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RESEARCH ARTICLE

*Neural Circuits*

# Sensorimotor integration during grasping is mediated by distinct M1 circuits

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## Abstract

Motor control relies on the dynamic interplay between excitatory and inhibitory influences shaping sensorimotor integration during hand movements. In this study, we investigated short-latency afferent inhibition (SAI)—a neurophysiological marker of sensorimotor integration—during different isometric grasping behaviors (precision vs. power grip). We applied transcranial magnetic stimulation (TMS) with different coil orientations [antero-posterior (AP) vs. postero-anterior (PA)] to engage distinct neuronal populations within the primary motor cortex (M1). We found increased SAI in the AP direction during grasp execution and enhanced corticospinal excitability for precision grip when tested with AP stimulation. These findings provide evidence that distinct cortical circuits within M1 are differentially engaged during different hand configurations. Notably, we observe no grip-specific modulation of SAI, which may reflect a less topographically precise distribution of thalamocortical afferents—along with their lower temporal resolution, potentially shaped by cholinergic modulation. Future studies should investigate SAI dynamics across different phases (i.e., preparation vs. execution) of naturalistic prehension.

**NEW & NOTEWORTHY** In the present study, we assessed SAI in M1 using different coil orientations (AP vs. PA) to determine whether distinct M1-S1 circuits are selectively engaged during rest and grasping behaviors (precision vs. power grip). We found increased SAI in the AP direction during grasp execution and greater corticospinal excitability for precision grip with AP stimulation, supporting the idea that distinct M1 circuits are differentially recruited depending on hand configuration and sensorimotor demands.

*current directions; power grip; precision grip; sensorimotor integration; short-latency afferent inhibition*

## INTRODUCTION

The interaction between the primary motor cortex (M1) and the primary somatosensory cortex (S1) plays a crucial role in the control of grasping behaviors (1–4). Multiple lines of evidence have documented the presence of dense projections from S1 to M1 (5). Specifically, S1 primarily projects to layers 2/3 and 5 of M1 (6), whereas M1 projects back to S1, mainly targeting layer 1 and layers 5/6 (7).

In nonhuman primates, neurophysiological studies have shown that both motor (8) and somatosensory cortical neurons (9, 10) exhibit significant activity during different grasping actions. Muir and Lemon (11) demonstrated that, within M1, a subset of neurons that project to motoneurons controlling hand muscles play a specific role in the precision grip but not in the power grip, even though the same target muscles may be active in both types of grasps. Gardner et al. (12) have shown that S1 neurons play a key role in prehension by encoding tactile feedback upon contact and the grip and load forces exerted during grasping.

In humans, more recent studies have shown that S1 activity varies across different hand postures during grasping (13). Furthermore, when tactile feedback is disrupted through local anesthesia, excessive grip force is exerted by the fingers during object manipulation (14). Intraoperative electrophysiological studies have shown that direct intracortical stimulation of S1 evokes responses in M1 (15, 16), and neuroimaging studies have revealed grasp-related neuronal responses in both M1 and S1, with distinct activation patterns during precision and power grip (17–19).

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The interaction between S1 and M1 can be investigated in humans noninvasively through short-latency afferent inhibition (SAI), which is believed to originate from thalamocortical projections to M1 via a relay through S1 (20, 21). SAI is an inhibitory phenomenon observed when peripheral nerve stimulation precedes a transcranial magnetic stimulation (TMS) pulse to M1 at interstimulus intervals of ~20 ms (22–24), providing a valuable tool for investigating how corticospinal excitability is modulated by sensory afferent input, which is essential for refining grasping behaviors (25, 26).

A substantial body of evidence from TMS studies has shown that power grip and precision grip engage distinct cortical circuits within M1 (27–29). This differential engagement has been explored by varying TMS coil orientations, which enables the selective targeting of partially distinct neural populations in M1 that project to pyramidal layer 5 neurons. Specifically, an antero-posterior (AP) current direction primarily stimulates superficial neuronal populations in layers 2 and 3 (L2 and L3)—which may play a more prominent role in sensorimotor integration—whereas a postero-anterior (PA) current direction preferentially targets deeper neurons in layer 5 (L5) (30, 31).

