **Table 2** further compares the number and location of activated voxels in each ROI during the pre- and posttests for each practice condition.

Pretest

For the NP group, Sequence A activation was found in the SMA, bilateral M1 and S1, contralateral (CONTRA)-PMA, and posterior parietal areas, while subcortical activity was found bilaterally in the cerebellum and thalamus. Cerebellar activity was extensive, though intensity and extent were greater ipsilateral (IPSI) than CONTRA. CONTRA-M1 and -S1 activations were contiguous and to a greater spatial extent than IPSI. The activation pattern for Sequence B was similar to Sequence A, except the posterior parietal region did not achieve threshold and cerebellar activity was less spatially extensive. CONTRA-M1 and -S1 activations were contiguous and of a greater intensity than for Sequence A.

For the MP group, activation during Sequence A was seen in the SMA, PMA, CONTRA-M1, and bilateral S1 areas and subcortically in the cerebellum (bilaterally) and CONTRA-thalamus. SMA and PMA activations were contiguous, though SMA activity alone was extensive and high intensity. Sequence B showed SMA, PMA, and CONTRA-M1 and -S1 activations, with bilateral activation in both the cerebellum and thalamus. CONTRA-M1 and -S1

Table 2.
Comparison of number of activated voxels and location of local maxima in cortical ROIs during pretest and posttest for each practice condition and each sequence. We obtained voxel numbers by comparing volume list in SPM to cluster labeling percentages from Automated Anatomical Labeling technique by Tzourio-Mazoyer et al. [Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage. 2002;15:273–89.] Voxel coordinates were obtained from SPM volume list where possible, although in cases where a coordinate was not matched to a region found in cluster label list, coordinates were determined manually.

Practice Condition	ROIs							
	SMA	PM-C	PM-I	M1-C	M1-I	S1-C	S1-I	PP
Control								
A-Pre	375 (2,–4,52) 6.87	11* (–26,–10,60) 5.51	0	42* (–26,–12,56) 5.51	13* (56,–2,32) 4.13	204 (–62,–18,18) inf	13* (56,–2,32) 4.13	14 (–32,–46,58) 4.66
A-Post	448 (2,0,60) 7.41	0	12* (34,–8,58) 4.52	118† (–42,–16,56) inf	1* (36,–10,56) 4.52	548† (–42,–26,56) inf	0	26 (–42,–16,56) inf
B-Pre	258 (0,–4,52) 6.66	24 (–48,16,–2) 4.33	0	96† (–50,0,32) 3.93	43 (56,4,28) 4.01	379† (–62,–20,20) inf	8 (58,2,14) 6.17	0
B-Post	367 (–4,–4,54) 7.59	57 (–44,8,6) 3.92	1 (4,16,42) 4.46	276 (–28,–8,54) 4.85	4† (58,4,16) 4.30	721 (–40,–20,52) inf	2† (60,0,16) 4.30	35 (–20,–50,64) 3.79
Mental								
A-Pre	339‡ (6,4,50) 7.19	122 (–54,10,0) 6.85	7‡ (18,2,66) 3.76	350† (–36,–20,62) inf	0	529† (–46,–30,56) 7.17	24 (60,–26,34) 5.15	0
A-Post	170 (–2,–6,54) inf	9 (–60,10,–4) inf	0	156† (–38,–16,64) inf	0	242† (–60,–18,14) 6.03	0	0
B-Pre	602 (4,–4,54) inf	76 (–54,10,6) 7.59	7 (20,–4,60) 3.67	351† (–36,–20,62) inf	0	717† (–60,–14,14) 7.73	0	0
B-Post	334 (0,–6,56) 7.58	16 (–56,8,2) 5.24	0	141† (–38,–16,64) 7.48	0	230† (–56,–10,16) 3.88	0	0
Physical								
A-Pre	174 (–2,–4,60) 4.95	0	0	187† (–38,–18,60) 6.09	6† (44,–16,58) 3.71	232† (–52,–20,44) 6.79	3† (46,–18,56) 3.71	0
A-Post	173 (0,–6,58) 5.82	0	0	237† (–38,–18,60) 5.53	0	469† (–46,–16,50) 4.27	12 (60,–10,20) 3.86	0
B-Pre	559 (0,–6,58) 6.52	0	0	289† (–38,–22,62) 7.34	0	450† (–44,–22,54) inf	0	9 (–36,–48,54) 5.01
B-Post	166 (–4,–6,52) 4.99	0	0	303 (–22,–30,52) 3.78	0	467 (–38,–24,54) 7.35	0	0

