Transcranial Magnetic Stimulation in Different Current Directions Activates Separate Cortical Circuits

Zhen Ni, Samer Charab, Carolyn Gunraj, Aimee J. Nelson, Kaviraja Udupa, I-Jin Yeh, and Robert Chen
Division of Neurology, Krembil Neuroscience Centre and Toronto Western Research Institute, University Health Network, University of Toronto, Toronto, Ontario, Canada

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Ni Z, Charab S, Gunraj C, Nelson AJ, Udupa K, Yeh I-J, Chen R. Transcranial magnetic stimulation in different current directions activates separate cortical circuits. J Neurophysiol 105: 749–756, 2011. First published December 8, 2010; doi:10.1152/jn.00640.2010. Transcranial magnetic stimulation (TMS) to the primary motor cortex (M1) produces a series of corticospinal descending waves, with a direct (D) wave followed by several indirect (I) waves. TMS inducing posterior–anterior (PA) current in the brain predominantly recruits the early I1-wave, whereas anterior–posterior (AP) directed current preferentially recruits the late I3-wave. However, it is not known whether I-waves elicited by different current directions are mediated by the same neuronal populations. We studied the neuronal mechanisms mediating I-waves by examining the influence of short-latency afferent inhibition (SAI) on various I-waves. SAI was tested with electrical median nerve stimulation at the wrist followed by TMS to the contralateral M1 at different current directions. Surface electromyograms and single motor units were recorded from the first dorsal interosseous muscle. SAI was weaker for the AP compared with that for the PA current direction. With increasing median nerve stimulation intensities, SAI increased for the PA direction but showed a U-shaped relationship for the AP direction. SAI produced more inhibition of late I-waves generated by PA than those generated by AP current direction. We conclude that late I-waves generated by PA and AP current directions are mediated by different neuronal mechanisms.

INTRODUCTION

Primary motor cortex (M1) works in association with other motor-related brain areas in the planning and execution of movements. The unique anatomical and physiological features of the M1 provide an opportunity to analyze the organization of cortical networks. Electrical stimulation of the M1 elicits a series of periodic, high-frequency descending corticospinal waves. The first wave is due to direct activation of corticospinal axons and is termed the direct (D) wave. Subsequent waves are caused by synaptic activities of interneurons in M1, which project to corticospinal neurons and are termed indirect (I) waves. Multiple I-waves are classified as early (I1, I2) or late (I3, etc.) (Patton and Amassian 1954; Rothwell et al. 1991). Studies using transcranial magnetic stimulation (TMS) in human M1 have shown that the order of recruitment of the different I-waves depends on the current direction. Posterior–anterior (PA) directed current in the brain predominantly recruits early I-waves. On the other hand, anterior–posterior (AP) current predominantly recruits late I-waves, whereas lateral–medial (LM) current preferentially recruits the D-wave (Day et al. 1989; Di Lazzaro et al. 2001; Sakai et al. 1997).

TMS is widely used in the diagnosis and treatment of neurological and psychiatric disorders (Chen et al. 2008; Kobayashi and Pascual-Leone 2003). However, the physiological basis of the I-wave generation is not fully understood. In particular, it is not known whether a specific I-wave (e.g., I3-wave) induced by different current directions is mediated by different mechanisms (Amassian et al. 1987; Rothwell et al. 1987). Corticospinal excitability is modulated by sensory afferent input. When TMS is preceded by electrical stimulation of the median nerve at the wrist with an interstimulus interval (ISI) of about 20 ms, the motor evoked potential (MEP) elicited by TMS is inhibited, a phenomenon termed short-latency afferent inhibition (SAI) (Tokimura et al. 2000). Recording of corticospinal waves showed that SAI inhibits late I-waves more than early I-waves generated by the PA current direction (Tokimura et al. 2000), similar to other inhibitory circuits such as short- and long-interval intracortical inhibition (SICI and LICI, respectively) (Di Lazzaro et al. 2004). SAI is more suited to test the properties of various I-wave generating neurons compared with intracortical inhibitory circuits elicited by paired-pulse TMS because SAI does not require conditioning stimulation (CS) with TMS, which is also influenced by different current directions. We hypothesize that different current directions may involve different neural populations to generate I-waves of similar latencies (model shown in Fig. 1A). This is tested by investigating the effects of SAI with TMS applied in PA and AP current directions.

