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ARTICLE

Somatosensory Electrical Stimulation Does Not Augment Motor Skill Acquisition and Intermanual Transfer in Healthy Young Adults—A Pilot Study

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Sensory input can modify motor function and magnify interlimb transfer. We examined the effects of low-intensity somatosensory electrical stimulation (SES) on motor practice-induced skill acquisition and intermanual transfer. Participants practiced a visuomotor skill for 25 min and received SES to the practice or the transfer arm. Responses to single- and double-pulse transcranial magnetic stimulation were measured in both extensor carpi radialis. SES did not further increase skill acquisition (motor practice with right hand [RMP]: 30.8% and motor practice with right hand + somatosensory electrical stimulation to the right arm [RMP + RSES]: 27.8%) and intermanual transfer (RMP: 13.6% and RMP + RSES: 9.8%) when delivered to the left arm (motor practice with right

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hand + somatosensory electrical stimulation to the left arm [RMP + LSES]: 44.8% and 18.6%, respectively). Furthermore, transcranial magnetic stimulation measures revealed no changes in either hand. Future studies should systematically manipulate SES parameters to better understand the mechanisms of how SES affords motor learning benefits documented but not studied in patients.

Keywords: electrical stimulation, interlimb transfer, motor evoked potential, transcranial magnetic stimulation

A brief period of motor practice (MP) improves finger acceleration (Lee, Hinder, Gandevia, & Carroll, 2010) and visuomotor skills, using finger (Cirillo, Todd, & Semmler, 2011), hand (Berghuis et al., 2016), and ankle (Perez, Lungholt, Nyborg, & Nielsen, 2004) movements. Unilateral MP can also increase motor performance in the nonpractice limb, resulting in intermanual transfer (Steinberg, Pixa, & Doppelmayr, 2016; Veldman et al., 2015).

Afferent input shapes motor output, and sensory dysfunctions contribute to motor deficits (Asanuma, 1981; Broeks, Lankhorst, Rumping, & Prevo, 1999; Porter, Sakamoto, & Asanuma, 1990; Sawaki, Wu, Kaelin-Lang, & Cohen, 2006). In contrast, an increase in afferent input through mechanical vibration or electrical stimulation can potentiate motor skill acquisition and intermanual transfer (Rothwell & Rosenkranz, 2005; Veldman, Maffiuletti, Hallett, Zijdewind, & Hortobágyi, 2014). Indeed, low-intensity (below motor threshold or eliciting paresthesia) somatosensory electrical stimulation (SES) alone or added to MP can enhance stroke patients' motor function (Conforto, Kaelin-Lang, & Cohen, 2002; Wu, Seo, & Cohen, 2006).

Although interlimb transfer of motor skills and muscle strength is clinically relevant (Ehrensberger, Simpson, Broderick, & Monaghan, 2016; Farthing & Zehr, 2014; Kwakkel et al., 2016; Urbin, Harris-Love, Carter, & Lang, 2015), the magnitude of transfer in healthy adults is small, ~7% (Munn, Herbert, Hancock, & Gandevia, 2005). Combining MP with afferent stimulation could increase intermanual skill transfer. However, the mechanisms of SES-induced facilitatory effects are poorly understood. Delivering SES to the practicing hand could raise the excitability of the primary motor cortex (M1) through connections between M1 and the primary and secondary sensory cortices (S1 and S2) and facilitate intermanual transfer (Veldman et al., 2014). Alternatively, delivering SES to the transfer-receiving hand instead of the practicing hand could also be effective for two reasons. First, although SES could facilitate MP, MP and SES delivered to the practicing hand could also interfere with each other. Such interference can occur either through two types of afferent input generated by MP and SES or through efferent motor commands generated by MP and afferent sensory signals generated by SES. Delivering SES to the transfer-receiving hand could avoid such interferences and might therefore be effective in enhancing intermanual transfer. Second, SES activates supplementary motor area (Han et al., 2003), an area that is also activated during intermanual transfer of motor skills (Perez, Wise, Willingham, & Cohen, 2007) due to its dense connections to the M1, premotor cortex, and supplementary motor area of the contralateral hemisphere (Liu, Morel, Wannier, & Rouiller, 2002). Therefore, transfer-hand SES could make the receiving right hemisphere more accessible and subsequently increase the magnitude of intermanual transfer. The bilateral activation of S2 by SES also contributes to the accessibility of the transfer hemisphere for inputs from the practice hemisphere (Veldman et al., 2014).