*M1 activity was contiguous with premotor activity.
†S1 activity was contiguous with M1 activity.
‡SMA activity was contiguous with premotor activity over 10 voxels.
inf = infinity
M1-C = contralateral primary motor area
M1-I = ipsilateral primary motor area
PM-C = contralateral premotor
PM-I = ipsilateral premotor
PP = posterior parietal
ROIs = regions of interest
SMA = supplementary motor area
SPM = statistical parametric map
S1-C = contralateral primary sensory area
S1-I = ipsilateral primary sensory area

activations were contiguous and extensive. Cerebellar activity was bilateral and extensive, while thalamic activity was bilateral.

For the PP group, Sequence A activation was found in the SMA and bilateral M1 and S1, while subcortical activation within the cerebellum and thalamus was IPSI only. S1 and M1 activations were contiguous in both hemispheres, with greater extent contralaterally. Sequence B activation was seen in the SMA, CONTRA-M1 and -S1, and the posterior parietal area as well as in IPSI-cerebellum and CONTRA-thalamus. IPSI-thalamic activity failed to achieve threshold.

Posttest

Similar to the pretest, activation during Sequence A for the NP group was seen in the SMA, CONTRA-M1 and -S1, PMA, posterior parietal area, and the cerebellum and thalamus (**Table 3**). Differences from the pretest were marked by a greater intensity and extent of activation in CONTRA-M1 and -S1 areas, as well as an increase in the intensity of activation in the posterior parietal region. Activation of IPSI-M1 was minimal while IPSI-S1 failed to reach statistical threshold. PMA activation shifted from CONTRA in the pretest to IPSI in posttest. Cerebellar activity was less extensive, and only IPSI-thalamus activity appeared. Activation for Sequence B on the posttest was seen in the SMA, bilateral M1 and S1, posterior parietal, CONTRA-PMA, and the cerebellum and IPSI-thalamus. CONTRA-M1 and -S1 activity was of greater magnitude and extent on the posttest. Cerebellar activity was bilaterally symmetrical, while the CONTRA-thalamus failed to reach statistical threshold and IPSI-thalamus activity was greatly reduced.

For the MP group, Sequence A activation was localized in the SMA, CONTRA-PMA, CONTRA-M1 and -S1, bilateral cerebellum, putamen, and CONTRA-thalamus. Notable changes from the pretest were the considerably less-extensive SMA and PMA activations, the shift of S1 activation from bilateral to contralateral only, and the addition of activity in the putamen. Cerebellar activation was bilaterally contiguous and reduced overall, with greater extent in the IPSI-hemisphere. Sequence B posttest activity appeared in the same cortical regions as Sequence A, with a reduction in activation extent for all areas. Sequence B activation of the cerebellum was bilateral and reduced compared with the pretest, with greater extent in the IPSI-hemisphere. No activation was seen in the thalamus or putamen, as was the case for Sequence A.

For the PP group, the extent of SMA activation during Sequence A was unchanged. M1 and S1 activations increased CONTRA and disappeared IPSI. The extent of IPSI-cerebellar activation was greatly reduced during the posttest, while the extent of CONTRA activity increased slightly. Thalamic activity increased CONTRA and decreased IPSI. Sequence B activation was less extensive in the SMA, while M1 and S1 activity increased slightly and posterior parietal activation disappeared. Cerebellar activation decreased IPSI and appeared as a small magnitude CONTRA. Thalamic activation remained CONTRA and relatively unchanged from the pretest.