METHODS

Subjects

We studied 12 right-handed healthy subjects (4 women and 8 men, aged 25–47 yr, mean age 36.1 ± 7.7 yr). Handedness (laterality quotient, 96.7 ± 7.8) was confirmed using the Oldfield Handedness Inventory (Oldfield 1971). All subjects provided written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the University Health Network (Toronto) Research Ethics Board.

Electromyographic recording

Surface electromyogram (EMG) was recorded from the right first dorsal interosseous (FDI) muscle with 9 mm diameter Ag/AgCl surface electrodes (except for experiment 2). The active electrode was placed over the muscle belly and the reference electrode over the metacarpophalangeal joint of the index finger. The signal was amplified (×1,000), band-pass filtered (2 Hz to 2.5 kHz, Model 2024F; Introx Technologies, Bolton, Ontario, Canada), digitized at 5 kHz by an A/D interface (Micro1401; Cambridge Electronics Design, Cambridge, UK), and stored in a computer for off-line analysis.
with a pen as the motor hot spot. Next, we determined the hot spot for optimal position for activation of the right FDI muscle was marked to produce the I1-wave (Di Lazzaro et al. 2001; Kaneko et al. 1996). The direction, corticospinal neurons are activated transynaptically and approximately perpendicular to the central sulcus. With this current coil points backward at 30–45° from the midsagittal line. It is PA and AP current directions were used for TS (Fig. 1). Sensory threshold (ST) with MNS was measured and was the lowest TS intensity needed to generate MEPs of >1 mV in ≥5 of 10 trials in the right FDI muscle when the muscle was completely relaxed. TS_{stim} and TS_{stim} were determined in a similar way. MEP latencies were measured with the intensity of TS_{stim}.

**Experiment 1: time courses of SAI**

A previous study reported that SAI was found at a range of ISIs, with peak inhibition at ISI of about 20 ms (Tokimura et al. 2000). We investigated the time courses of SAI for both PA and AP current directions in all 12 subjects. Eight ISIs (16, 18, 20, 22, 24, 26, 28, 30 ms) were tested. CS intensity was adjusted to produce a slight thumb twitch (Abbruzzese et al. 2001). This CS intensity was equal to 3.47 ± 0.52 ST (n = 12). TS intensity was TS_{stim} for different current directions. Ten trials for each ISI and 20 trials for TS alone (total of 100 trials) were delivered in random order for each subject. Different TS current directions (PA and AP) were tested in separate runs.

**Experiment 2: single motor unit study**

In experiment 1, we recorded surface EMG that reflects the superimposed activities of many motor units. In this study, we investigated how single motor units (SMUs) responded to TMS and distinguished different descending waves in SMU recordings by analyzing components with different latencies to a given TMS pulse. Five subjects were studied. Active motor threshold (AMT) was defined as the lowest TMS intensity that could generate a small MEP (<200 μV from surface EMG recording) in 5 of 10 consecutive trials when the subject contracted the FDI muscle at background EMG of 20% of maximum. AMTs for different current directions were determined. SMU recordings were made via a concentric needle electrode (disposable type DCN50, 26G; Medtronic, Skovlund, Denmark) inserted into the FDI muscle. The signal was amplified and filtered as for surface EMG recordings. Subjects were trained to fire the SMU at <10 Hz with the aid of audiovisual feedback. This required a slight and constant voluntary muscle contraction of <5% of maximum. TS intensity was set at 120% AMT for each current direction, which produced about 30% firing probability of the SMU (Hanajima et al. 2002). CS intensity was adjusted to produce a slight thumb twitch. The ISI for which peak SAI was found in experiment 1 was used and was adjusted individually (20 or 22 ms). One hundred trials for CS–TS and TS alone (200 trials in total) were delivered in random order. PA and AP current directions were tested in separate runs. In addition, SMU recording with TS alone in the LM current direction was recorded to determine the latency for the D-wave. We simultaneously recorded the surface EMG to monitor MEP amplitudes during the SMU recording and moved the active electrode for surface EMG slightly away from the motor point of the FDI muscle to allow placement of the needle electrode.

**Experiment 3: effects of different TS intensities on SAI**

Twelve subjects participated. Three TS intensities were tested: TS_{stim}, TS_{stim}, and TS_{stim}. Three stimulators and two Bistim modules (Magstim) were used to deliver TS. Two stimulators were connected via a Bistim module. This Bistim module and the third Magstim 200 stimulator were connected to a second Bistim module. The TMS coil was connected to the second Bistim module. This setup allowed us to deliver TS with different intensities through the same coil at a short intertrial interval (Ni et al. 2009). CS was adjusted to
produce a slight thumb twitch. The ISI with peak SAI for each subject based on the results of experiment 1 was tested. The stimulus configuration consisted of six states: TS alone and CS–TS at three different TS intensities. Ten trials for each state were delivered in random order. Data for PA and AP current directions were collected in separate runs.

