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Pilot fMRI investigation of representational plasticity associated with motor skill learning and its functional consequences

Ela B. Plow and

Department of Biomedical Engineering, Lerner Research Institute, Department of Physical Medicine and Rehabilitation, Neurological Institute, Center for Neurological Restoration, Neurological Institute, Cleveland Clinic, 9500 Euclid Avenue, ND20, Cleveland, OH 44195, USA
plowe2@ccf.org

Program in Rehabilitation Science, University of Minnesota, Minneapolis, MN 55455, USA

James R. Carey

Program in Physical Therapy, University of Minnesota, University of Minnesota Medical School, University of Minnesota, 388 MMC, 420 Delaware St SE, Minneapolis, MN 55455, USA

Abstract

Complex skill learning at a joint initiates competition between its representation in the primary motor cortex (M1) and that of the neighboring untrained joint. This process of representational plasticity has been mapped by *cortically-evoking simple movements*. We investigated, following skill learning at a joint, 1) whether comparable processes of representational plasticity are observed when mapping is based on *volitionally produced complex movements* and 2) the consequence on the skill of the adjacent untrained joint. Twenty-four healthy subjects were assigned to either finger- or elbow-skill training or no-training control group. At pretest and posttest, subjects performed complex skill movements at finger, elbow and ankle concurrent with functional magnetic resonance imaging (fMRI) to define learning and allow mapping of corresponding activation-based representations in M1. Skill following both finger- and elbow-training transferred to the ankle (remote joint) ($p=0.05$ and 0.05); however, finger training did not transfer to the elbow and elbow training did not transfer to the finger. Following finger training, location of the trained finger representation showed a trend ($p=0.08$) for medial shift towards the representation of adjacent untrained elbow joint; the change in intensity of the latter representation was associated with elbow skill (Spearman's $\rho=-0.71$, $p=0.07$). Following elbow training, the trained elbow representation and the adjacent untrained finger representation increased their overlap ($p=0.02$), which was associated with finger skill (Spearman's $\rho=-0.83$, $p=0.04$). Thus, our pilot study reveals comparable processes of representational plasticity with fMRI mapping of complex skill movements as have been demonstrated with cortically-evoked methods. Importantly, these processes may limit the degree of transfer of skill between trained and adjacent untrained joints. These pilot findings that await confirmation in large-scale studies have significant implications for neuro-rehabilitation. For instance, techniques, such as motor cortical stimulation, that can potentially modulate processes of representational plasticity between trained and adjacent untrained representations, may optimize transfer of skill.

Keywords

Motor cortex; Learning; Skill; Representation; Plasticity; functional Magnetic Resonance Imaging (fMRI)

Introduction

Primary motor cortex (M1) lies at the epicenter of motor skill learning-based plasticity (Butefisch et al. 2000; Classen et al. 1998; Muellbacher et al. 2002b). Learning novel spatiotemporal features of movement and/or coordinated sequences initiates cortical plasticity/reorganization (Nudo et al. 1996; Plautz et al. 2000; Kleim et al. 1998; Pascual-Leone et al. 1993). The neural networks implicated in such reorganization include representations in M1 (Conner et al. 2003; Monfils et al. 2005). These motor cortical representations possess unique characteristics, such as extensive connectivity (Hess and Donoghue 1994; Huntley and Jones 1991) and flexible organization (Dechent and Frahm 2003; Beisteiner et al. 2001; Schieber 2001), which make them ideal candidates to reorganize with learning.

Numerous studies have illustrated processes of learning-based reorganization. As skill is acquired at a joint, its trained representation in M1 expands at the expense of neighboring representations (Nudo et al. 1996a; Molina-Luna et al. 2008; Kleim et al. 1998), shifts towards, (Pearce et al. 2000; Elbert et al. 1995) or shares with (Hlustik et al. 2001; Tyc et al. 2005) the adjacent untrained representation. Essentially, efficient motor strategy, enhanced input, and acquisition of novel movement sequences create a demand and competition that tips the representational balance in favor of the trained representation (Plautz et al. 2000; Pascual-Leone et al. 1993, 1995). Two important questions, however, linger in regard to learning-based reorganization.

First, the consequences of learning-based competitive reorganization on the skill of the adjacent untrained joints remain unexplored, even though studies have shown a relinquishing of territory from untrained representations to the trained representations. The consequence of such relinquished representation territory becomes critical when considering lesions or disuse, which enhance the potential for reorganization of representations in M1. In stroke (Nudo and Milliken 1996), deafferentation (Sanes et al. 1988; Franchi 2000; Huntley 1997) and amputations (Wu and Kaas 1999), representations of affected joints lose territory to those of adjacent less-affected joints. Contrarily, re-training affected joints rectifies the imbalance through adaptive reorganization (Nudo and Milliken 1996; Nudo et al. 1996b; Liepert et al. 2001). Knowing how learning-induced reorganization affects skill of adjacent untrained joints will help develop novel neuro-rehabilitative interventions that restore representational balance in lesions and disuse.

Second, most studies have defined representations through *simple evoked movements* with intracortical micro-stimulation (ICMS) in animals (Plautz et al. 2000; Nudo et al. 1996a; Kleim et al. 2004; Molina-Luna et al. 2008) or transcranial magnetic stimulation (TMS) in humans (Pascual-Leone et al. 1993, 1995; Tyc et al. 2005; Pearce et al. 2000). However, since *complex volitional movements* recruit more extensive resources (Park et al. 2008; Carey et al. 2006; Gerloff et al. 1998) and their representations are key predictors of skill (Ramanathan et al. 2006), defining volitional maps may reflect learning-based reorganization more accurately. Mapping complex skill movements in healthy subjects would also establish a model that could be applied to study mechanisms underlying skill-based rehabilitation in neurological recovery.

The objectives of the present pilot study were twofold: 1) investigate in healthy subjects the effect of skill learning at a trained joint on the skill of untrained adjacent and remote joints, and 2) examine the associated representational plasticity defined by functional magnetic resonance imaging (fMRI)-based mapping of complex skill movements. Participants were assigned to finger skill training, elbow skill training, or no-training control group. The training involved computer-based visuomotor tracking with the designated joint. Training was founded on principles, such as variability of practice and provision of feedback (Schmidt 2003; Schmidt and Lee 1999), to optimize learning. Overall training duration, i.e. the total number of sessions, for each subject depended upon the time required to achieve criterion level of skill, a strategy shown to be associated with key mechanisms of plasticity (Plautz et al. 2000; Nudo et al. 1996a). At pretest and posttest, subjects were tested on visuomotor tracking for finger, elbow and ankle joints during fMRI scanning. This test determined the effect of learning at the finger or elbow on 1) the skill of adjacent untrained joint and at a remote untrained joint—the ankle, and 2) the fMRI activation-based representations of the adjacent trained and untrained joints and the ankle. Extraneous movements (Liu et al. 2000) and poor reproducibility can confound fMRI activation (Veltman et al. 2000); thus, multiple methodological and analytical controls were instated to ensure validity and reliability of findings. Prior to the pretest and posttest fMRI sessions, we employed surface electromyography (EMG) in mock MRI to ensure that activation associated with one joint was not confounded by contraction of muscles around another. Analyses of reliability investigated whether activation-based representations were reproducible.

Materials and methods

Subjects

Twenty-four healthy volunteers (20 females; 4 males) with a mean ($\pm$ SD) age of 25.7 ($\pm$ 2.9) years were enrolled. All subjects met the inclusion criteria of ages between 21 and 35 years and right handedness (Oldfield 1971). Subjects were excluded if they presented with a neuromuscular or musculo-skeletal condition that affected the arm/hand (verified through medical history), indwelling metal or medical devices incompatible with MRI testing, claustrophobia, or pregnancy. Subjects were assigned randomly to one of three groups: finger skill training group (Finger_{Group}, $n=8$, 1 male), elbow skill training group (Elbow_{Group}, $n=8$, 1 male), or no-training (Control_{Group}, $n=8$, 2 males). The study was approved by the Institutional Review Board of the University of Minnesota. The experiments were undertaken with the understanding and written consent of each subject and the study conformed with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Groups

Subjects in the Finger_{Group} and the Elbow_{Group} were trained on a computer-based visuomotor tracking task involving only the designated joint on the right side for 30 min daily at the same time every day. Tracking required subjects to view a target waveform on a computer screen and spatiotemporally track the cursor along the target using flexion-extension of the designated joint. A custom electrogoniometer fitted with a potentiometer (ETI Systems, Carlsbad, CA) recorded movement of the designated joint. Subjects were seated during training. Because of the difference in mass between the forearm and the finger, all tracking movements were performed with gravity-eliminated support so that extraneous co-contractions could be minimized. For the Elbow_{Group}, the upper arm, flexed to 90° and internally-rotated, rested on a table while subjects flexed and extended their elbow in the transverse plane during tracking. For the Finger_{Group}, the forearm rested on a

table in a pronated position while subjects flexed and extended their index finger at the metacarpophalangeal joint in the frontal plane during tracking.

Each session was composed of 100 total trials, of which 84 involved training on visuomotor tracking, 13 involved rest at specific times, and 3 involved test probes (see description below). The tracking trials varied in waveform (triangle, square, sine, cosine, sawtooth-left, sawtooth-right), amplitude (varying percentages of 90° range of motion set between 0° extension and 90° flexion), waveform frequency (0.2, 0.4, 0.6, 0.8, 1.0 Hz), trial duration (5, 10, 20, 30 s), and stimulus–response (S–R) compatibility. S–R compatibility was occasionally altered by changing the polarity of the potentiometer so that flexion of the joint produced motion of the cursor in the intuitively opposite direction. Variability of these tracking trials afforded complexity to training, an important founding principle of effective motor learning (Carey et al. 2005; Schmidt and Lee 1999). The rest trials (20 s each) were presented after every 6 training trials.

