# ATTENTION MODULATES SPECIFIC MOTOR CORTICAL CIRCUITS RECRUITED BY TRANSCRANIAL MAGNETIC STIMULATION

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**Abstract**—Skilled performance and acquisition is dependent upon afferent input to motor cortex. The present study used short-latency afferent inhibition (SAI) to probe how manipulation of sensory afference by attention affects different circuits projecting to pyramidal tract neurons in motor cortex. SAI was assessed in the first dorsal interosseous muscle while participants performed a low or high attention-demanding visual detection task. SAI was evoked by preceding a suprathreshold transcranial magnetic stimulus with electrical stimulation of the median nerve at the wrist. To isolate different afferent intracortical circuits in motor cortex SAI was evoked using either posterior–anterior (PA) or anterior–posterior (PA) monophasic current. In an independent sample, somatosensory processing during the same attention-demanding visual detection tasks was assessed using somatosensory-evoked potentials (SEP) elicited by median nerve stimulation. SAI elicited by AP TMS was reduced under high compared to low visual attention demands. SAI elicited by PA TMS was not affected by visual attention demands. SEPs revealed that the high visual attention load reduced the fronto-central P20-N30 but not the contralateral parietal N20-P25 SEP component. P20-N30 reduction confirmed that the visual attention task altered sensory afference. The current results offer further support that PA and AP TMS recruit different neuronal circuits. AP circuits may be one substrate by which cognitive strategies shape sensorimotor processing during skilled movement by altering sensory processing in premotor areas. © 2017 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: transcranial magnetic stimulation, monophasic, current direction, indirect waves, motor, attention.

## INTRODUCTION

Afferent input to motor cortex is integral to the acquisition and performance of motor skills. Short-latency afferent inhibition (SAI) (Tokimura et al., 2000) offers a method to probe the modulatory effects of somatosensory afference upon motor cortex excitability and plasticity. SAI involves transcranial magnetic stimulation (TMS) over motor cortex timed to coincide with the arrival of somatosensory afference evoked by stimulation of the corresponding peripheral nerve (~20 ms for distal muscles of the hand). The inhibition evoked by the somatosensory afference is cortical in origin with spinal excitability unaffected (Tokimura et al., 2000). That at least part of the SAI network is driven by somatosensory afference to motor cortex is evidenced by increasing inhibition as the intensity of the peripheral nerve stimulus is increased (Fischer and Orth, 2011). Further, the positive relationship between the N20-P25 somatosensory-evoked potential (SEP) and magnitude of SAI suggests that at least part of the network mediating SAI is dependent upon thalamo-cortical projections to somatosensory cortex (Bailey et al., 2016). Although there is a strong relationship between somatosensory afference and SAI, SAI is a malleable phenomenon modulated by movement timing and the relevance of a muscle to voluntary movement (Voller et al., 2006; Asmussen et al., 2013, 2014). Central cholinergic involvement, in addition to $GABA_A$, in the generation of SAI (Ziemann et al., 2014) makes it a potential method to probe the effect of cognition on motor cortex excitability through attention-related afferent modulation.

To date all the aforementioned studies have quantified SAI by pairing posterior–anterior (PA) monophasic magnetic stimulation with peripheral electrical stimulation. However, it has been demonstrated that SAI evoked with less frequently employed anterior–posterior (AP) monophasic current isolates different circuits of inhibitory neurons (Ni et al., 2011). Functionally, networks recruited by PA and AP stimulation have been differentially linked model-free and model-based learning (Hamada and Galea, 2014). AP-sensitive, but not PA-sensitive, circuits mediate individual responsiveness to plasticity-inducing protocols like theta burst stimulation (Hamada et al., 2013) that are mechanistically similar to those that underlie motor learning (Censor and Cohen, 2011). These same plasticity-inducing protocols are sensitive to attention demands and allocation (Stefan et al., 2004; Conte et al., 2007; Kamke et al., 2012, 2014) suggesting that the AP circuit may be sensitive to attention. Suppressing cortical areas linked to cognitive control, like dorsolateral prefrontal cortex, to minimize their influence of sensorimotor processing enhances procedural learning (Galea et al., 2010; Zhu et al., 2015). The common involvement of AP-sensitive circuits in mediating SAI and plasticity-inducing protocols raises the possibility that at least some of the networks involved in generating SAI

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may reflect a volitional cognitive modulation of sensory-motor processing (Paul and Ashby, 2013).