In the present study, we assessed SAI in M1 using different coil orientations (AP vs. PA) to investigate whether distinct M1-S1 circuits might be selectively engaged during rest and grasping behaviors (i.e., precision and power grip), reflecting their different sensorimotor demand.

## METHODS

### Ethical Approval

All the participants were informed about the experimental procedure, and they provided written informed consent according to the last update of the Declaration of Helsinki. The experiment was approved by the ethical committee "Comitato Etico Unico della Provincia di Ferrara" (Approval No. 170592).

### Participants

Sample size estimation was guided by previous studies that investigated comparable neurophysiological mechanisms using similar TMS protocols and task designs (32–36). A total of 30 healthy participants were recruited for the study, which consisted of two separate experimental sessions investigating different TMS current directions. The sessions involved independent participant groups to ensure feasibility and minimize dropouts, due to the lengthy protocol involving multiple repeated measures, pauses, and EEG montage for SEP measurement. Sixteen participants (means ± SD age 23.69 ± 2.5 yr; 7 males, 9 females) completed the anterior-posterior (AP) stimulation session, whereas 14 participants (means ± SD age 23.57 ± 3.3 yr; 6 males, 8 females) completed the posterior-anterior (PA) stimulation session. The gender distribution was balanced across groups.

### Somatosensory-Evoked Potential (N20 Component) Recording

The experiment started with the acquisition of the somatosensory-evoked potential (SEP), aimed at determining the individualized latency of the N20 component for each participant. SEPs were elicited by stimulating the median nerve on the dominant right side with 500 stimuli, while the first dorsal interosseous (FDI) remained at rest. The latency of the individualized N20 component was determined by averaging 500 raw sweeps. Electrical stimuli (2 Hz; sampling rate: 5 kHz; pulse width: 200 μs) were delivered to the median nerve at the wrist using a constant-current stimulator (Digitimer DS7AH) via cup electrodes (cathode proximal). The stimulus intensity was adjusted to just above motor threshold, as determined by a visible twitch in the thenar muscle (37). The N20 component was recorded using cup electrodes applied to the scalp contralateral to the stimulated median nerve, following appropriate skin preparation. A bipolar montage was used, with the active electrode placed at CP3 and the reference electrode at Fz, in accordance with the 10–20 system. The signal was amplified (gain: 5,000) and bandpass filtered (low cut: 10 Hz; high cut: 500 Hz) using a Digitimer D360 system before being digitized by a Power1401 interface (Cambridge Electronic Design Ltd.) connected to a computer running Signal 6.05 (Cambridge Electronic Design).

### Experimental Task

During the execution of the three task conditions (rest, precision grip, or power grip; Fig. 1), short-latency afferent inhibition (SAI) was assessed. The experiment consisted of three blocks presented in randomized order. To determine each participant's maximal voluntary contraction (MVC), subjects first performed three brief abductions of the right index finger, each separated by 30 s, during which they exerted their MVC for 3 s. The 10% MVC value was then used to ensure a consistent level of muscle contraction (~10%) during both the precision and power grip conditions. In the precision grip, participants grasped a cylinder [diameter: 1.18 cm; length: 10.9 cm; weight: 86 g (38)] between their thumb and index finger, whereas in the power grip, they used their entire hand to grasp the same cylinder, flexing all fingers against the palm. The cylinder was maintained vertically throughout, and participants were instructed to sustain an isometric contraction of the first dorsal interosseous (FDI) muscle (39). In the rest condition, SAI was tested while the participant was fully relaxed. The wrist and forearm remained in their natural positions during the experiment. Before the start, practice trials were conducted to ensure that participants were able to perform the tasks with the appropriate level of EMG activity. In addition, during each trial, the experimenter visually monitored the EMG signals and provided verbal feedback to help participants maintain the target muscle contraction. The FDI muscle was selected due to its consistent involvement in the examined actions and its high sensitivity to task-dependent variations in corticospinal drive (29, 38, 40).

