Somatosensory changes associated with motor skill learning

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Abstract

Trial-and-error motor adaptation has been linked to somatosensory plasticity and shifts in proprioception (limb position sense). The role of sensory processing in motor skill learning is less understood. Unlike adaptation, skill learning involves the acquisition of new movement patterns in the absence of perturbation, with performance limited by the speed-accuracy tradeoff. We investigated somatosensory changes during motor skill learning at the behavioral and neurophysiological level. Twenty-eight healthy young adults practiced a maze-tracing task, guiding a robotic manipulandum through an irregular 2D track featuring several abrupt turns. Practice occurred on days 1 and 2. Skill was assessed before practice on day 1 and again on day 3, with learning indicated by a shift in the speed-accuracy function between these assessments. Proprioceptive function was quantified with a passive two-alternative forced choice task. In a subset of 15 participants, we measured short latency afferent inhibition (SAI) to index somatosensory projections to motor cortex. We found that motor practice enhanced the speed-accuracy skill function ($F_{4,108} = 32.15$, $p < 0.001$) and was associated with improved proprioceptive sensitivity at retention ($t_{22} = 24.75$, $p = 0.0031$). Further, SAI increased after training ($F_{1,14} = 5.41$, $p = 0.036$). Interestingly, individuals with larger increases in SAI, reflecting enhanced somatosensory afference to motor cortex, demonstrated larger improvements in motor skill learning. These findings suggest that SAI may be an important functional mechanism for some aspect of motor skill learning. Further research is needed to test what parameters (task complexity, practice time, etc) are specifically linked to somatosensory function.

New & Noteworthy

Somatosensory processing has been implicated in motor adaptation, where performance recovers from a perturbation such as a force field. We investigated somatosensory function during motor skill learning, where a new motor pattern is acquired in the absence of perturbation. After skill practice, we found changes in proprioception and short latency afferent inhibition (SAI), signifying somatosensory change at both the behavioral and neurophysiological level. SAI may be an important functional mechanism by which individuals learn motor skills.

Introduction

Motor learning is the improvement in performance associated with repetitive practice. Learning can generally be categorized into either modifying a well-learned movement in response to a perturbation (i.e. adaptation) or acquiring a new set of movement patterns in the absence of a perturbation (i.e. skill learning) (McGrath and Kantak 2016; Reis et al. 2009; Shmuelof et al. 2012). Motor adaptation and skill learning differ also differ in timescale. With adaptation, error reduction plateaus within minutes and reaches a level of performance close to baseline (Bastian 2008; Krakauer and Mazzoni 2011). A simple motor skill with straightforward kinematics (i.e. planar straight reaches or finger button presses) may show improvements in speed or accuracy on the order of minutes, but more complex motor skill learning may continue to show improvements over multiple training sessions (e.g., improving a tennis serve over days, weeks, months, years) (Dayan and Cohen 2011).

There are several overlaps between the known neural substrates of adaptation and skill learning. The cerebellum is important for both motor adaptation and the early stage of learning a new motor skill (Cantarero et al. 2015; Galea et al. 2011; Spampinato and Celnik 2017, 2018). Primary motor cortex (M1) has been tied to a later stage of learning involved in the retention of learned movements in both skill learning and adaptation paradigms (Galea et al. 2011; Reis et al. 2009; Richardson et al. 2006; Robertson 2005). With skill learning, altering M1 activity affected performance between sessions, or offline learning processes involving consolidation (Reis et al. 2009). Altering M1 activity with non-invasive brain stimulation in visuomotor rotation, a form of motor adaptation, influenced the rate of forgetting (i.e. retention) after the perturbation was removed; however, it did not affect the rate of adaptation (Galea et al. 2011).

While much motor adaptation and motor skill learning research has focused on the motor system, there is significant evidence of somatosensory involvement in these processes. Spatial shifts in proprioceptive estimates of hand/limb position have been observed following visuomotor adaptation (Cressman and Henriques 2009; Henriques and Cressman 2012; Salomonczyk et al. 2012), as well as force field adaptation (Ostry et al. 2010). Force field adaptation has been associated with changes in somatosensory evoked potentials (Nasir et al. 2013) and changes in resting state functional connectivity in networks involving S1 (Vahdat et al. 2011, 2014). Lesions to somatosensory cortex have been found to impair motor skill learning in animal models (Pavlides et al. 1993). Further, noninvasive brain stimulation over somatosensory cortex has been shown to influence motor skill learning in both neurologically intact individuals and stroke survivors (Brodie et al. 2014; Meehan et al. 2011; Vidoni et al. 2010).

Despite the accumulation of evidence highlighting the role of somatosensory processing in motor learning, the majority of previous studies in this area concerns motor adaptation or relatively simple motor skills (i.e. planar straight reaches or finger button presses) (Cuppone et al. 2018; Ostry and Gribble 2016; Wong et al. 2011). While there is no set definition as to what makes a skill “complex”, we and others suggest that it involves coordinating and sequencing different arm movements with temporal and spatial constraints (Kantak et al. 2018, 2017; McGrath and Kantak 2016). A relatively more complex motor skill is likely to be more kinematically demanding; e.g., a motor pattern with several abrupt turns requiring a series of movements by different joints to execute the pattern accurately. With practice, the kinematics become smoother, indicative of better planning and overall improvement in the movement *quality* (Kantak et al. 2018; Shmuelof et al. 2012). Gains in motor skill are best captured by a shift in the speed-accuracy function (Kantak et al. 2017; McGrath and Kantak 2016; Reis et al. 2009; Shmuelof et al. 2012). In other words, the motor pattern is executed more accurately at a range of movement speeds.

Here we asked whether learning a relatively complex skill, confirmed by a shift in the speed-accuracy tradeoff, is associated with changes in somatosensory function. At the behavioral level, we assessed proprioceptive function before and after skill learning. Given reciprocal links between sensory and motor systems (Ostry and Gribble 2016) and that skill learning reflects improved motor acuity (Shmuelof et al. 2012), we expected skill learning to also be associated with enhanced proprioceptive acuity. If skill learning is associated with changes in proprioceptive function, we would also expect changes in sensory processing at the cortical level. To investigate this, we used transcranial magnetic stimulation (TMS) and peripheral median nerve stimulation to measure short latency afferent inhibition (SAI) before and after skill learning. SAI provides a measure of the inhibitory somatosensory projections to motor cortex. The magnitude of SAI is associated with the excitability of somatosensory cortex and is thought to reflect sensorimotor integration (Bailey et al. 2016; Turco et al. 2017). However, the association between SAI magnitude and behavior is less clear. SAI magnitude was not related to performance involving tactile function or manual dexterity (Turco et al. 2018). Whether SAI changes in the context of more complex skill learning has not been investigated. A working model of SAI proposes that the level of inhibition is related to GABA levels in somatosensory cortex (Turco et al. 2017). If somatosensory cortex is critical for motor skill learning, we hypothesized that motor skill learning will be associated with increased SAI, reflective of enhanced afferent input to S1.

Methods

Participants

Twenty-eight right-handed young adults (17 female), aged 18-30, with no known neurological disorders, participated in the experiment. Of these, 15 subjects received TMS measurements (11 female, aged 18-30). The study was approved by the Indiana University Institution Review Board. All participants gave written informed consent before participating in the study.

