Sensorimotor Adaptation Changes the Neural Coding of Somatosensory Stimuli

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ABSTRACT

Motor learning is reflected in changes to the brain's functional organization as a result of experience. We show here that these changes are not limited to motor areas of the brain and indeed that motor learning also changes sensory systems. We test for plasticity in sensory systems using somatosensory evoked potentials (SEPs). A robotic device is used to elicit somatosensory inputs by displacing the arm in the direction of applied force during learning. We observe that following learning there are short latency changes to the response in somatosensory areas of the brain that are reliably correlated with the magnitude of motor learning: Subjects that learn more show greater changes in SEP magnitude. The effects we observe are tied to motor learning. When the limb is displaced passively such that subjects experience similar movements but without experiencing learning, no changes in the evoked response are observed. Sensorimotor adaptation thus alters the neural coding of somatosensory stimuli.
INTRODUCTION

Is the neuroplasticity that is associated with motor learning limited to motor areas of the brain or do the effects of learning extend into non-motor areas and notably into sensory systems? It is known that there are substantial anatomical interconnections linking the brain's motor and somatosensory regions. Cortical motor areas receive direct inputs from primary (Jones et al., 1978; Darian-Smith et al., 1993) and second somatosensory cortex (Krubitzer and Kaas, 1990; Cipolloni and Pandya, 1999) and from parietal areas 5 and 7 (Petrides and Pandya, 1984; Ghosh and Gattera, 1995). Somatosensory areas get direct cortical inputs from primary motor cortex (Jones et al., 1978; Darian-Smith et al., 1993; Krubitzer and Kaas, 1990), premotor cortex (Cipolloni and Pandya, 1999) and from supplementary motor area (Jones et al., 1978; Cipolloni and Pandya, 1999). A change in somatosensory function in association with motor learning would seem to be a natural by-product of this anatomical connectivity. However, apart from behavioral studies (Haith et al., 2008; Cressman and Henriques, 2009; Ostry et al., 2010; Wong et al., 2011) and a recent analysis of changes to resting-state networks in association with motor learning (Vahdat et al. 2011), there is little direct evidence that motor learning produces changes in sensory systems. Here we show that motor learning indeed alters the response of somatosensory areas of the brain. The changes we observe are substantially linked to motor learning in the sense that they vary in magnitude with motor learning and they are not obtained when subjects passively experience the same movement kinematics, but do not experience learning.

We studied motor learning using a force-field adaptation paradigm (Shadmehr and Mussa-Ivaldi, 1994) in which subjects had to reach straight ahead to a single visual target while a robot applied forces in a lateral direction in proportion to movement velocity. We assessed changes to sensory function that occur in conjunction with motor learning by using EEG to record somatosensory evoked potentials (SEPs) before and after learning. Instead of using electrical stimulation which
is infeasible in the case of elbow and shoulder muscles, we developed a technique in which we recorded SEPs while the robot mechanically displaced the subject’s arm in a direction that was aligned with the newly learned force field, orthogonal to the direction of movement.

SEPs have been recorded previously in response to mechanical stimulation. Typically, flexion or extension of the fingers has been used to elicit the SEPs. The earliest responses occur between 35 and 60 ms depending on the speed of the imposed displacement (Papakostopoulos et al., 1974; Mima et al. 1996; Alary et al., 1998). Current source estimates show initial responses in primary and second somatosensory cortex (Alary et al. 2002). In the one study that we are aware of, in which SEPs were recorded in conjunction with visuomotor learning, using median nerve stimulation, the authors report a transient SEP reduction early in learning followed by a return to baseline values by the time that learning reached asymptotic levels (Bernier et al., 2009).

In the present study, in addition to examining the effects of motor learning on the response of the somatosensory system, we considered the possibility that factors other than learning might produce changes in the response of the brain's sensory areas to the displacement of the limb. Factors such as exposure to the kinematic pattern experienced during training, exposure to an altered statistical distribution of movement directions, or to altered visual information could all possibly lead to changes in the sensory response without requiring learning. Accordingly, we carried out a control study in which we tested for the possibility that sensory change results from these factors rather than from motor learning per se. In the control test, the force-field learning trials were replaced with a control sequence in which the limb was displaced passively by the robot arm to replicate the entire sequence of trajectories experienced by subjects in the active learning condition (Ostry et al., 2010). Thus, subjects in the passive control condition experienced the same movement trajectories, the same distribution of movement directions and the same visual inputs as subjects that moved actively. The difference was that they did not experience
learning. By recording SEPs during this procedure, at the same points in the experimental sequence as in the primary experimental manipulation, we show that changes in the neural response to somatosensory stimuli are tied to motor learning.