During each session, 3 probe trials were presented as the 7th, 50th and 100th trials. The parameters of these probe trials, i.e. S–R compatible triangle waveform, 60° amplitude, 0.4 Hz frequency and 10-sec duration, were different from any other trial used in training or testing. Accuracy on these probe trials defined the individual learning curve for each subject, ultimately helping determine the overall length/duration of training. When an average 80% criterion level of accuracy (see below) on probe trials was achieved in two consecutive training sessions, training was deemed complete and the participant was scheduled for the posttest. For the Finger_{Group} and the Elbow_{Group}, the elapsed time between pretest and the start of training was 24–48 hrs. The time between the end of training and the posttest was the same.

To facilitate learning, subjects in both training groups, Finger_{Group} and Elbow_{Group}, were given feedback regarding their accuracy and quality of tracking, called the knowledge of results (KR) and knowledge of performance (KP), respectively (Blackwell and Newell 1996; Kohl and Guadagnoli 1996; Schmidt and Lee 1999; Shumway-Cook and Woollacott 2001). KR was delivered in a faded-frequency format (Kohl and Guadagnoli 1996; Anderson et al. 2005), once every two trials initially and once every 30 trials towards the end of training. KP was provided by the investigator on 5 trials per session when it was noted that the subject was lagging or leading the target or was spatially inaccurate. In this case, the investigator manually assisted during practice of the trial.

The Control_{Group} had no training and was instructed to continue with their normal daily routine following the pretest. The elapsed time between pretest and posttest for the Control_{Group} was based upon a matching procedure. Based on sequence of enrollment in the study, we created triads of 3 subjects composed of one subject from each group. The mean time interval that elapsed between pretest and posttest for the members of the two training groups defined the time interval between the pretest and posttest for the subject from the Control_{Group} in the triad.

Pre-screening in mock MRI

Before both pretest and posttest, we conducted prescreening with surface EMG as a methodological control to ensure that fMRI activation-based mapping of representations of complex skill was not confounded by extraneous movements or unnecessary co-contractions. In a mock MRI set-up, we coached subjects to only use muscles at the designated joint while performing the tracking test during fMRI. A 4-channel EMG amplifier (Sierra Wedge, Cadwell, Kennewick, WA; bandwidth 20–2000 Hz, gain 50 μV /division) was used to identify co-contractions of arm and forearm muscles during finger tracking practice and finger and shoulder muscles during elbow tracking practice.

respectively. Self-adhesive electrodes (2.2 cm×2.5 cm) (Cadwell, Kennewick, WA) were attached to the right anterior and middle deltoid, right and left biceps and triceps, first dorsal interosseous and extensor digitorum over different trials. A ground electrode (4.5 cm×3.1 cm) was applied to the dorsum of the right hand. Electrogoniometers were positioned at the right index finger, elbow, and ankle to allow subjects to practice tracking with each of the 3 joints prior to final testing during fMRI. EMG activity from muscles around ankle was not recorded because our main aim was to ensure that contraction of finger muscles did not confound activation during elbow tracking test and vice versa with fMRI testing. Subjects were closely observed, however, and were instructed to only move joints that were designated in specific practice trials.

While lying in the mock scanner, subjects viewed the target waveform (0.4 Hz, 10 s duration, sine waveform, 15–85% of maximum range at joint) on a projection screen through a mirror attached to the artificial head coil. This waveform was different than the trials used in training in the Finger_{Group} and in the Elbow_{Group}. More importantly, this target waveform differed in certain respects from the one used for pretest and posttest during fMRI (details below). In the mock scanner, all subjects practiced finger and ankle tracking in the sagittal plane, and elbow tracking in the frontal plane while EMG activity was monitored. In order to minimize the chances of muscle co-contractions, movements of joints occurred with gravity-eliminated support. Proximal joints were well-supported on foam bolsters. For instance, during index finger tracking, elbow/forearm and wrist rested on a pad, while during elbow tracking, shoulder and upper arm remained supported. Since this was a pre-screening session, the number of tracking trials that the subjects practiced varied (between 2 and 4) based on their ability to minimize co-contractions. Once activity of the extraneous muscles was reduced to an average of less than 50 μ V over 10 s of tracking trial, it was deemed that the muscle was quiescent. Extraneous EMG activity in muscles beyond the designated joint occurred only occasionally, which was eliminated with simple instruction.

Data acquisition

Subjects performed a tracking test in a 3-Tesla MRI scanner (Siemens Trio, Munich, Germany) simultaneous with fMRI scanning. The tracking test was presented as a block design, comprised of 12 tracking trials (4 trials each for finger, elbow and ankle with a duration of 30 s each) alternating with 13 rest trials (duration of 30 s each). The order of presentation of finger, elbow and ankle trials was pseudo-randomized across subjects. The target used for tracking with fMRI scanning included a random sine-waveform that varied in amplitude between 15% and 85% of a 90° range of flexion/extension at the finger and elbow and between 15% and 85% of a 70° range of dorsiflexion/plantarflexion at the ankle. The frequency was 0.4 Hz.

The parameters of the tracking test were consistent across joints but differed from other trials used during training. Although the duration and shape of the waveform of the tracking test used with fMRI in 3 T scanner differed from that used in the mock scanner, their frequency and amplitude were similar. By ensuring that the two tasks differed to some degree, we aimed to reduce the possible confound of practice-related performance effects on learning-related skill change measured simultaneously with fMRI. At the same time, by maintaining some consistency between the two tasks, we are confident that the ability to reduce extraneous muscle activity during tracking in the mock scanner translated to tracking with fMRI in the 3 T scanner.

Electrogoniometers were connected to the right index finger, elbow and ankle, which were connected to three computers (Dell Inc., USA) (60 Hz sampling rate). We monitored the three joints simultaneously using multiple computers to ensure that movements at joints other than the designated joint could be ruled out. For instance, we confirmed that during

finger tracking, elbow and ankle were silent and during ankle tracking, finger and elbow did not move. The tracking waveform was projected on a screen, which the subjects viewed while lying in the scanner through a rearview mirror attached to the head coil. They moved their index finger and ankle in the sagittal plane and elbow in the frontal plane with similar type of gravity-eliminated support for joints as provided in the mock scanner during EMG pre-screening.

Blood Oxygen Level-Dependent (BOLD) fMRI data were collected while subjects performed the tracking test. High-resolution T_2^* -weighted images ($1.5 \times 1.5 \times 1.5 \text{ mm}^3$) were obtained in the transverse plane using a gradient Echo Planar Imaging (EPI) sequence (TE=36 msec, TR=3000 msec, FA=80°, FOV=256 mm×256 mm). Isomorphic 1.5 mm^3 spatial resolution was chosen since it optimally captures task-related activation in M1 (Hyde et al. 2000). Each volume covered a cortical depth of 63 mm in 42 interleaved slices. In total, 300 imaged volumes were collected for a total acquisition time of 15 min. The first 3 volumes were dismissed to account for signal saturation effects. High-resolution (1 mm^3), T_1 -weighted, 3D anatomical images (3D FLASH, TR=20 msec, FA=30°, acquisition time=10:44 min) were acquired over the entire brain to define the template for fMRI analysis.

Data analysis

Skill—Based on performance on the tracking test in the MRI scanner, visuomotor tracking skill for finger, elbow and ankle joints was defined. For each tracking trial included in the tracking test, accuracy was calculated using an accuracy index (AI) (Carey 1990). AI is given by

$$AI = 100 * (P - E) / P$$

where E is the root mean square (rms) error between the target waveform and subject's response, and P is the magnitude of the target waveform, measured as the rms difference between the target waveform and the midline separating the upper and the lower phases of the target waveform. The maximum possible score is 100%. Average AI across 4 tracking trials each for finger, elbow and ankle was computed and termed as AI_{FINGER} , AI_{ELBOW} and AI_{ANKLE} respectively.

fMRI variables—Brain Voyager QX (Brain Innovation B.V., v 2.0, Maastricht, Netherlands) software was used to analyze fMRI data. Data were first preprocessed (corrected for differences in slice scan time acquisition, head motion artifacts and temporal linear trends). Data were not spatially smoothed to permit accurate localization of even the slightest changes in activation. Preprocessed functional data were registered with processed high-resolution T_1 -weighted images (isotropic 1 mm^3 voxels) to identify landmarks. Analysis of functional data were restricted to the region of left M1, which was defined based on anatomical landmarks described previously (Bhatt et al. 2007; Dassonville et al. 2001) and was drawn manually for each individual subject. A trained investigator (E.P.), blinded to group assignments and testing sequence (pretest or posttest), drew these regions.

For each subject, BOLD signal during tracking test was analyzed using a multi-factorial General Linear Model (GLM). Although our main interest was to explore activation related to finger, elbow and ankle tracking trials, head motion-related predictors (x, y, z translation and x, y, z rotations) were added to the model to exclude effect of any movement artifact on the variability of BOLD signal (Lund et al. 2005).

In GLM analysis, statistical contrasts identified voxels within left M1 with significantly higher BOLD signal intensity during finger, elbow and ankle tracking compared to rest. The threshold for significance was set using Bonferroni correction (0.05/total voxels within left M1), which was in the range of 10^{-6} . The minimum cluster size was set to 10 active voxels. Voxels significantly active across 4 tracking trials of finger were called the Finger_{VOLUME} representation; those significantly active during 4 elbow trials were called the Elbow_{VOLUME} representation, and those that were active during 4 ankle trials were defined as the Ankle_{VOLUME} representation. Voxels significantly active during both finger and elbow tracking trials were called the “Overlap” representation (Plow et al. 2010).

FMRI analysis generated the following dependent variables.

Size: To understand whether the size of trained and untrained representations changed with learning, we analyzed the number of active voxels comprising Finger_{VOLUME}, Elbow_{VOLUME} and Ankle_{VOLUME} representations.