Experimental Design

Each participant completed three sessions of proprioception and motor tasks over three consecutive days. Both tasks entailed sitting in front of a 2D virtual reality apparatus and grasping the handle of a KINARM Endpoint 2D robotic manipulandum (BKIN) with the right hand (Fig. 1A). The task display, viewed in a mirror, appeared in the plane of the manipulandum. The mirror and a drape over the shoulders prevented direct vision of the arm, hand, or manipulandum. Subjects wore a wrist brace to reduce wrist flexion/extension, so that the movement was mostly at the shoulder and elbow. On day 1, a baseline speed-accuracy function was assessed. On days 1 and 2, proprioception was evaluated before and after motor skill training, while retention of proprioception and motor skill speed-accuracy function was assessed on day 3 (Fig.

1B). In the subset of subjects receiving neurophysiological measurements, we delivered transcranial magnetic stimulation (TMS) to assess motor corticospinal excitability and short latency afferent inhibition (SAI) before and after the behavioral tasks on day 1 and day 2 (Fig.1B).

Motor Skill Training and Speed-Accuracy Function Assessment

In the 2D task display (Fig. 1A), participants navigated a visual cursor (white circle, 10mm diameter) through an irregular shaped track (20x20 cm space, 1.5 cm width) using the robotic manipulandum (Fig. 1C). This design is similar to that of Kantak and colleagues (Kantak et al. 2018, 2017; McGrath and Kantak 2016), with 6 straight-line segments connected by abrupt turns. The white cursor was displayed veridically, centered at the top of the manipulandum handle. Subjects were instructed to move as accurately as possible within the desired movement time range. The track's design required subjects to coordinate and sequence movements at shoulder and elbow to traverse the track within the temporal and spatial constraints (Kantak et al. 2018, 2017; McGrath and Kantak 2016). For example, one possible sequence of joint movements would be (1) elbow flexion with shoulder adduction (first horizontal section), (2) elbow extension with shoulder abduction (diagonal portion), (3) elbow extension with shoulder abduction (second horizontal section), (4) elbow extension with shoulder flexion (first sagittal section), (5) elbow extension with shoulder abduction (third horizontal section), and (6) elbow extension + shoulder flexion (second sagittal section). These different movements could be captured by multiple sub-movements, requiring subjects to manage the acceleration/jerk of tracing a track with several abrupt turns, which would not be observed in a simple planar reaching task in which subjects move in a straight line to a target.

Each trial began with a starting red square, centered at the body midline. After 1 second, the starting square turned green and the irregular shaped track appeared with a green square at the end of the final track segment. Participants were instructed to move the white cursor into the starting square, and when ready, to follow the track to the end green square as accurately as possible. The trial was complete once the cursor entered the end green square. After each movement, subjects received feedback on their movement time (too slow, too fast, good speed) and accuracy in the form of points. They were instructed to first prioritize movement speed, and then work on improving their accuracy throughout practice. Subjects were rewarded with 5 points for trials of good speed, and received an additional 1, 2, or 3 points for higher levels of accuracy. 0 points were given if they moved too slowly or too quickly for the desired speed range, regardless of how accurate they were. Subjects were told that during the speed-accuracy tradeoff skill assessment the desired speed range may change, and to use the feedback to help guide their subsequent movements.

During motor skill assessment on day 1 and day 3 (Fig. 1B), the motor skill was performed over 5 movement time (MT) ranges to assess a speed-accuracy tradeoff in five separate blocks of trials (MT 1: 300-600 ms; MT 2: 600-850 ms; MT 3: 850-1100 ms; MT 4: 1100-1400 ms: MT 5: 1400-1700 ms). Order of MT ranges was randomized across participants, with 10 trials at each MT range collected, before proceeding to the next block with a different MT (Kantak et al. 2018, 2017; McGrath and Kantak 2016). Motor skill assessment took approximately 5-10 minutes. During motor skill practice on day 1 and day 2 (Fig. 1B), participants trained at a fixed MT range (MT 3) for 120 trials and 150 trials, respectively. Subjects were told that the desired speed range would remain constant, and to work on improving their accuracy with practice. The trials were performed in blocks of 30 trials, with ~2 minutes rest in between, to minimize fatigue. Motor training on each day took approximately 20-30 minutes.

For each individual trial (Fig. 1D), we calculated movement time (MT) and percentage of movement trajectory inside the track (in-track accuracy). MT was defined as the difference in time between when the cursor exited the start square and when the cursor entered the end square. Only trials of the correct MT were analyzed. All subjects had 120 and 150 trials of practice, and 10 trials per MT bin in the skill assessment, as trials outside of the prescribed MT range were repeated (McGrath and Kantak 2016; Shmuelof et al. 2012). For the motor skill assessment blocks, mean in-track accuracy and MT were computed separately for each MT bin.

Proprioception Assessment Task

The sense of hand position was assessed in a passive movement two-alternative forced choice task (2AFC). The robotic manipulandum passively moved the participant's hand to different test positions using movements that followed a bell-shaped velocity profile (Fig. 2A). At each test position, participants verbally reported their perceived hand position in relation to a visual reference marker (white circle), which was always present during the task (Wilson et al. 2010). Between individual trials, passive distractor movements in random directions were applied to minimize the possibility of subjects adapting their responses based on the previous response (Wong et al. 2011). The distractor movements varied in 2D and ranged in movement time between 500-1500 ms. Proprioception was assessed in the horizontal dimension (left/right of visual reference) in all participants and in the sagittal dimension (forward/backward of visual reference) in all but 5 participants who completed the study before the sagittal assessment was added. The order of dimension of testing was randomized across participants. While proprioceptive assessments in motor adaptation studies are often done near the end of the movement path, where motor error is greatest, we placed the visual reference at the center of the track where the horizontal and sagittal track sections intersected. Others have also tested proprioception at the center of the workspace (e.g. Wong et al. 2011). The task was to stay in the track all the way along from beginning to end, and the trial only ended when subjects reached the end of the track. We therefore hypothesized that proprioception would likely be important at many points along the track, including the center.

For test positions in the horizontal dimension, the sagittal position remained constant and vice versa. The test positions were determined using an adaptive staircase algorithm based on the Parameter Estimation by Sequential Testing method (PEST) (Block et al. 2019; Hoseini et al. 2015; Ostry et al. 2010; Taylor and Creelman 1967). The first trial of each staircase began with moving the subject's hand to the visual reference where it was held for 2 seconds, and subjects received explicit knowledge that their hand was at the reference position (Wilson et al. 2010; Wong et al. 2011). After a distractor movement, the hand was positioned 6 cm away from the visual reference. If the subject's response was correct (i.e. "left" when the hand was 6 cm to the left of the reference), the subsequent test positions were 2 cm closer to the visual reference until the subject's reported judgment reversed. With each reversal, the step size decreased by half so that more judgments were made near the perceptual boundary, or position at which the subject is equally likely to report left/right or forward/backward. The staircase terminated after the subject had reversed their judgment 4 times. In each dimension, 4 staircases were performed, with 2 staircases beginning to the left or in right of the visual reference (horizontal dimension) and 2 staircases beginning to in front or behind the visual reference (sagittal dimension) (Fig. 2B). Since we used an adaptive staircase algorithm, the number of trials depended upon each subject's responses during the testing. In order to get to 4 reversals, there could be a number of combinations of potential judgements that contribute to a different number of trials. Each dimension of testing took approximately 3-5 minutes to complete.