Experiment 4: effects of different CS intensities on SAI

The effects of different CS intensities were investigated in seven subjects. Six CS intensities, varying from 1ST to 6ST in 1ST increments, were tested at the ISI for peak SAI from experiment 1. TS used TS1mV. Ten trials for TS alone and for CS–TS were delivered in random order. Data for different CS intensities and TS current directions (PA and AP) were collected in separate runs.

Experiment 5: effects of voluntary contraction on SAI

We investigated the effects of voluntary contraction on SAI in seven subjects. The subjects abduced their index finger to produce 20% of maximum EMG with the aid of visual and auditory feedback. The CS intensity was adjusted to produce a slight thumb twitch. The ISI for peak SAI was tested based on experiment 1. Since voluntary contraction greatly increases MEP amplitude (Rothwell 1997), we adjusted the TS intensity to produce about 1 mV MEP during muscle contraction. This intensity is termed TS1mVActive. Both TS1mV and the adjusted TS intensity were used as TS. The stimulus configuration consisted of four states: TS alone with TS1mV or TS1mVActive and CS followed by TS1mV or TS1mVActive. Ten trials for each state were delivered in random order. Data for PA and AP current directions were collected in separate runs. SAI during voluntary muscle contraction was compared with that at rest.

Data analysis and statistical analysis

MEP amplitudes were measured peak to peak. The MEP amplitude evoked by CS–TS was expressed as a percentage of the mean MEP amplitude of TS alone. Values <100% indicate inhibition and values >100% indicate facilitation. Values are reported as mean ± SE. For SMU recording, spike numbers after TMS were counted. Peristimulus time histograms (PSTHs) were constructed for each SMU. The bin size was set at 0.2 ms to distinguish the different descending waves. Four PSTHs under different stimulus conditions (TS alone and CS–TS with PA and AP current directions) were compared.

A two-way repeated-measures ANOVA was used to examine the time course of SAI under different TS current directions in experiment 1. Two-way repeated-measures ANOVA was used in experiments 3–5 to examine the effects of current direction and TS intensity (experiment 3), CS intensity (experiment 4), and voluntary muscle contraction (experiment 5). Paired t-tests with Bonferroni correction for multiple comparisons were performed as post hoc tests if ANOVA showed a significant main effect. SPSS software (v. 10.0; SPSS, Chicago, IL) was used for statistical analysis. The significance level was set at \( P < 0.05 \).

Results

\( \text{TS}_{1 \text{mV}}(n = 12) \) was 49.9 ± 10.1% of maximum stimulator output for the PA current direction and generated MEP of 1.26 ± 0.23 mV in amplitude. For the AP current direction, \( \text{TS}_{1 \text{mV}} \) at 72.6 ± 16.4% maximum stimulator output produced MEP of 1.20 ± 0.26 mV in amplitude. MEP amplitudes for PA and AP current directions were matched. In addition, \( \text{TS}_{1 \text{mV}} \) was 57.7 ± 12.6% of maximum stimulator output for the LM current direction and generated MEP of 1.25 ± 0.15 mV in amplitude. The three current directions tested generated MEPS with significantly different latencies [Fig. 2; \( F_{(2,11)} = 58.56, P < 0.001 \)]. The MEP latencies (\( n = 12 \)) were 22.6 ± 1.9 ms for LM, 23.1 ± 2.0 ms for PA, and 24.7 ± 2.4 ms for AP current direction (comparisons between LM and PA, \( P < 0.01 \); between PA and AP, \( P < 0.001 \); between LM and AP, \( P < 0.001 \)). The shortest MEP latency for LM current direction confirmed that the D-wave was generated by this current direction.

Experiment 1: time courses of SAI

Figure 3 shows that the peak inhibition caused by the preceding MNS occurred at ISIs of 20 and 22 ms for both PA and AP current directions. This is consistent with previous studies (Di Lazzaro et al. 2000; Tokimura et al. 2000). The two-way ANOVA showed significant main effects of ISI [\( F_{(7,77)} = 17.65, P < 0.001 \)] and current direction [\( F_{(1,77)} = 6.90, P = 0.023 \)], the latter indicating that there was a greater degree of inhibition for the PA than for the AP current direction. Post hoc tests confirmed greater SAI at ISIs of 20, 22, and 24 ms for the PA than for the AP current directions.
(P < 0.05 for all comparisons). The interaction between current direction and ISI was not significant.