Conjunction Analysis of Differences Between Pre- Versus Posttest Activation

We performed a multisubject conjunction analysis on the pre- versus posttest difference contrasts for participants in each training condition. **Figure 3(a)** to **(l)** displays the SPMs for activation increases and decreases between the pre- and posttest that were common with each participant in the practice groups. **Table 4** provides a further comparison of increases and decreases in activation.

For the NP condition, the only change was an increase of five voxels in the CONTRA-thalamus for Sequence B. For the MP condition, activation increased for Sequence A in the PMA, CONTRA-M1, bilateral cerebellar, caudate, and putamen. No ROI showed a decrease in activation during Sequence A or an increase during Sequence B. For Sequence B, activation decreased in the PMA, IPSI-S1, and bilateral cerebellum. For the PP condition, activation increased during Sequence A in the SMA, PMA, IPSI-S1, caudate, putamen, and IPSI-thalamus. Decreases were found during Sequence A in the cerebellum bilaterally. For Sequence B, the caudate and IPSI-thalamus increased, while the CONTRA-M1 and IPSI-cerebellum decreased significantly.

DISCUSSION

Following 1 week of practice, motor behavior improved more following PP than motor imagery-based MP or NP, while the motor imagery-based MP group improved more than the NP group. Changes in functional cerebral and cerebellar activations following PP and MP were robust in some ROIs, while other ROIs changed variably. Relatively few changes in activation accompanied NP. While improved motor behavior is consistent

Table 3.
Comparison of number of activated voxels and location of most significant voxel in subcortical ROIs during pretest and posttest for each practice condition and each sequence. We obtained voxel numbers by comparing volume list in SPM to cluster labeling percentages from Automated Anatomical Labeling technique by Tzourio-Mazoyer et al. [Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage. 2002;15:273–89.] Voxel coordinates were obtained from SPM volume list where possible, although in cases where a coordinate was not matched to a region found in cluster label list, coordinates were determined manually.

Practice Condition	ROIs					
	Cer-C	Cer-I	Caud	Put	Thal-C	Thal-I
Control						
A-Pre	508*	655*	0	0	42	24
	(–36,–56,–40)	(20,–68,–22)			(–8,–18,6)	(10,–20,4)
	4.97	7.41			5.21	5.99
A-Post	9	174	0	0	0	11
	(–22,–62,–30)	(14,–64,–22)				(10,–18,6)
	3.93	6.25				3.98
B-Pre	148*	236*	0	0	56	58
	(–32,–56,–28)	(26,–52,–30)			(–10,–18,4)	(14,–8,8)
	5.78	7.52			5.97	4.54
B-Post	324	285	0	0	0	9
	(–32,–56,–30)	(16,–64,–20)				(12,–18,2)
	7.69	6.26				3.94
Mental						
A-Pre	446	582	0	0	18	0
	(–16,–68,–22)	(22,–70,–22)			(–16,–20,4)	
	6.01	6.47			3.95	
A-Post	177*	276*	0	4	10	0
	(–16,–66,–22)	(2,–70,–20)		(–26,–4,–8)	(–10,–20,4)	
	5.29	7.18		4.14	3.97	
B-Pre	386	539	0	0	15	10
	(–28,–58,–28)	(22,–64,–26)			(–12,–20,6)	(14,–18,8)
	6.69	7.41			4.3	4.36
B-Post	26	496	0	0	0	0
	(–20,–66,–22)	(18,–60,–24)				
	4.90	5.78				
Physical						
A-Pre	0	806	0	0	0	11
		(18,–70,–22)				(10,–22,4)
		7.36				4.26
A-Post	21*	455*	0	0	3	0
	(–8,–72,–10)	(6,–64,–16)			(–14,–14,8)	
	4.30	6.25			3.69	
B-Pre	0	863	0	0	30	0
		(18,–62,–20)			(–12,–14,4)	
		5.93			4.01	
B-Post	27*	521*	0	0	22	0
	(–4,–66,–10)	(12,–60,–24)			(–12,–18,8)	
	3.80	6.10			4.12	

*Cerebellar activity was bilateral with contiguous activation.
Caud = caudate,
Put = putamen
Cer-C = contralateral cerebellum
Cer-I = ipsilateral cerebellum
inf = infinity
ROIs = regions of interest
SPM = statistical parametric map
Thal-C = contralateral thalamus
Thal-I = ipsilateral thalamus

