

Cortical Plasticity During Three-Week Motor Skill Learning

Petr Hluštík,† Ana Solodkin,* Douglas C. Noll,‡ and Steven L. Small*†§*

Abstract: The authors studied motor behavior and primary motor (M1) and somatosensory (S1) cortical representations of movement during hand motor skill acquisition over 3 weeks. During four functional MRI sessions 1 week apart, subjects performed simple movements of single fingers and wrist, and a sequential movement of the middle three fingers, contrasted with rest. Half of the subjects practiced the sequential movement, whereas the other half practiced a gross motor task (squeezing a sponge). In both groups, motor performance gradually improved both on the practiced sequence and also on unrelated tests of general hand performance. Similarly, gradual expansion of active M1 and S1 areas was observed with the practiced sequence and with the unpracticed single-finger and wrist movements. Motor practice enhanced overlaps and sharing of cortex (significantly more so in the fine-skill group), preserving somatotopy and the overall extent of the hand representations. Even a limited amount of practice on a complex task can thus lead to both specific and nonspecific improvements in behavior and to expansion of M1 and S1 movement representations. Finally, the extent of active M1 and S1 was significantly correlated with out-of-scanner performance on sequential finger movement and may reflect the current motor ability of the individual.

Key Words: Motor skill learning, Primary motor cortex, Primary somatosensory cortex, Somatotopy, Training, Hand.

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Human functional brain mapping studies have begun to separate the neural correlates of different cognitive, perceptual, and motor processes that participate in acquisition of motor skills (e.g., Grafton et al., 1992; Jueptner et al., 1997; Karni et al., 1995; Kawashima et al., 1994; Schlaug et al.,

1994; Seitz and Roland, 1992; Toni et al., 1998). Longitudinal changes of brain activity related to skill acquisition have been observed in multiple cortical areas that normally participate in motor execution, e.g., primary motor cortex (M1), supplementary motor area, and premotor cortex.

Motor cortices may encode the newly acquired skill through change in movement representations (Grafton et al., 1992, 1995; Karni et al., 1995). The studies of Karni et al. (1995, 1998) showed that learning over a longer term (weeks) may be necessary to cause such changes, possibly requiring a process of motor memory consolidation (Shadmehr and Holcomb, 1997).

The primary motor cortex is a natural focus for the investigation of changes associated with motor skill acquisition for two reasons: (1) its functional organization is well described in nonhuman primates as well as humans, and (2) this organization appears to be readily subject to plastic change, even in adults (Nudo et al., 2001).

Several human motor learning studies have reported that movement practice leads to recruitment of additional primary motor cortex, with the appearance of new active cortical fields (Kawashima et al., 1994) and expansion of the cortical territory corresponding to the practiced muscles/movements of several millimeters up to several centimeters (Karni et al., 1995; Pascual-Leone et al., 1994). Karni et al. (1995) compared primary motor cortical activation caused by two sequential finger movements involving the same fingers. One of the sequences was repeatedly practiced over several weeks. Although the extent of cortex activated with each sequence was similar at the beginning of the study, this changed after a few weeks of training, as the activation by the practiced finger sequence became significantly larger than the activation caused by the nonpracticed sequence. The area of evoked response in M1 for the trained sequence did not extend beyond the hand representation, which was mapped in a subset of the subjects by independent finger movements.

It is possible that expansion of one motor representation influences other motor representations occupying adjacent cortical territory. For example, in a nonhuman primate model of cortical reorganization after stroke, nonuse of impaired fingers caused shrinking of the primary motor cortical representation of finger muscles and invasion of other arm muscles into their territory, whereas rehabilitation of the impaired

Departments of *Neurology and §Radiology, University of Maryland, Baltimore, Maryland, U.S.A.; †Center for Neuroscience, University of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A.; and ‡Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, U.S.A.

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Address correspondence and reprint requests to Dr. Petr Hluštík, Department of Neurology, Palacký University, I. P. Pavlova 6, 77520 Olomouc, Czech Republic; e-mail: phlustik@upol.cz.

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fingers led to preservation of their cortical representation (Nudo and Milliken, 1996; Nudo et al., 1996b). These results would lead to a prediction that during motor learning and the associated expansion of cortical movement representations, cortical representations of nonpracticed movements would shrink. Alternatively, it is possible that in the absence of cortical lesion, learning would preserve preexisting movement representations and lead to increased sharing of cortical territory. This would reflect the behavioral observation that acquiring a new motor skill does not impair the performance of skills acquired previously. Lastly, because the effects of across-session learning on the extent of primary motor cortical representations are only been detected after the motor skill is acquired (Karni et al., 1995), it is not clear whether cortical changes evolve concurrently with behavioral performance over the entire learning period or whether the cortical expansion occurs only at the end of learning.

These outstanding questions led to the present study of motor and somatosensory cortical plasticity during human motor skill learning. This study examined changes in cortical representations of a newly learned skilled movement and other, unpracticed movements. The investigation focused on the spatial relationships among the individual cortical movement representations as they changed over several weeks. Subjects underwent repeated fMRI of motor and somatosensory cortical areas during performance of a learned sequential finger movement and several other unpracticed hand movements. Over the course of these 3 weeks, subjects were also monitored on behavioral performance of these tasks. The following three hypotheses summarize the main predictions of the study. First, learning-induced expansion of one motor cortical representation will lead neither to competition for cortical territory nor to reduction in the size of other cortical representations. Instead, learning will increase the overlapping and sharing among cortical representations of the individual movements. Importantly, such sharing is known to be a common property of primary motor cortical movement representations (Hluštík et al., 2001; Schieber and Hibbard, 1993; Schieber and Poliakov, 1998). Second, the somatotopic arrangement within the hand area (Hluštík et al., 2001) will be unaffected by motor learning. Third, the temporal evolution of cortical changes will correlate with the behavioral improvement.

To test the first hypothesis, we assessed changes in the spatial relationship of cortical movement representations over the course of learning. To test the second hypothesis, we studied the somatotopic arrangement of centers of mass of the cortical representations over time. To test the third hypothesis, we evaluated the relationship of performance on the practiced task to measures of cortical activation.