MATERIALS AND METHODS

Subjects. Twenty-seven right-handed male subjects between the ages of 18 and 32 yrs (mean age of 22.5 yrs) participated in the study. Fifteen subjects were tested in the experimental group, twelve were tested in a passive control condition. Subjects had no history of sensory or motor disorders. The McGill University Research Ethics Board approved all experimental procedures.

Experimental setup. A two-degree of freedom planar robotic arm (InMotion2, Interactive Motion Technologies) was used for psychophysical part of study (Figure 1a). Subjects were seated in front of the robot and grasped the handle with their right hand. They either performed reaching movements to a single target in the horizontal plane or simply held the handle of robot arm while robot displaced the limb under position servo-control. The start position, target and a cursor that represented the position of the subject’s hand were all projected on a semi-silvered mirror that was placed horizontally just above the subject’s arm. Two white circles, 20 mm in diameter, indicated the start and target points while a yellow circle, 12 mm in diameter, represented the location of the hand. Subjects were not able to see their arm or hand at any point during the experiment and all studies were conducted with low ambient light levels. The movement start point was defined on a per subject basis, at a handle position 20 cm from trunk in the mid-sagittal plane. The seat height was adjusted to have an 80° abduction angle at the shoulder. The position of robot handle was recorded by means of 16-bit optical encoders at the robot joints (Gurley Precision Instruments). Subject applied forces to the handle were measured using a force-torque transducer (ATI Industrial Automation).
Reaching movements. Subjects were asked to move as straight as possible. The movement amplitude was 20 cm. EEG data were not recorded during this phase of experiment. A desired maximum tangential velocity was set at 0.5 ± 0.04 m/s. Visual feedback of both hand position and the target were presented throughout. Visual feedback of movement speed was also provided as soon as the subject’s hand entered the target zone. The feedback was used to encourage subjects to move within the desired speed range but trials were not removed from the analysis if the movement fell outside this range. At the end of each movement, the robot returned the subject’s hand to the start point. The next trial began after a random delay of 1500 ± 500 ms. The start of each trial was signaled by a visual cue and subjects were told that reaction time was unimportant.

In total, subjects completed 250 reaching movements, 100 as null field movements followed by 150 in a counter clock-wise force field. The force field was applied according to Equation 1.

\[
\begin{bmatrix}
    f_x \\
    f_y
\end{bmatrix} = \begin{bmatrix}
    0 & -18 \\
    18 & 0
\end{bmatrix} \begin{bmatrix}
    v_x \\
    v_y
\end{bmatrix} \tag{1}
\]

In this equation, \(x\) and \(y\) are lateral and sagittal directions, \(f_x\) and \(f_y\) are the commanded force to the robot and \(v_x\) and \(v_y\) are hand velocities in Cartesian coordinates.

Passive reaching movements. For control subjects, we replaced the force-field training trials with a set of passive movements in which the limb was guided under position servo control by the robot along the desired trajectory. Each of the 150 force-field trials was replaced with the corresponding mean trajectory for that trial, which was obtained from the first 12 of 15 subjects that performed the task under active conditions. Thus, subjects in the control condition experienced similar average trajectories and similar average spatial distribution of movements as subjects in the experimental condition, but they did not experience force-field learning. As in the
experimental condition, subjects in the passive control, first produced the 100 null field movements actively. Next, during the passive movement phase, to make sure that subjects attended to the passive movement task, on 10% of trials, the cursor that represented the subjects’ hand was removed from the screen either in the first or second half of the trajectory. Subjects were required to report whenever the cursor was removed. Ten subjects reported all such occasions, one subject missed one of these trials and another missed three.

Washout trials were not included in the present experiments. We have previously used a similar procedure in which both somatosensory function and learning were assessed in conjunction with force-field adaptation and matched passive control trials (Ostry et al. 2010). Under these conditions, we found that after-effects were present in washout trials following force-field learning. No after-effects were observed in washout trials in the passive control condition. This is consistent with the idea that there is limited motor learning in passive condition movements.

Electroencephalographic (EEG) data were obtained at a sampling frequency of 512 Hz using a 64-channel BioSemi ActiveTwo system (Figure 1b). The electrodes were mounted on an elastic cap that used the standard 10-20 system of electrode placement. Additional electrodes were placed on both ear lobes, at the outer canthus of each eye, and above and below the right eye.