For each proprioception assessment, we calculated the proportion of trials that a participant responded left (horizontal dimension) or down (sagittal dimension) across the different test positions. The data were fitted with a logistic function upon which proprioceptive bias and sensitivity were calculated. Bias was defined as the 50% point of the fitted function (perceptual boundary). Subjects have naturally idiosyncratic biases in proprioception that vary in direction (Henriques and Cressman 2012; Liu et al. 2018; Salomonczyk et al. 2012). It is possible that motor skill training could alter bias direction (e.g., from right to left). However, there is no evidence to suggest that a directional change, by itself, would be functionally an improvement. Our goal was to detect improvement in proprioception, which in this context would be a reduction in bias *magnitude*; we therefore used absolute bias in all group analyses. Sensitivity (uncertainty range) was defined as the distance between the 25% and 75% points of the fitted function (Wilson et al. 2010; Wong et al. 2011) (Fig. 2C).

Neurophysiological Assessment

Surface electromyography (EMG) was recorded from the right first dorsal interosseus (FDI) muscle and abductor pollicis brevis (APB) muscle in a belly-tendon montage with a common ground electrode over the right ulnar styloid process. EMG signals were amplified (AMT-8; Bortec Biomedical, Calgary, Canada), band-pass filtered (10-1000 Hz), sampled at 5000 Hz, and recorded using Signal software (Cambridge Electronic Design Ltd, United Kingdom).

During TMS, participants were seated with their arms relaxed on a pillow. Single pulses of TMS were delivered using a Magstim 200^2 stimulator (Magstim Company LTD, United Kingdom) with a 70-mm figure-of-eight coil. The coil was held tangentially over the left motor cortical representation of the hand with the handle 45 degrees to the midline to evoke posterior-to-anterior current in the cortex. The optimal scalp position was determined by the largest and most consistent motor evoked potentials (MEP) in the relaxed right FDI. We registered the coil position and trajectory of the FDI hotspot in a BrainSight neuro-navigation system (Rogue Research, Montreal, Canada). At the beginning of day 1 and day 2, we found resting motor threshold (RMT), defined as the minimum stimulator intensity to evoke MEPs > 50 microvolts in at least 10 out of 20 trials (Rossini et al. 2015), and the stimulus intensity that would evoke a 1 mV MEP on average over 10 trials (SI_1mV).

Two neurophysiological measurements were made pre- and post-training: Motor corticospinal excitability (SI_1mV) and short latency afferent inhibition (SAI). The order of the SI_1mV block and SAI block were randomized across participants. During the SI_1mV block, we delivered 20 single pulses at SI_1mV with a 5 s inter-trial interval, with the same intensity pre- and post-training, to evaluate changes in motor corticospinal excitability. An additional 40 pulses were delivered for the SAI block.

To elicit SAI, a TMS pulse at SI_1mV was delivered 22 ms after an electrical stimulus over the median nerve at the right wrist (Tokimura et al. 2000; Turco et al. 2017). Electrical stimuli were delivered using a Grass Instruments S88 stimulator (Astro-Med; RI, USA) with in-series stimulus isolation unit (SIU-5) and constant-current unit (CCU-1) (square wave pulse, 0.2 ms duration, cathode proximal). The intensity was set based on a visible thumb twitch and adjusted as needed to evoke a consistent M-wave amplitude in the APB. By keeping the M-wave constant across the study, we rule out the possibility that any changes in SAI are be due to differences in stimulation intensity across time (Bailey et al. 2016; Turco et al. 2017).

During the SAI block, 20 conditioned MEPs (TMS + median nerve stimuli) and 20 unconditioned MEPs (TMS alone) were delivered in a random order with a 5 s intertrial interval. Since the magnitude of SAI is sensitive to the amplitude of the unconditioned MEP (Ni et al. 2011; Turco et al. 2017; Udupa et al. 2009), the TMS intensity needed to evoke an unconditioned 1mV response was re-assessed post-training. If needed, the TMS intensity was adjusted so that there was an average unconditioned response of 1mV in both the pre and post-training SAI block. This allows us to infer changes in somatosensory projections to motor cortex independent of any underlying changes in

M1 excitability (Tokimura et al. 2000; Turco et al. 2017). There was no adjustment of the TMS intensity on a trial-by-trial basis because the intensity is based on an average response of unconditioned MEPs.

For all trials in the SI_1mV block and SAI block, peak-to-peak MEP amplitudes were analyzed. Trials with muscle activity in the 100 ms before the TMS pulse, defined as root mean square EMG exceeding 15 microvolts, were discarded from analysis. 3.6% of the 3600 total trials were discarded. SAI was expressed as a percentage of the unconditioned MEP amplitude. Lower values indicate higher levels of MEP suppression by the somatosensory afferent volley.

Statistical Analysis

Motor skill learning (shift in speed-accuracy function) was computed by comparing accuracy across the five MT bins at baseline versus retention using a Day (Baseline, Retention) x MT Bin (MT 1, MT 2, MT 3, MT 4, MT 5) repeated measures ANOVA. To verify that any differences in accuracy were not due to changes in average MT across the five MT bins, we also ran a Day (Baseline, Retention) x MT Bin repeated measures ANOVA on MT. We did not perform statistical analysis on the motor practice data performed at MT 3 because performance at a single speed is not a good indicator of skill learning (McGrath and Kantak 2016; Shmuelof et al. 2012; Wickelgren 1977), as the speed-accuracy function is not necessarily linear (Wickelgren 1977). Motor skill was thus only *assessed* at two time points in this study: baseline on day 1 and retention on day 3.

Within-session training effects on proprioceptive bias and sensitivity in each dimension were evaluated with a Day (Day 1, Day 2) x Time (Pre- and Post-training) repeated measures ANOVA. Retention of proprioceptive changes was evaluated by a paired sample t-test comparing values on day 3 to baseline on day 1.

For each neurophysiological outcome variable (MEPs evoked by SI_1mV and SAI), we ran a Day (Day 1, Day 2) x Time (Pre-Training, Post-Training) repeated measures ANOVA. To evaluate whether any changes in neurophysiology were related to the magnitude of motor skill learning, we ran separate correlations comparing change in MEP amplitude (evoked from SI_1mV) or change in SAI versus total skill learning. Total skill learning was calculated by taking the cumulative difference in accuracy across 5 movement times at baseline on day 1 compared to that at retention on day 3. The neurophysiological changes were averaged across day 1 and day 2.

For ANOVAs involving MT bin, post-hoc pairwise comparisons were performed after significant Day x MT Bin interactions using Tukey's HSD. Given the exploratory nature of this research, we did not adjust p-values to account for analyzing multiple outcome measures. Statistically significant results are therefore indicative of a need for further study.

Results

Motor Skill

Total skill learning averaged 32.3%, but some subjects made large gains in skill (Fig. 3A) while others showed no improvement or even a slight loss (Fig. 3B). Total skill learning thus varied considerably across subjects, ranging from -10.8% to 94.9%.