While SES applied before MP can be used to temporally prime skill acquisition, we hypothesize that spatially priming the transfer-receiving left hand with SES could have greater effects on interlimb transfer than the crossed effects produced by SES delivered to the practice hand. We thus examined the effects of MP on skill acquisition and intermanual transfer by delivering SES either to the practicing or to the transfer-receiving hand. We supplemented the behavioral data with transcranial magnetic stimulation (TMS) measures to examine the potential underlying mechanisms involved in skill acquisition and its intermanual transfer.

Materials and Methods

Participants

In total, 34 right-handed healthy adults (age 22 ± 2.31 years, range 18–27, 16 men) volunteered for the study (Oldfield, 1971). Participants were free of neurological disorders, were not pregnant, were not taking drugs that affected functioning of the central nervous system, and had no contraindications to receiving TMS (Rossi, Hallett, Rossini, Pascual-Leone, & Safety of TMS Consensus Group, 2009). Each participant gave written informed consent, and the study protocol was conducted according to the declaration of Helsinki. The local Medical Ethical Committee approved the study protocol.

Experimental Design

To establish the number of participants required for the study, we performed power analysis for a repeated-measures analysis of variance using G*Power 3.1.7 (Faul, Erdfelder, Lang, & Buchner, 2007). According to the power analysis, seven participants per group were enough to detect changes in the measured variables at a power of 80% and effect size of 0.25.

Participants were randomly assigned to right MP alone (motor practice with right hand [RMP], $n = 8$), to right MP while receiving SES to the left (motor practice with right hand + somatosensory electrical stimulation to the left arm [RMP + LSES], $n = 10$), to the right (motor practice with right hand + somatosensory electrical stimulation to the right arm [RMP + RSES], $n = 9$) median and radial nerves (Figure 1), or to a control group ($n = 7$) that performed only the visuomotor familiarization trials and the pre- and posttests. We used these data to correct skill acquisition and intermanual transfer for the familiarization and testing effects. Two TMS protocols were applied to each hemisphere before and after intervention. In one run, we measured corticospinal excitability (CSE), short-interval intracortical inhibition (SICI), and intracortical facilitation (ICF). In a second run, we measured ipsilateral silent period (iSP) to measure interhemispheric inhibition (IHI) and contralateral facilitation (CLF) to quantify the magnitude of the associated activity and also the facilitation of motor evoked potentials (MEPs). The order of the two runs and the two hemispheres was randomized between participants.