### EMG Recording

Surface EMG was recorded from the first dorsal interosseous (FDI) muscle of the right hand using a wireless system (Zerowire EMG, Aurion, Italy) with a tendon-belly montage. EMG signals were digitized (5 kHz; LP and HP filters: 1st order, 6 dB/octave; bandwidth: 10–500 Hz) and acquired by a CED Micro Power1401 mk II board (Cambridge Electronic Design, Cambridge, UK). All the acquired data were stored for offline

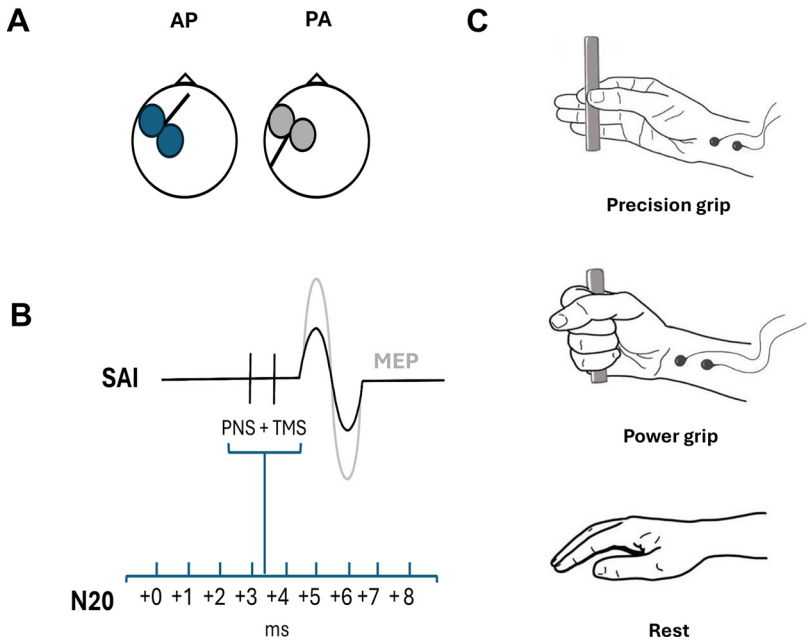


**Figure 1.** Schematic representation of the experimental conditions. *A*: illustration of the two current directions tested: antero-posterior (AP) and postero-anterior (PA). *B*: short-latency afferent inhibition (SAI), assessed by delivering peripheral nerve stimulation (PNS) before transcranial magnetic stimulation (TMS) over M1. The black schematic MEP represents the response conditioned by median nerve stimulation, while the gray trace represents the unconditioned MEP. *C*: hand actions performed during the experiment: precision grip (grasping a small cylinder between the index finger and thumb), and power grip (grasping a small cylinder using all flexed fingers with a palmar opposition grip) and rest (hand relaxed, without grasping). MEP, motor-evoked potential.

analysis using the software Signal 6.05 (Cambridge Electronic Design).