Nonetheless, at the group level, changes in in-track accuracy during motor skill speed-accuracy function assessment suggest that subjects were able to learn the motor skill in the training time allotted (Fig. 4A). We found a main effect of Day ($F_{1,108} = 32.15$, $p < 0.001$), indicating a shift in the speed-accuracy function from baseline to retention (Fig. 4A). There was also a main effect of MT bin ($F_{4,108} = 218.04$, $p < 0.001$), suggesting different accuracy at different MTs, as expected, and a significant Day x MT Bin interaction ($F_{4,108} = 7.32$, $p < 0.001$). Post-hoc contrasts indicated higher accuracy at MT1, MT2, and MT3 ($p<0.0001$, $p<0.0001$, $p = 0.003$, respectively) at retention compared to baseline. The higher accuracy levels at MT4 and MT5 were not statistically significant ($p = 0.09$, $p = 0.069$, respectively).

The shift in speed-accuracy tradeoff cannot be attributed to differences in speed at baseline compared to retention, which ranged from -18.23 ms (slower at retention) to 24.94 ms (faster at retention), with a mean difference of 7.38 ms across the 5 MT bins (Fig. 4B). Accordingly, there was no main effect of Day ($F_{1,108} = 2.48$, $p = 0.13$).

Only the motor skill speed-accuracy assessment blocks were used to *assess* motor skill learning (Kantak and Winstein 2012; Soderstrom and Bjork 2015), but mean subject performance and inter-individual variability during motor practice on day 1 and day 2 are shown for illustrative purposes in Fig. 4C.

Proprioception

In the sagittal dimension, proprioceptive sensitivity decreased (improved) after training on day 1 (45.2 mm on pre compared to 33.5 mm on post, representing ~35% improvement), and remained consistently low on day 2 (Fig. 5A). This is supported by a borderline significant interaction between Day and Time ($F_{1,22} = 4.25$, $p = 0.051$) and main effects of Day ($F_{1,22} = 7.79$, $p = 0.011$) and time ($F_{1,22} = 10.29$, $p = 0.0041$). At retention, sensitivity was enhanced compared to baseline ($t_{22} = 24.75$, $p = 0.0031$). While there appears to be greater variability at baseline, 18 out of the 23 participants demonstrated an improvement in proprioceptive sensitivity at retention (ranging between 9 mm and 78 mm of improvement). To verify the significant improvement was not driven by higher initial variability at baseline, we identified the four most extreme participants (more than 1.5 interquartile ranges above the upper quartile). However, we found a significant improvement in sensitivity ($p = 0.0163$) even without these four individuals, suggesting the change in sensitivity is robust. Proprioceptive sensitivity in the horizontal dimension was consistently better (i.e., smaller) than in the sagittal dimension at all time points (Fig. 5A). Thus, a floor effect may explain why horizontal sensitivity was not modulated across training days, with no significant main effects or interactions, and no significant difference at retention (all $p > 0.50$).

Proprioceptive bias in the sagittal dimension improved similarly each day (Fig. 5B), as indicated by a main effect of Time ($F_{1,22} = 6.52$, $p = 0.018$) but not Day ($F_{1,22} = 1.64$, $p = 0.21$). There was no Day x Time interaction ($p > 0.90$). Interestingly, bias at retention was similar to baseline ($t_{22} = 5.84$, $p = 0.54$) (Fig. 5B). Together, these results suggest that training-related improvements in bias were not retained from day to day. As with sensitivity, proprioceptive bias in the horizontal dimension was consistently better (i.e., smaller) than in the sagittal dimension at all time points (Fig. 5B), and there were no significant main effects, interaction, or change at retention (all $p > 0.41$).

Neurophysiology

RMT on day 1 and day 2 was 42.9 ± 9% (mean ± standard deviation) and 43.3 ± 9% of stimulator output, respectively. The stimulus intensity needed to evoke a 1mV MEP on day 1 and day 2 before training was 53.5 ± 12% and 54.2 ± 13%, respectively.

SAI showed a main effect of time ($F_{1,14} = 5.41$, $p = 0.036$), indicating that within each day, SAI increased from pre- to post-training (Fig. 6A). There was no effect of Day ($F_{1,14} = 2.00$, $p = 0.18$) and no Day x Time interaction ($F_{1,14} = 0.091$, $p = 0.77$). MEP amplitude elicited by SI_1mV was not modulated by training or across days (Fig. 6B). There was no main effect of Day ($F_{1,14} = 0.32$, $p = 0.58$) or Time ($F_{1,14} = 0.69$, $p = 0.42$), and no Day x Time interaction ($F_{1,14} = 0.50$, $p = 0.49$).

Interestingly, subjects who showed greater learning of the motor skill were more likely to also have greater increases in SAI within each day (Fig. 3B), whereas subjects who did not learn the motor skill often had a reduction in SAI (Fig. 3D). This pattern was borne out at the group level: Individual changes in SAI from pre- to post-training (averaged across days) were associated with the baseline-to-retention magnitude of motor skill learning (R = -0.52, p = 0.048, Fig. 7). In other words, subjects whose SAI increased after training were those that showed larger magnitude of skill learning at retention. SAI increase was not correlated with total number of training trials, which varied due to repetition of trials outside the desired speed range (R = 0.38, p = 0.15), or with training time (R = -0.14, p = 0.62).

Discussion

Motor skill training was associated with changes in proprioceptive function and SAI, suggesting a prominent role for the somatosensory system in some aspect of motor skill learning. At the group level, SAI increased each day after training, reflecting increased somatosensory afference to motor cortex. Greater motor skill learning, as indicated by the speed-accuracy function, was associated with greater increases in SAI.

Behavioral evidence of motor skill learning

Motor learning has traditionally been studied using single session training studies of already well-learned movements in the absence of a perturbation, or with systematic perturbations associated with motor adaptation. A hallmark of skill learning is a shift in the speed-accuracy tradeoff; i.e., improvements in speed without sacrificing accuracy or improvements in accuracy without sacrificing speed. Our behavioral paradigm was adapted from Kantak et al., which employed an irregular shaped track (Kantak et al. 2018, 2017; McGrath and Kantak 2016). In the present study, two days of motor training at a fixed speed shifted the speed-accuracy function and enhanced motor skill accuracy at untrained movement speeds, consistent with previous literature. Since movement times were unaltered at baseline compared to retention, the results suggest that training resulted in an improvement in a complex motor skill.

While there is no set definition as to what makes a skill “complex”, we and others suggest that in a reaching task, it involves coordinating and sequencing different arm movements to traverse the track with temporal and spatial constraints (Kantak et al. 2018, 2017; McGrath and Kantak 2016). The skill considered in the present study is certainly not as complex as a skill that would take weeks or years to perfect, such as a golf swing or bowing a violin. However, navigating the track requires a well-timed sequence of elbow and shoulder movements; to improve accuracy, subjects must get better at managing their acceleration and smoothness as well as interaction torques and other forces caused by the presence of abrupt turns in the track. These demands would be absent in a straight-line reaching task.