% Overlap: We evaluated the percentage of overlap (Plow et al. 2010; Alkadhi et al. 2002; Hlustik et al. 2001, 2004; Kapreli et al. 2007) between Finger_{VOLUME} and Elbow_{VOLUME} representations to understand whether trained representation increased its overlap with the adjacent untrained representation with learning.

$$\% \text{ Overlap} = \frac{(\text{No. of Overlapping Voxels})}{\left[(\text{Finger}_{\text{VOLUME}} + \text{Elbow}_{\text{VOLUME}}) - \text{No. of Overlapping Voxels} \right]} * 100$$

Location: We described the location for each representation (Finger_{VOLUME}, Elbow_{VOLUME}, Ankle_{VOLUME}) using the Talairach x coordinate of the peak of activation (POA) voxel, i.e. the voxel with the highest BOLD signal intensity in the representation. POA has low intrasession and intersession variability (Loubinoux et al. 2001; Waldvogel et al. 2000) and is an important marker for somatotopy and reorganization (Plow et al. 2010). However, since, location of voxel with highest mean BOLD signal amplitude can be influenced by varying confounds, such as change in signal-to-noise ratio, etc., we chose the POA voxel strategically. Within the representation, ten voxels with highest fMRI signal intensity were identified. Mean and standard deviation (SD) of fMRI signal for this cluster was calculated. The voxel with highest intensity was chosen as POA voxel only if its intensity was within a range of mean+2 (SD) of the average intensity of the cluster. Voxels whose intensity was higher than mean+2 (SD) of the intensity of the cluster were discarded and the voxel with the next highest level of intensity that fulfilled criteria for POA was instead chosen. We decided to only analyze the x-dimension of the 3-dimensional POA based on findings from our previous research report (Plow et al. 2010). In that report, we had witnessed that the POAs of the representations of index finger and elbow in M1, when studied using fMRI-based activation, showed difference only along the x-axis. The POA of representation of the index finger was located lateral to that of the elbow. Thus, we expected that the change in POA of trained representations (Finger_{VOLUME} or Elbow_{VOLUME}), following learning, would only be apparent in the x-dimension.

Intensity of activation: Signal intensity is an indicator of local increases in neural activity (Logothetis and Pfeuffer 2004). Percent signal intensity change during a task compared to rest is a reliable measure of activation (Cohen and DuBois 1999). We defined the percent change in BOLD signal intensity for each representation (Finger_{VOLUME}, Elbow_{VOLUME}, Ankle_{VOLUME}) during its corresponding tracking trial versus rest. The formula was given by

$$\% \text{ Signal Intensity} = \frac{(\text{Intensity during Tracking} - \text{Voxels During Rest})}{(\text{Intensity During Rest})} * 100$$

Statistical analysis

Since our functional aim was to evaluate the effect of motor skill training at a joint on the skill of adjacent and remote untrained joints, we compared the 3 groups on AI_{FINGER} , AI_{ELBOW} and AI_{ANKLE} using separate Analyses of Variance (ANOVAs). As the sample sizes were small, we set *a priori* contrasts, without adjusting for multiple comparisons, to compare skill as *direct* effect of training at that joint, *indirect* effect of training at another joint versus no training at all (test-retest effects). Thus, using one-way ANOVAs, contrasts compared at posttest, a) AI_{FINGER} between $\text{Finger}_{\text{Group}}$ vs. $\text{Control}_{\text{Group}}$ (*direct*) as well as $\text{Elbow}_{\text{Group}}$ and $\text{Control}_{\text{Group}}$ (*indirect*), b) AI_{ELBOW} between $\text{Elbow}_{\text{Group}}$ and $\text{Control}_{\text{Group}}$ (*direct*) as well as $\text{Finger}_{\text{Group}}$ vs. $\text{Control}_{\text{Group}}$ (*indirect*), and c) AI_{ANKLE} between $\text{Finger}_{\text{Group}}$ vs. $\text{Control}_{\text{Group}}$ (*indirect*) as well as $\text{Elbow}_{\text{Group}}$ vs. $\text{Control}_{\text{Group}}$ (*indirect*). Post-hoc Least Significant Difference (LSD) tests were used to analyze between-group differences.

The purpose of fMRI analysis was to investigate reorganization of trained and untrained representations in M1. Again, due to small sample sizes, we set *a priori* contrasts, without correcting for multiple comparisons. These included comparing from pretest to posttest the change in a) size and location of POA of $\text{Finger}_{\text{VOLUME}}$ representation as *direct* (in $\text{Finger}_{\text{Group}}$) vs. *indirect* effect (in $\text{Elbow}_{\text{Group}}$) of training vs. test-retest effect (no-training $\text{Control}_{\text{Group}}$), b) size and location of POA of $\text{Elbow}_{\text{VOLUME}}$ representation as a *direct* (in $\text{Elbow}_{\text{Group}}$) vs. *indirect* effect (in $\text{Finger}_{\text{Group}}$) of training vs. test-retest effect (no-training $\text{Control}_{\text{Group}}$), and c) % Overlap as an effect of training ($\text{Finger}_{\text{Group}}$ and $\text{Elbow}_{\text{Group}}$) vs. none ($\text{Control}_{\text{Group}}$). We, thus, compared the three groups on reorganization of $\text{Finger}_{\text{VOLUME}}$ and $\text{Elbow}_{\text{VOLUME}}$ using separate two-way (Group X Test) repeated measures ANOVAs (RMANOVA). Regarding intensity, within-group pair-wise comparisons were conducted separately. Post-hoc LSD analysis compared groups on posttest minus pretest difference.

Further, to understand which specific processes of reorganization were associated with change in skill at the adjacent untrained joint, we conducted correlation analyses. Specifically, in the training groups, association between change in skill at the adjacent untrained joint (AI_{ELBOW} in $\text{Finger}_{\text{Group}}$ and AI_{FINGER} in $\text{Elbow}_{\text{Group}}$) and fMRI variables was explored using 2-tailed tests of significance at $\alpha=0.05$. We considered *p*-values ranging from 0.05 to 0.09 to represent trends towards statistical significance.

Since poor reproducibility of activation-based representations can confound learning-related M1 reorganization, we employed analytical schemes to determine the test-retest reliability of fMRI variables. The following strategies were adopted.

Analyzing voxels commonly active at both tests—Change in location of POA and % signal intensity was studied for voxels commonly active at both pretest and posttest. These voxels, when identified for each representation, $\text{Finger}_{\text{VOLUME}}$, $\text{Elbow}_{\text{VOLUME}}$, and $\text{Ankle}_{\text{VOLUME}}$, were respectively termed, $\text{Finger}_{\text{PREPOST}}$, $\text{Elbow}_{\text{PREPOST}}$, and $\text{Ankle}_{\text{PREPOST}}$. Reorganization of location of POA, and % intensity within $\text{Finger}_{\text{PREPOST}}$, $\text{Elbow}_{\text{PREPOST}}$, and $\text{Ankle}_{\text{PREPOST}}$ was analyzed using pair-wise within-group t-tests; if voxels commonly active at pretest and posttest demonstrated similar changes as their parent representations, we argued, that representational reorganization could be considered valid.

Reliability coefficients of activation—A main method of analysis of test-retest reliability of activations expresses reproducibility as a ratio of the voxel numbers commonly active across both sessions (called Volume_{PREPOST}, see section above, 2-F-a) to the voxels active in either session (Clement and Belleville 2009; Havel et al. 2006; Rombouts et al. 1998). We calculated this ratio for each representation, i.e. Finger_{VOLUME}, Elbow_{VOLUME}, and Ankle_{VOLUME}, in the Control_{Group} using the following formula. Values of reliability coefficient can vary between 0 and 1 (Clement and Belleville 2009).

$$\text{Reliability Coefficient} = \frac{[2 * \text{Volume}_{\text{PREPOST}}]}{[\text{Volume}_{\text{Pretest}} + \text{Volume}_{\text{Posttest}}]}$$

Intraclass Correlation Coefficient (ICC)—One limitation of the reliability coefficient is that it can be influenced by the level of statistical threshold (Havel et al. 2006). To investigate whether the activation defined at pretest was in agreement with that at posttest, two-way random average measure absolute agreement ICC model (Portney and Watkins 2000) was used for the center of mass (COM) location of Finger_{VOLUME}, Elbow_{VOLUME}, and Ankle_{VOLUME} across three groups. COM is defined as the geographic center of all active voxels (Lotze et al. 2000; Plow et al. 2010; Loubinoux et al. 2001; Waldvogel et al. 2000) within a representation. Lack of agreement between COM at pretest and at posttest for a representation, we theorized, would suggest poor repeatability in mapping. Although shift in COM may signify representational plasticity with learning, the training duration in the current study was too short to allow structural synapto-genesis that would underlie gross expansion of representations (Kleim et al. 2004). Thus, we chose COM as a marker of reproducibility rather than plasticity.

Results

The Finger_{Group} achieved the mean criterion AI in (mean±SD) 5.14±1.07 days of training, while the Elbow_{Group} achieved it in 5.14±2.12 days. Accordingly, the yoked subjects in the Control_{Group} were tested on posttest an average of 5.81±2.99 days after the pretest. Finger_{Group} and Elbow_{Group} were analyzed with 7 subjects each because one subject from each group was deemed an outlier (based on AI values that were more than 3 SD below the group mean). The Control_{Group} was analyzed with 8 subjects.