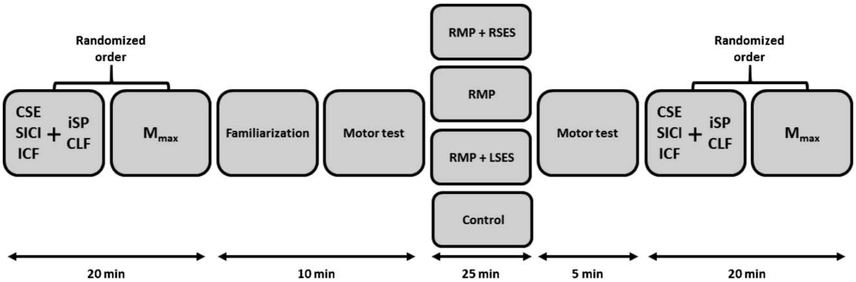

Figure 1 — A schematic illustration of the experimental design. Baseline measurements including CSE, SICI, ICF, CLF, iSP, and M_{max} were repeated after participants were familiarized with the visuomotor task or completed one of the three interventions and the motor tests. The total time of the experiment was 80 min. CSE = corticospinal excitability; SICI = short-interval intracortical inhibition; ICF = intracortical facilitation; iSP = ipsilateral silent period; CLF = contralateral facilitation; M_{max} = maximal compound action potentials; RMP = motor practice with right hand; RMP + RSES = motor practice with right hand + somatosensory electrical stimulation to the right arm; RMP + LSES = motor practice with right hand + somatosensory electrical stimulation to the left arm.

Behavioral Data Acquisition and Analysis

We previously reported the details of participant's positioning, the template-matching visuomotor task, the speed of the templates, familiarization with the task, and the testing protocol (Veldman et al., 2015; Veldman, Zijdewind, Maffiuletti, & Hortobágyi, 2016). A similar paradigm was also used in previous studies (Cirillo et al., 2011; Jensen, Marstrand, & Nielsen, 2005). Briefly, subjects sat in a chair in front of a computer monitor and followed preprogrammed templates appearing on the screen as accurately as possible by flexing and extending the wrist. After three familiarization trials, visuomotor performance was tested using 12 trials before and after each of the three interventions and the control period. The templates that were used during the testing session were different from the training templates. In total, six different test templates appeared in random order and duration, varying between 4 and 6 s, on the screen. Participants received the same set of templates before and after the intervention. The MP intervention consisted of 300 visuomotor training trials, divided into five blocks of 60 trials with 2 min of rest between blocks. To reduce the attentional drift, participants counted backward by seven after every 15 trials, starting from a random two-digit number.

The two intervention groups received SES in either the left or the right arm during MP with the right hand. We described in detail the equipment, the stimulation parameters, and the type, size, and location of the stimulating electrodes used (Veldman et al., 2015, 2016). Briefly, two electrodes were placed over the radial and median nerve above the elbow. We delivered 1,500 trains and 7,500 pulses in total at 1 Hz consisting of five square wave pulses (pulse width = 1 ms).

The five pulses were delivered at 10 Hz over 500 ms, resulting in a 50% duty cycle, at an intensity of twice the perceptual threshold, determined as the lowest stimulation intensity sensed by the participant using the descending method of limits. When the backward counting attention task was performed, the SES was paused. In the MP-only and the control group, as a placebo, the electrodes were placed over the radial and median nerve of the right arm above the elbow with the stimulator on, but the stimulation intensity was set to zero.

Electromyographic Recording

We recorded electromyographic (EMG) activity of extensor carpi radialis (ECR) and flexor carpi radialis in both hands using 37 × 26 × 15 mm, 14 g, wireless, preamplified surface parallel-bar sensors (Trigno™ Wireless System, Delsys, Natick, MA) affixed to the skin with a four-slot adhesive skin interface. EMG activity was sampled at 4 kHz with a bandwidth of 20–450 Hz, amplified 909 times, with a channel noise less than 0.75 μV and a common mode rejection ratio over 80 dB using data acquisition interface and software (Power 1401 and Signal 5, Cambridge Electronics Design, Cambridge, UK).

TMS and Peripheral Nerve Stimulation Data Acquisition and Analysis

MEPs from ECR muscles were evoked by a figure of eight-shaped magnetic coil connected to two Magstim 2002 through a BiStim2 module (Magstim, Whitland, UK). The optimal locations to stimulate the left and right ECR, the so-called hotspots, were determined systematically by moving the coil in steps of 0.5 cm over the right and left M1 area, starting at the vertex with the handle pointing backward at ~45° away from the sagittal plane. The locations of the hotspots were marked on a cap placed over the scalp to ensure the same spots were stimulated before and after the intervention. Resting motor threshold (rMT) was determined as the nearest 1% of maximum stimulator output that evoked MEPs in the ECR of at least 50 μV in five out of 10 subsequent stimuli (Rothwell et al., 1999). To examine the excitability of the corticospinal path and inhibitory and excitatory intracortical circuits, 10 single pulses at 1.2 rMT (CSE) and 20 paired-pulses at 0.8 and 1.2 rMT (intracortical excitability) were delivered 10% variation in intertrial interval to reduce anticipation by the participant. Paired-pulses SICI and ICF were delivered at an interstimulus interval of 2 and 10 ms, respectively (Kujirai et al., 1993), targeting different populations of interneurons in M1. The intensities of the subthreshold conditioning pulse and suprathreshold test pulse were set at 0.8 and 1.2 rMT, respectively.