Based on the motor practice data illustrated in Fig. 4C, it may be tempting to conclude that learning quickly reached an asymptote on day 1, or that there were no offline gains between day 1 and day 2. However, because this data represents motor performance at a single speed, it is not a good metric for motor skill learning (Shmuelof et al. 2012; Wickelgren 1977). One reason is that the speed-accuracy function can have different shapes for different tasks, and cannot be assumed to be linear (Wickelgren 1977); in many tasks, including apparently ours (Fig. 4A), there is a limit to performance accuracy such that giving subjects a very long time to execute the motor pattern doesn't result in much increase in accuracy (Wickelgren 1977). If a single speed is chosen for learning assessment and it happens to be near this asymptote, learning may be substantially underestimated compared to gains in skill over a larger speed range. Even though performance in some subjects may appear to plateau for the training speed (MT 3), we cannot infer anything about the skill as a whole; online or offline changes at other speed ranges could have occurred. Because we only assessed the full speed-accuracy tradeoff at baseline and retention, we cannot infer anything about the time course of skill learning other than that significant learning had occurred by day 3.

Proprioceptive changes associated with skill learning

Previous research investigating associations between proprioceptive function and learning has largely been limited to adaptation paradigms and relatively simple reaching movements. Motor adaptation paradigms that considered proprioception have primarily considered the effect of adaptation on proprioceptive bias (Cressman and Henriques 2009; Henriques and Cressman 2012; Ostry et al. 2010; Ostry and Gribble 2016) rather than sensitivity. Improvements in proprioceptive sensitivity have been observed following repetitive reaching movements in the absence of a perturbation (Wong et al. 2011). Though the reaching movements in the Wong et al. study were relatively simpler, learning was still observed based on improvements in movement time. They found ~11% improvement in proprioceptive sensitivity whereas we found ~35% improvement after one day of training. However, it is important to acknowledge that in the Wong study, proprioceptive sensitivity at baseline was better (10.5 mm), and this was in the horizontal dimension. They did not assess proprioceptive function in the sagittal dimension. Several methodological differences may relate to the baseline differences and amount of improvement. We assessed proprioception in reference to a visual marker, while the Wong study proprioceptive judgments were in relation to a previously-remembered location. Thus, our method relies on simultaneous visual judgments while the Wong et al. method relies on working memory. In the Wong study, the elbow was supported with the shoulder abducted, whereas here, the elbow was unsupported without shoulder abduction. Assessing proprioception in these different postures, by itself, is enough to yield differences in measured proprioception, apart from any differences associated with motor training (Klein et al. 2018).

Here we observed improvements in both proprioceptive bias and sensitivity, on different time scales. The changes were only apparent in the sagittal dimension, which may be a function of the spatially complex motor task. One possibility is that for the sagittal dimension, there was a relatively larger deficit at baseline, allowing more room for improvement than the horizontal dimension (floor effect). The time scale of proprioceptive changes associated with motor learning has also been investigated primarily in motor adaptation paradigms. Changes in proprioceptive bias do not follow the same course as visuomotor (Cressman and Henriques 2009; Henriques and Cressman 2012; Salomonczyk et al. 2012) or force field (Ostry et al. 2010; Ostry and Gribble 2016) adaptation, suggesting some degree of independence from motor learning. When learning a motor skill, consolidation of motor memory occurs 4-6 hours after practice and is influenced by sleep (Berghuis et al. 2015). Similar mechanisms appear to be important for retention of proprioceptive changes (Cuppone et al. 2018). Our results are only partially consistent with Cuppone and colleagues; in their study the bias improvements were retained up to three days after practice whereas sensitivity improvements persisted up to 10 days after practice. Such differences may relate to the duration and complexity of motor training. Taken together with Cuppone et al.'s findings, there is evidence for slightly different processes that mediate changes in proprioceptive bias versus sensitivity.

It is unclear whether proprioceptive enhancement is specific to the training workspace (i.e. the center of the track), or if it generalizes to other portions of the track and/or the untrained workspace. Due to time constraints, we were unable to assess proprioceptive at other portions of the track; however, the center of the track seemed most relevant since this is where the horizontal and sagittal sections intersected, and we were interested in proprioceptive function in two dimensions. Proprioceptive changes associated with visuomotor adaptation have been shown to generalize to positions outside of the training target region (Mostafa et al. 2015). If improvement in proprioceptive function transfers or generalizes for more complex skills, this would further support the idea of parallel processes underlying sensory and motor learning.

In the present study, we acknowledge that the proprioceptive judgements involved a visuo-proprioceptive transformation, since all judgements of hand position were in relation to a visual reference. While this might be a limitation, findings from Wilson et al. (2010) suggest similar mappings of proprioceptive function whether subjects judge hand position from a proprioceptive reference or a visual reference (Wilson et al. 2010). Like the current study, the visual reference was maintained in the same position and the hand was returned to the visual reference. Further, distractor movements were put in between trials. In the absence of performance feedback, the amount of information subjects receive by starting the trial at the reference marker is the same at all points in the experiment, so is unlikely to account for changes in proprioceptive sensitivity. Also, it is important to give aligned visual and proprioceptive information periodically to reduce the likelihood of proprioceptive drift (Brown et al. 2003a, 2003b). One potential limitation of this study is that we did not have a passive control group to assess whether proprioceptive function changes were related to the passage of time and/or repetition of making proprioceptive judgements. However, previous research has demonstrated in control groups that proprioception does not change over time or with passive motor training (Ostry et al. 2010; Wong et al. 2011).

Passive training with a visuo-proprioceptive mismatch can elicit proprioceptive recalibration (Cressman and Henriques 2010), but the present study did not have such a mismatch.

The design of this study was correlational, so we cannot make any speculations on the causation of the observed proprioceptive improvements. Proprioceptive function may have improved which then enhanced motor learning or vice versa. It is also unclear which aspects of the task may have been important for the changes in proprioceptive function. For example, proprioceptive improvements could be tied to the linking of a series of submovements, requiring subjects to manage their acceleration and smoothness while tracing a track with several abrupt turns; or it could simply be that subjects made a large number of movements, and a similar number of movements in a straight-line reaching task would have a similar outcome. Further research is needed to test what movement parameters (complexity, time, difficulty, etc) cause, or are affected by, changes in proprioceptive function.

Neurophysiological changes

We investigated SAI to examine how complex motor skill training influences sensory afferent projections to motor cortex (M1). At the group level, SAI increased after training on both day 1 and day 2. SAI changes may reflect enhanced connections between somatosensory cortex (S1) and M1, through enhanced somatosensory processing in S1, or altered thalamocortical projections to S1 and/or M1. Given that skill learning is also associated with changes in proprioceptive sensitivity and that motor corticospinal excitability evoked at a fixed intensity (SI_1mV) was unaltered, we speculate the SAI changes to be mediated at the level of S1. The changes in SAI without corresponding changes in M1 corticospinal excitability suggests an important role in S1 in mediating learning and memory. It is possible that SAI changes occur in conjunction with changes in long-latency afferent inhibition, thought to be mediated by higher order association areas including posterior parietal cortex and premotor cortex (Sailer 2003).