METHODS

Subjects and Tasks

Ten healthy right-handed volunteers (seven men and three women; age range, 23 to 34 years; mean age, 26.6 years) without any history of neurologic or developmental illness participated in the study. All were right-hand dominant according to the Edinburgh Inventory (Oldfield, 1971), with a group laterality score of 0.73 ± 0.20 , and provided informed consent before the study, according to a protocol approved by the University of Maryland Institutional Review Board. Participants were assigned to two groups of five subjects.

At the beginning of the study, all subjects performed a set of behavioral tests to assess general motor function of both hands: index finger tapping speed test (Shimoyama et al., 1990), a test of hand grip strength (dynamometry), and the nine-hole peg test (Mathiowetz et al., 1985). The hand performing more poorly on the index finger tapping test (always the nondominant left hand) was used for subsequent practice and testing. These general motor tests were performed again at the final imaging session.

Subjects were then instructed on the four movements to be performed during the functional imaging sessions. Three simple movements involved repetitive flexion-extension movements of either thumb (Thumb), little finger (Little), or wrist (Wrist). The fourth movement consisted of successive finger flexions, pressing the keys 1 to 6–8 to 3–9 to 4 on a numerical keypad using the three middle fingers, a task requiring fine motor skill. This task was performed with one finger for each column of keys (index finger = left column, middle finger = middle column, ring finger = right column). Each subject underwent a single short (about 1 minute) practice session that aimed to make the subject capable of performing the sequence without visual control.

Performance of the sequence task with the left hand and with eyes closed was then evaluated quantitatively using a computerized test designed in the PsyScope software (Cohen et al., 1993). During this 2.5-minute test, the subject repeatedly executed the sequence, while the presence of each keypress, the name of the key pressed, and the time required to press the key were all recorded in a computer data file. These records were processed to provide the count of keypress sequences per minute and the success rate (percentage of keypresses belonging to a correct sequence). The right hand was then tested in the same manner.

Starting the day after the first functional imaging and behavioral assessment session, subjects in the first (fine-skill) group practiced the keypress sequence for 15 minutes per weekday, whereas the second (gross-skill) group practiced an unskilled sponge-squeezing task. The practice continued over the 3-week study period (between the baseline and final imaging sessions). During keypad practice in the fine-skill

group, keypresses and movement times were recorded and then analyzed quantitatively as during the assessment periods. Out-of-scanner performance of the sequence task in the gross-skill subjects was limited to the one 2.5-minute testing block per hand each week, just before each imaging session.

At the time of the final imaging session, all assessments of hand motor performance (index finger tapping test, nine-hole peg test, and hand grip strength) were repeated in all subjects. TABLE 1 summarizes the temporal distribution of the different behavioral and imaging procedures throughout the 3-week study.

Functional MRI

After the initial behavioral testing, all subjects underwent a baseline MRI session. Subjects performed the tasks in a blocked paradigm consisting of alternating 24-second blocks of each hand movement (little finger, thumb, sequence, wrist) and rest, with blocks separated by 6-second breaks. Movements were paced at 2 Hz by short beeps heard in pneumatic headphones. High-frequency beeps marked the periods of hand movement, whereas low-frequency beeps were presented during rest periods. Blocks of movements were performed in different random orders during each of five 10-minute runs, with the order of movements counter-balanced across runs to prevent nonspecific order and time effects (Rajah et al., 1998). Subjects received instructions about the type of movement to be performed over headphones during the breaks between movements and kept their eyes closed throughout the experiment.

All MRI data were acquired on a 1.5-T Signa scanner (GE Medical Systems, Milwaukee, WI, U.S.A.) with a standard head coil. Twelve oblique axial slices were prescribed parallel to the intercommissural (AC-PC) line and adjusted to cover the superior part of the cortex including the superior convexity. To perform accurate image alignment over a 3-week period, a three-dimensional slice prescription algorithm was followed. It proceeded from a straight axial scout, through an oblique coronal perpendicular to the longitudinal

fissure, to an oblique sagittal through the longitudinal fissure and the third ventricle, and to the final triple-oblique axial, parallel to the AC-PC line. Furthermore, the vertical distance from the AC-PC line to the center of the most superior imaged slice was recorded during the first imaging session. In the subsequent sessions, the position of the slices was adjusted so that the distance of the top slice from the AC-PC line was the same as during the first session.

Anatomic images were T1-weighted (550-millisecond repetition time, 6-millisecond echo time, 70° flip angle, two excitations, spin echo). Functional (T2*-weighted) data used blood oxygen level-dependent contrast and was acquired with four-shot spiral technique (Noll et al., 1995, 1999) with 60° flip angle, 35-millisecond echo time, and a repetition time of 1500 milliseconds per spiral, providing 1.6 × 1.6 mm (inplane) × 3 mm (slice thickness) resolution. Two scans were added at the beginning of each functional scanning series (run) and the data discarded to reach a steady-state magnetization before acquisition of the experimental data. Scanning started 3 seconds after the experimental paradigm to compensate for part of the hemodynamic delay. We also acquired two-dimensional phase contrast magnetic resonance angiography data sensitized to slow venous flow (gradient echo, 25° flip angle, 6-millisecond echo time, 25-millisecond repetition time, 192 × 256 matrix, velocity encoding 10 cm/second, sensitive to all flow directions). Slice locations exactly matched the functional and anatomic scans. A three-dimensional T1-weighted spoiled gradient echo volume scan (6-millisecond echo time, 24-millisecond repetition time, 40° flip angle, 124 slices, 1.5-mm slice thickness, 24-cm field of view, 192 × 256 matrix) provided thin slices to allow identification of neuroanatomy with high resolution in all three orthogonal planes. The follow-up imaging sessions had the same design as the initial session and the MRI data were processed in the same way.