**Experiment 2: different degrees of SAI in various I-waves (single motor unit study)**

The firing probability of SMU increased within the time window of 20–30 ms after TMS. In any given trial, the SMU fired no more than once within this window. The changes in I-waves generated by PA and AP current directions were analyzed separately by PSTH. It is possible to record the firing properties of more than one SMU in intrinsic hand muscles (Enoka 1995) if the tip of the electrode is located close to multiple SMUs. Multiple SMUs in a single subject were identified by the shapes of different waveforms. Four subjects had two SMUs each and one subject had one (total of nine SMUs from five subjects), which showed constant firing in all four experimental conditions (TS alone and CS–TS with PA and AP current directions). Figure 4A shows the PSTH from one SMU. The three current directions produced different sets of descending waves. For all SMUs (n = 9), LM directed current produced two distinct peaks with latencies of 22.0 ± 0.4 and 23.4 ± 0.5 ms, corresponding to D- and I1-waves. PA current produced three peaks with latencies of 23.4 ± 0.5, 24.6 ± 0.4, and 26.1 ± 0.5 ms, corresponding to I1-, I2-, and I3-waves. AP current produced two peaks with latencies at 26.1 ± 0.5 and 27.6 ± 0.4 ms, corresponding to I3- and I4-waves. In addition, PA current also produced a small I4 peak, whereas AP current produced a small I2 peak in some SMUs. A typical SMU shown in Fig. 4A recorded I1-, I2-, and I3-waves with PA directed current. The I2- and I3-waves were inhibited by the preceding MNS, whereas the I1-wave did not change. On the other hand, AP directed current produced I3- and I4-waves. Both waves were moderately inhibited by the preceding MNS. The simultaneously recorded surface EMG (Fig. 4B) confirmed the results of experiment 1 that MEP was less inhibited in AP than that in PA directed current. The PSTH counts (100 trials) for the different I-waves are summarized in Table 1. Paired t-tests showed that the I3-wave generated by the PA current direction was more inhibited than that generated by the AP current direction (t = 5.43, df = 8, P < 0.001).

**Experiment 3: effects of different TS intensities on SAI**

Figure 5 shows that SAI decreased with higher TS intensities for PA directed current but slightly increased with increasing TS intensities for AP current. The two-way ANOVA revealed significant main effects of TS intensity [F(2,22) = 3.94, P = 0.034] and current direction [F(1,22) = 20.04, P < 0.001] on SAI, the latter confirming the results of experiment 1. In addition, the interaction between the two main effects was also significant [F(2,22) = 11.88, P < 0.001], indicating that the
TABLE 1. Counts and degree of SAI (mean ± SD) for different I-waves generated by PA and AP current directions measured in the peristimulus time histogram

<table>
<thead>
<tr>
<th>Current Direction</th>
<th>I1</th>
<th>I2</th>
<th>I3</th>
<th>I4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS alone</td>
<td>11.7 ± 1.4</td>
<td>12.1 ± 1.1</td>
<td>14.7 ± 2.1</td>
<td>0.9 ± 0.8</td>
</tr>
<tr>
<td>CS–TS</td>
<td>11.1 ± 1.3</td>
<td>6.8 ± 1.7</td>
<td>6.8 ± 1.7</td>
<td>—</td>
</tr>
<tr>
<td>Degree of SAI</td>
<td>4.5 ± 5.8%</td>
<td>43.5 ± 16.1%</td>
<td>60.7 ± 11.0%</td>
<td>—</td>
</tr>
<tr>
<td>AP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS alone</td>
<td></td>
<td>0.4 ± 0.5</td>
<td>22.2 ± 3.3</td>
<td>11.0 ± 2.6</td>
</tr>
<tr>
<td>CS–TS</td>
<td></td>
<td>—</td>
<td>16.2 ± 2.2</td>
<td>8.8 ± 1.9</td>
</tr>
<tr>
<td>Degree of SAI</td>
<td></td>
<td>—</td>
<td>25.8 ± 13.3%</td>
<td>18.5 ± 14.9%</td>
</tr>
</tbody>
</table>

Data are from nine single motor units. Degree of SAI is normalized as a percentage of decrease in the counts produced by CS–TS to that produced by TS alone (0 means no inhibition and 100% means maximum inhibition). AP, anterior–posterior; CS, conditioning stimulus; I-wave, indirect wave; PA, posterior–anterior; SAI, short-interval afferent inhibition; TS, test stimulus.

effects of TS intensity on SAI are different for PA and AP directed currents. Post hoc testing showed greater SAI for PA than that for AP current direction at TS0.5mV (P < 0.001) and TS1mV (P < 0.05), but not at TS2mV.