Skill

Between-group differences at pretest were not significant for either AI_{FINGER} (Fig. 1a), AI_{ELBOW} (Fig. 1b) or AI_{ANKLE} (Fig. 1c), indicating equivalence at baseline. At posttest, however, one way ANOVA comparing groups on AI_{FINGER} showed a trend for statistical significance ($F_{2, 21}=3.12$, $p=0.07$); retrospective analysis determined that the overall effect size of difference on the ANOVA was medium (0.49). Post-hoc LSD testing showed that at posttest AI_{FINGER} was higher for the Finger_{Group} than the Control_{Group} ($p=0.02$) (Fig. 1d); differences between Elbow_{Group} and the Control_{Group} however remained non-significant. Similarly, analysis of AI_{ELBOW} between groups demonstrated a weak trend towards significance ($F_{2, 21}=2.62$, $p=0.09$) at posttest, for which the effect size was small-to-medium (0.45). While the difference between the Elbow_{Group} and Control_{Group} was significant ($p=0.03$) (Fig. 1e), that between Finger_{Group} and Control_{Group} was not. Analysis of skill of the remote comparator joint, AI_{ANKLE} revealed findings that contrasted with that for AI_{FINGER} and AI_{ELBOW}. At posttest, one-way ANOVA showed a trend for significant difference between groups ($F_{2, 21}=3.01$, $p=0.07$) with a medium effect of 0.48. Importantly, however, both Finger_{Group} and Elbow_{Group} demonstrated higher AI_{ANKLE} than the Control_{Group} ($p=0.05$ and 0.05 , respectively) (Fig. 1f).

fMRI results

Size—From pretest to posttest, group X test RMANOVA failed to show any main or interaction effects for either representation, Finger_{VOLUME} or Elbow_{VOLUME}, or Ankle_{VOLUME}, across groups. Retrospective power analysis revealed that the statistical power for group X test interaction was inadequate for the size of most representations; while power for comparing Finger_{VOLUME} and Ankle_{VOLUME} was 27.22% and 59.67% respectively, that for investigating Elbow_{VOLUME} change was 74.05%. We deduced that, to obtain 80% power, future studies using a comparable design would require a total of 33 individuals to find significant differences in the size of Elbow_{VOLUME} and as many as 78 to explore changes in Finger_{VOLUME}.

% Overlap—Since at baseline Finger_{Group} had a lower % Overlap compared to the other groups, the pretest value was included as a covariate in the RMANOVA. We found a significant group X test interaction ($F_{2, 15}=7.54$; $p=0.02$). Post hoc LSD analysis revealed that from pretest to posttest the Elbow_{Group} demonstrated an increase in % Overlap, extent of which was significantly greater than the change observed in the Finger_{Group} ($p=0.03$) and showed a trend for being higher than the difference noted in the no-training Control_{Group} ($p=0.08$) (Fig. 2). These differences are also exemplified in representative examples from each group (Fig. 3).

Location—Analysis of location of POA of Finger_{VOLUME} showed a trend for Group X Test interaction ($F_{2, 18}=2.86$; $p=0.08$). Based on post-hoc LSD analysis, we found that the Finger_{Group} showed a medial shift of the POA of its Finger_{VOLUME}; the degree of such shift had a trend for being larger than the shift noted in the Elbow_{Group} ($p=0.06$), while it was significantly greater than the change observed in the no-training Control_{Group} ($p=0.03$) (Fig. 4a). These differences are exemplified in representative examples from each group in Fig. 5. Contrarily, analysis of location of POA of neither Elbow_{VOLUME} nor Ankle_{VOLUME} showed any interaction effect over time. Since we expected a relative change in location of POA of Elbow_{VOLUME} in the Elbow_{Group} across time, we conducted retrospective power analysis. We found that the statistical power to find significant differences between groups, across time, was only 56.34%; future studies, we calculated, would require at least 36 individuals to demonstrate a change in location of POA of Elbow_{VOLUME} following elbow training. Still, the non-significant shifts are plotted in Fig. 4b and c.

Intensity of representations—Pair-wise, within-group comparisons analyzing intensity of the Finger_{VOLUME} representation failed to show any significant change from pretest to posttest for any group [Finger_{Group} ($p=0.33$), Elbow_{Group} ($p=0.13$), Control_{Group} ($p=0.73$)]. Analysis of intensity of the Elbow_{VOLUME} representation, however, demonstrated an increase for the Finger_{Group} and the Elbow_{Group} [$(t_{6, .05}=2.44, p=.05)$ and $(t_{6, .05}=2.24, p=.07)$ respectively] while there was no change for the Control_{Group} ($p=0.98$). Analysis of intensity of Ankle_{VOLUME} representation indicated that Finger_{Group} showed higher intensity ($t_{6, .05}=2.45, p=.05$), while the Elbow_{Group} showed a trend towards increase in intensity from pretest to posttest ($t_{6, .05}=2.24, p=.07$); Control_{Group} did not demonstrate a significant change ($p=0.46$) in intensity of Ankle_{VOLUME}.

Correlation results

In the Finger_{Group}, shift of location of POA of Finger_{VOLUME} representation was associated positively with the change in AI_{ELBOW} ($r=0.75, p=0.05, n=7$) (Fig. 6a). Shift of POA of Finger_{VOLUME}, however, was associated negatively with change in intensity of Elbow_{VOLUME} ($r=-0.65, p=0.05, n=7$) (Fig. 6b), which was negatively associated with change in AI_{ELBOW} (Spearman's Rho= $-0.71, p=0.07, n=7$) (Fig. 6c). We recommend caution in interpreting these findings as the correlation can be easily affected by extreme

values in such a small sample. Although preliminary, the patterns observed in the small groups, such as in the Finger_{Group}, are still significant to generate testable hypotheses for future. Detailed subject-by-subject analysis suggests that the Finger_{Group} subjects, who showed a medial shift in the POA location of their Finger_{VOLUME} (represented by values >0 on the x-axis in Fig. 6a), showed higher gain in AI_{ELBOW}. Instead, those who showed a smaller medial shift or even a lateral shift of the POA (represented by values close to 0 on the x-axis in Fig. 6b) tended to show highest increase in intensity of Elbow_{VOLUME}. Only subjects who experienced smallest gains in intensity of Elbow_{VOLUME} demonstrated highest gains in AI_{ELBOW} (represented by values close to 0 on the x-axis in Fig. 6c). Thus, although the strength of association in 6a and 6b may be limited by small sample size and influence of extreme values, the patterns are informative for the future.

In the Elbow_{Group}, the only process that correlated with skill was the extent of overlap between Finger_{VOLUME} and Elbow_{VOLUME}. The change in % overlap was associated negatively with the change in AI_{FINGER} (Spearman's $Rho = -0.83$, $p = 0.04$, $n = 6$) (Fig. 6d). Five out of six subjects who demonstrated an increase in overlap only experienced minor gain in AI_{FINGER}.

Validity and reliability analysis

- a. In the Finger_{Group}, analysis of Finger_{PREPOST} yielded a trend towards medial shift of the POA ($p = 0.06$), a result that is comparable to that of the parent representation, Finger_{VOLUME}. Similarly, the Elbow_{Group} showed higher intensity of Finger_{PREPOST} ($p = 0.003$) and Elbow_{PREPOST} ($p = 0.037$) representations, analogous to their respective original representations.
- b. Within the Control_{Group}, reliability coefficients for measuring test-retest reliability of Finger_{VOLUME}, Elbow_{VOLUME} and Ankle_{VOLUME} representations were low at a conservative statistical threshold (10^{-6}). These values were 0.18 ± 0.04 , 0.18 ± 0.04 and 0.17 ± 0.07 , respectively.
- c. Across all groups, ICC analysis measuring agreement between COM values for pretest and posttest for Finger_{VOLUME}, Elbow_{VOLUME}, and Ankle_{VOLUME} showed moderate reliability. Average measure ICC values were 0.67 ($p = 0.01$), 0.52 ($p = 0.06$) and 0.62 ($p = 0.007$) respectively.

Discussion

This pilot study shows that skill learning at one joint, whether distal (index finger) or proximal (elbow), transfers to *certain* untrained joints. Untrained joints remote to the trained joint, such as the ankle, received the benefit of skill transfer, whereas untrained joints adjacent to the trained joint, such as the elbow or the finger, did not receive benefit. Using fMRI-based mapping of complex volitional skill, we demonstrate that unique mechanisms of representational plasticity, including competitive interactions between *adjacent* representations of trained and neighboring untrained joints, limit skill transfer between them. These preliminary findings hold implications for designing future neuro-rehabilitative treatments; modulating mechanisms of representational plasticity through behavioral or cortical stimulation techniques may prove to enhance the effectiveness of motor learning-based rehabilitation.

Representational plasticity: relation to skill transfer

The idea that skill transfers following learning at a targeted joint emerged in the fields of kinesiology and physical education. As long as the S-R properties of the task remained the same, the abstract, effector-independent level of skill was believed to generalize to other

joints (Imamizu and Shimojo 1995; van Mier and Petersen 2006; Weigelt et al. 2000). However, the degree of skill transfer may be incomplete due to differences in effector-specific properties of trained and untrained joints (Brashers-Krug et al. 1996; Vangheluwe et al. 2006; Verwey and Wright 2004; Wigmore et al. 2002; Panzer et al. 2006; Bays et al. 2005; Krakauer et al. 1999). This may partially explain the limited transfer between adjacent finger and elbow in the present study. However, since the transfer between trained joint (finger or elbow) and the remote comparator joint, i.e. the ankle, was significant, differences in effector-specific properties alone do not explain the limited transfer of skill between finger and elbow.

Competitive interference in skill exchange between trained and adjacent untrained joints, we believe, can instead be explained by complex processes of representational plasticity. A key innovation of our study lies in the demonstration of such mechanisms using high-resolution fMRI mapping. Following skill training at the finger, the region of peak activity in the trained finger representation came to lie medially towards the adjacent untrained elbow representation. Shift of the region of peak activity was associated with change in intensity of the elbow representation, which was negatively related to the skill at the untrained elbow (Fig. 6a, b, c). Likewise, when skill learning at the elbow was emphasized, the trained elbow and adjacent untrained finger representations enhanced their overlap, a process that was negatively associated with gain in skill at the untrained index finger (Fig. 6d). These preliminary results suggest that mechanisms of representational plasticity may limit transfer of skill from trained to adjacent untrained joints.