Spiral image reconstruction was performed off-line on a SGI Origin2000 server (Silicon Graphics Inc., Mountain

TABLE 1. Distribution of tests and practice throughout the learning study

Session	Day	Hand motor testing	Task instruction	Sequence testing	EMG	Imaging	Sequence practice	Squeeze practice
Session 1	0	*	*	*	*	*		
Intersession	1–6						F	G
Session 2	7			*		*		
Intersession	8–13						F	G
Session 3	14			*		*		
Intersession	15–20						F	G
Session 4	21	*		*	*	*		

EMG, electromyography; F, fine-skill group; G, gross-skill group; *, both

View, CA, U.S.A.). Automated Image Registration (AIR) software version 3.0 (Woods et al., 1998) with a three-dimensional rigid model and least-squares cost function for alignment and a trilinear model for reslicing was used on the functional images to correct for movement within and between sessions. For AIR, data were gaussian-blurred during the estimation phase with 1.6-mm full width at half-maximum and initialization files were used to facilitate convergence for between-session registration. The reference T2*-weighted image volume was chosen to be in the middle of the third out of five experimental runs of the first session to minimize the necessary alignment within that session. The in-plane anatomic images and angiograms were registered to the same reference using AIR with a three-dimensional rigid model and variance-ratio cost function for alignment and a trilinear model for reslicing. For phase-contrast angiograms, alignment was performed using a flow-enhanced set of images, the estimated correction was then applied to the background-suppressed vascular images from the same acquisition.

The skull and meninges were manually segmented out before cross-modality registration. Anatomic landmarks visible in all modalities (such as cortical sulci, especially the central sulcus) were used to evaluate the success of the cross-modality registration. If a residual in-plane displacement of the registered image against reference was found, the registered images were manually shifted within the plane to the correct position. This manual correction never exceeded one voxel. Functional data from the top and bottom slices were excluded from subsequent analysis because of interpolation artifacts from image registration.

Voxel-by-Voxel Analysis

Voxel-by-voxel analysis was performed using the MCW AFNI package (Cox, 1996) to calculate cross-correlation of the linearly detrended vector of signal intensities over time with a modified sinusoidal model waveform (Bandettini et al., 1993) using positive and negative half-sinusoids in place of the selected task blocks to be compared. The time-points acquired during 6-second breaks and the task blocks not involved in the current comparison were excluded from the waveforms. Both a single-voxel statistical threshold $r = 0.37$ and a three-dimensional contiguity threshold of three voxels (Forman et al., 1995) were used to determine which voxels are active. Monte Carlo simulation (Forman et al., 1995) from MCW AFNI estimated the corresponding overall (whole-brain) alpha level as less than 0.05.

Vascular artifacts (voxels activated as a result of macroscopic venous blood flow) were removed using a mask based on magnetic resonance angiograms (Hluštík et al., 1998). Briefly, the angiograms were gaussian-blurred to the resolution of the T2*-weighted images and thresholded at mean + 2 standard deviations to create a binary image of

draining veins. Activation colocalized with the venous mask was removed.

Regions of Interest

Regions of interest (ROIs) were defined *a priori* on anatomic T₁-weighted images using MNI-Display software (Montreal Neurologic Institute, Montreal, Canada). The primary motor cortex was identified on the anterior bank of the central sulcus, and, in the most superior slices (above the level of the confluence of precentral and superior frontal gyri), also on the posterior part of the precentral gyrus. Here, precentral gyrus was traced from within central sulcus out to the most lateral point on the convexity, which was used as the anterior limit of M1 (Rademacher et al., 1993). The primary somatosensory cortex was outlined on the postcentral gyrus to include areas 3a, 3b, 1, and 2 using the precentral and postcentral sulci as delimiting landmarks (Brodmann, 1909; Geyer et al., 1999). Premotor cortex encompassed both banks of precentral sulcus and of the adjoining superior frontal sulcus. The anterior limit of premotor cortex was defined using a coronal plane perpendicular to the intercommissural line and containing the anterior commissure. Supplementary motor area was defined on the mesial surface, with the same anteroposterior extent as the premotor cortex. The inferior limit was defined to be just superior to the dorsal bank of cingulate gyrus.

Regional Measures: Volumes, Overlaps, Somatotopy, and Spatial Complexity of Movement Representations

The volumes of activation and the centers of mass (centroids) of significantly activated voxels within each ROI were calculated for each movement–rest comparison. For centroid calculation, the contribution of each voxel was weighted by its correlation coefficient to enhance the contribution of voxels containing a greater proportion of active tissue. When the movement representation consisted of multiple noncontiguous clusters, the regional center of mass was again calculated as a weighted average, using the average correlations for each cluster as the weight. To assess the degree of overlap between cortical representations of individual movements, the volume of cortex shared by two different movements was expressed as the percentage of the area activated by either of the movements. Presence of a somatotopic gradient was evaluated by comparing the arrangement of movement representation centroids in three orthogonal coordinates (x: medial-lateral, y: anterior-posterior, z: inferior-superior) with the expected order of movements along the central sulcus (Hluštík et al., 2001). Measuring the three-dimensional (Euclidean) distance of the extreme ends of an area including voxels activated with any finger movement (Thumb, Little, or Sequence) provided an estimate of the sizes of the hand representations. Finally, to assess the spa-

tially distributed nature of regionally activated cortex for each movement, we calculated two additional measures. The cluster count was defined as the number of clusters of significant activation in each ROI. The percentage of the total ROI volume activation contained in the largest cluster was called the primary cluster size (Hlušík et al., 2001).

Statistical Analysis

Group results are reported as the mean ± standard deviation. Repeated-measures analyses of variance (RM-ANOVA) were performed to study the effects of group (fine skill, gross skill), movement (Thumb, Little, Wrist, Sequence) and session (1–4) on behavioral measures (sequences per block, success rates) and the previously described measures of ROI brain activation: volume of activated cortex, cluster count, primary cluster size, and center of mass (x, y, z). Where a significant main effect was found, individual movements or sessions were compared pairwise using the Student-Neuman-Keuls (*post hoc*) test. Repeated-measures ANOVA was also used to test the hypothesis that neither group nor session has an effect on the extent of M1 and S1 hand representations. Planned contrasts were conducted to compare the change of overlaps of M1 and S1 movement representations over the duration of the study between the fine-skill and gross-skill groups. The expected linear relationship between brain measures (volumes of active M1 and S1 cortex) and behavioral measures (sequence count per minute) was assessed with a Spearman correlation coefficient. An alpha level of 0.05 was used for all statistical tests.