In a separate TMS run, IHI and excitability were measured through iSP and CLF, respectively. First, we determined the maximum voluntary contraction of the right and left ECR. After five TMS pulses at an intensity of 1.6 rMT to the M1 ipsilateral to the hand at rest, participants received an additional 10 TMS pulses at 1.6 rMT to the same M1 when they produced wrist extension at 20% maximum voluntary contraction for 5 s, with the hand ipsilateral to the stimulated M1, to induce an iSP, detected as a disruption of ongoing EMG activity (Solnik, Rider, Steinweg, DeVita, & Hortobágyi, 2010). This 1.6 rMT stimulation also evoked MEPs in the resting contralateral ECR, allowing us to measure CLF in the resting hand in conjunction with wrist extension of the other hand. The reference line for the 20% wrist extension maximum voluntary contraction was displayed on a projection screen.

The radial nerve was stimulated above the elbow through custom-made gauze electrodes (Hortobágyi, Taylor, Petersen, Russell, & Gandevia, 2003) using a constant-current stimulator (Digitimer model DS7A, Hertfordshire, UK) to evoke a maximal muscle response, an M-wave. The electrodes were designed to apply a current to the nerve with approximately 3 cm between the two poles. The stimulation intensity was increased until the amplitude of the M-wave did not increase any further (maximal compound action potential). We checked whether a plateau was reached by delivering a single pulse at 120% of the intensity at which the maximal M-wave was seen. The maximum M-wave amplitude was used to express and normalize the MEPs.

Data Analysis and Statistical Analysis

We report the data as mean ± standard deviation. All data were checked for normal distribution using the Shapiro–Wilk test. Variables that were not normally distributed were log transformed. The analyses were done on the transformed data using SPSS (version 22.0), but all variables are reported in the nontransformed form. Motor performance was calculated as the mean absolute vertical deviation from the preprogrammed template in degrees using a custom Matlab script (MathWorks, Natick, MA). Per trial, a mean deviation was calculated for a complete template. This value was then averaged for 12 trials to calculate an average per participant. Percentage differences between the average visuomotor performance at each time point were calculated to quantify motor skill acquisition. In addition, net skill acquisition was calculated as the magnitude of learning in intervention groups (RMP, RMP + RSES, and RMP + LSES) minus the magnitude of learning in the control group.

Test pulses were normalized by maximal compound action potential, and SICI and ICF were expressed as a percent of test pulse MEP. CLF was calculated as the ratio of $MEP_{contraction}/MEP_{rest}$. An adjusted version of the Teager–Kaiser energy operator (Solnik et al., 2010) was used to detect disruption of ongoing EMG activity during iSP using a signal-to-noise ratio. Visuomotor performance and cortical changes were compared by a three (Group: RMP, RMP + RSES, and RMP + LSES) by two (Time: pre and post) repeated-measures analysis of variance. When there was a between-group difference at the pretest, an analysis of covariance was performed, using pretest values as a covariate. In case of a significant F value, Tukey's post hoc analysis was performed to identify means that differed at $p < .05$. In order to determine if pretest values and changes in visuomotor performance were associated with change in neuronal excitability, Pearson's correlations were computed.