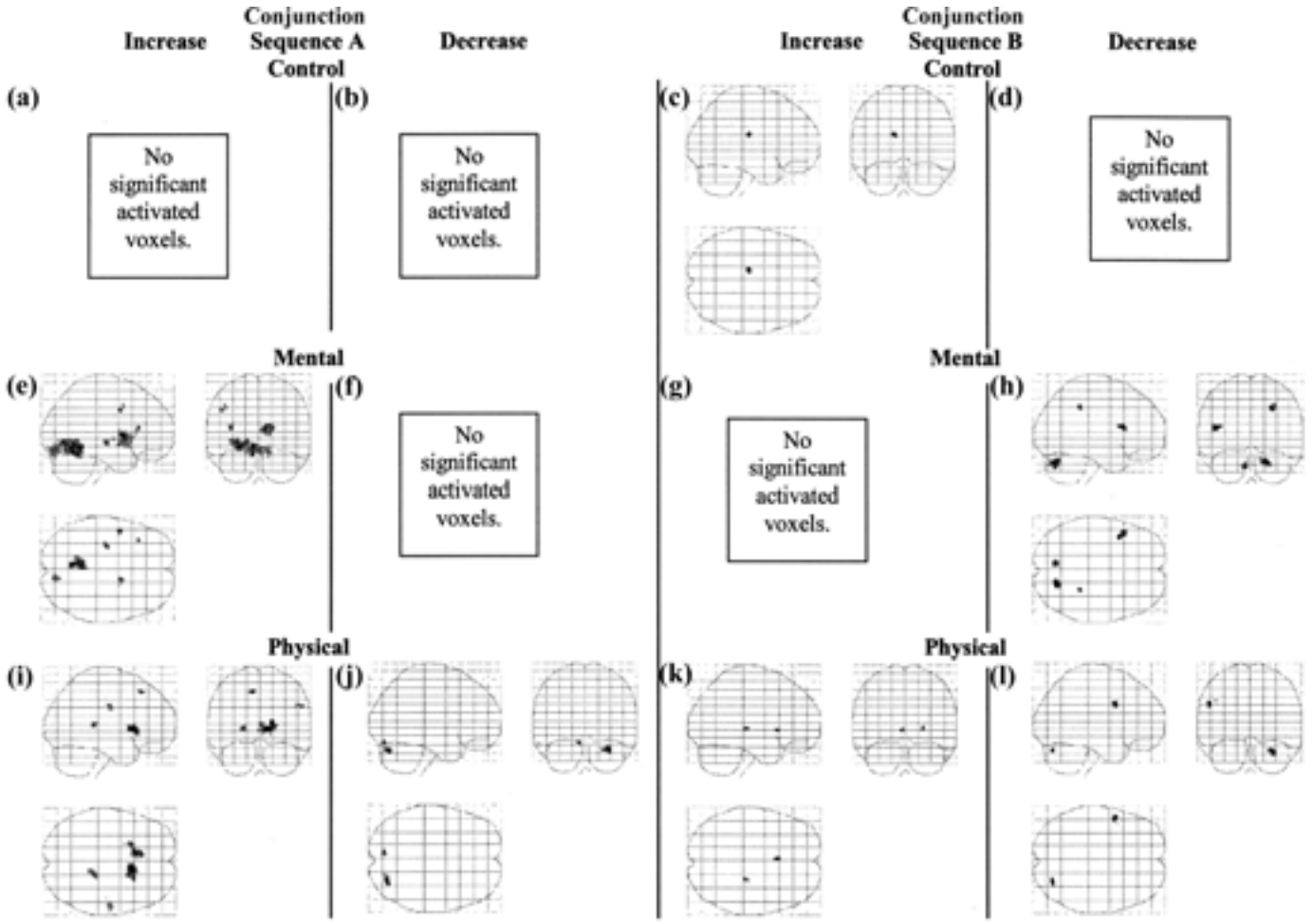

Figure 3.
(a)–(l): Glass brains displaying significantly activated voxels ($p < 0.001$, uncorrected) in regions of interest (ROIs) from a conjunction analysis (n = 13, degree of freedom = 1,079) performed on the participants in each of three practice groups (no practice, mental practice, and physical practice) for Sequences A and B during pretest and posttest. **Note:** Significantly activated voxels in non-ROIs are deleted from glass brains.

with previous findings [39,43], systemic changes in cerebral and cerebellar activations accompanying MP of a sequential hand movement are reported here for the first time.