RESULTS

The goal of this study was to evaluate the effect of motor learning on movement representations in motor and somatosensory cortices. Specifically, it focused on the relationship among the expanding representation of the learned sequential movement and the representations of other unpracticed hand movements. Behavioral data were examined first, to determine whether general and specific hand motor behavior has changed during learning. Then, cortical movement representations of different movements were evaluated over time. Finally, the changes in behavior were correlated with the changes in cortical representations.

Behavioral Results

General Motor Behavior

Performance on general hand motor tests improved during the study, although there were no group differences ($P > 0.1$ for all three tests). Index finger tapping speed over the 3-week study period improved only in the fine-skill group ($F_{1,8} = 6.0, P = 0.04$, session × group interaction, RM-ANOVA), with no significantly change over sessions when the groups were collapsed ($P > 0.1$). Performance on the nine-hole peg test and the grip strength improved signifi-

cantly in both groups ($F_{1,8} = 11.4, P = 0.0097, F_{1,8} = 22.7, P = 0.0014$, respectively, RM-ANOVA).

Behavioral Results

Motor Sequence

Both the fine-skill and gross-skill group improved their performance of the six-key sequence over time, while keeping a high success rate. Subjects in the fine-skill group gradually increased their speed from 34.6 ± 4.6 sequences per minute before session one to 50.4 ± 5.5 sequences per minute at the time of session four. The gross-skill group improved during the same period from 19.9 ± 4.7 to 29.7 ± 3.8 sequences per minute (see Fig. 1). In contrast to their similar performance on general hand motor tests, the fine-skill group performed the sequence overall faster than the gross-skill one (45.5 ± 2.6 versus 25.2 ± 2.0 sequences per minute). Repeated-measures ANOVA showed a significant learning (session) effect and a significant group difference (session ($F_{3,21} = 20.8, P < 0.0001$), and group ($F_{1,7} = 12.1, P = 0.010$)). The rate of improvement did not differ significantly between the two groups, although there was a clear trend toward more pronounced sequence learning in the fine-skill group (session by group interaction, $P = 0.058$).

Even though performance on the sequence task improved throughout the 3-week period, learning was most dramatic in the earliest phase of the study period and tapered off later. Statistical analysis of this learning suggested that most of this learning occurred between the first and second sessions (Student-Neuman-Keuls *post hoc* analysis of the session main effect revealed significant pairwise differences of sequence performance between sessions 1–2, 1–3, and

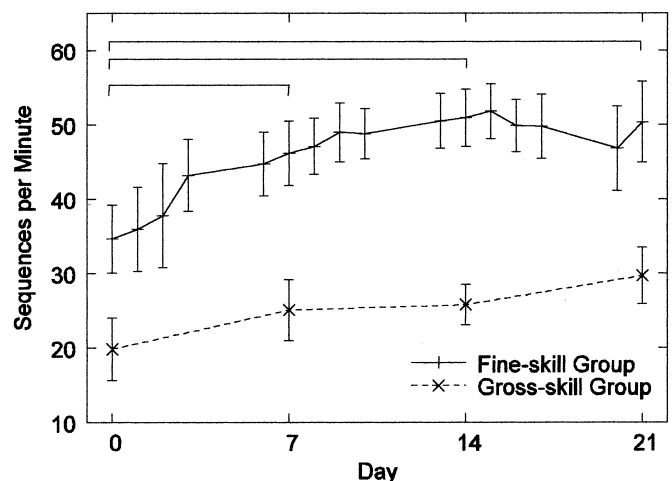


FIGURE 1. Behavioral performance of keypad sequence (correct sequences per minute) in the fine-skill (solid line) and gross-skill (dashed line) groups plotted over time. Brackets show significant posthoc differences between sessions. Values represent group means ± standard errors of the mean.

1–4). Subjects' sequence performance improved also in the right (nonpracticed) hand, although the left hand improved significantly more (hand by session interaction, $P = 0.027$). Fine-skill and gross-skill groups did not differ in this respect (hand by session by group interaction, $P = 0.35$).

Whereas performance speed changed over the course of the study, accuracy did not change, indicating no speed-accuracy trade-off; there also was no group difference in accuracy (RM-ANOVA: no effect of session or group, all $P > 0.6$). The overall success rate in the behavioral testing laboratory was $93\% \pm 8\%$ (both groups collapsed). Accuracy was also measured during performance of the sequence task in the scanner, where it was significantly lower than in the behavioral laboratory ($64\% \pm 15\%$) but likewise did not change over the 3-week study period or differ by group (RM-ANOVA: environment: $P = 0.001$; no effect of session and group, $P > 0.9$; no interaction between session and group, $F_{3,21} = 2.7$, $P = 0.069$).

Changes in Contralateral Primary Motor Cortical Activation

The mean volume of active M1 in the fine-skill group was greater than that of the gross-skill group when collapsed over sessions ($794 \pm 309 \text{ mm}^3$ versus $585 \pm 280 \text{ mm}^3$), but this group difference was not significant ($F_{1,8} = 3.9$, $P = 0.084$, RM-ANOVA). Because the session by group interaction was also not significant ($P = 0.60$), the following two results reflect data collapsed across both groups.

The representations of movements in M1 increased in volume over the course of learning (main effect of session, $F_{3,24} = 5.4$, $P = 0.0054$, RM-ANOVA). Most of the increase occurred between the first two sessions (Student-Neuman-Keuls *post hoc* analysis: significant pairwise differences between session one and every other session), when volumes increased by about 30% (from $563 \pm 262 \text{ mm}^3$ to $724 \pm 347 \text{ mm}^3$), with the volume remaining high thereafter for the remainder of the study period (see Fig. 2).