Experimental procedure. Subjects were tested in a single session that lasted approximately 2.5 hours, including the explanation of the procedure and setup. Subjects completed five blocks of trials in total. In the first, third and fifth blocks of experiment, somatosensory evoked potentials (SEP) were recorded in response to position servo-controlled displacements of the arm. In blocks two and four, subjects were trained to make straight reaching movements to a single target.
Somatosensory evoked potentials. Mechanical perturbations were used to elicit somatosensory evoked potentials. The subject’s hand was positioned at the movement start position in the center of workspace. Subjects were asked to hold their hand in this central location and not to resist the action of the robot. In each set of SEP trials, four hundred displacements were applied under position servo control. The set was divided into four subsets that were separated by two to three minute rest periods. Position servoed displacements were applied pseudo-randomly to the right or the left of subjects’ midsagittal plane (two hundred in total in each direction). The displacements were programmed to be 4 cm in amplitude and to last for 1000 ms (300 ms rise time, 300 ms hold time and 400 ms fall time). Subjects were required to wait at the target position for a random interval of $1500 \pm 500$ ms between perturbations.

The EEG signal that was recorded in response to the displacements was band-pass filtered between 0.75 and 30 Hz using a 2nd order Butterworth filter and referenced to the average across all 64 channels. Individual SEP epochs extended from 100 ms before perturbation onset to 250 ms after. All epochs were time aligned at the initiation of the force pulse. The mean of the pre-perturbation part of the signal was subtracted before conducting further analyses. Epochs in which the voltage, at any of the 64 electrode locations or at electrodes placed externally around the eyes, exceeded $50 \mu V$ were excluded from analysis. We also looked for presence of alpha-wave activity and rejected subjects in which these patterns occurred in over 50% of trials. On this basis, 3 subjects from the passive condition were excluded from further analysis.

The recorded scalp voltage distribution was displayed graphically as a scalp map (Matlab based EEGLAB toolbox) that showed as a function of time statistically reliable changes in activation following learning (Delorme and Makeig, 2004). At each time point and each electrode location, $t$-scores were computed based on the SEP change following learning, using all trials across all
subjects. The $t$-scores displayed in Figure 4 were thresholded, as described below, at $p < 0.01$ (one-tailed) after correcting for family-wise error rate. This error rate was determined at each time point by computing the distribution of maximum $t$-statistics that were obtained by randomly permuting trials from before and after learning SEP sets. Each random permutation gave rise to 64 $t$-scores corresponding to the 64 electrode locations and gave a single maximum $t$-value. The entire procedure was repeated 5000 times and resulted in a distribution of maximum statistics, under the null hypothesis that SEPs are equal before and after learning. From this distribution we obtained the critical $t$-value that was used to threshold the displayed scalp images (Pantazis et al., 2005).

Current source estimation. The Brain Electrical Source Analysis software (BESA Research 5.3) was used to obtain estimates of the current source location underlying the recorded scalp voltage distribution. For the purpose of estimation, we used mean SEP values over all subjects and trials at each of the 64 electrode locations and focused on a 20 ms window centered about the first peak at electrode location C3. We used discrete dipole source analysis techniques and also distributed imaging methods (sLORETA, standardized low-resolution electromagnetic tomography, Pascual-Marqui et al., 1994) to obtain estimates of the current source. For the discrete technique, we first established the number of dipoles by using Principal Components Analysis (PCA). We found that the first principle component accounted for more than 97% of the variance in the scalp voltage distribution for both the pre-learning and the post-learning analyses as well as for their difference. Accordingly, we used a single dipole to model the current source in each case. Anatomical labels for the resulting dipole locations were obtained using Talairach Client (Lancaster et al, 2000). We used sLORETA to obtain the current density map. For purposes of comparison with the single dipole solution, we found the location corresponding to the point of maximum current density.
Data analysis. Hand position and subject-applied forces to the robot handle were each sampled at
400 Hz. The recorded signals were subsequently low pass filtered at 40 Hz using a zero phase lag Butterworth filter. Position signals were numerically differentiated to produce velocities. The start and end of each trial were defined at the time that hand tangential velocity went above or fell below 5% of peak velocity. The resulting data were time normalized to have the same number of samples in each trial. For purposes of data analysis, the maximum perpendicular deviation of the hand (PD) from straight line connecting movement start and end of movement was calculated.

For statistical analyses, learning was assessed using mean PD over the last 10 baseline trials, and the first ten and last ten force-field trials. Statistical tests were conducted using a split-plot ANOVA where the force-field training and passive control groups were a between subjects factor and the three kinematic measures were a within subjects factor.

To conduct statistical analyses of SEPs, mean SEP magnitudes were converted into z-scores on a per subject basis. A window of 8 ms around the first SEP peak was used for this purpose. z-scores were obtained using the mean and standard deviation of all trials for each subjects’ three SEP tests. Statistical tests were conducted using repeated measures ANOVA.