Results

Behavioral Measures

The control group improved their performance by 2.0° (9%) in the right hand and by 2.3° (9%) in the left hand. We report the net effects of MP on motor performance and intermanual transfer by subtracting the improvements of control group from the effects produced by the interventions. After only 25 min of MP, the net mean absolute deviation from the preprogrammed template decreased in the trained right hand (30.8%), but SES added to MP did not augment skill acquisition when delivered to the right (27.8%) or left arm (44.8%), resulting in a significant effect of time, $F(1, 24) = 53.4$, $p = .001$, but no significant effect of group by time interaction, $F(2, 24) = 1.6$, $p = .232$; Figure 2; Table 1. Baseline performance in the visuomotor skill was different for RMP + RSES (17°) and RMP + LSES (22.1°; $p = .041$) in the nonpractice left transfer hand. While controlling for these differences using an analysis of covariance, we found no significant effect of intervention (RMP: 13.6%, RMP + RSES: 9.8%, and RMP + LSES: 18.6%) on intermanual transfer, $F(2, 24) = 0.618$, $p = .548$. Table 1 shows the data for the pre- and postintervention in the three groups. There were no correlations between the improvements in the right and left hand (all ps > .05). Altogether, MP produced significant skill acquisition and transfer, but regardless of which hand received SES, it did not further augment skill acquisition or transfer.

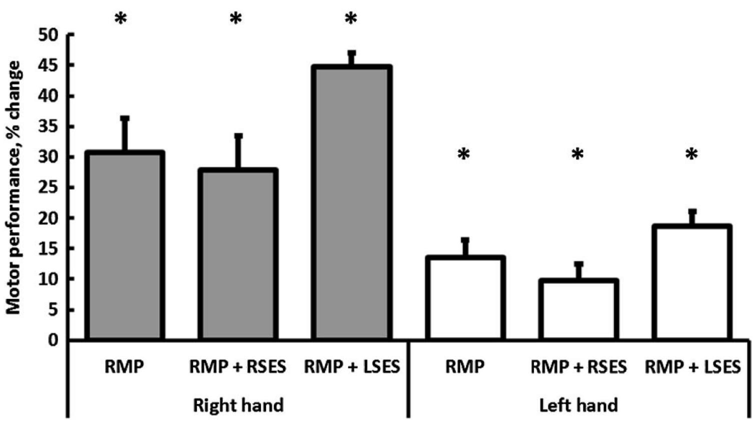

Figure 2 — Intervention effects on motor skill acquisition in the right practiced hand and nonpracticed left transfer hand in the three intervention groups. Twenty-five minutes of MP decreased mean absolute deviation from the preprogrammed template in both the right practiced hand and nonpracticed left transfer hand, but SES added to MP did not augment skill acquisition when delivered to the right or left arm. The time main effect shows significant motor skill acquisition and interlimb transfer in all three groups. Vertical bars denote +1 standard deviation. RMP = motor practice with right hand; RMP + RSES = motor practice with right hand + somatosensory electrical stimulation to the right arm; RMP + LSES = motor practice with right hand + somatosensory electrical stimulation to the left arm. *$p < .05$.

Table 1 Intervention Effects on Motor Skill Acquisition in the Right Practiced Hand and Nonpracticed Left Transfer Hand

		Pre	Post
		M (±*SD*)	*M* (±*SD*)
Right (practiced)	RMP	19.6 (2.4)	11.8 (0.8)
	RMP + RSES	18.2 (2.3)	11.5 (0.8)
	RMP + LSES	21.0 (2.2)	9.7 (0.8)
Left (nonpracticed)	RMP	19.9 (1.5)	15.4 (1.6)
	RMP + RSES	17.0 (1.4)	13.8 (1.5)
	RMP + LSES	22.1 (1.4)	16.0 (1.4)

Note. Values are in degrees, expressing the mean absolute error from the target. RMP = motor practice with right hand; RMP + RSES = motor practice with right hand combined with somatosensory electrical stimulation to the right median and radial nerve; RMP + LSES = motor practice with right hand combined with somatosensory electrical stimulation to the left median and radial nerve.