The volumes of M1 representations differed across movements, with Sequence activating the greatest extent of cortex, followed by Wrist, Thumb, and Little. The difference across movements was significant ($F_{3,24} = 43.5$, $P < 0.0001$, RM-ANOVA) with *post hoc* analysis indicating that the movements all differed from each other except little finger and thumb movements. That is, sequential movements differed from each of the other movements (Sequence–Wrist, Sequence–Little, Sequence–Thumb) and wrist movements differed from each of the other movements (Wrist–Sequence, Wrist–Little, Wrist–Thumb), and thumb and little finger movements differed from each of the other movements except for each other. Although the volumes of cortex active with the different movements did not change in the same manner over time (significant session by movement interaction, $F_{9,72} = 2.2$, $P = 0.034$), no specific pattern of change

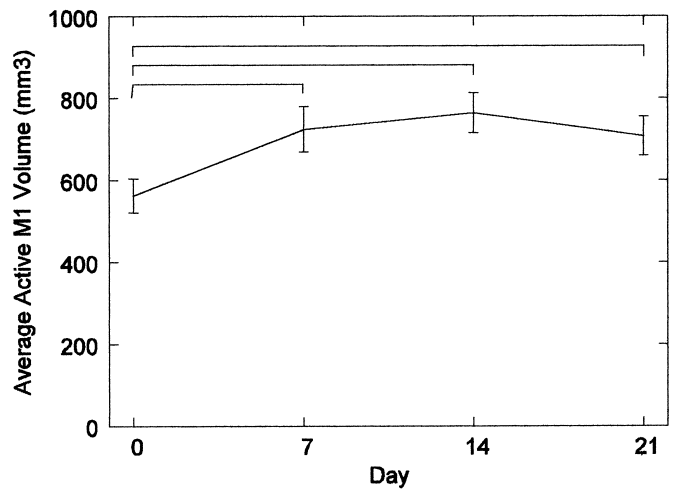


FIGURE 2. Volume of active M1, averaged across movements and groups and plotted over time. Brackets show significant *post hoc* differences between sessions. Values represent means \pm standard errors of the mean.

was apparent, e.g., expansion was not limited to the Sequence representations (see Fig. 3). None of the movement representations reduced its size over the course of the study.

Changes in Contralateral Primary Somatosensory Cortical Activation

Overall, the fine-skill group had greater mean volume of S1 activation than did the gross-skill group ($819 \pm 438 \text{ mm}^3$ versus $588 \pm 375 \text{ mm}^3$), but not significantly ($F_{1,7} = 2.7$, $P = 0.15$), nor was there a significant change in this

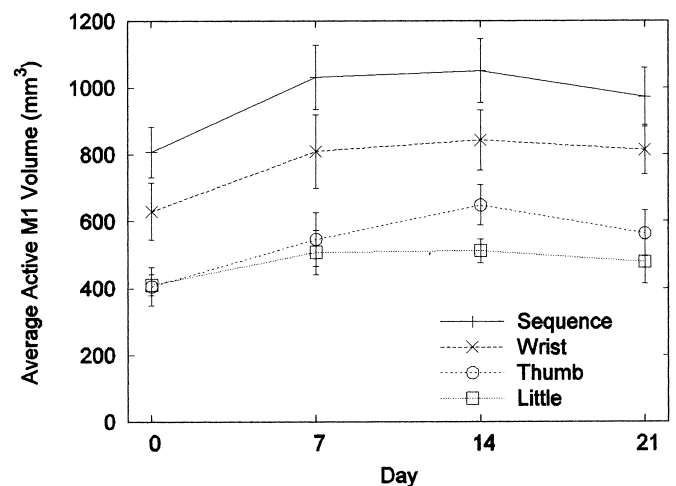


FIGURE 3. Volume of M1 active with individual movements (sequence = solid line, wrist = long dashes, thumb = short dashes, little = dotted line), averaged across groups and plotted over time. Values represent means \pm standard errors of the mean.

relationship over time (session by group interaction, $P = 0.73$, all RM-ANOVA). The following two results thus reflect data collapsed across both groups.

The volume of movement representations in S1 also increased during the study period ($F_{3,21} = 3.6$, $P = 0.030$, RM-ANOVA), but not so rapidly as in M1. By session 3, the volume of activation increased by about 40% (from $588 \pm 338 \text{ mm}^3$ to $825 \pm 347 \text{ mm}^3$), which was a statistically significant difference against session one (Student-Neuman-Keuls test; see Fig. 4).

There were significant differences in the volume of active S1 cortex across the different types of movements ($F_{3,21} = 26.7$, $P < 0.0001$), and *post hoc* analysis indicated the results in S1 to be analogous to those in M1, i.e., that all pairs of movements differed significantly, except for the comparison of little finger movement and thumb movement.

Changes in Contralateral M1 and S1 Overlaps

Pairwise overlaps of cortical representations of movements were significantly greater in M1 than in S1 for all pairs of movements, except Thumb and Wrist, where the M1-S1 difference did not reach significance ($P = 0.065$, RM-ANOVA). With both groups combined, movement overlaps increased during learning in both M1 and S1 by $4.5\% \pm 16.5\%$ and $3.6\% \pm 16.3\%$, respectively, although the increase was not significant in either cortex ($P = 0.39$, $P = 0.49$, RM-ANOVA). There was no group difference in the amount of overlap within M1 and S1 (both $P > 0.05$, RM-ANOVA). Baseline M1 overlaps were greater in the fine-skill group, though not significantly ($49\% \pm 4\%$ versus $39\% \pm 7\%$ in the gross-skill group) but with training increased more significantly in this group (by $8.1\% \pm 11.8\%$)

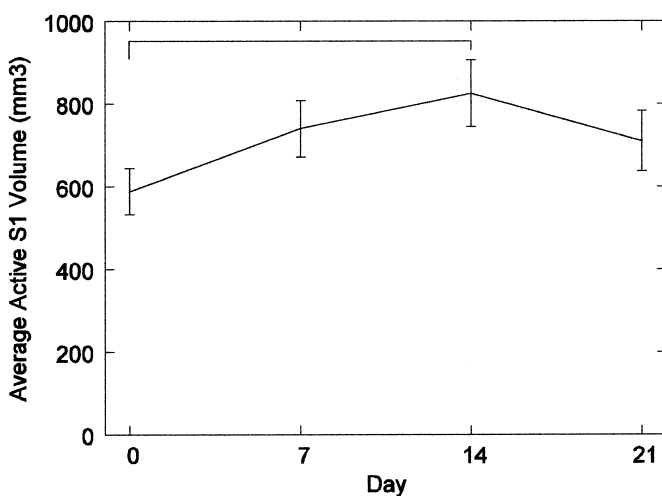


FIGURE 4. Volume of active S1, averaged across movements and groups and plotted over time. Brackets show significant *post hoc* differences between sessions. Values represent means \pm standard errors of the mean.

than in the gross-skill group ($0.9\% \pm 19.7\%$, $P = 0.044$, planned contrast; one-sided, unpaired *t*-test).