RESULTS

The experimental sequence is given in Figure 2a. We obtained SEPs at three points during the experiment: (1) at the start of the experimental session, (2) after a series of null field movement trials (no load) and (3) after motor learning. Figure 2a also shows the pattern of limb movement over the course of training. Kinematic performance was quantified by computing the mean perpendicular deviation from a line joining movement start and end (PD). Values for PD are shown, averaged over subjects. Data are shown for both the primary manipulation involving
active force-field learning and for the passive-movement control condition. It is seen that movements are straight in the null (no-load) condition, they are deflected laterally with introduction of load and reach asymptotic levels at the end of training. In the passive control condition, subjects first produce active movements in the absence of load (null condition). Then, in lieu of force-field trials, the limb is passively guided under position-servo control through a complete set of 150 trials in which the trajectory sequence is matched on a trial-by-trial basis to the mean of the first 12 of 15 subjects in the force-field learning condition. Representative hand paths, averaged over subjects, are shown in Figure 2b for both the active learning and passive movement conditions. Note that in each case initially curved movements return to near baseline values with training. ANOVA confirmed reliable changes in curvature, in both the force-field learning and passive movement conditions over the course of training \((F(2,50)=123.13, p < 0.001)\). The pattern was similar for passive movement and force-field subjects \((F(1,25)=0.34, p > 0.50)\). By the end of training, movement curvature for both groups had returned to baseline levels \((p > 0.90, \text{Bonferroni-corrected post-hoc comparison})\).

Somatosensory evoked potentials were elicited before and after training using robot-controlled displacements of the passive limb. The robot was programmed to produce a sequence of arm displacements under position servo control with random timing and in random order to the left and the right. The displacement was 4 cm in amplitude and the limb was held in position for 300 ms and then returned to the center. Mean displacement magnitudes were similar for the three SEP tests for subjects in both the experimental and the passive control groups \((F(2,28)=1.56, p > 0.20, F(2,22)=0.23, p > 0.70, \text{respectively})\).

In order to confirm that subjects’ hands were passively displaced by the robot for purpose of eliciting SEPs and that there was no active motor outflow during this procedure, we compared the forces applied by the robot and the measured forces at the handle that reflect the subjects’
resistance to the perturbation. Figure 2c shows a sequence of commanded displacements and measures of restoring forces acting against the robot handle. It can be seen that the pattern of restoring forces closely matches the pattern of applied load (see Figure 2c). The difference in magnitude between applied and measured forces to hand was small, averaging 0.24 N. The mean applied force was 3.42 ± 0.15 N (mean ± SE) and the mean sensed force was 3.64 ± 0.15 N. This means that there is little active force production on the part of the subject during the somatosensory measurement phase of the experiment. Moreover, there were no differences in the magnitude of the sensed force over the course of the three SEP tests for subjects in either the experimental or the passive control conditions (F(2,28) = 0.17, p > 0.80, F(2,22)=1.26, p > 0.30). Hence, there is no evidence of differences in forces applied by the robot to elicit SEPs that might account for changes in SEP magnitude.

Figures 3a and 3d show SEPs recorded over contralateral somatosensory cortex (electrode locations C3 and CP3, see Figure 1b, negative values are shown in a downward direction) aligned with the initiation of limb displacement. The figure shows mean SEP ± SE for force-field learning trials and comparable data in the passive-movement control condition. Peaks in the SEP are first evident between 70 and 80 ms following the start of limb displacement. There is a later peak at about 170 ms (see also Figure 4). If sensory change occurs in conjunction with motor learning, we should expect it to be present in the region of the first positive peak since this peak reflects the immediate consequences of sensory stimulation and is centered on somatosensory areas of the brain. The later negative peaks likely reflect the propagation of any changes due to learning to other brain areas and could possibly reflect factors that are cognitive in nature.

It can be seen that at both C3 and CP3, the magnitude of the early positive peak is unchanged following null field movements (baseline versus before training) but after a similar interval involving force-field learning there is a systematic SEP reduction (Figures 3a and 3d). No
changes in the magnitude of the early positive peak are observed in the passive-movement control trials (Figures 3b and 3e) which is consistent with the idea that no learning resulted from the passive manipulation. The later negative peak of the evoked response shows a different pattern at the two electrode locations, which is reflected in differences in the distribution of scalp voltage at longer latencies (see Figure 4).

SEP magnitudes averaged across subjects (± SE) are shown in Figure 3 for both force-field learning and passive control movements at electrode locations C3 (Figure 3c) and CP3 (Figure 3f). Values are expressed in z-score units relative to the mean over the three phases of the SEP procedure. Separate z-score calculations were conducted for the force-field learning and passive movement subjects. The figure gives values for the short latency peak as these measures are directly associated with the activation at electrode locations above somatosensory cortical areas. It is seen that at both C3 and CP3 electrode locations, SEPs change reliably following motor learning. A repeated measures ANOVA followed by Bonferroni corrected post-hoc tests found significant changes in SEP following learning at both C3 and CP3 (F(2,28) = 7.02, p < 0.005, F(2,28) = 10.0 p < 0.001, respectively). At both electrode locations, after-learning SEP values differed reliably from both pre-learning SEP measures (p < 0.03 or smaller in all cases). There were no differences between the baseline and before training SEPs (p > 0.40 or above). Following passive control trials, there are no reliable changes in SEP (F(2,16) = 0.10, p > 0.90, F(2,16) = 2.39, p > 0.10, for C3 and CP3 respectively).