The current study assessed the effect of attention load on the specific afferent intracortical motor circuits recruited by different current directions. SAI was elicited using either PA or AP TMS to preferentially recruit distinct motor cortical circuits (Ni et al., 2011) during a visual detection task of varying attentional demand. While it is well known that PA SAI scales with peripheral stimulation intensity, somatosensory afference can similarly be scaled by intrinsic factors such as attention (Staines et al., 2002; Meehan and Staines, 2009) and movement intention (Legon et al., 2008, 2010). Tasks with high perceptual loads draw attention resources away from task-irrelevant sensory processing leading to suppression of the irrelevant afference (Lavie, 2005). In the somatosensory system such attention-related suppression can occur as early as the N20-P25 thalamo-cortical afferent projections (Staines et al., 2002; Legon and Staines, 2006; Meehan et al., 2009), the same projections are shown to underline SAI magnitude (Bailey et al., 2016). Therefore, we hypothesized that an increasingly attention-demanding visual detection task would reduce somatosensory afference and thereby reduce SAI elicited by both PA- and AP-sensitive networks. We further hypothesized that any reduction would be greater for AP SAI. The latter hypothesis was based upon a collection of past observations involving the relationship between theta burst stimulation and late I-wave recruitment (Hamada et al., 2013), reduced efficacy of theta burst stimulation when attention is withdrawn (Kamke et al., 2012) and that SAI predominantly works on later I-waves more readily recruited by AP TMS (Tokimura et al., 2000; Ni et al., 2011). In a second independent experiment, we quantified the change in the parietal N20-P25 and frontal P20-N30 SEPs to index somatosensory gating induced by the different attention demands of the visual detection tasks.

## EXPERIMENTAL PROCEDURES

### Participants

Twelve self-reported right-handed adults participated in the original TMS experiment assessing SAI under different visual attention demands (Experiment 1; 6 males, 6 females, 22 ± 5 years). An independent sample of thirteen self-reported right-handed adults participated in the post hoc SEP experiment (Experiment 2; 6 males, 7 females, 22 ± 5 years). All participants across both experiments provided written informed consent; the Institutional Review Board of the University of Michigan Medical School (IRBMED) approved the study protocol.

### Visual detection task

For both experiments visual attention load was manipulated using a visual detection task with two levels of difficulty (Schwartz et al., 2005; Kamke et al., 2012). The visual detection task required participants to monitor a stream of different color upright and inverted crosses presented at a rate of 4 Hz. For the low attention task

participants counted the number of red crosses in the stream regardless of orientation (Fig. 1A). In the high attention variant participants counted the number of upright yellow or inverted green crosses (Fig. 1B). Participants verbally reported the count at the end of the trial. For both experiments behavioral performance was assessed by comparing mean accuracy across the low and high attention load variants of the visual detection task.

### Transcranial magnetic stimulation (TMS)

For Experiment 1, motor-evoked potentials (MEP) elicited by TMS were recorded using LabChart 7 software in conjunction with a Dual BioAmp and PowerLab 8/30 acquisition system (AD Instruments, Colorado Springs, CO). Participants were seated with both arms resting on a pillow placed upon their lap. Surface electromyography electrodes (Ag-AgCl) were placed over the right first dorsal interosseous muscle using a tendon-belly montage. Surface electromyography recording was triggered using a 5 V TTL pulse with an epoch of −0.3 to 0.5 s. During acquisition, data were amplified ($\times 1000$), digitized ($\times 40,000\ Hz$) and filtered (band pass filtered 5–1000 Hz, notch filter − 60 Hz). Surface electromyography data were subsequently down-sampled to 5000 Hz during offline analysis. The MEP was defined as the peak-to-peak amplitude of the maximal electromyographic response between 20 and 50 ms post-TMS stimulation. Trials where baseline root mean square error (−50 to 0 ms) in the first dorsal interosseous muscle exceeded 15 μV were excluded from subsequent analysis. Less than 2% of all trials were excluded as a result of excessive muscle activity during the baseline period.

TMS was delivered using a MagVenture MagPro X100 with option stimulator (MagVenture Inc., Atlanta, GA) and a figure-8 coil (MC-B70). Two different current configurations were delivered. For posterior–anterior (PA) stimulation the coil was held ~45° to the midline and current direction specific as "reverse" using the stimulator's onboard software (Fig. 1D). For anterior–posterior (AP) stimulation the coil orientation was identical with that for PA stimulation but current direction was current was set to "normal" via the stimulator's onboard software (Fig. 1D).

The left first dorsal interosseous motor cortical hotspot was defined as the scalp position that elicited the largest and most consistent response following PA stimulation. The location and trajectory of the coil on the scalp at the hotspot was recorded using the BrainSight™ stereotactic system (Rogue Research, Montreal, QC). The same hotspot was used for AP stimulation (Sakai et al., 1997). Resting motor threshold was independently defined for the PA- and AP-induced currents as the percentage of stimulator output (to the nearest 1%) that elicited an MEP of $\geq 50$ μV peak-to-peak on 10 out of 20 trials (Rossini et al., 2015). TMS intensity for SAI was set to the stimulator output that elicited a peak-to-peak MEP amplitude of ~1 mV (in the absence of peripheral stimulation) for each current direction.