Other reports on the functional relevance of SAI have been mixed. Recently, Turco et al. (2018) demonstrated that SAI was not related to tactile measures or manual dexterity (Turco et al. 2018). Like the current study, SAI was evaluated at rest in the absence of concurrent task performance. Others have shown that SAI is modulated by motor planning and execution, with greatest release of inhibition involved in muscles utilized in the movement (Asmussen et al. 2013, 2014). Functionally, this is similar to surround inhibition and represents an efficient way for releasing inhibition to increase muscle contraction needed for movement. Interestingly, the magnitude of SAI increase in the present study was related to the total magnitude of skill learning at retention. In other words, individuals with a larger SAI increase after training, reflecting enhanced somatosensory cortical activity, had larger skill improvement. The effect size of this relationship (R=0.52) is considered “large” (Cohen 2013). However, the marginal significance value suggests our study may have been underpowered to detect this effect. A relationship between SAI change and skill learning would need to be confirmed in a larger study, but it appears unlikely that the increase in SAI was simply due to movement repetition or time spent practicing rather than learning. The number of trials actually completed during training varied across subjects since trials outside the desired speed range were repeated; we found that SAI change was not correlated with either total number of training trials or with amount of time spent training.

It is important to consider that the SAI changes and motor skill retention assessment took place on separate days. While SAI at baseline on the training days was consistent, it was the change in SAI after training that was associated with learning. In other words, the state of sensorimotor networks after training (captured by SAI) may contribute to offline consolidation processes important for learning. This interpretation is consistent with work that suggests that the state of primary motor cortex after training contributes to retention. For instance, altering M1 activity after training resulted in impaired skill performance assessed 12 hours after training (Robertson 2005). Further, changes in M1 corticospinal excitability after motor training were associated with motor skill retention assessed on a subsequent day (Hirano et al. 2015). Similarly, the magnitude of LTP-like plasticity after training was related to the amount of skill retention on a subsequent day (Cantarero et al. 2013a, 2013b; Spampinato and Celnik 2017). Here, the relationship between SAI changes after training and motor skill retention is consistent with the idea that the state of the brain after training contributes to mechanisms involved in learning.

It should be noted that the neurophysiological measurements were assessed for the hand, even though the motor skill task required movements of the shoulder and elbow. We made this choice because our goal was to assess somatosensory changes related to hand perception: the goal of the task was to navigate a visual cursor that corresponded to hand position, and proprioceptive estimation was done at the hand. Proprioception is thought to be most salient when the limb endpoint (i.e., hand) position is estimated, rather than focusing on joint angles (Fuentes and Bastian 2010). It is unclear whether training would be associated with changes in SAI and motor corticospinal excitability in muscles spanning the shoulder and/or elbow. SAI is most commonly assessed at the hand, but previous research suggests a similar magnitude of SAI in FDI versus a forearm and biceps muscle (Bailey et al. 2016; Helmich et al. 2005).

Conclusions

We found that motor skill learning was associated with improved proprioceptive function and increased SAI, reflective of enhanced afferent input to SI. Further, the changes correlated with magnitude of skill learning: Greater increases in SAI were associated with greater skill learning. This suggests that proprioception could be important for kinematically complex motor skill learning, a role that may be mediated by inhibitory somatosensory projections to M1.

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Figure Legends

Fig. 1 A. Experimental setup. 2D virtual reality apparatus used for the proprioception and motor tasks. Subjects grasped the manipulandum handle in their right hand. Visual stimuli were displayed on a horizontal television (top) for the subject to view in a horizontal mirror (black shape). **B.** Experimental design. TMS: Neurophysiological measurements performed before and after the behavioral tasks on day 1 and day 2. These included short latency afferent inhibition (SAI) and single pulses at SI_1mV. Proprioception: Assessment of proprioceptive function. Motor Skill: Assessment of motor skill learning, using 5 different speed ranges to evaluate changes in speed-accuracy tradeoff. Motor Training: Practice of skill at a single speed range. **C.** Bird's eye view of motor skill task display. Subject was seated in the direction of the negative y-axis, centered with the track. Subjects navigated the white cursor with the robotic manipulandum through the irregular shaped track, moving from the lower green starting square to the upper green end square. **D.** Representative movement trajectory used to compute movement time (MT) and in-track accuracy. Blue line represents parts of the movement path that were inside the track. Magenta line represents parts of the movement path that were outside the track.

Fig. 2 A. Bird's eye view of passive proprioception assessment. Participants judged the position of their unseen right hand in relation to a visual reference (white circle), located at the center of the motor skill track. Proprioception was assessed in the horizontal dimension, where participants indicated whether their hand was to the left or right of the reference, and sagittal dimension, where participants indicated whether their hand was in front or behind the visual reference. **B.** Depiction of proprioceptive test positions across trials for an example subject. 4 lines represent the 4 staircases that were performed in each dimension. **C.** Example subject proprioceptive data fitted with logistic function. Bias was defined as the 50% point of the fitted function. Sensitivity was defined as the difference between the 25% and 75% points of the fitted function. For this subject, the bias, or perceptual boundary, was computed as -13.55 mm and the sensitivity was 23.83 cm.

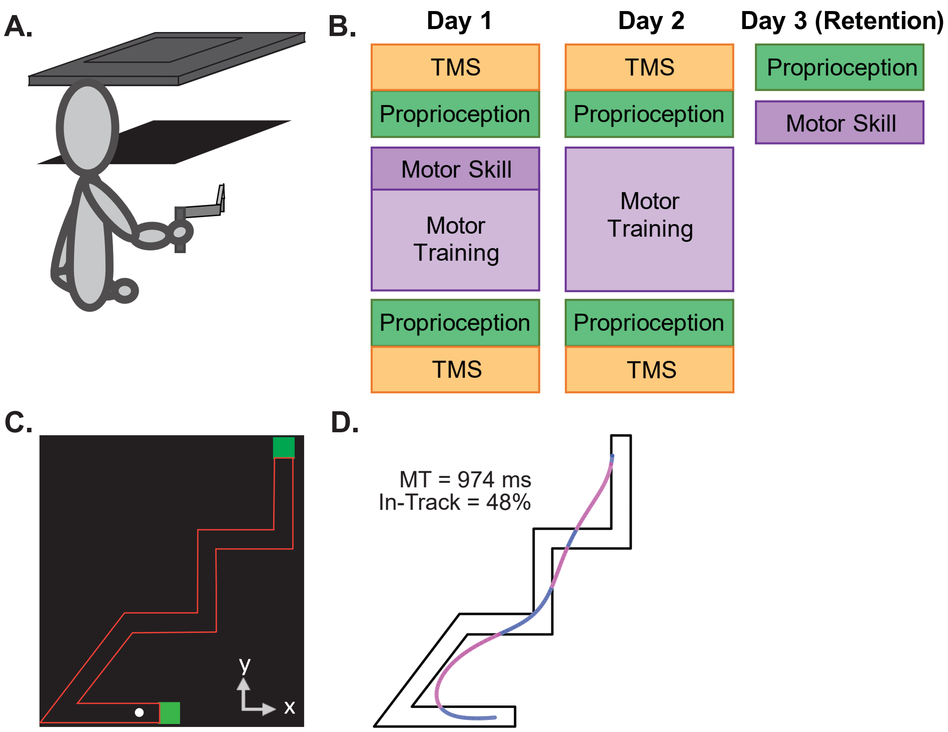
Fig. 3. Motor skill learning and SAI results from two example subjects. Top row: The subject demonstrated improvements in motor skill at retention, with total skill learning of 63.9% (**A**). The same subject had an increase in SAI after training each day (lower numbers on post relative to pre), 78.26% on average (post SAI/pre SAI) (**B**). Bottom row: This subject showed a different pattern, with total skill learning of -4.3% (worse at retention) (**C**) and a decrease in SAI after training each day (higher numbers on post relative to pre) that averaged 137.27% (post SAI/pre SAI) (**D**). Error bars represent standard error of the mean.