We verified that the magnitude of the first positive peak was matched between force-field learning and passive control subjects prior to the learning sequence. A split-plot ANOVA revealed no differences in the magnitude of the first positive SEP peak. Specifically, we observed no differences between the two baseline SEPs (F(1, 23) = 0.006, p > 0.90, F(1, 23) = 1.18, p > 0.30, at C3 and CP3, respectively) and no differences in SEP magnitude between experimental
and control subjects (F(1, 23) = 1.12, p > 0.30, F(1, 23) = 1.49, p > 0.20, at C3 and CP3). Thus in
terms of the short latency peak in the SEP response, the only difference we see between
experimental and passive control subjects is that for experimental subjects SEPs are reduced
following learning. No SEP reduction occurs with passive control movements.

While experimental and control groups were equated in terms of the magnitude of the first
positive peak of the SEP (prior to learning), the magnitude of the later negative peak differed in
the two experimental conditions. This difference in the evoked response can be seen at electrode
locations C3 and at CP3 by comparing the magnitude of the later negative peak in Figure 3b and
3e with that of Figure 3a and 3d respectively. At both electrode locations, subjects that underwent
force-field learning showed larger non-specific SEP amplitudes at the later negative peak. The
fact that the difference is present even under null conditions before learning, rules out the
possibility that it is learning related. Indeed nothing, other than the participants involved and the
positioning of the electrode cap on the skull, differed for the SEPs elicited prior to learning (both
groups produced active movements for the null field trials). It is presumably one of these factors
that accounts for the observed differences in SEPs at the later negative peak.

We also conducted tests to assess possible differences in SEP for subjects in the experimental
group depending on the direction of the perturbation. We found no directional differences (left
versus right directed perturbation) in SEP magnitude over the three phases of the SEP procedure
(F(2,28) = 0.06, p > 0.90, F(2,28) = 0.22, p > 0.80, for C3 and CP3 respectively).

Figure 4 gives topographic probability maps, that is, the distribution, as a function of time, of
scalp locations at which sensory activity changes reliably due to learning (p < 0.01, corrected for
family-wise error rate, see Methods) and corresponding changes in activation in the passive
control condition. The upper two rows of the figure map out changes in activation at different
times over the course of the first positive peak in the SEP (as shown in Figure 3). The lower two
rows give changes over the course of the later negative peak. It can be seen that motor learning
results in short latency changes to sensory function that are greatest over contralateral
somatosensory cortex. Longer latency changes are seen over electrode locations in both
contralateral and ipsilateral premotor areas. Thus, we see that the same sensory stimulus
(displacement of the limb) results in different evoked responses after motor learning.

Comparable changes in activation are not observed when SEPs are elicited following passive
control trials. Probability maps in the second row of Figure 4 show that there are no short latency
changes (relative to baseline) in SEP (the example shown here is given at a p < 0.05 indicating
the absence of even marginal effects in the control condition). Reliable differences in SEP under
passive conditions are observed at longer latencies and are centered over more posterior locations
in parietal cortex.

We assessed the relationship between motor learning and the magnitude of the first peak of the
evoked response. For each of the electrode locations at which SEP magnitudes changed reliably
with motor learning, we calculated the correlation between the amount of learning and changes in
the magnitude of the somatosensory response. We repeated this calculation for each of the time
points shown in Figure 4, using a 15 ms window centered on each point to obtain measures of
SEP change. We quantified motor learning by using changes in average perpendicular deviation
(PD) between the first ten and last ten training trials. We found that changes in SEPs at electrode
locations over somatosensory cortex were reliably correlated with the magnitude of motor
learning: Subjects that learned more showed a greater reduction in SEP magnitude. Figure 4c
shows a representative example of this relationship at electrode location C5. For the first peak of
the evoked response, at 63 ms, there was a reliable reduction in SEPs with learning at electrode locations CP1, CP3 and CP5 \((r = -0.61, p < 0.02; r = -0.61, p < 0.02; r = -0.62, p < 0.02, \text{ respectively})\). At 71 ms, the SEP reduction was reliable at C3, CP1 and CP3 \((r = -0.54, p < 0.05; r = -0.61, p < 0.02; r = -0.60, p < 0.02, \text{ respectively})\). At 79 ms, the correlations were reliable at C5 and CP5 \((r = -0.57, p < 0.03; r = -0.55, p < 0.04)\).