Experiment 4: effects of different CS intensities on SAI

The degree of SAI for both PA and AP current directions changed with increasing CS intensities [Fig. 6; ANOVA, main effect of CS intensity, F(5,30) = 8.37, P < 0.001]. The effect of current directions was also significant [F(1,30) = 26.82, P = 0.002]. In addition, ANOVA showed that the interaction between CS intensity and TS current direction was significant [F(5,30) = 6.34, P < 0.001], indicating that the difference between two current directions depends on the CS intensity used. Figure 6 shows that with the increasing CS intensities, SAI generated by PA current direction increased. On the other hand, SAI generated by AP current direction initially increased with higher CS intensity, but further increases in CS intensity decreased the inhibition. Post hoc testing confirmed that at CS intensities >2ST, there was greater SAI for the PA than that for the AP current direction (3ST and 4ST, P < 0.05; 5ST and 6ST, P < 0.01).

Experiment 5: effects of voluntary contraction on SAI

The results are shown in Fig. 7. ANOVA showed a main effect of voluntary contraction conditions (active SAI with unadjusted TS intensity, active SAI with adjusted TS intensity and similar test MEP size, resting SAI) [F(2,12) = 6.42, P = 0.013] on SAI. The main effect of current direction was not significant [F(1,12) = 2.10, P = 0.197]. This is different from the results in relaxed muscle (experiments 1, 3, and 4), suggesting that the difference in SAI between PA and AP was largely abolished by voluntary muscle contraction. The interaction between current direction and muscle contraction was significant [F(2,12) = 5.14, P = 0.025], indicating that the effect of voluntary muscle contraction on SAI is different for the two current directions tested. Figure 7 shows that voluntary contraction reduced SAI in the PA current direction but not in...
that used higher TMS intensity (130% AMT) and stronger voluntary contraction (20% of maximum) recorded the I4-wave with implanted epidural electrodes for both the PA and AP current directions (Di Lazzaro et al. 2001). The descending waves with different latencies (the interval between adjacent waves was about 1.5 ms, with the D-wave appearing first in the LM direction) accounted for the different MEP latencies for the three current directions (Fig. 2). It should be noted that differences in MEP latencies among various current directions are shorter than those in the descending waves. This can be explained by temporal summation of multiple descending waves on the spinal motoneuron caused by relatively higher TS intensity used in the rest condition (Ilic et al. 2002; Ziemann and Rothwell 2000).

PA and AP directed current activate different late I-waves

In other paired-pulse TMS inhibitory paradigms, such as SICI and LICI, late I-waves are predominantly inhibited (Di Lazzaro et al. 2004). Previous studies investigating SAI in PA current direction also reported that SAI inhibits late I-waves (Di Lazzaro et al. 2005; Sailer et al. 2003; Tokimura et al. 2000), suggesting that the cortical circuits mediating late I-waves are more susceptible to cortical inhibition than those mediating early I-waves. Consistent with these previous studies, we found that sensory afferent input inhibited the output from M1 at the ISIs around 20 ms not only for PA but also for AP current direction. PSTH studies confirmed that SAI predominantly inhibited the late I-waves for both PA and AP current directions, similar to the recordings from implanted cervical epidural electrodes for the PA direction (Tokimura et al. 2000).

Importantly, the present study showed that sensory afferent input had fewer inhibitory effects on MEP produced by the PA than those produced by the PA current direction. This was confirmed by the investigations of different ISIs (experiment 1), TS intensities (experiment 3), CS intensities (experiment 4), and the different degrees of inhibition in various I-waves measured by PSTH (experiment 2). We examined peak SAI at an individual ISI with comparable test MEP size for both current directions. Because PA directed current generated both early and late I-waves, whereas AP directed current generated only late I-wave, AP directed current should have produced more late I-waves than the PA directed current. If late I-wave generating neurons activated by PA and AP current directions were mediated by the same neural population, stronger SAI for the AP than that for the PA current direction would be expected. However, the opposite results that SAI produced greater inhibition for the PA direction than that for the AP direction were obtained in all experiments. Therefore these findings support the notion that different neuronal populations were involved in the late I-waves generated by PA and AP directed currents. This is consistent with a previous study demonstrating that late I-waves generated by the PA direction have latencies different from those generated by the AP direction (Di Lazzaro et al. 2001).