Motor Behavior

Relative improvements of motor behavior following PP, MP, and NP are consistent with prior studies [4,39] and demonstrate a clear behavioral effect of MP on sequential motor behavior in this experiment. The effect size (*d*) of MP versus NP was larger than reported in meta-analyses and may be related to the relatively long duration of practice used here (i.e., 75 total minutes of practice). The mean increase in completed sequences for the NP group during Sequences A and B indicates that even a brief exposure to the motor task during the pretest session (i.e., four 30 s epochs) was sufficient to produce large improvements in behavior. Future experiments might consider using more complex movement sequences to minimize the potentially confounding effects of test-related learning.

NP Effects on Activation

A NP control condition was used to assess intersession activation differences for comparison with PP and MP conditions [53,54]. Activation changes across tests for the NP group would imply extraneous effects such as habituation on the BOLD signal. Although the 40 percent

Table 4.
Comparison of number of activated voxels and location of most significant voxel in ROIs that increased or decreased from pretest to posttest for each practice condition and each sequence. We obtained voxel numbers by comparing volume list in SPM to cluster labeling percentages from Automated Anatomical Labeling technique by Tzourio-Mazoyer et al. [Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage. 2002;15:273–89.] Voxel coordinates were obtained from SPM volume list where possible, although in cases where a coordinate was not matched to a region found in cluster label list, coordinates were determined manually.

Practice	ROIs												
Condition	SMA	PM	M1-C	M1-I	S1-C	S1-I	PP	Cer-C	Cer-I	Caud	Put	Thal-C	Thal-I
Control													
A-Inc	0	0	0	0	0	0	0	0	0	0	0	0	0
A-Dec	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Inc	0	0	0	0	0	0	0	0	0	0	0	5	0
												(–12,–20,20) 4.57	
B-Dec	0	0	0	0	0	0	0	0	0	0	0	0	0
Mental													
A-Inc	0	59	10	0	0	0	0	100	25	7	30	0	0
	(–36,26,14) 4.28		(–50,2,38) 3.99					(–8,–60,–10) 4.53	(12,–84,–14) 3.94	(14,4,6) 3.80	(–28,–14,–4) 4.32		
A-Dec	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Inc	0	0	0	0	0	0	0	0	0	0	0	0	0
B-Dec	0	67	0	0	0	9	0	21	76	0	0	0	0
		(–44,18,14) 4.50				(26,–40,40) 4.04		(–8,–72,–34) 3.89	(18,–70,–28) 4.26				
Physical													
A-Inc	2	10	0	0	0	18	0	0	0	138	22	0	7
	(–8,28,50) 4.24	(–12,24,52) 4.24				(56,–12,30) 3.69				(10,18,2) 5.09	(–22,14,4) 3.83		(16,–34,8) 4.03
A-Dec	0	0	0	0	0	0	0	39	10	0	0	0	0
								(–8,–80,–20) 3.89	(26,–78,–28) 4.81				
B-Inc	0	0	0	0	0	0	0	0	0	5	0	0	2
										(–4,16,0) 4.27			(24,–24,2) 3.73
B-Dec	0	0	11	0	0	0	0	0	11	0	0	0	0
			(–52,6,32) 3.86						(28,–74,–26) 4.04				