We observed no reliable correlations at the later epochs, 87 ms or 90 ms. At the later negative peak of the evoked response, we found no systematic relationship between SEP change and learning. For this peak, none of the observed changes in SEP magnitudes at any of the time points shown in Figure 4 was correlated with motor learning \((p > 0.05 \text{ in all cases})\). Thus, while learning was systematically related to short latency SEP reductions at electrode locations over somatosensory cortex, the SEP changes observed at the later negative peak, although statistically reliable, were not related to learning, per se.

The changes in the scalp voltage distribution that accompany learning reflect plasticity in the underlying neuronal population. Figure 5 shows scalp topographic maps at the first SEP peak, before and after motor learning. The values are obtained by averaging over all subjects in the force-field learning condition. It is seen that both before and after learning, positive SEPs are located over contralateral parietal cortex and negative values are in frontal cortex. The peak of the positive evoked response following learning is over electrode location CP3. It can also be seen that both before and after learning the positive voltage pattern in parietal cortex is relatively focal whereas the negative pattern in frontal cortex is diffuse. This is presumably the reason that reliable changes in the evoked response following learning were seen only at electrode locations over parietal cortex (see Figure 4a).
We computed characteristics of the dipole current source as a way to quantify neural plasticity. We obtained estimates of each of the position, orientation, and strength of the underlying dipole current source before and after learning (see Methods for details). For SEPs elicited before learning, a single dipole in area 2 of left primary somatosensory cortex (Talaraich coordinates [-45, -22, 48], orientation vector [-0.3, -0.9, -0.4], current source strength, 11.36 nAm) accounted for 97.3% of the variance in the scalp voltage. Following learning, a single dipole in area 3 (location [-45, -23, 51], orientation [-0.3, -0.8, -0.5], current source strength, 9.83 nAm) accounted for 96.4% of the variance. Following learning the estimated dipole locations changed by 0.34 cm, the orientation changed by 7.7 deg and there was reduction in strength of 1.53 nAm. Thus the estimated current source is a single dipole located within somatosensory cortical areas and oriented in a posterior direction. This orientation is consistent with the scalp topographic maps shown in Figure 5.

We also obtained estimates of current source density associated with SEPs before and after learning using sLORETA. Activity peaks before and after learning were in areas 3 and 2, ([-44, -20, 42] and [-45, -22, 47] respectively), with a distance of 0.55 cm between the peaks. Thus both procedures give estimates of the current source location for the first SEP peak in the left primary somatosensory cortex.

We additionally obtained an estimate of the current source location for the SEP change following motor learning. In this case, the peak activity was in area 2 (Talaraich coordinates [-41, -24, 29]). A single dipole at this location accounted for 87.8% of the scalp voltage variance. In summary, consistent with the scalp map in Figure 4, SEPs following motor learning are centered about locations in contralateral somatosensory cortical areas.
In further analyses, we examined the difference in the estimated current source location for SEPs associated with leftward and rightward displacements of the arm. Although we found no significant difference in the magnitude of the SEPs for displacements in these two directions (see above), these two different perturbation directions presumably recruit different neuronal populations and this should be reflected in differences in the estimated current source. Using single dipole analyses, we found that the current source locations were located in areas 2 and 3 of left primary somatosensory cortex, and in all cases, accounted for more than 91% of the scalp voltage variance. Before learning the estimated current source was in areas 3 in the response to both leftward and rightward perturbations (Talaraich coordinates [-47, -20, 51] and [-41, -22, 44] respectively). Following learning for leftward perturbations, the estimated source moved to area 2([-46, -24, 52]), while for rightward perturbations, the estimated source remained in area 3([-44, -21, 50]). This suggests that both before and after motor learning, leftward and rightward perturbations recruit different neuronal populations.

DISCUSSION

We have shown that motor learning has short-latency effects on the response of somatosensory cortex even when measured after the end of training. Motor learning appears to be the determining factor behind these effects in that changes in SEP magnitude vary with the extent of learning and changes in SEPs are not obtained for yoked control movements that do not involve learning (but are matched on kinematic characteristics). The absence of SEP change following null field movements suggests that it is motor learning and not simply efferent outflow that is required to produce the somatosensory change. The presence of changes to SEPs that occur in conjunction with motor learning reveals a new dimension to plasticity in sensory and motor systems. Motor learning does not occur in isolation, but rather leads to changes in sensory areas
of the brain. Motor learning is thus associated with changes in a distributed network that involves
the brain's motor and sensory regions.