There are several other factors that should be considered. First, rather than different neuronal populations, the same group of cortical neurons may be activated by PA and AP current directions at different sites. Since higher TS intensities were used for AP current, it was possible that neuronal popu-
lutions in deeper and wider areas were activated. Nevertheless, this possibility still indicates that different subsets of the same neuronal population are activated by PA and AP current directions. Second, there may be interactions between early and late I-waves. Specifically, the presence of early I-waves may affect late I-waves in the PA direction, whereas in the AP direction the late I-waves are not affected by such interaction. Third, we examined the time course of SAI with ISI resolution of 2 ms and a more detailed time course (ISI 1 ms) might better identify the peak SAI. However, the finding that the whole time course of SAI shifted to less inhibition for the AP current direction (Fig. 2) made it unlikely that SAI at the optimal ISI would be similar for PA and AP directed current. Fourth, sensory afferent input might be affected differently by PA and AP current directions, with the afferent input being partially blocked by the AP but not by the PA current direction. We cannot exclude this possibility but consider it unlikely because only one TMS pulse was given and would have to simultaneously affect the sensory input and the corticospinal output of the M1 to change MEP amplitude. There was also no evidence that sensory input to the M1 was affected by current directions of TMS.

Our results also suggest that TS current directions have different effects for SAI and SICI because SICI inhibits MEP generated by the AP current direction more than that generated by the PA current direction (Hanajima et al. 1998). This is consistent with the different effects of benzodiazepines on SICI and SAI. SICI is increased by both lorazepam and diazepam but SAI is only slightly increased by diazepam and is reduced by lorazepam (Di Lazzaro et al. 2005). Therefore the cortical circuits activated by SAI and SICI are likely to be different. Moreover, SICI involves TMS for both CS and TS. Since CS even at subthreshold intensity is able to raise the excitability of early and late I-wave generating neurons, the SICI paradigm may lead to complex interactions between early and late I-waves.

We found that MEP generated by the AP current direction in which more late I-waves were produced was less inhibited compared with MEP generated by the PA direction. This result suggested that the AP directed current activated different neuronal populations of late I-wave generating neurons that were less sensitive to SAI than those activated by the PA current direction. Moreover, increasing the strength of CS (experiment 4, Fig. 6) initially increased SAI for both PA and AP current directions, but further increases in CS intensity reduced the inhibition in the AP current direction. The finding may potentially be explained by sensory afferent inputs having both inhibitory and facilitatory effects on late I-wave generating neurons for the AP current direction with the facilitatory component having higher threshold. Recruitment of the facilitatory component partially canceled the inhibitory effect and at very high CS intensity (Fig. 6, 6ST) the net outcome changed from inhibition to facilitation. This is similar to the coexistence of SICI and short-interval intracortical facilitation, where the facilitation has a higher threshold (Ilic et al. 2002; Ni and Chen 2008; Peurala et al. 2008). The facilitatory component may be present throughout the range of ISIs in which SAI is observed (Fig. 3). The different effects of voluntary contraction on SAI produced by PA and AP current directions also suggest the existence of the facilitatory component of late I-waves. Voluntary muscle contraction reduced SAI for the PA direction, similar to the finding in SICI (Ridding et al. 1995). SAI for the AP directed current did not change with voluntary contraction (Fig. 7), suggesting the facilitatory component generated by the AP direction was less modulated by voluntary contraction. However, further studies are required to substantiate the existence of facilitation caused by sensory input to late I-wave generating neurons of the AP direction. The effects of voluntary muscle contraction on SAI likely depend on the strength of contraction since the SMU study that required much weaker contraction (<5% maximum) showed results similar to those obtained at rest.

Conclusion

In summary, the present study showed that the corticospinal waves produced by TMS at different current directions are mediated by different mechanisms. Recruitment of these neural circuits depends on the stimulus parameter (e.g., current direction) and is modulated differently by the input to M1.

DISCLAIMER

No conflicts of interest, financial or otherwise, are declared by the authors.

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