Caud = caudate
Cer-C = contralateral cerebellum
Cer-I = ipsilateral cerebellum
M1-C = contralateral primary motor area
M1-I = ipsilateral primary motor area
PM = premotor
PP = posterior parietal
Put = putamen
ROIs = regions of interest
SMA = supplementary motor area
SPM = statistical parametric map
S1-C = contralateral primary sensory area
S1-I = ipsilateral primary sensory area
Thal-C = contralateral thalamus
Thal-I = ipsilateral thalamus

increase in completed sequences indicates some learning occurred during the pretest session, activation changes across tests were negligible compared with MP and PP. An overall reduction of cerebral activation observed during the posttest might be attributable to either habituation [54,55], a shift from controlled to automatic processing [56] or selective inhibition of unnecessary muscle activity [57] or all three. The small expansion of SMA and CONTRA-M1/S1 activations suggests that even a brief exposure to the motor task during the pretest session was sufficient to induce some functional plasticity of the sensorimotor system.

Physical Practice Effects on Activation

Altered signal intensity in ROI following PP indicates structures that might mediate motor skill acquisition, providing a baseline comparison for the effectiveness of other practice strategies, such as MP on sensorimotor plasticity.

The ROIs selected for this study include those structures previously identified as being active during sequential motor behavior **(Figure 1**).

Depending on the statistical model, our data showed both increased M1 activation and no change in activation. If the number of activated voxels in an M1 cluster during each test is compared (i.e., extent), greater activity in the CONTRA-M1 cluster occurred during the posttest, confirming Karni et al. and others [43,58,59]. With a week of extensive PP, the sequential task is likely consolidated, with expanded networks controlling motor performance [60].

If differences in signal intensity from pre- to posttest are examined rather than extent during each test (**Figure 3** and **Table 4**), the conclusion is that the change in M1 signal intensity associated with PP was negligible. A methodological constraint might explain the discrepancy in findings between the two statistical models. Because M1 activation is correlated with movement rate [61], consistent signal intensity across tests might be an artifact of constraining movement rate during the test sessions (i.e., 2 Hz). In fact, studies reporting no change in M1 activation also used a constrained movement rate [17,37]. Expanded extent of M1 activation following practice is believed to reflect enhanced movement representation [43,62] and may be a more valid indicator of practice-related effects than differences of signal intensity in suprathreshold voxels when rate is constrained.

M1 output is influenced by widespread cortical and subcortical input; practice-related changes in these secondary structures are expected to accompany M1 plasticity. Following practice, SMA and PMA activations were less extensive than during the pretest, while CONTRA-S1 was strongly activated. The decrease in SMA activation is incompatible with previous sequential motor learning studies [37,38], but might be explained by a design limitation (discussed later). The decrease in PMA, on the other hand, is consistent with Toni et al. [38]. It is possible that as the motor task becomes increasingly automated, the prefrontal loop, including PMA and SMA, becomes less engaged and control is redirected to striatal circuits [63]. While this study did not use a dual task to specifically probe for automatic processing, the extent of practice and level of motor performance during the posttest suggests the task may have become automatic.

Subcortical regions activated during the pretest were bilateral cerebellum and thalamus. Following practice, cerebellar activation decreased bilaterally, although the decrease was greater contralaterally. Bilateral dissociation of practice-related cerebellar plasticity is consistent with prior studies [37,38,63] and implies a shift to IPSI-control of learned movements. Posttest activation was maximal in the IPSI-posterior lobe (declive), which may be part of an internal feedback circuit regulating cortical motor programs [64].

Activation of caudate, putamen, and globus pallidus failed to exceed threshold during either test; however, differences in signal intensity between pre- and posttest did exceed threshold in the caudate and putamen. Both of these structures participate in the control of automated movements, and their increased activation might imply a shift from controlled to automatic processing. Increased putamen activation was seen previously [65,66]; however, the caudate has been shown to be more active during a new task [17,38]. Increased caudate activity here might indicate consolidation of the sequence in memory, because this structure was recently found to participate in motor and nonmotor skill learning [67–69].

The major subcortical inputs to M1 are channeled through the thalamus [64]. Thalamic activation was bilateral during the pretest and CONTRA during the posttest. The reduction in IPSI-activation reflects reduced activation in IPSI-M1 and CONTRA-cerebellum. Maintenance of CONTRA-activation in the ventral posterior lateral nucleus during the posttest is consistent with active cerebrocerebellar networks.