The SEP changes observed in the present study follow the same pattern as psychophysical
measures of perceptual change (Ostry et al. 2010, Vahdat et al. 2011). Both SEP magnitudes and
measures of sensed limb position vary with the extent of learning, and neither is observed to
change in the context of passive movement that does not involve learning. The SEP reduction
observed in the present study thus serves as an electrophysiological correlate of limb position
change that is measured using psychophysical techniques. The SEP changes following motor
learning presumably reflect plasticity in the neuronal population as evidenced by shifts in the
estimated current source location and magnitude. Thus, motor learning alters the somatosensory
cortical map.

The evoked potentials recorded in the present study had estimated current source locations in
primary somatosensory cortex both before and after motor learning. Single dipoles in these areas
accounted for large proportions of the variance in the scalp voltage distribution. Previous studies
that have used mechanical displacement of the fingers or wrist to elicit somatosensory evoked
potentials have reported topographic maps similar to those observed here with a frontal negative
and a parietal positive voltage distribution and with similar dipole orientations (Bötzel et al.,
1997; MacKinnon et al., 2000; Seiss et al., 2002). However, in the MacKinnon and Seiss papers,
the estimated current source was more anterior than here, in primary motor cortex. Our EEG
techniques do not permit us to conclusively determine whether the present somatosensory effects
are in sensory or motor areas of the brain. Accordingly, it remains to be determined whether
motor learning leads to changes in somatosensory function in sensory or motor areas or the two in
combination. Having somatosensory effects in motor areas of the brain would not be all that
surprising as there is ample evidence that cortical motor areas are extensively involved in somatosensory function (Rosén and Asanuma, 1972; Wong et al., 1978; Romo et al., 2004).

More generally, sensory change can be seen to play a functional role in the learning process. A common observation in studies of motor learning is that in the washout phase at the end of training there is persistent error in the sense that movements do not return to previous baseline levels (Shadmehr and Holcomb, 1997; Caithness et al., 2004). Our behavioral results suggest that this occurs because learning changes both motor and somatosensory systems in parallel. In Ostry et al. (2010), it is observed that after motor learning, movements follow trajectories that are aligned with shifted perceptual boundaries. Thus, in effect, the functional role of the observed sensory change is that in combination with motor learning, the two act together to keep motor and sensory systems in register.

The present findings complement the results of recent studies in which we have used fMRI under resting-state conditions to assess changes that occur in association with motor learning in the functional connectivity between the brain's sensory and motor regions (Vahdat et al. 2011). In that work, it was observed that changes in brain networks that occur in conjunction with learning can be partitioned into those that are primarily motor in nature and those that reflect the perceptual changes that occur in combination with motor learning. We find that changes in functional connectivity, which are related to perceptual change, occur between second somatosensory cortex (SII) and frontal motor areas (ventral premotor cortex and supplementary motor area). The sensory networks that were strengthened in conjunction with motor learning are the same as those involved in perceptual learning and perceptual decision-making in primates (Romo et al., 2002, 2004).
We have measured SEP changes that occur in conjunction with learning immediately following the adaptation procedure. It is difficult to have any sense of their durability. Nevertheless, there is considerable evidence that force-field adaptation produces durable changes in motor behavior at considerable delays after initial training (Nezafat et al., 2001). The somatosensory changes associated with motor learning, when measured behaviorally, likewise show persistence at least for 24 hours. Thus it appears that there may be durable changes that are associated with quite short period of sensorimotor training.

Transient reductions in SEPs have been reported previously in conjunction with finger and limb movement (Papakostopoulos et al., 1975; Rushton et al., 1981; Starr and Cohen, 1985). The reduction has been attributed to the idea that the nervous system suppresses sensory inflow associated with self-initiated movement. Typically SEPs decrease about 100 ms before EMG onset and remain depressed through to the end of the movement, but not longer. It is unlikely that the SEP reduction observed in the present study is a manifestation of the SEP suppression seen in association with movement. First, SEP changes are observed here in the absence of active movement. That is, they are present in testing that is conducted following the completion of the training phase of the experiment. It is also unlikely that the SEP change that we observe here arises due to repeated suppression over the course of learning. Bernier et al. (2009) report that an SEP reduction occurs early in visuomotor learning, but it dissipates quickly such that SEPs are back to baseline levels well before the end of the training. A further reason for thinking that the effects that we have seen here are not simply the persistence of a sensory suppression mechanism is that sensory suppression is typically associated with a reduction in acuity, rather than shifts in perceptual boundaries that are observed in conjunction with motor learning (Haith et al., 2008; Cressman and Henriques, 2009; Ostry et al., 2010; Vahdat et al., 2011). Cortical motor areas are densely interconnected with somatosensory cortex. There are ample opportunities for interactions
between sensory and motor areas that extend beyond the reduction of sensory signals in conjunction with movement.