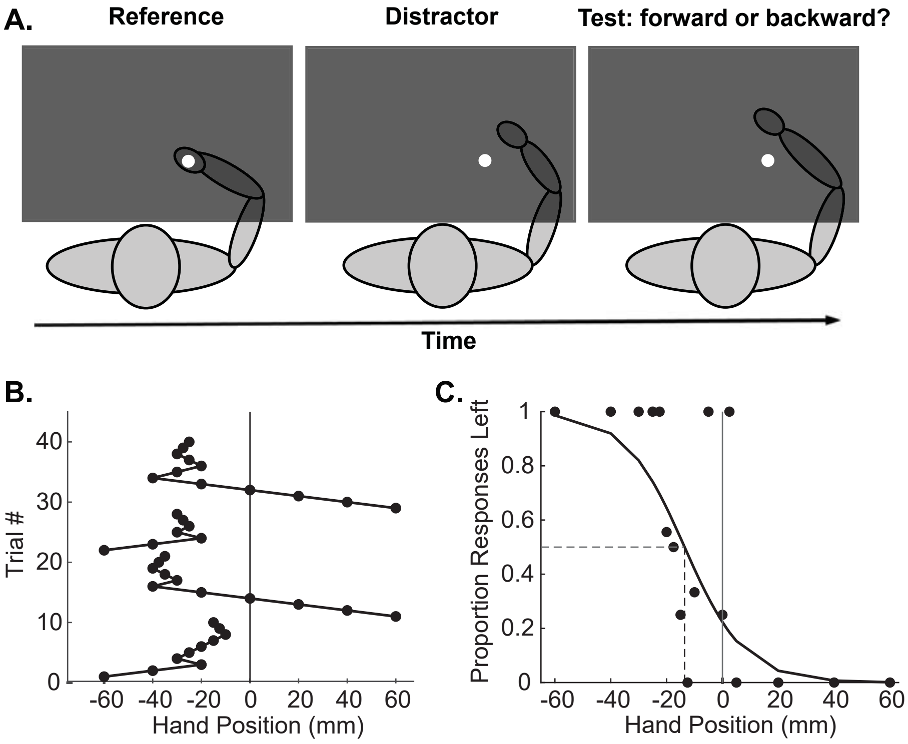
Fig. 4 A. In-track accuracy on motor skill assessment across five movement time bins. The speed-accuracy tradeoff shifted significantly from baseline to retention, suggesting that skill learning occurred. **B.** Mean movement time on motor skill did not change significantly across sessions. Error bars represent standard error of mean. **C.** In-track accuracy during motor practice at a single movement time (MT 3: 850-1100 ms) on day 1 and day 2. Vertical dashed line delineates training day 1 from training day 2. B0 denotes the performance during the skill assessment at MT3 at baseline. * denotes post-hoc contrasts, all $p < 0.003$

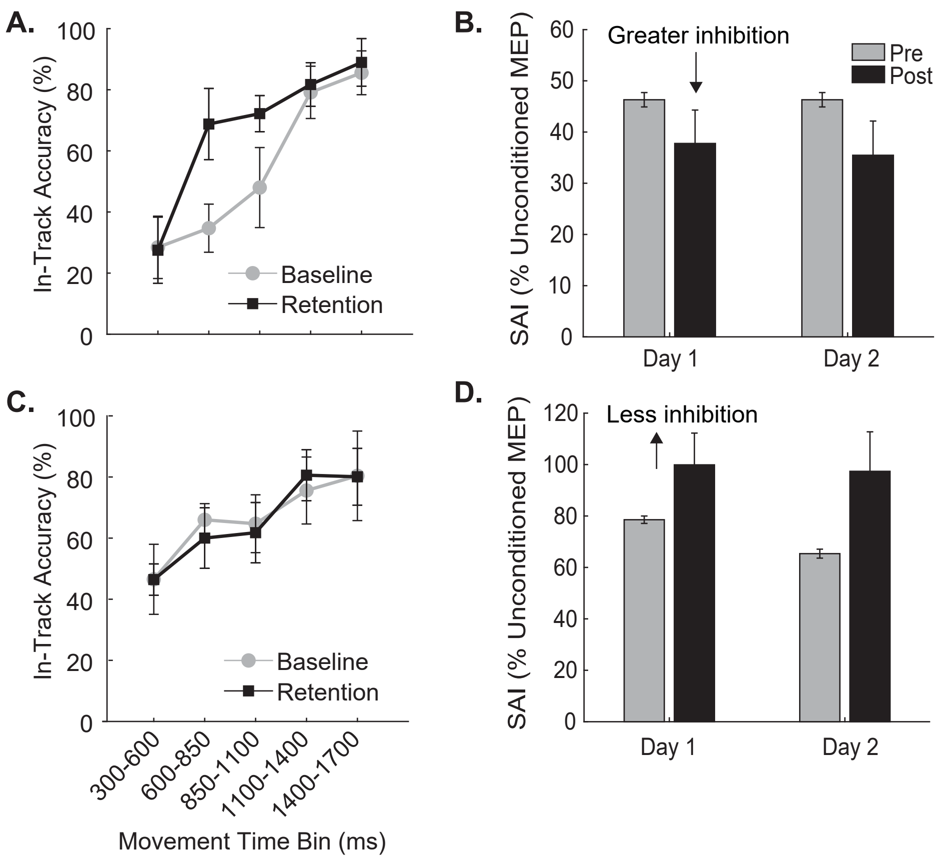
Fig. 5 A. Proprioceptive sensitivity improved from day to day only in the sagittal dimension. Lower values denote better performance. Vertical dashed lines delineate pre-training and post-training on day 1 and day 2. **B.** Absolute proprioceptive bias improved after training each day, but improvements were not retained. Lower values denote better performance. Vertical dashed lines delineate pre-training and post-training on day 1 and day 2. Error bars represent standard error of the mean. * $p < 0.05$, ** $p < 0.005$