The demonstration of representational plasticity in the current study is in agreement with conclusions drawn in the previous literature; complex skill acquisition creates demand and competition for cortical resources that shapes the dynamic constructs of trained and adjacent untrained representations (Pascual-Leone et al. 1993, 1995; Xerri et al. 1996). Processes of representational plasticity witnessed in our study using mapping of complex volitional skill validate findings from both motor and somatosensory studies involving evoked mapping (Kleim et al. 1998; Nudo et al. 1996a; Plautz et al. 2000; Elbert et al. 1995; Pascual-Leone et al. 1993, 1995; Jenkins et al. 1990; Coq and Xerri 1998; Xerri et al. 1996). However, our study, to the best of our knowledge, represents an elemental attempt relating representational plasticity to the consequence on skill of the adjacent untrained joints.

An important caveat nevertheless requires further consideration. Mechanisms of representational plasticity manifest differently with training of different joints. While learning at the finger initiated a shift in the region of peak activity in the direction of the neighboring untrained elbow representation, learning at the elbow was accompanied by greater overlap between trained and adjacent untrained representations. These characteristically distinct findings, revealed by training two different within-limb joints, are supported by two seemingly different viewpoints on process of representational plasticity. Whereas the predominant view discusses that acquiring novel skills tips the balance between adjacent representations to favor the trained joint (Kleim et al. 1998; Nudo et al. 1996a; Plautz et al. 2000; Elbert et al. 1995; Pascual-Leone et al. 1993, 1995; Jenkins et al. 1990; Coq and Xerri 1998; Xerri et al. 1996), a differing view argues that adjacent representations increase their overlap following training at a segment (Kossut and Siucinska 1998; Hlustik et al. 2004). By training two different joints, we have witnessed both patterns of representational plasticity; while skill training of the index finger demonstrated cortical mechanisms supporting the former view, training of elbow was accompanied by processes that are in line with the latter view. Distinct mechanisms of plasticity are potentially related to neurophysiologic reasons. Since proximal segments, such as elbow/forearm, receive fewer (Jankowska et al. 1975; Wassermann et al. 1992) and weaker corticomotorneuronal projections (McKiernan et al. 1998) and have smaller representations (Luft et al. 2002)

compared to the distal joints, training of elbow joint may require greater sharing with its well-endowed neighboring representation, the index finger. By testing representational plasticity at two levels- learning at a distal joint and a proximal joint, the current pilot exploratory study harmonizes the varied views of representational plasticity as it demonstrates that they have similar impact on transfer of skill.

Functional significance of representational plasticity for rehabilitation

To analyze the significance of our elemental findings for neurorehabilitation, we borrow concepts from empirical (Ziemann et al. 2002; Bjorkman et al. 2004, 2009) and clinical (Rosen et al. 2006; Lundborg and Rosen 2007; Muellbacher et al. 2002a) models involving de-afferentation and de-efferentation. Virtual or actual lesions, such as de-afferentation and de-efferentation, initiate cortical disinhibition. In a disinhibited state, competitive interactions between adjacent M1 representations are unmasked. For instance, during experimental de-afferentation (Ziemann et al. 1998), increasing activity of the hand representation (using repetitive TMS, rTMS) leads to inhibition of activity of the adjacent elbow representation. This competitive, activity-driven phenomenon is termed across-representational plasticity that manifests only between adjacent M1 representations, such as hand and elbow/arm (Ziemann et al. 2002).

Our model of complex motor skill learning may have similarly initiated across-representational plasticity. Learning creates a disinhibited, plastic cortical state (Monfils and Teskey 2004; Rioult-Pedotti et al. 1998; Hess and Donoghue 1994) through release of GABA-related inhibition (Ziemann et al. 2001; Floyer-Lea et al. 2006; Stagg et al. 2011; Butefisch et al. 2000) and activation of NMDA receptors (Butefisch et al. 2000). Within such a dynamic environment, shifts in peak activity of adjacent representations (Ziemann et al. 2002; Bjorkman et al. 2009), as signified by medial shift in the finger training group and higher overlap in the elbow training group, in the present study, mark across-representational plasticity. Therefore, our study is innovative because it illustrates that learning initiates comparable markers of across-representational plasticity as have been classically emphasized in lesions and disuse.

Importantly, our pilot study demonstrates the relationship between learning-based across-representational plasticity and skill, thereby suggesting that modulating representational plasticity carries therapeutic relevance. Through behavioral, pharmacologic and/or motor cortical manipulations, representational plasticity can potentially be modulated to optimize acquisition of skill across joints. For instance, altering representational balance using techniques, such as rTMS, in conjunction with skill acquisition at affected regions, in peripheral nerve injuries or stroke, may augment efficacy of rehabilitation. Along similar lines, pharmacologic manipulations that oppose maladaptive representational plasticity could enhance responsiveness to rehabilitation. Once confirmed in large-scale studies in the future, these foundational findings will guide novel applications in neuro-rehabilitation.

Plasticity versus reproducibility

Low validity and reproducibility of fMRI activation from one session to another though (Veltman et al. 2000; Liu et al. 2000; Kimberley et al. 2008) can seemingly diminish the confidence that can be placed upon findings of plasticity. Therefore, we adopted methodological controls to monitor the influence of confounds on the significance of our results. By using offline surface EMG in a mock-scanner and online multi-joint monitoring in the real scanner, we attempted to mitigate the effects of muscle co-contractions that could affect the ability to accurately map complex movement-based representations. Since subjects learned to only move muscles around designated joints after brief instruction in the mock

scanner, we believe that extraneous muscle contractions only minimally affected activation-based representations derived from in-scanner experiments.

Next, varying forms of reliability and validity analyses were utilized. Within subset of voxels that were commonly active at pretest and at posttest, we witnessed comparable changes in location of peak and level of intensity as in the parent representations. This finding validates that observed changes in trained and adjacent untrained representations signified representational plasticity, rather than confounds of reproducibility.

Further, the agreement between the geographic centers of representations from pretest to posttest, measured using ICC, was moderate yet significant. Values of ICC are moderate in especially those studies that employ complex tasks versus simple automatic motor tasks because former paradigms generate higher activation compared to the latter (Lee et al. 2010). Nevertheless, ICC greater than 0.5 is considered acceptable in fMRI studies (Manoach et al. 2001; Kimberley et al. 2008). ICC values in our study crossed this criterion.

The between-session reliability coefficient, however, was lower than in other studies (Clement and Belleville 2009; Havel et al. 2006). The dissociation between ICC and reliability coefficient emerges from the nature of their calculation (Lee et al. 2010; Havel et al. 2006; Clement and Belleville 2009). Poor activators show high session-to-session ICC but their activation is too low to cross statistical threshold to be included in the calculation of reliability coefficient (Lee et al. 2010), whereas good-activators show low ICC while demonstrating high activation that inflates the reliability coefficient. As statistical thresholds are made stricter, reliability coefficients reduce (Havel et al. 2006). Since we utilized a complex task with stringent statistical threshold and still demonstrated acceptable ICCs, we believe that the reliability of activation-based representations was reasonable.

Strengths and future directions

Several follow-up questions linger that could inform the design of future studies. Findings of the present study can be further validated using a double-dissociation design; incorporating learning at ankle joint could help validate processes noted with upper limb training. Future investigations also can potentially address an important factor that seemingly differs between our study and previous reports of learning-related plasticity. We failed to witness a relative change in size of trained versus adjacent untrained representation as shown previously (Nudo et al. 1996a; Plautz et al. 2000; Kleim et al. 1998; Pascual-Leone et al. 1993, 1995). Perhaps, the average training duration was too short (5 days). Kleim et al. discuss that changes in sizes of representations only occur in late phases of skill learning (Kleim et al. 2004). Similarly, in humans, relative gain in size of trained versus adjacent untrained representations occurs after extensive years of skill learning (Pascual-Leone et al. 1993, 1995; Elbert et al. 1995). Therefore, we might have only witnessed early reorganization of M1 representations. Setting higher criterion skill and serial fMRI measurements could help address stages of representational plasticity. Last, a potential, yet important, confound that could affect the interpretation of our results is the small-scale nature of the study; since 22 subjects, assigned to 3 separate groups, were tested on 2 measurements, we acknowledge that the study may not have been adequately powered to reveal statistically-significant behavioral skill transfer or underlying representational plasticity, rather only trends. Unequal distribution of males versus females across the study may have further confounded the pilot findings since males show higher tracking accuracy (Carey et al. 1994). Nevertheless, the pilot and exploratory nature of the present results can guide the design of future large-scale studies and estimate optimal sample sizes.

We contend that despite its pilot exploratory nature, our study contributes significantly to the fields of motor learning, neuroscience and neuro-rehabilitation. Our primary contribution

is the development of a model of complex voluntary skill that could be uniformly applied across joints to define their respective fMRI activation-based representations. Simultaneous with fMRI, our model of mapping complex movements would be more accurately reflective of skill than mapping based on electrically-evoked simple movements (Plautz et al. 2000; Nudo et al. 1996a; Kleim et al. 1998; Pascual-Leone et al. 1995; Elbert et al. 1995; Tyc et al. 2005). Second, compared to classical studies, we discuss comprehensive markers of representational changes, including location of peak activity, size, overlap and intensity of activation that could guide data analysis for future. Third, we employed extensive methodologic and analytical controls that could be customized to suit specific designs in future studies to validate fMRI-based mapping. Fourth, through planned behavioral controls, including comparator joint and comparative no-training control group, we defined the degree to which skill learning at joint transfers to remote versus adjacent joints, which can inform study design on a large scale. More importantly, we defined cortical markers signifying transfer of skill, which could generate ideas for future involving modulation of plasticity to optimize learning.

Conclusions

Thus, using fMRI-based mapping of complex skill, we defined the proof-of-concept of comparable processes of learning-related representational plasticity as witnessed previously with evoked movement-based mapping (ICMS and TMS), a finding that warrants confirmation in larger-scale studies. Using various methodological and analytical strategies, we note acceptable reliability in mapping fMRI-based representations of complex skill movements; the present paradigm may offer unique perspective in understanding motor cortical mechanisms underlying learning-based rehabilitation. Further, by employing stringent behavioral controls, we preliminarily suggest that these mechanisms signify incomplete skill transfer for adjacent untrained joints. Ultimately, by modulating mechanisms of representational plasticity witnessed here, through behavioral, pharmacologic and/or cortical neuromodulatory techniques, greater adaptive functional gains can be achieved in rehabilitation.