Another possibility is that the changes observed here in the response to mechanical input are primarily attributable to changes in reflexes rather than cortical function. The latency of the observed SEPs in the present paper would be consistent with an interpretation based on the timing of the long-latency reflex response (MacKinnon et al., 2000). While this remains a possibility for the data presented here, other observations suggest that the present results are substantially cortical in nature. In particular, changes in somatosensory perceptual function are observed in the context of identical motor learning paradigms that do not involve reflex elicitation (Haith et al., 2008; Cressman and Henriques, 2009; Vahdat et al., 2011). Moreover there are changes in resting-state cortical somatosensory networks following motor learning under conditions where there is no experimental task at all (Vahdat et al., 2011).

It should be noted that it is not possible under passive movement conditions to fully equate both the movement trajectory and force simultaneously. Thus, forces experienced during the passive control movements differ in magnitude from those experienced during learning. Typically, the maximum lateral force at the hand in the passive condition is about half of that experienced during active force-field learning (Ostry et al., 2010). However, if the SEP change that we have observed following learning was attributable to experienced force during learning, then a nonzero SEP change should be evident in the passive movement condition, since forces differ from those that are experienced in conjunction with movements under baseline conditions. This is not what was observed.

We considered using alternative control tests which involved active rather than passive movements. One idea was to apply perturbations randomly in either a clockwise or
counterclockwise direction during active movement to the target location used for force-field learning. Under such conditions, there should be no learning, but subjects would experience perturbations that as in learning, are related to movement. If changes in SEPs are due to learning, it could be argued that no changes in SEPs should be expected under these conditions. However, it is known that when subjects experience unlearnable force-fields, antagonist muscle cocontraction is increased to maintain stability (Burdet et al., 2001). Cocontraction levels change over the course of training (Darainy et al., 2008; Franklin et al., 2008) and its possible effects on SEPs would need to be considered. If SEPs were observed to change under these conditions, it would be difficult to rule out the possibility that the changes were not due to impedance learning.
Figure 1. Experimental setup to study motor learning. A. Subjects moved the handle of a robot arm to a single visual target. Vision of the arm was occluded. In the force-field condition, the robot applied forces to the handle that varied with movement velocity. B. Scalp map showing EEG electrode locations.

Figure 2. Behavioral results for the force-field learning group and the passive control condition. A. Experimental sequence. Somatosensory evoked potentials were obtained before and after training (gray vertical bars). All subjects produced active movements in baseline trials (gray and black). The main experimental manipulation involved a force-field training sequence (red). Learning was assessed using the mean perpendicular deviation of the hand from a line joining movement start and end points. A group of control subjects was tested in a passive condition (cyan) in which subjects held the handle of the robot arm while the robot reproduced the entire series of movements of subjects in the force-field training condition. B. Mean hand paths for the force-field training (left) and passive-movement (right) conditions. C. Somatosensory evoked potentials were elicited as subjects held the handle of the robot arm. The limb was perturbed laterally using a sequence of servo-position controlled displacements (upper panel). The lower panel shows that subject applied forces sensed at the robot handle were closely matched to the commanded forces that displaced the arm.

Figure 3. Motor learning changes sensory evoked responses at electrode locations above contralateral somatosensory cortex. A and B. Mean somatosensory evoked responses (SEPs) at electrode location C3 before and after training for force-field learning (A) and passive movement (B). Changes to the first peak are observed following force-field learning but not under passive movement conditions. C. Z-scores for the first positive peak of the SEP averaged over subjects.
decrease reliably following force-field learning but not after passive movement. D, E, F. SEP changes with learning at electrode location CP3 are similar to those in the upper panel.

Figure 4. Topographic probability maps showing electrode locations at which evoked responses change reliably following training. Activation differences following learning (given as $t$ values, thresholded at $p < 0.01$) are shown at times associated with the first positive and later negative peaks of the SEP. A. Force-field learning results in reliable changes in activation at the first peak of the SEP at electrode locations over contralateral somatosensory cortical areas (upper panel). There are no changes in the passive movement condition (lower panel). B. Force-field learning also results in changes in activation at the second peak of the SEP at bilateral electrode locations over premotor areas (upper panel). Passive training leads to changes in activation over posterior parietal cortex (lower panel).

Figure 5. Scalp topographic maps averaged over subjects at the first positive peak of the somatosensory evoked response. A. Scalp voltage distribution before motor learning. B. Voltage distribution after learning.
REFERENCES


Force-field learning

First peak

Passive movement

T=63 ms  T=71 ms  T=79 ms  T=87 ms  T=90 ms

Second peak

Passive movement

T=157 ms  T=169 ms  T=180 ms

SEP change (μV)

Adaptation amount

$C5$

$r = -0.55$

$p < 0.03$
Before learning

After learning

SEP (μV)

-0.3  -0.1  0.1  0.3  0.5