CSE Data

Results of TMS measures for RMP and RMP + RSES are already published in our previous manuscript (Veldman et al., 2015). The remaining of the results will focus on the spatial effects of SES on TMS metrics. The rMT was similar in RMP + LSES and in RMP + RSES group for the left (47 ± 5% of maximal stimulator output, range 41–57%; 47 ± 7%, range 37–57%, respectively) and for the right (48 ± 7%, range 41–64%; 45 ± 10%, range 33–62%, respectively) hemispheres, $t(17) = 0.1$, $p = .916$; $t(17) = 0.5$, $p = .594$, respectively.

Table 2 shows the pre- and postintervention values and the relative changes in five TMS measures in each hemisphere. CSE did not change in the practiced left and nonpracticed right M1. Neither did the location of SES affect CSE in either hemisphere (all effects $p > .05$). The improvements in motor performance and changes in CSE did not correlate in the right hand ($R^2 = .145$) or the left hand ($R^2 = .003$).

Intracortical Excitability Data

Table 2 shows that SICI and ICF did not change in the practiced left and nonpracticed right M1. Neither did the location of SES affect SICI and ICF in either hemisphere (all effects $p > .05$). There was no group by time interaction in SICI, $F(1, 17) = 0.389$, $p = .541$, nor in ICF, $F(1, 17) = 0.042$, $p = .840$.

Interhemispheric Excitability Data

The iSP was measured pre- and postintervention as an index of IHI. There were no group or time main effects or group by time interaction in iSP in the left M1 and the right M1 (all effects $p > .05$). There was no group by time interaction for CLF in either hemisphere; however, there was a time main effect for CLF in the right hemisphere, $F(1, 17) = 6.130$, $p = .025$. There was no association between CLF of the trained right hand and motor performance ($R^2 = .003$). Table 2 summarizes percent and absolute changes in interhemispheric data.

Table 2 Summary of Absolute and Percent Changes in TMS Metrics in the Left-Intervention and Right-Transfer M1

		Pre	Post	
		M (±*SD*)	*M* (±*SD*)	% Changes
Right M1				
CSE	RMP + RSES	12 (7)	9 (4)	−13.7
	RMP + LSES	9 (4)	8 (4)	11.6
SICI	RMP + RSES	58.5 (26.0)	73.8 (31.2)	41.4
	RMP + LSES	58.0 (36.0)	64.4 (25.5)	44.4
ICF	RMP + RSES	175.8 (99.0)	157.6 (69.1)	−2.2
	RMP + LSES	98.7 (26.5)	114.4 (30.5)	20.4
iSP	RMP + RSES	27.2 (7.4)	24.9 (5.4)	−1.8
	RMP + LSES	25.5 (6.1)	25.8 (5.6)	3.2
CLF	RMP + RSES*	188.8 (68.7)	153.4 (34.8)	−14.8
	RMP + LSES	197.1 (69.7)	181.8 (53.9)	−4.8
Left M1				
CSE	RMP + RSES	9 (7)	10 (8)	18.9
	RMP + LSES	10 (4)	9 (3)	−8.4
SICI	RMP + RSES	58.1 (33.3)	54.5 (31.7)	1.6
	RMP + LSES	68.8 (35.1)	57.6 (24.6)	−4.1
ICF	RMP + RSES	146.2 (61.1)	136.2 (48.6)	1.5
	RMP + LSES	135.4 (24.4)	131.9 (18.7)	−2.8
iSP	RMP + RSES	28.1 (8.4)	27.6 (7.0)	−1.1
	RMP + LSES	30.0 (11.4)	24.8 (5.1)	−11.1
CLF	RMP + RSES	222.8 (141.4)	214.1 (113.9)	1.1
	RMP + LSES	235.4 (79.7)	246.8 (148.0)	6.6