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Abbreviations

M1	Primary Motor Cortex
ICMS	Intra Cortical Micro Stimulation
TMS	Transcranial Magnetic Stimulation
KR	Knowledge of Results
KP	Knowledge of Performance
S-R	Stimulus–Response
Finger_{Group}	Finger Tracking Training Group

Elbow_{Group}	Elbow Tracking Training Group
Control_{Group}	No Training Control Group
EMG	Electromyography
MRI	Magnetic Resonance Imaging
fMRI	Functional Magnetic Resonance Imaging
BOLD	Blood Oxygen Level-Dependent
EPI	Echo Planar Imaging
TE	Echo Time
TR	Repetition Time
FA	Flip Angle
FOV	Field of View
AI	Accuracy Index
AI_{FINGER}	Average Accuracy Index for 4 finger tracking trials during tracking test
AI_{ELBOW}	Average Accuracy Index for 4 elbow tracking trials during tracking test
AI_{ANKLE}	Average Accuracy Index for 4 ankle tracking trials during tracking test
GLM	General Linear Model
Finger_{VOLUME}	Finger representation, defined by voxels significantly active during finger tracking trials with fMRI
Elbow_{VOLUME}	Elbow representation, defined by voxels significantly active during elbow tracking trials with fMRI
Ankle_{VOLUME}	Ankle representation, defined by voxels significantly active during ankle tracking trials with fMRI
POA	Peak of Activation
Finger_{PREPOST}	Voxels within finger representation that are commonly active at pretest and posttest
Elbow_{PREPOST}	Voxels within elbow representation that are commonly active at pretest and posttest
Ankle_{PREPOST}	Voxels within ankle representation that are commonly active at pretest and posttest
ICC	Intraclass Correlation Coefficient
COM	Center of Mass

References

- Alkadhi H, Crelrier GR, Boendermaker SH, Golay X, Hepp-Reymond MC, Kollias SS. Reproducibility of primary motor cortex somatotopy under controlled conditions. *AJNR. American Journal of Neuroradiology*. 2002; 23(9):1524–1532. [PubMed: 12372742]
- Anderson DI, Magill RA, Sekiya H, Ryan G. Support for an explanation of the guidance effect in motor skill learning. *Journal of Motor Behavior*. 2005; 37(3):231–238. [PubMed: 15883120]
- Bays PM, Flanagan JR, Wolpert DM. Interference between velocity-dependent and position-dependent force-fields indicates that tasks depending on different kinematic parameters compete for motor working memory. *Experimental Brain Research*. 2005; 163(3):400–405.

- Beisteiner R, Windischberger C, Lanzenberger R, Edward V, Cunnington R, Erdler M, et al. Finger somatotopy in human motor cortex. *NeuroImage*. 2001; 13(6 Pt 1):1016–1026. [PubMed: 11352607]
- Bhatt E, Nagpal A, Greer KH, Grunewald TK, Steele JL, Wiemiller JW, et al. Effect of finger tracking combined with electrical stimulation on brain reorganization and hand function in subjects with stroke. *Experimental Brain Research*. 2007; 182(4):435–447.
- Bjorkman A, Rosen B, Lundborg G. Acute improvement of hand sensibility after selective ipsilateral cutaneous forearm anaesthesia. *European Journal of Neuroscience*. 2004; 20(10):2733–2736. [PubMed: 15548216]
- Bjorkman A, Weibull A, Rosen B, Svensson J, Lundborg G. Rapid cortical reorganisation and improved sensitivity of the hand following cutaneous anaesthesia of the forearm. *European Journal of Neuroscience*. 2009; 29(4):837–844. doi:10.1111/j.1460-9568.2009.06629.x. [PubMed: 19250441]
- Blackwell JR, Newell KM. The informational role of knowledge of results in motor learning. *Acta Psychologica*. 1996; 92(2):119–129. [PubMed: 8712035]
- Brashers-Krug T, Shadmehr R, Bizzi E. Consolidation in human motor memory. *Nature*. 1996; 382(6588):252–255. [PubMed: 8717039]
- Butefisch CM, Davis BC, Wise SP, Sawaki L, Kopylev L, Classen J, et al. Mechanisms of use-dependent plasticity in the human motor cortex. *Proceedings of the National Academy of Sciences of the United States of America*. 2000; 97(7):3661–3665. [PubMed: 10716702]
- Carey JR. Manual stretch: effect on finger movement control and force control in stroke subjects with spastic extrinsic finger flexor muscles. *Archives of Physical Medicine and Rehabilitation*. 1990; 71(11):888–894. [PubMed: 2222157]
- Carey JR, Bogard CL, King BA, Suman VJ. Finger-movement tracking scores in healthy subjects. *Perceptual and Motor Skills*. 1994; 79(1 Pt 2):563–576. [PubMed: 7808897]
- Carey JR, Bhatt E, Nagpal A. Neuroplasticity promoted by task complexity. *Exercise and Sport Sciences Reviews*. 2005; 33(1):24–31. [PubMed: 15640717]
- Carey JR, Greer KR, Grunewald TK, Steele JL, Wiemiller JW, Bhatt E, et al. Primary motor area activation during precision-demanding versus simple finger movement. *Neurorehabilitation and Neural Repair*. 2006; 20(3):361–370. [PubMed: 16885422]
- Classen J, Liepert J, Wise SP, Hallett M, Cohen LG. Rapid plasticity of human cortical movement representation induced by practice. *Journal of Neurophysiology*. 1998; 79(2):1117–1123. [PubMed: 9463469]
- Clement F, Belleville S. Test-retest reliability of fMRI verbal episodic memory paradigms in healthy older adults and in persons with mild cognitive impairment. *Human Brain Mapping*. 2009; 30(12):4033–4047. doi:10.1002/hbm.20827. [PubMed: 19492301]
- Cohen MS, DuBois RM. Stability, repeatability, and the expression of signal magnitude in functional magnetic resonance imaging. *Journal of Magnetic Resonance Imaging*. 1999; 10(1):33–40. [PubMed: 10398975]
- Conner JM, Culbertson A, Packowski C, Chiba AA, Tuszynski MH. Lesions of the Basal forebrain cholinergic system impair task acquisition and abolish cortical plasticity associated with motor skill learning. *Neuron*. 2003; 38(5):819–829. doi:S0896627303002885[pil]. [PubMed: 12797965]
- Coq JO, Xerri C. Environmental enrichment alters organizational features of the forepaw representation in the primary somatosensory cortex of adult rats. *Experimental Brain Research*. 1998; 121(2):191–204.
- Dassonville P, Lewis SM, Zhu XH, Ugurbil K, Kim SG, Ashe J. The effect of stimulus–response compatibility on cortical motor activation. *NeuroImage*. 2001; 13(1):1–14. [PubMed: 11133304]
- Dechent P, Frahm J. Functional somatotopy of finger representations in human primary motor cortex. *Human Brain Mapping*. 2003; 18(4):272–283. [PubMed: 12632465]
- Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. Increased cortical representation of the fingers of the left hand in string players. *Science*. 1995; 270(5234):305–307. [PubMed: 7569982]
- Floyer-Lea A, Wylezinska M, Kincses T, Matthews PM. Rapid modulation of GABA concentration in human sensorimotor cortex during motor learning. *Journal of Neurophysiology*. 2006; 95(3):1639–1644. doi:10.1152/jn.00346.2005. [PubMed: 16221751]

- Franchi G. Reorganization of vibrissal motor representation following severing and repair of the facial nerve in adult rats. *Experimental Brain Research*. 2000; 131(1):33–43.
- Gerloff C, Corwell B, Chen R, Hallett M, Cohen LG. The role of the human motor cortex in the control of complex and simple finger movement sequences. *Brain*. 1998; 121(Pt 9):1695–1709. [PubMed: 9762958]
- Havel P, Braun B, Rau S, Tonn JC, Fesl G, Bruckmann H, et al. Reproducibility of activation in four motor paradigms. An fMRI study. *Journal of Neurology*. 2006; 253(4):471–476. doi:10.1007/s00415-005-0028-4. [PubMed: 16283098]
- Hess G, Donoghue JP. Long-term potentiation of horizontal connections provides a mechanism to reorganize cortical motor maps. *Journal of Neurophysiology*. 1994; 71(6):2543–2547. [PubMed: 7931533]
- Hlustik P, Solodkin A, Gullapalli RP, Noll DC, Small SL. Somatotopy in human primary motor and somatosensory hand representations revisited. *Cerebral Cortex*. 2001; 11(4):312–321. [PubMed: 11278194]
- Hlustik P, Solodkin A, Noll DC, Small SL. Cortical plasticity during three-week motor skill learning. *Journal of Clinical Neurophysiology*. 2004; 21(3):180–191. [PubMed: 15375348]
- Huntley GW. Correlation between patterns of horizontal connectivity and the extend of short-term representational plasticity in rat motor cortex. *Cerebral Cortex*. 1997; 7(2):143–156. [PubMed: 9087822]
- Huntley GW, Jones EG. Relationship of intrinsic connections to forelimb movement representations in monkey motor cortex: a correlative anatomic and physiological study. *Journal of Neurophysiology*. 1991; 66(2):390–413. [PubMed: 1723093]
- Hyde JS, Biswal BB, Jesmanowicz A. Optimum voxel size in fMRI. *Proceedings of the International Society for Magnetic Resonance in Medicine*. 2000; 8:240.
- Imamizu H, Shimojo S. The locus of visual-motor learning at the task or manipulator level: implications from intermanual transfer. *Journal of Experimental Psychology. Human Perception and Performance*. 1995; 21(4):719–733. [PubMed: 7643045]
- Jankowska E, Padel Y, Tanaka R. Projections of pyramidal tract cells to alpha-motoneurons innervating hind-limb muscles in the monkey. *The Journal of Physiology*. 1975; 249(3):637–667. [PubMed: 1177109]
- Jenkins WM, Merzenich MM, Ochs MT, Allard T, Guic-Robles E. Functional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulation. *Journal of Neurophysiology*. 1990; 63(1):82–104. [PubMed: 2299388]
- Kapreli E, Athanasopoulos S, Papathanasiou M, Van Hecke P, Keleki D, Peeters R, et al. Lower limb sensorimotor network: issues of somatotopy and overlap. *Cortex*. 2007; 43(2):219–232. [PubMed: 17405668]
- Kimberley TJ, Birkholz DD, Hancock RA, VonBank SM, Werth TN. Reliability of fMRI during a continuous motor task: assessment of analysis techniques. *Journal of Neuro-imaging*. 2008; 18(1): 18–27. doi:10.1111/j.1552-6569.2007.00163.x.
- Kleim JA, Barbay S, Nudo RJ. Functional reorganization of the rat motor cortex following motor skill learning. *Journal of Neurophysiology*. 1998; 80(6):3321–3325. [PubMed: 9862925]
- Kleim JA, Hogg TM, VandenBerg PM, Cooper NR, Bruneau R, Remple M. Cortical synaptogenesis and motor map reorganization occur during late, but not early, phase of motor skill learning. *Journal of Neuroscience*. 2004; 24(3):628–633. doi:10.1523/JNEUROSCI.3440-03.2004. [PubMed: 14736848]
- Kohl RM, Guadagnoli MA. The scheduling of knowledge of results. *Journal of Motor Behavior*. 1996; 28(3)
- Kossut M, Siucinska E. Learning-induced expansion of cortical maps—what happens to adjacent cortical representations? *Neuroreport*. 1998; 9(18):4025–4028. [PubMed: 9926841]
- Krakauer JW, Ghilardi MF, Ghez C. Independent learning of internal models for kinematic and dynamic control of reaching. *Nature Neuroscience*. 1999; 2(11):1026–1031.
- Lee JN, Hsu EW, Rashkin E, Thatcher JW, Kreitschitz S, Gale P, et al. Reliability of fMRI motor tasks in structures of the corticostriatal circuitry: implications for future studies and circuit function.