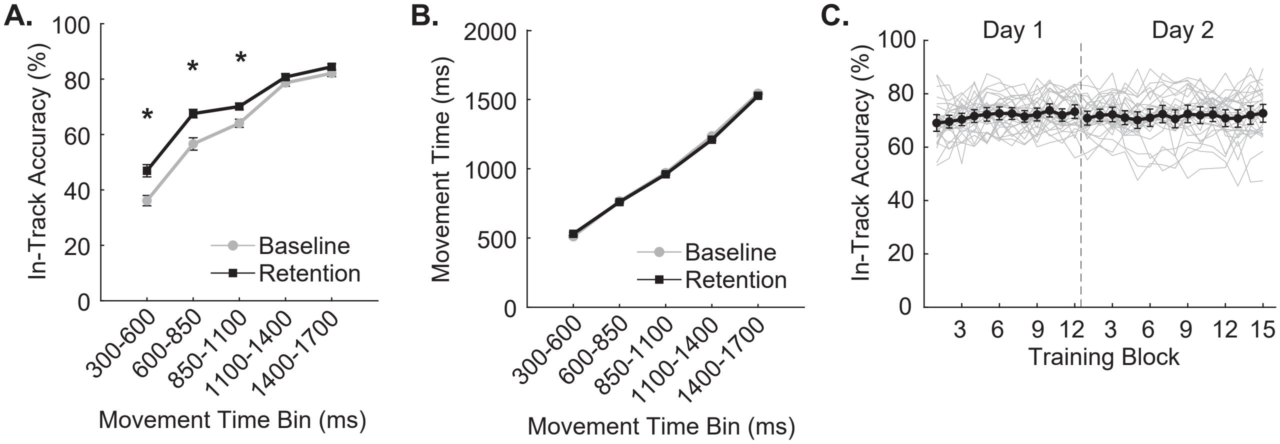
Fig. 6. Neurophysiological values measured pre- and post training on day 1 and day 2. **A.** Mean SAI expressed as a percentage of the unconditioned MEP amplitude, with lower values denoting greater inhibition evoked from the afferent volley. **B.** Mean MEP amplitude evoked from single TMS pulses at fixed stimulus intensity (SI_1mV determined pre-training). All error bars represent standard error of the mean. * Main effect of measurement time ($p = 0.036$).

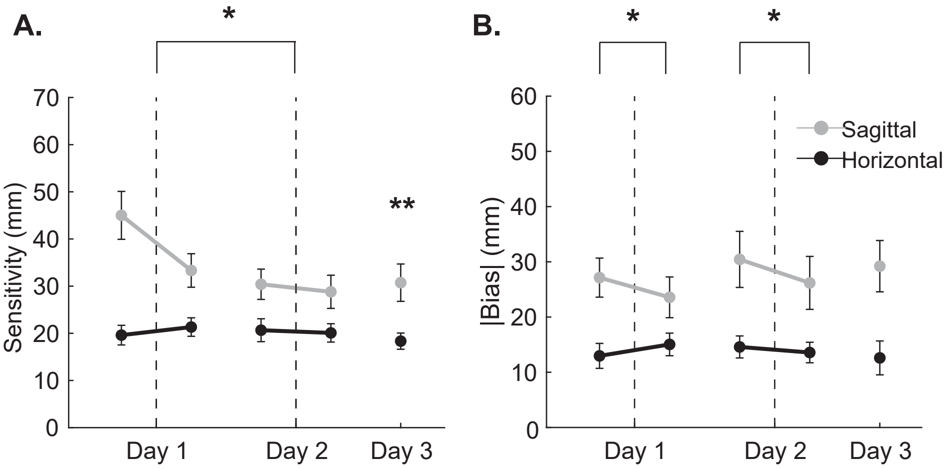
Fig. 7. Correlation between average within-day SAI change and total magnitude of skill learning. Subjects who acquired the most motor skill were those most likely to show increased SAI each day. Shaded region represents 95% confidence interval.

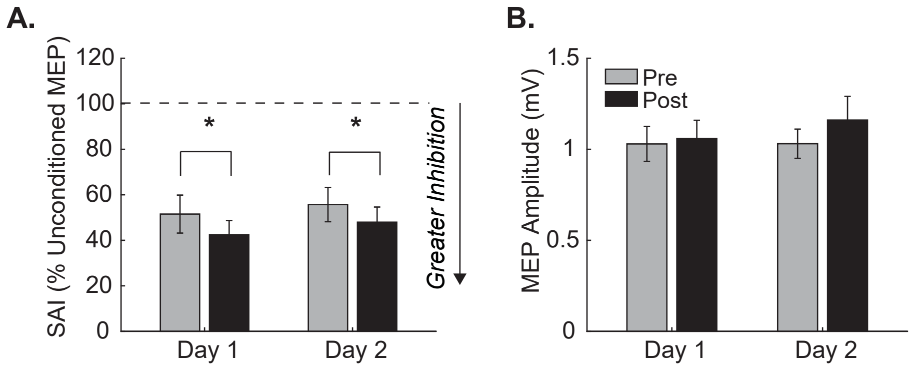

A.
B.
Day 1
Day 2
Day 3 (Retention)
TMS
Proprioception
Motor Skill
Motor Training
Proprioception
TMS
TMS
Proprioception
Motor Training
Proprioception
TMS
Proprioception
Motor Skill
C.
y
x
D.
MT = 974 ms
In-Track = 48%

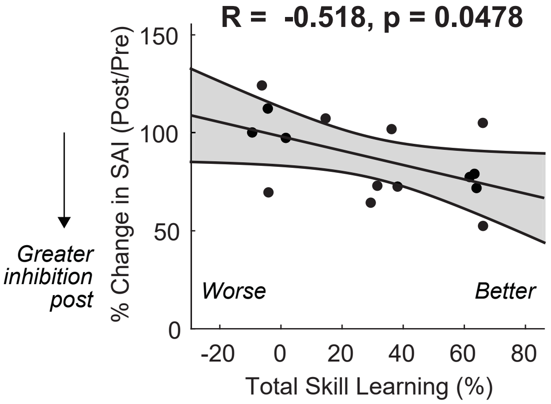

A.
Reference
Distractor
Test: forward or backward?
Time
B.
Trial #
0
10
20
30
40
-60
-40
-20
0
20
40
60
Hand Position (mm)
C.
Proportion Responses Left
0
0.2
0.4
0.6
0.8
1
-60
-40
-20
0
20
40
60
Hand Position (mm)


A.
In-Track Accuracy (%)
0
20
40
60
80
100
Baseline
Retention
B.
SAI (% Unconditioned MEP)
0
10
20
30
40
50
60
Greater inhibition
Pre
Post
Day 1
Day 2
C.
In-Track Accuracy (%)
0
20
40
60
80
100
Baseline
Retention
300-600
600-850
850-1100
1100-1400
1400-1700
Movement Time Bin (ms)
D.
SAI (% Unconditioned MEP)
0
20
40
60
80
100
120
Less inhibition
Day 1
Day 2


A.
In-Track Accuracy (%)
100
80
60
40
20
0
*
*
*
Baseline
Retention
300-600
600-850
850-1100
1100-1400
1400-1700
Movement Time Bin (ms)
B.
Movement Time (ms)
2000
1500
1000
500
0
Baseline
Retention
300-600
600-850
850-1100
1100-1400
1400-1700
Movement Time Bin (ms)
C.
Day 1
Day 2
In-Track Accuracy (%)
100
80
60
40
20
0
3
6
9
12
3
6
9
12
15
Training Block


A.
B.
*
*
*
**
70
60
50
40
30
20
10
0
Sensitivity (mm)
Day 1
Day 2
Day 3
60
50
40
30
20
10
0
|Bias| (mm)
Sagittal
Horizontal
Day 1
Day 2
Day 3


A.
SAI (% Unconditioned MEP)
120
100
80
60
40
20
0
*
*
Greater Inhibition
Day 1
Day 2
B.
MEP Amplitude (mV)
1.5
1
0.5
0
▨ Pre
■ Post
Day 1
Day 2


R = -0.518, p = 0.0478
% Change in SAI (Post/Pre)
150
100
50
0
Greater inhibition post
Worse
Better
-20
0
20
40
60
80
Total Skill Learning (%)