Note. Percent change values are mean percent changes based on individually computed changes. CSE = corticospinal excitability (% maximal compound action potential); SICI = short-interval intracortical inhibition (% test pulse size, positive change denote decreases in inhibition); ICF = intracortical facilitation (% test pulse size); iSP = ipsilateral silent period (ms, positive change denote decreases in inhibition); CLF = contralateral facilitation (% MEP during contralateral hand contracting and MEP during contralateral hand resting); RMP + RSES = motor practice with right hand combined with somatosensory electrical stimulation to the right median and radial nerve; RMP + LSES = motor practice with right hand combined with somatosensory electrical stimulation to the left median and radial nerve; MEP = motor evoked potential.

*Time main effect, $p < .05$.

Discussion

Contrary to our hypothesis, spatial priming did not augment intermanual transfer as the magnitude of transfer was similar when SES was delivered to the transfer-receiving left hand (18.6%) and the practicing right hand (9.8%). Further, SES did not modify CSE, SICI, ICF, iSP, and CLF. We discuss these results with a perspective on the mechanisms of how low-intensity electrical stimulation interacts with motor skill acquisition and intermanual transfer.

Location of SES Does Not Affect Motor Skill Acquisition and Intermanual Transfer

Although there is some evidence that SES applied concurrently with MP can increase motor learning in stroke patients (Celnik, Hummel, Harris-Love, Wolk, & Cohen, 2007), both the present study and our previous study (Veldman et al., 2015) showed that SES to the practiced hand and nonpracticed hand combined with MP did not further increase motor skill acquisition (27.8% and 44.8%, respectively) compared with MP alone (30.8%) in healthy participants. Application of SES in an asynchronous manner, for example, priming skill acquisition by applying SES before MP appears to improve stroke patients' motor function after several sessions (Conforto et al., 2010) but not after a single session of SES intervention (Celnik et al., 2007).

Because our previous study (Veldman et al., 2015) showed that SES to the practiced hand combined with MP did not augment interlimb transfer, we hypothesized that priming the transfer-receiving left hand with SES, that is, spatial priming, could raise the excitability state of the transfer-receiving hemisphere directly and therefore could have greater effects on interlimb transfer than the crossed effects produced by SES delivered to the practiced hand (Bonato et al., 1996). However, SES did not enhance motor performance in the nonpracticed hand, regardless of location (Table 1). Although there are some indications that SES has spatially specific effects (Koesler, Dafotakis, Ameli, Fink, & Nowak, 2008; Wu et al., 2006), there are notable methodological differences between the present study and previous studies examining spatial specificity of SES that could explain the disparate findings between studies, including SES frequency, intensity, and duration. However, the present results are comparable with studies that showed that 2 hr of SES delivered to peroneal, sural, and tibial nerves of the ipsilateral leg failed to enhance stroke patients' and healthy adults' hand motor function (Koesler et al., 2008; Wu et al., 2006). Such null results may be related to the absence of additional adaptations in neuronal plasticity when SES is added to MP, as discussed in the next section. Altogether, the present results show that priming the transfer-receiving hand with SES failed to augment intermanual transfer of a visuomotor skill.

Location of SES Failed to Affect Neurophysiological Mechanisms as Assessed by TMS

We observed increases in CSE in the M1 controlling the practicing hand after MP (43.6%), in accordance with previous studies showing that increased motor performance (23%) was accompanied by increased CSE (20%; Cirillo et al., 2011; Perez et al., 2004). MP of a similar visuomotor task in the present study, using wrist muscles, produced intermanual transfer (13.6%) in absence of adaptations in CSE (1.3%). Delivering SES to the practicing hand in the present study did not further increase the magnitude of motor skill acquisition (Table 1;

Figure 2). In addition, while MP and SES alone increased CSE in the trained and nontrained M1 in previous studies (Bonato et al., 1996; Veldman et al., 2015), SES did not affect CSE in the left and right M1 when SES was applied during MP to the right hand (18.9% and −13.7%, respectively) or the left hand (−8.4% and 11.6%, respectively). One possible explanation is that afferent motor and sensory information not only interfered with each other when SES was applied to the right, practiced arm but also when SES was applied to the left, nonpracticed arm, and therefore SES could not augment interlimb transfer. Altogether, in contrast to our hypothesis, we found no evidence for spatial priming by SES to affect key TMS parameters, even though long-term potentiation-like mechanisms are known to be involved in the immediate effects of MP (Bütefisch et al., 2000; Kaelin-Lang et al., 2002; Koesler et al., 2008; Sorinola, Bateman, & Mamy, 2012).