M1 and S1 Somatotopy

The average somatotopic arrangement of M1 and S1 corresponded to that found previously (Hluštík et al., 2001). The centroids of M1 and S1 movement representations lay approximately in the somatotopic order suggested by Penfield and Boldrey (1937) with thumb, sequence, little finger, and wrist positioned progressively more medially, posteriorly, and superiorly along the course of the central sulcus. M1 centroid Euclidean distances were as follows: Thumb–Sequence, $2.26 \pm 1.51 \text{ mm}$; Thumb–Little, $2.70 \pm 1.84 \text{ mm}$; Thumb–Wrist, $3.64 \pm 2.68 \text{ mm}$. The location of the centroids differed significantly across the four different movements on two of the three orthogonal coordinates. The medial-lateral (x) and anterior-posterior (y) coordinates showed a small (see above) but statistically highly significant spatial separation (x: $F_{3,27} = 15.2$, $P < 0.0001$, y: $F_{3,27} = 9.3$, $P = 0.0002$, RM-ANOVA), whereas the superior-inferior (z) coordinate did not show separation ($P = 0.3$). The location of the centroids was preserved throughout the study (no session effect: $P > 0.3$ for x, y, z).

An even stronger somatotopic result was found for S1, where the centroid distances were larger (Thumb–Sequence, $3.78 \pm 6.55 \text{ mm}$; Thumb–Little, $4.44 \pm 6.59 \text{ mm}$; Thumb–Wrist $4.95 \pm 6.29 \text{ mm}$) and the spatial separation was statistically significant along all three orthogonal directions (x: $F_{3,21} = 15.9$, $P < 0.0001$, y: $F_{3,21} = 9.9$, $P = 0.0003$, $F_{3,21} = 10.9$, $P < 0.005$). There was no change in this somatotopic arrangement over the period of active learning, despite the increasing volume of cortical activation.

The spatial extent of M1 and S1 within-hand somatotopy estimated by measuring Euclidean distances between Thumb and Little centroids or Thumb and Wrist centroids did not significantly change from the first to fourth sessions (M1: Thumb–Little, $P = 0.89$, Thumb–Wrist, $P = 0.69$; S1: Thumb–Little, $P = 0.43$, Thumb–Wrist, $P = 0.11$; paired *t*-test).

The fine-skill and gross-skill groups differed significantly in the medial-lateral spatial locations of movement representations in S1 (across all sessions). The extent of M1 and S1 hand representations (M1: $43 \pm 7 \text{ mm}$, S1: $49 \pm 8 \text{ mm}$) did not significantly change across sessions and did not differ between groups (RM-ANOVA).

Distributed Properties of M1 and S1 Representations

Representations of movement in M1 and S1 are distributed into multiple noncontiguous clusters (Hluštík et al., 2001; Sanes et al., 1995). In M1, cluster count and primary cluster size were not different between the groups ($P = 0.23$, $P = 0.13$, respectively) nor were they different across the

different movements studied ($P = 0.77$, $P = 0.06$, respectively). The cluster count did not significantly change over the course of the study ($P = 0.35$), but the primary cluster size did ($F_{3,24} = 3.9$, $P = 0.021$, all RM-ANOVA). The percentage of M1 activation contained in the largest cluster first increased and then decreased somewhat, suggesting that the M1 representations relatively consolidated in the course of the study.

In S1, the fine-skill group had cortical representations distributed into more clusters than the gross-skill group ($F_{1,7} = 7.0$, $P = 0.033$) and the different movement representations were not distributed to the same degree (the main effect of movement on cluster count was significant: $F_{3,24} = 4.1$, $P = 0.020$). Most notably, the movement representation of the sequence contained more clusters than any of the other movements. The number of S1 clusters monotonically decreased while the primary cluster size increased over the course of the study, indicating that during learning, the S1 movement representations became less distributed. For cluster count, the session main effect was not significant ($F_{3,24} = 2.2$, $P = 0.12$) but a *post hoc* linear contrast was significant ($F_{1,24} = 0.037$). For the primary cluster size, both the main effect of session and linear contrast were significant ($F_{3,24} = 4.9$, $P = 0.010$; $F_{1,24} = 11.6$, $P = 0.011$, respectively).

Brain–Behavior Correlation

As described, subject performance on the sequence task (outside the scanner) improved significantly across sessions. In these trials, subjects were instructed to perform the task as quickly as possible without making errors. By contrast, subjects were constrained during the scanning sessions to perform the sequence task at a fixed rate of two movements per second. It is this slower paced performance that served as the driving force for the functional brain activation, and nevertheless, the volumes of cortex active during the sequence task expanded across sessions, thereby correlating with behavioral ability rather than performance. In both cases, the most significant change occurred between the first and second sessions.

The volume of M1 and S1 cortex active during the sequence task was significantly correlated with out-of-scanner performance of the sequence task (M1: $r = 0.35$, $P < 0.05$; S1: $r = 0.50$, $P < 0.01$; see Fig. 5). Similarly, the volume of active M1 and S1 cortex summed over all four movements correlated significantly with out-of-scanner performance of sequence (M1: $r = 0.45$, $P < 0.01$, S1: $r = 0.58$, $P < 0.01$).