MP Effects on Activation

The main focus of this experiment was to test whether improvements in sequential motor behavior and accompanying changes in cerebral and cerebellar activation are similar following motor imagery-based MP and PP. The analysis of MP-related plasticity, therefore, centered on those sensorimotor structures that were previously reported to be active during episodic motor imagery or that comprise the large-scale cerebral and cerebellar motor network (**Figure 1**).

Beginning with cortical structures, if activation extent (i.e., number of activated voxels) in a ROI during the pre- and posttest is compared, the conclusion is that CONTRA-M1 activation decreases following MP. If signal intensity differences between pre- and posttests are examined instead, the conclusion is that CONTRA-M1 activation increases. At least two explanations exist for these disparate findings. First, while the extent of CONTRA-M1 activation decreases because of increased efficiency in muscle recruitment patterns [70], focal

signal intensity might increase because of expanded small-scale representation of the practiced sequence. A second explanation is that the spatial location of activated voxels during the pretest was more consistent across group members than during the posttest. Accordingly, the locus of CONTRA-M1 activation became more variable across group members because of inconsistent MP strategies (i.e., decreased extent of common activation), while increased signal intensity indicates one focal area where sequence-related activation was consistently enhanced through MP. A critical difference between PP and MP is that while PP is observable and produces error-based feedback, MP is unobservable and produces no perceived feedback. Despite detailed instructions and pretraining, group members may have adopted varying motor control strategies during practice, leading to variations in activated networks. With a conjunction analysis, intersubject variability decreases voxelwise activation intensities and could mask robust changes that are spatially variable.

In contrast to CONTRA-M1, neither did activation of IPSI-M1 exceed threshold on either test nor did activation of any voxels exceed threshold when test differences were examined. Both executed and imagined sequential movements have been shown to activate IPSI-M1 as well as CONTRA-M1 during early learning [71]. When we compared tests in this study, IPSI-M1 activation decreased substantively following both PP and MP, although the amount of reduction is greater following PP. Given that PP also leads to greater improvements in motor behavior than MP, a relationship between motor skill improvement and IPSI-M1 deactivation may exist.

SMA and PMA activations decreased following practice for Sequences A and B. No subregions of SMA were found showing increased or decreased signal intensity; however, signal intensity did increase in a large subregion of the PMA. Bilateral S1 activation also decreased, with the greatest decrease occurring contralaterally. While no published data exist on secondary motor area plasticity and MP, practice of both motor and nonmotor tasks leads to reduced prefrontal activity as performance shifts from controlled to automatic processing [17,37,56]. Reduced prefrontal activation with MP might also reflect a shift from a controlled- to automated-processing mechanism that accompanied PP but not NP.

Changes in cerebellar activation also accompanied MP. Specifically, while the extent of cerebellar activation decreased in both hemispheres with practice, the extent of IPSI-cerebellum was more active both before and after practice. In contrast to decreases in extent, signal intensity of a subregion in both hemispheres increased, with the largest increase in the CONTRA-hemisphere. The increase in CONTRA-cerebellum is inconsistent with PP, suggesting a differential response of the cerebellum to MP and PP conditions. As with PP, however, evidence exists for a bilateral dissociation of cerebellar activation following MP.

Basal ganglia structures were not activated above threshold before or after practice; however, signal intensity increased in striatal circuits, specifically the putamen and caudate. Striatal plasticity is associated with early acquisition of motor skills via PP routines when cognitive and working memory processes mediate motor behavior [37,72]. Striatal circuits may also mediate the learning and memory of stimulus-response "habits" [73] as well as motor procedures [74]. Increased activation of the striatum with MP indicates that motor imagery-based therapeutic interventions may lead to long-term storage of movement sequences prior to PP-based interventions [75].