Although γ-aminobutyric acid-mediated SICI was reduced in the nonintervention right-ipsilateral M1 (41.4%) after RMP + RSES, but not in the left intervention M1 (1.6%; Veldman et al., 2015), location of SES did not affect intracortical inhibition. Further, the present study demonstrated that there were no changes in ICF regardless of location of SES. After prolonged SES, changes in ICF tend to be inconsistent, as ICF did not change in healthy adults (17%, $p > .05$) after 2 hr of median nerve SES in one study (Kaelin-Lang et al., 2002), but it increased in stroke patients (36%) after ulnar and median nerve stimulation in another study (Celnik et al., 2007). Altogether, location of SES did not affect γ-aminobutyric acid-mediated SICI and *N*-methyl-d-aspartate-mediated ICF-related mechanisms under the present experimental conditions.

Our previous study showed that IHI, quantified by iSP duration, increased after RMP, decreased after SES, and remained unchanged after RMP + RSES (Veldman et al., 2015), suggesting that excitability of interhemispheric connections is modified to preserve or even increase motor independence of the two hands (Veldman et al., 2015). However, sensory input can modify the state of the nonintervention M1 by producing afferent volleys that reach S1 and bilaterally S2 (Allison, McCarthy, Wood, Williamson, & Spencer, 1989; Golaszewski et al., 2004; Hari et al., 1984, 1990), resulting in a modified excitability state of the ipsilateral M1 through neuroanatomical connections (Shin & Sohn, 2011). We hypothesized that delivering SES to the hand that performs MP may cause a cancelation or interference effect (Veldman et al., 2015). Therefore, we determined whether delivering SES to the transfer-receiving left hand during right-handed MP would modify IHI differently by canceling the interference effect. Previous studies showed that reductions in glutamatergic interhemispheric fibers mediating IHI have been associated with increased intermanual transfer of skill and strength (Hortobágyi et al., 2011), suggesting that a less-inhibited cortex could generate outputs faster (Perez et al., 2007). However, our results showed that IHI was not modified differently when applying SES to the transfer-receiving hand, which is in line with our observation that location of SES did not affect intermanual transfer.

Limitations and Conclusion

One limitation is that the optimal SES parameters may differ between patients and healthy adults, underlying in part our results. It is possible that the TMS results can be different when assessed at rest and during muscle contraction, a relevant condition in a motor learning study (Berghuis et al., 2015; Opie, Catcheside, Usmani, Ridding, & Semmler, 2013). Further, the study involved small groups of participants, and some of the measurements showed large variation. High levels of interindividual variability known to be associated with TMS-derived measures, the responses to motor learning, and the effects of SES may have prevented us from detecting whether SES added to visuomotor practice would improve motor performance and interlimb transfer. Future studies should examine the ideas presented here in clinical populations that could potentially benefit from SES-aided MP in the acute rehabilitation of unilateral motor dysfunctions. Finally, although the prestudy power analysis revealed that seven subjects per group is sufficient to detect changes in the measured variables, the large variability in the data may have prevented us from detecting significant changes, suggesting that TMS studies require the inclusion of a greater number of participants.

In conclusion, the present study showed that SES did not further increase the magnitude of skill acquisition and intermanual transfer, which was independent of the location of SES. Future studies should systematically manipulate SES parameters to better understand the mechanisms of how SES affords motor learning benefits documented but not studied in patients.

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