- NeuroImage. 2010; 49(2):1282–1288. doi:10.1016/j.neuroimage.2009.09.072. [PubMed: 19818409]
- Liepert J, Uhde I, Graf S, Leidner O, Weiller C. Motor cortex plasticity during forced-use therapy in stroke patients: a preliminary study. *Journal of Neurology*. 2001; 248(4):315–321. [PubMed: 11374097]
- Liu JZ, Dai TH, Elster TH, Sahgal V, Brown RW, Yue GH. Simultaneous measurement of human joint force, surface electromyograms, and functional MRI-measured brain activation. *Journal of Neuroscience Methods*. 2000; 101(1):49–57. [PubMed: 10967361]
- Logothetis NK, Pfeuffer J. On the nature of the bold fmri contrast mechanism. *Magnetic Resonance Imaging*. 2004; 22(10):1517–1531. [PubMed: 15707801]
- Lotze M, Erb M, Flor H, Huelsmann E, Godde B, Grodd W. fMRI evaluation of somatotopic representation in human primary motor cortex. *NeuroImage*. 2000; 11(5 Pt 1):473–481. [PubMed: 10806033]
- Loubinoux I, Carel C, Alary F, Boulanouar K, Viallard G, Manelfe C, et al. Within-session and between-session reproducibility of cerebral sensorimotor activation: a test–retest effect evidenced with functional magnetic resonance imaging. *Journal of Cerebral Blood Flow and Metabolism*. 2001; 21(5):592–607. [PubMed: 11333370]
- Luft AR, Smith GV, Forrester L, Whittall J, Macko RF, Hauser TK, et al. Comparing brain activation associated with isolated upper and lower limb movement across corresponding joints. *Human Brain Mapping*. 2002; 17(2):131–140. [PubMed: 12353246]
- Lund TE, Norgaard MD, Rostrup E, Rowe JB, Paulson OB. Motion or activity: their role in intra- and inter-subject variation in fMRI. *NeuroImage*. 2005; 26(3):960–964. [PubMed: 15955506]
- Lundborg G, Rosen B. Hand function after nerve repair. *Acta Physiologica*. 2007; 189:207–217. [PubMed: 17250571]
- Manoach DS, Halpern EF, Kramer TS, Chang Y, Goff DC, Rauch SL, et al. Test-retest reliability of a functional MRI working memory paradigm in normal and schizophrenic subjects. *The American Journal of Psychiatry*. 2001; 158(6):955–958. [PubMed: 11384907]
- McKiernan BJ, Marcario JK, Karrer JH, Cheney PD. Corticomotoneuronal postspike effects in shoulder, elbow, wrist, digit, and intrinsic hand muscles during a reach and pre-hension task. *Journal of Neurophysiology*. 1998; 80(4):1961–1980. [PubMed: 9772253]
- Molina-Luna K, Hertler B, Buitrago MM, Luft AR. Motor learning transiently changes cortical somatotopy. *Neuro-Image*. 2008; 40(4):1748–1754. doi:10.1016/j.neuroimage.2007.11.018. [PubMed: 18329289]
- Monfils MH, Teskey GC. Skilled-learning-induced potentiation in rat sensorimotor cortex: a transient form of behavioural long-term potentiation. *Neuroscience*. 2004; 125(2):329–336. doi:10.1016/j.neuroscience.2004.01.048. [PubMed: 15062976]
- Monfils MH, Plautz EJ, Kleim JA. In search of the motor engram: motor map plasticity as a mechanism for encoding motor experience. *The Neuroscientist*. 2005; 11(5):471–483. doi: 10.1177/1073858405278015. [PubMed: 16151047]
- Muellbacher W, Richards C, Ziemann U, Wittenberg G, Weltz D, Boroojerdi B, et al. Improving hand function in chronic stroke. *Archives of Neurology*. 2002; 59(8):1278–1282. [PubMed: 12164724]
- Muellbacher W, Ziemann U, Wissel J, Dang N, Kofler M, Facchini S, et al. Early consolidation in human primary motor cortex. *Nature*. 2002; 415(6872):640–644. [PubMed: 11807497]
- Nudo RJ, Milliken GW. Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. *Journal of Neurophysiology*. 1996; 75(5):2144–2149. [PubMed: 8734610]
- Nudo RJ, Milliken GW, Jenkins WM, Merzenich MM. Use-dependent alterations of movement representations in primary motor cortex of adult squirrel monkeys. *Journal of Neuroscience*. 1996; 16(2):785–807. [PubMed: 8551360]
- Nudo RJ, Wise BM, SiFuentes F, Milliken GW. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. *Science*. 1996; 272(5269):1791–1794. [PubMed: 8650578]
- Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*. 1971; 9(1):97–113. [PubMed: 5146491]

- Panzer S, Wilde H, Shea CH. Learning of similar complex movement sequences: proactive and retroactive effects on learning. *Journal of Motor Behavior*. 2006; 38(1):60–70. [PubMed: 16436363]
- Park JW, Kwon YH, Lee MY, Bai D, Nam KS, Cho YW, et al. Brain activation pattern according to exercise complexity: a functional MRI study. *NeuroRehabilitation*. 2008; 23(3):283–288. [PubMed: 18560146]
- Pascual-Leone A, Cammarota A, Wassermann EM, Brasil-Neto JP, Cohen LG, Hallett M. Modulation of motor cortical outputs to the reading hand of braille readers. *Annals of Neurology*. 1993; 34(1): 33–37. [PubMed: 8517678]
- Pascual-Leone A, Nguyet D, Cohen LG, Brasil-Neto JP, Cammarota A, Hallett M. Modulation of muscle responses evoked by transcranial magnetic stimulation during the acquisition of new fine motor skills. *Journal of Neurophysiology*. 1995; 74(3):1037–1045. [PubMed: 7500130]
- Pearce AJ, Thickbroom GW, Byrnes ML, Mastaglia FL. Functional reorganisation of the corticomotor projection to the hand in skilled racquet players. *Experimental Brain Research*. 2000; 130(2):238–243.
- Plautz EJ, Milliken GW, Nudo RJ. Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use versus learning. *Neurobiology of Learning and Memory*. 2000; 74(1):27–55. [PubMed: 10873519]
- Plow EB, Arora P, Pline MA, Binstock MT, Carey JR. Within-limb somatotopy in primary motor cortex-revealed using fMRI. *Cortex*. 2010; 46(3):310–321. doi:10.1016/j.cortex. 2009.02.024. [PubMed: 19446804]
- Portney LG, Watkins MP. *Foundations of clinical research: Applications to practice* (2nd ed.). 2000
- Ramanathan D, Conner JM, Tuszynski MH. A form of motor cortical plasticity that correlates with recovery of function after brain injury. *Proceedings of the National Academy of Sciences of the United States of America*. 2006; 103(30):11370–11375. doi:10.1073/pnas.0601065103. [PubMed: 16837575]
- Rioult-Pedotti MS, Friedman D, Hess G, Donoghue JP. Strengthening of horizontal cortical connections following skill learning. *Nature Neuroscience*. 1998; 1(3):230–234. doi:10.1038/678.
- Rombouts SA, Barkhof F, Hoogenraad FG, Sprenger M, Scheltens P. Within-subject reproducibility of visual activation patterns with functional magnetic resonance imaging using multislice echo planar imaging. *Magnetic Resonance Imaging*. 1998; 16(2):105–113. doi:10.1016/S0730-725X(97)00253-1. [PubMed: 9508267]
- Rosen B, Bjorkman A, Lundborg G. Improved sensory relearning after nerve repair induced by selective temporary anaesthesia - a new concept in hand rehabilitation. *J Hand Surg [Br]*. 2006; 31(2):126–132.
- Sanes JN, Suner S, Lando JF, Donoghue JP. Rapid reorganization of adult rat motor cortex somatic representation patterns after motor nerve injury. *Proceedings of the National Academy of Sciences of the United States of America*. 1988; 85(6):2003–2007. [PubMed: 3162322]
- Schieber MH. Constraints on somatotopic organization in the primary motor cortex. *Journal of Neurophysiology*. 2001; 86(5):2125–2143. [PubMed: 11698506]
- Schmidt RA. Motor schema theory after 27 years: reflections and implications for a new theory. *Research Quarterly for Exercise and Sport*. 2003; 74(4):366–375. [PubMed: 14768837]
- Schmidt, RA.; Lee, TD. *Motor control and learning: A behavioral emphasis*. Human Kinetics; Champaign: 1999.
- Shumway-Cook, A.; Woollacott, MH. *Motor control: Theory and practical applications*. 2nd ed.. Lippincott Williams and Wilkins; Baltimore: 2001.
- Stagg CJ, Bachtar V, Johansen-Berg H. The role of GABA in human motor learning. *Current Biology*. 2011; 21(6):480–484. doi:10.1016/j.cub.2011.01.069. [PubMed: 21376596]
- Tyc F, Boyadjian A, Devanne H. Motor cortex plasticity induced by extensive training revealed by transcranial magnetic stimulation in human. *European Journal of Neuroscience*. 2005; 21(1):259–266. doi:10.1111/j.1460-9568.2004.03835.x. [PubMed: 15654863]
- van Mier HI, Petersen SE. Intermanual transfer effects in sequential tactuomotor learning: evidence for effector independent coding. *Neuropsychologia*. 2006; 44(6):939–949. [PubMed: 16198379]