DISCUSSION

In the current study, several weeks of practicing a complex movement caused both specific and more general improvements on hand behavioral tasks. The major corresponding cerebral changes were threefold: (1) skill acquisi-

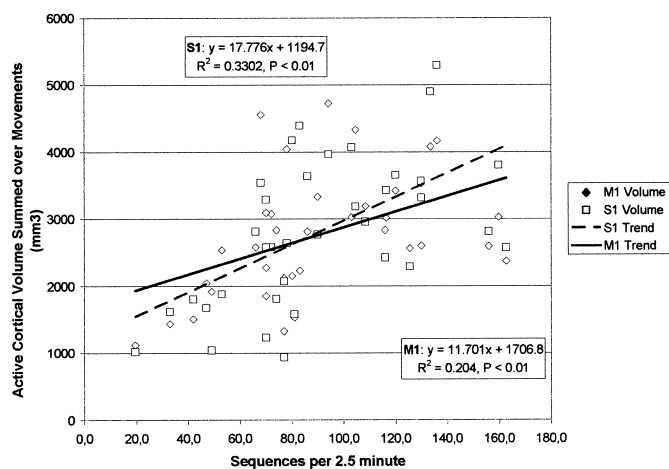


FIGURE 5. Relationship of behavioral performance on the keypad sequence and volume of active M1 (filled symbols, solid regression line) and S1 (open symbols, dashed regression line) cortex summed over the five different movements. Each point represents one subject at a particular session.

tion is accompanied by an expansion of primary motor and somatosensory representations and their increased overlaps, (2) somatotopy is preserved during this process, and (3) the volume of cortical movement representations increases in parallel and is correlated with the behavioral ability of the subjects. Also noted was the presence of changes in the distributed character of movement representations over the course of motor learning, due to a transient increase of M1 primary cluster size and a linear increase of S1 primary cluster size. In addition, in S1, concomitant with this increase in the size of the largest cluster was the decrease in the total number of noncontiguous clusters constituting each movement representation.

Motor Behavior–Specific and Nonspecific Improvements

The behavioral data show that subjects' performance on the practiced sequence improved over the 3-week training period, with most of the change occurring early (between the first and second sessions). Over this same period, performance also improved on the three other tests of hand performance. One possible interpretation could be that lower baseline dexterity of the nondominant hand makes any task relatively novel and leads to general improvement, irrespective of the type of training. However, other studies of motor skill learning found behavioral improvement limited to the practiced sequence (Karni et al., 1995). We favor an alternative explanation. Both older (Adams, 1953, 1957; Lintern, 1991; Wightman and Lintern, 1985) and recent behavioral and brain imaging studies (Cohen et al., 1990; Grafton et al., 1998; Keele et al., 1995) bear witness to the phenomena of transfer and generalization, where learning a particular task

(e.g., the serial reaction time task) can improve performance on other motor tasks (generalize) or improve performance of the same task with another body part or effector (transfer).

Differences in behavioral outcome in different motor learning studies likely reflect differences in the nature of the tasks used for learning and for assessment of primary effects and generalization. In particular, execution of the finger opposition task of (Gordon et al., 1994), whereas the serial reaction time task or the sequential typing task used in the present study depends more on spatial coordinates of an outside object (the keypad). Another difference may involve attentional mechanisms. In the task of Karni et al. (1995), attention is focused on the hand alone; in the other tasks, attention to the interaction between subject's hand and an object is necessary.

It is possible that performance of the finger opposition sequence in the Karni et al. (1995) study, relying on person-centered (e.g., body- or hand-centered) coordinates, may explain the lack of generalization to the other sequence and leads to the representation of this particular sequence in a highly lateralized primary motor cortex contralateral to the hand used. However, external (object-centered) coordinates may play a significant role in encoding of the sequence used in the present study. Similarly, Grafton et al. (1998) suggest that because the component movements of the serial reaction time task are simple and overlearned, learning of the composite task may primarily occur at a higher level of abstract response, encoded in higher motor and sensory cortices with less somatotopic segregation and more bilateral representation of movements. Their study provided neuroimaging evidence supporting separable functional anatomic substrates for effector-specific (i.e., nontransferable) and effector-independent (i.e., transferable) representations of the serial reaction time task (Grafton et al., 1998).

Although the fine-skill subjects had better overall performance of the practiced sequence than did the gross-skill groups, the amount of sequence learning in the fine-skill and gross-skill groups was not significantly different. This can be attributed to several factors. First, the gross-skill subjects actually did practice the sequence, during laboratory performance testing before each weekly imaging session and also during imaging. Because the preponderance of learning occurred early, with the only statistically significant learning occurring between session one and two, even this limited amount of practice may have been sufficient. Second, the fine-skill group performed the sequence faster at baseline and could be considered more advanced learners. As already mentioned, learning gains are expected to diminish over time as subjects approach the maximum possible hand and finger mobility (about five finger movements per second, Shimoyama et al., 1990). Because of the similarity in degree of learning between the two groups, some of the results across both groups are interpreted together (when appropriate).

Although learning progressed and subjects were able to perform the sequence progressively faster (up to five keypresses per second in the fine-skill group), the imaging sessions still called for movement executed at 2 Hz. There is a concern that performing the paced movement at a constant speed makes it progressively more dissimilar to the one practiced. However, behavioral evidence shows that subjects are able to slow down the rate of performing a keypress sequence and still retain the same patterns of the performance, e.g., delays between individual keypresses on a keyboard scale up proportionally to the whole sequence (Rosenbaum, 1991, p. 273ff). This supports the notion that slowing down the sequence performance does not change the nature of the task.

Improvement on index finger tapping limited to the fine-skill group could relate to their overall faster performance while practicing and being tested on the finger sequence, which included index finger tapping components. Index finger tapping is relatively overlearned compared with the sequence and the higher finger movement rate in the fine-skill group might have been necessary to produce further improvement.

Expansion of Primary Motor and Sensory Representations and Increased Overlaps

The first major imaging result was that skill acquisition is accompanied by an expansion of primary motor and somatosensory representations. Activated regions in primary motor cortex gradually expanded, similar to previous experiments where frequency and type of movement were held constant over learning (Grafton et al., 1998). Moreover, a similar expansion occurred in primary somatosensory cortex.