Experimental Design Limitation

A possible design limitation is that both PP and MP were performed as rapidly as possible during practice, while the task was visually paced at 2 Hz during the test sessions. This design controlled for the potentially confounding interaction of movement rate and learning on the change in BOLD signal intensity [76]; however, the control of rate may have created a secondary confounding effect by varying the spatiotemporal requirements of the task between practice and test conditions. Indeed, the behavioral data show that the posttest performance rates exceeded 5 Hz for the PP group and nearly 4 Hz for the MP group. It is possible the incongruous spatiotemporal requirements of the posttest necessitated an acute change in functional processing to accommodate the slower-paced requirement inside the scanner. The adoption of an incongruous spatiotemporal structure during the posttest may have altered attention or other sensorimotor processing demands during the test, yielding activity that might have confounded chronic practice effects and acute performance effects [63,77]. While no evidence exists to indicate this confounding occurred, a comparison of pre- and posttest activation during maximal task performance rather than at a controlled pace and with rate as a statistical covariate might have produced different results and should be considered as an experimental condition in future skill acquisition and cerebral plasticity experiments.

Motor Imagery-Based MP for Neuromotor Rehabilitation

Altered brain structure and function accompany neurological disease and injury, such as Parkinson's Disease [78], SCI [78], stroke [79], and multiple sclerosis [80], and are both a precursor and sequelae to motor impairment. Jackson et al. recently proposed a model emphasizing the role of MP for the rehabilitation of patients with motor impairments from cerebral injury or disease [81]. This experiment demonstrates the potential efficacy of MP as a therapeutic intervention for targeting activation of cerebral and cerebellar sensorimotor networks damaged by injury or disease or whose structure and function remain sufficiently intact to provide a substrate for compensatory motor control. For example, successful motor recovery following stroke is associated with increased activation of IPSI motor areas as well as premotor and somatosensory areas [82,83]. Activating these structures through MP interventions may be efficacious to complement or precede interventions such as constraint-induced therapy [84].

Three features characterized both PP- and MP-related functional plasticity in this experiment that might be exploited for neuromotor rehabilitation. The first is an expansion/contraction of focal M1/S1 activation that is believed to index changes in movement or limb representation [43,85]. The second is a general reduction in activation extent that may be related to selective inhibition of unnecessary muscular activity [57]. The third is a shift in functional activation loci that may be explained by a transition from controlled to automatic processing structures [56,86]. The value of MP for neuromotor rehabilitation might therefore be as a substitute or complement to PP for targeting activation of compensatory sensorimotor networks to substitute for damaged networks before or during physical rehabilitation.

Neuroimaging for Assessing Efficacy of Therapeutic Interventions

If practice-related changes in sensorimotor activation are found to be reliable and robust, signal intensity and extent in ROIs may provide useful information to quantitatively assess skill acquisition when overt motor behavior cannot be directly measured because of pathology or chronic immobilization [87]. For example, the effectiveness of MP techniques for priming motor systems before physical rehabilitation in patients who cannot move may be difficult to assess without a covert measure of motor function. A predictable change in cerebral processing subsequent to an intervention might provide important information about preparedness for physical rehabilitation. Neuroimaging might also be a useful to assess cerebral sensorimotor processing changes that precede measurable changes in motor function. Future studies using a healthy human model might focus on the dynamic functional changes in cerebral activity that precede or follow observable changes in motor behavior, so the effectiveness of cognitive interventions on improving neuromotor function might be better understood.

CONCLUSION

Motor learning for neuromotor rehabilitation involves a dynamic shift in the magnitude and location of functional activation loci of the sensorimotor system [88]. The shift in activation following PP and MP in this experiment is similar in a subset of sensorimotor structures, while a striking difference in functional plasticity was seen in other regions. Physical practice-related improvements in motor behavior were associated primarily with increases in CONTRA-M1/S1 and striatal activation and decreases in cerebellar activation. MP-related improvements were also associated with increases in CONTRA-M1 and striatal activation, but to a lesser magnitude. The extent of cerebellar activation decreased bilaterally as with PP; however, there was an increase in the magnitude of CONTRA-cerebellum during MP that was not seen following PP. The most striking differences between PP and MP were the extensive changes outside the ROI following MP that were not seen following PP or NP. These effects will be reported elsewhere. While the pattern of functional plasticity is similar following PP in a subset of the sensorimotor structures, clearly, an alternative neuronal substrate exists that is affected by MP and not by PP.

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