- Vangheluwe S, Suy E, Wenderoth N, Swinnen SP. Learning and transfer of bimanual multifrequency patterns: effector-independent and effector-specific levels of movement representation. *Experimental Brain Research*. 2006; 170(4):543–554.
- Veltman DJ, Friston KJ, Sanders G, Price CJ. Regionally specific sensitivity differences in fMRI and PET: where do they come from? *NeuroImage*. 2000; 11(6 Pt 1):575–588. doi:10.1006/nimg.2000.0581. [PubMed: 10860787]
- Verwey WB, Wright DL. Effector-independent and effector-dependent learning in the discrete sequence production task. *Psychological Research*. 2004; 68(1):64–70. [PubMed: 12955505]
- Waldvogel D, van Gelderen P, Immisch I, Pfeiffer C, Hallett M. The variability of serial fMRI data: correlation between a visual and a motor task. *Neuroreport*. 2000; 11(17):3843–3847. [PubMed: 11117501]
- Wassermann EM, McShane LM, Hallett M, Cohen LG. Noninvasive mapping of muscle representations in human motor cortex. *Electroencephalography and Clinical Neurophysiology*. 1992; 85(1):1–8. [PubMed: 1371738]
- Weigelt C, Williams AM, Wingrove T, Scott MA. Transfer and motor skill learning in association football. *Ergo-nomics*. 2000; 43(10):1698–1707.
- Wigmore V, Tong C, Flanagan JR. Visuomotor rotations of varying size and direction compete for a single internal model in motor working memory. *Journal of Experimental Psychology. Human Perception and Performance*. 2002; 28(2):447–457. [PubMed: 11999865]
- Wu CW, Kaas JH. Reorganization in primary motor cortex of primates with long-standing therapeutic amputations. *Journal of Neuroscience*. 1999; 19(17):7679–7697. [PubMed: 10460274]
- Xerri C, Coq JO, Merzenich MM, Jenkins WM. Experience-induced plasticity of cutaneous maps in the primary somatosensory cortex of adult monkeys and rats. *Journal of Physiology, Paris*. 1996; 90(3–4):277–287.
- Ziemann U, Hallett M, Cohen LG. Mechanisms of deafferentation-induced plasticity in human motor cortex. *Journal of Neuroscience*. 1998; 18(17):7000–7007. [PubMed: 9712668]
- Ziemann U, Muellbacher W, Hallett M, Cohen LG. Modulation of practice-dependent plasticity in human motor cortex. *Brain*. 2001; 124(Pt 6):1171–1181. [PubMed: 11353733]
- Ziemann U, Wittenberg GF, Cohen LG. Stimulation-induced within-representation and across-representation plasticity in human motor cortex. *Journal of Neuroscience*. 2002; 22(13):5563–5571. [PubMed: 12097507]

Fig. 1.

Skill: Between-group comparisons of mean ($\pm$ s.e.m.) AI_{FINGER}, AI_{ELBOW} and AI_{ANKLE} are depicted at pretest (a–c) and at posttest (d–f). At pretest, no differences between groups existed for AI_{FINGER}, AI_{ELBOW} or AI_{ANKLE}. At posttest, differences between the trained groups and the Control_{Group} became apparent in relation to the skill of the trained joint [(AI_{FINGER} in the Finger_{Group}, d) and (AI_{ELBOW} in the Elbow_{Group}, e)] and the remote untrained joint (AI_{ANKLE} in the Finger_{Group} and the Elbow_{Group}, f). Note that the skill of the adjacent untrained joint [(AI_{ELBOW} in the Finger_{Group}, e) and (AI_{FINGER} in the Elbow_{Group}, d)] did not differ significantly between the trained groups and the Control_{Group} at posttest. ‘*’ denotes $p < 0.05$. Thus, finger and elbow tracking skill transferred significantly to remote, untrained ankle joint (f), but benefit for adjacent untrained joints, elbow (e) and finger (d) respectively, was non-significant

Fig. 2.

Percentage Overlap: Illustration of pretest to posttest change in % Overlap (sharing of Finger_{VOLUME} and Elbow_{VOLUME}) in groups. Symbols '*' and '‡' reflect the comparison of pretest to posttest change in % overlap between groups. '*' denotes $p < 0.05$, '‡' denotes $p = 0.08$. The pretest value for each group represents the raw level of % overlap at baseline, but since baseline differed across groups, we incorporated it as a covariate in the 2-way (group X time) repeated measures ANOVA. Although in this figure the height of the bars at pretest represents raw, unadjusted values, the model adjusted the pretest value at 36.26% overlap for all groups. While the Finger_{Group} witnessed a change to 24.66% and the Control_{Group} showed a change to 31.19%, the Elbow_{Group} showed an increase % overlap to 48.8%. These preliminary results show that % Overlap between trained and adjacent untrained representations increased following skill training at elbow but a comparable effect following training of the finger was not observed.

Fig. 3. Percentage Overlap- Comparison of fMRI Activation-based Representations of Representative Subjects: Shows change in % Overlap (between $\text{Finger}_{\text{Volume}}$ and $\text{Elbow}_{\text{Volume}}$ representations) for 3 representative subjects, one from each group. FMRI activation has been masked to the region of M1. Threshold for significant activation has been set at Bonferroni corrected p -level (10^{-6}). Note that the subject in the $\text{Elbow}_{\text{Group}}$ shows a more dramatic increase in % overlap ($z=49$, change from 44.02% to 53.12%) compared to the subject in the $\text{Finger}_{\text{Group}}$ ($z=56$, change from 33.26% to 32.00%) and that in the $\text{Control}_{\text{Group}}$ ($z=60$, change from 60.4% to 60.84%)

Fig. 4.

Location of POA of Representations: Comparison of pretest to posttest change in location of POA (Talairach X coordinate) of Finger_{VOLUME} (a), Elbow_{VOLUME} (b) and Ankle_{VOLUME} (c) representations between groups (note: higher magnitude on the y-axis indicates more lateral position in left M1). ‘*’ denotes $p < 0.05$, ‘†’ denotes $p = 0.06$. Our elementary findings indicate that following finger skill training, as a *direct effect*, location of POA of trained representation tends to shift medially towards that of the adjacent untrained elbow representation (4a). An analogous process following elbow skill training, however, is not evident (4b)

Fig. 5.

Location of POA of Representations- Comparison of fMRI Activation Maps of Representative Subjects: Change in Location of Talairach X-coordinate of POA of Finger_{VOLUME} representation depicted for 3 representative subjects, one from each group. While the 3 images on the *top* row illustrate pretest assessments for the 3 representative subjects, the *bottom* row shows the corresponding posttest assessments. FMRI activation has been masked to the region of M1. The color bar depicted along side the images illustrates values of 't' based on the statistical test of significance conducted using single-subject general linear model (GLM) analysis. The GLM tests the level of BOLD signal change across 288 fMRI volumes for all voxels in the brain. Threshold for significant activation has been set at Bonferroni corrected p -level (10^{-6}). T-value listed with the color bar shows that voxels shown in the MRI images are significantly active as they cross the critical value of t at 4.65. The location of the POA is denoted by a green dot. For Finger_{VOLUME}, note that the subject from the Finger_{Group} shows a large medial shift (thick red arrow) in the location of POA of Finger_{VOLUME} representation (from -41 to -30 mm) from pretest (*top*) to posttest (*bottom*). Subjects from Elbow_{Group} (-42 to -42 mm) and Control_{Group} (-54 to -54 mm) demonstrate no shift (thin red arrows) from pretest (*top*) to posttest (*bottom*)

Fig. 6. Association between Change in Skill and Representational Plasticity: Association between cortical reorganization processes apparent in the Finger_{Group} (**a**, **b**, **c**) and the Elbow_{Group} (**d**) with change in skill of the adjacent untrained joints (AI_{ELBOW} and AI_{FINGER}) respectively. In the Finger_{Group}, change in location of POA within the trained representation and increase in intensity of adjacent untrained representation, both, appeared to be related to change in skill at adjacent untrained elbow (**a**, **c**). In the Elbow_{Group}, higher sharing between trained and neighboring untrained representations was associated with limited skill gain at the untrained finger joint (**d**). These correlation results suggest, preliminarily, that mechanisms of representational plasticity may limit absolute transfer of skill from trained to adjacent untrained joints