Increases, decreases, and no changes in motor cortical activation have been observed in mapping studies of human motor skill learning (Doyon et al., 1996; Karni et al., 1995; Kawashima et al., 1994; Pascual-Leone et al., 1994, 1995), but exact comparison across studies is difficult for several reasons. Most important methodological differences among these studies include the duration of learning (hours to weeks), phase of learning (early versus complete asymptotic), type of learning (implicit versus explicit), and nature of the task, as discussed previously.

Studies in nonhuman primates provide further support for expansion of cortical fields with practice. Premovement cortical field potentials in premotor and motor cortex of the monkey increased during learning a skilled conditioned movement and stabilized when the movement was learned (Sasaki and Gamba, 1982). Nudo et al., (1996a) found enlargement of the M1 representation of the muscles/elementary movements used during learning of a food retrieval task by monkeys. Karni et al. (1995, 1998) mention this result in support of their speculation that expanded M1 activation represents the local network specifically representing the

trained motor sequence. However, because Nudo et al. (1996a) used intracortical stimulation to map the M1 output to muscles, rather than the representations of natural movements, the enlargement may be nonspecific and all natural movements employing the same muscles and/or elementary movements might benefit from this expansion. We speculate that such mechanism could underlie the expansion of M1 representations of the unpracticed simple movements observed in the present study. Other studies have shown that S1 representations also expand after increased utilization (Nudo et al., 1990; Recanzone et al., 1992).

The present results showed that as the volumes of individual representations increased, the degree of overlap among representations of individual movements in M1 and S1 increased as well, while the extent of the hand area (expressed as a union of all the finger movement representations) did not. In M1, overlaps increased significantly more in the fine-skill group than in the gross-skill group. A nonspecific training effect would be expected to affect the gross-skill group more, because the baseline overlaps were smaller there. Because the observed increase occurred in the fine-skill group instead, we believe this to be a specific effect of fine-skill learning.

A similar expansion of behaviorally significant cortical fields accompanied by increase in overlaps with adjacent cortical representations has been observed in mouse somatosensory cortex (Kossut and Siucinska, 1998). It is likely that in the absence of lesion, movement representations do not compete for cortical surface, but that instead, many representations coexist in the same cortical area (Kossut and Siucinska, 1998). We have replicated our previous observation (Hluštík et al., 2001) that the movement representation overlaps are more prominent in M1 than in S1, reflecting the more integrated nature of M1.

It is likely that the observed expansion of the cortical representations of simple hand movements does not reflect independent learning of these movements, because test-retest studies of simple finger movements do not demonstrate systematic change over time (Noll et al., 1997; Yetkin et al., 1996). Over the course of several weeks, primary motor and somatosensory activation with simple motor tasks is more likely to decrease (Loubinoux et al., 2001). Instead, cortical expansion and behavioral improvement in the present study are more likely to be generalized effects of practicing and learning the skilled movement.

Preservation of Somatotopic Arrangement Within M1 and S1

The second major imaging finding was that the M1 and S1 somatotopy did not change over time in the present study. The overall extent of the hand representations was preserved, and the ordering and the spatial separation of centroids of individual M1 and S1 movement representations did not

change. Although changes have been observed in other studies, these typically resulted from learning over much longer periods than the 3-week period used in the current experiment. Magnetoencephalographic data from Elbert et al. (1995) suggest that the S1 representations of the left fingers are farther apart than the right fingers in violin players than in nonmusicians. Furthermore, Volkman et al. (1998) found that the dominant hemisphere has a bigger M1 finger representation than the nondominant hemisphere (although somatotopy was not detected in that study). Perhaps the existence of larger individual representations eventually (over months or years) leads to their shift farther apart in the larger cortical hand territory.

Brain–Behavior Correlation

The third major result of the study was that the volume of cortical movement representations is correlated with the behavioral ability of the subjects. The similar temporal evolution of hand performance and movement-related M1/S1 volumes and the significant correlation of these measures suggest that in our paradigm, the size of cortical movement representations follows the behavioral ability over the whole course of learning. Previously, Grafton et al. (1994) found a within-subject correlation between rate of behavioral improvement and the rate of cerebral blood flow change, although in their study, improved performance in their study was manifested as increased rate of movement during brain imaging. This increase in total amount of movement may have confounded the results because, independent of learning, faster performance of finger movements proportionally increases both blood flow and fMRI signal change (Rao et al., 1996; Sadato et al., 1997).

Changes in Spatial Distribution of Contralateral M1/S1 Representations

Although somatotopy did not change in the present study, the spatial complexity of S1, but not M1, did change. In particular, the spatial complexity of S1 representations decreased over the course of learning, as the number of clusters linearly decreased and the primary cluster size linearly increased. In comparison, M1 showed no clear evidence of such monotonic change, even though total volume of activation increased in a similar degree to the increase found in S1. The spatial complexity of M1 activation seemed to decrease in the previous fMRI study of motor learning, as assessed by the observation of the “filling in” of originally patchy activation patterns (Karni et al., 1995, 1998). However, other data support changes in the opposite direction. One study in the oculomotor system reported fractionation of primary motor cortical stimulation maps after acquisition of a more precise smooth pursuit movement (Humphrey et al., 1997). Difference of the mapping methods as well as specific details of the tasks, such as their dependence on internal or

external spatial coordinates (discussed previously), may be crucial when considering these different effects of motor practice on cortical organization.

CONCLUSION

Long-term practice of a sequential finger movement task improved both performance on the practiced task and more general hand motor abilities. These changes were accompanied by expansion of the primary motor and somatosensory cortical representations of the practiced motor sequence and the representations of simple finger and wrist movements. Practice lead to increased overlaps of primary motor cortical representations, although the overall extent of the M1 and S1 hand representations and the somatotopic gradients in M1 and S1 did not change. The volume of cortical movement representations correlated significantly with performance on the finger sequence.

These results suggest that cortical representations of movement can be modified even by a modest amount of behavioral experience, and that the volume of engaged cortical tissue relates not only to the amount of movement being performed, but also to the current motor ability of the subject and to the history of movement performance and practice.

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