### Transcranial Magnetic Stimulation and Short-Latency Afferent Inhibition

During the experimental procedure, participants were seated comfortably in an armchair positioned in front of a table. The single-pulse TMS (sp-TMS) was administered through a 70 mm figure-of-eight focal coil connected to a Magstim BiStim2 monophasic stimulator (The Magstim Company, Whitland, UK). The FDI optimal scalp position (OSP) was identified by moving the coil in 0.5 cm steps over the left primary motor cortex hand area using a slightly supra-threshold stimulus. Resting motor threshold (rMT) was defined as the lowest intensity that elicited a motor-evoked potential (MEP) with >50 μV amplitude in 5 of 10 consecutive trials while the participants kept the FDI muscle relaxed (41, 42). Active motor threshold (aMT) was determined as the minimum intensity required to elicit MEPs of >200 μV (peak-to-peak) above the background EMG activity (~10% of maximal voluntary contraction), in ≥5 of 10 consecutive trials (27, 38). SAI was tested following the protocol described by Tokimura et al. (22). Specifically, MEPs were conditioned by electrical stimulation of the right median nerve at the wrist, with interstimulus intervals (ISIs) based on the individual latency of the N20 component of the somatosensory evoked potential. A total of 150 trials were acquired for each action condition (rest, precision grip, and power grip). SAI was tested at nine different ISIs during each action condition, ranging from N20 + 0 ms to N20 + 8 ms, with 15 trials at each interval, plus 15 unconditioned MEPs. The trials were randomized. The conditioning stimulus (CS) was delivered via bipolar electrodes at an intensity set just above the peripheral motor threshold, defined as the minimal current needed to evoke a visible twitch in the thenar muscles. The test magnetic stimulus (the conditioned MEP) was set to 120% of aMT and rMT in the active and resting conditions, respectively. Specifically, MEPs at rest were elicited using 120% rMT, while during the action conditions (precision and power grip), stimulation was delivered at 120% aMT. The same procedure was followed in both the PA and AP coil orientations (Fig. 1).

### Data and Statistical Analysis

#### *Motor-evoked potentials.*

First, we extracted the peak-to-peak amplitude for each trial, defined as the difference between the first major positive and negative deflections after MEP onset, and the latency of unconditioned MEPs at rest, measured as the time from TMS pulse release to MEP onset. Trials were visually inspected for artifacts, and data acquisition was considered valid with a minimum of 10 valid trials per condition. For every participant, we then computed the mean MEP amplitude for each tested condition. To assess corticospinal excitability across different action conditions and coil orientations, we performed a $3 \times 2$ mixed-design ANOVA on unconditioned MEP amplitude, with "action condition" (rest, precision grip, and power grip) as a within-subject factor and "coil orientation" (PA and AP) as a between-subject factor. To determine whether our data exhibited an ~1.5-ms MEP latency delay—associated with the recruitment of distinct M1 neural circuits in different cortical layers (29, 38, 35)—we conducted a two-tailed independent Student's $t$ test on MEP latencies at rest, comparing those elicited by PA and AP TMS stimulation.

#### *Short-interval afferent inhibition.*

SAI magnitude was calculated as the ratio of conditioned MEP to unconditioned MEP, expressed as a percentage:

$$SAI = \left(\frac{\text{conditioned MEP}}{\text{unconditioned MEP}}\right) \times 100.$$

To characterize the temporal profile of SAI and assess the influence of coil orientation, we performed a $9 \times 2$ mixed-design ANOVA on the mean SAI ratios computed for each

participant at each ISI, with "ISIs" (9 levels, N20 + 0 ms to N20 + 8 ms) as a within-subject factor and "coil orientation" (PA and AP) as a between-subject factor.

***ΔSAI: measuring the difference of SAI at rest and during actions.***

To investigate the modulation of SAI induced by muscle activation (i.e., precision vs. power), we measured the difference between SAI during action and at rest and expressed this difference as a percentage:

$$\Delta SAI_{\text{PRECISION}} = (SAI_{\text{PRECISION}} - SAI_{\text{REST}}) \times 100;$$
$$\Delta SAI_{\text{POWER}} = (SAI_{\text{POWER}} - SAI_{\text{REST}}) \times 100.$$

To evaluate the effect of different coil orientations on the time course of SAI during the actions of interest, we performed a $2 \times 9 \times 2$ mixed-design ANOVA on the mean ΔSAI values computed for every participant for each condition, with "action condition" (precision grip vs. power grip) and "ISIs" (from N20 + 0 ms to N20 + 8 ms) as within-subject factors and "coil orientation" (PA vs. AP) as a between-subject factor. All analyses were conducted in JASP 0.19.1.

## RESULTS

### Motor-Evoked Potentials

Figure 2 illustrates mean unconditioned MEP amplitudes across Action conditions (rest, precision grip, and power grip) and Coil orientations (PA, AP). Statistical analysis revealed a significant main effect of action condition ($F_{2,56} = 41.489$, $P < 0.001$) and coil orientation ($F_{1,28} = 9.888$, $P = 0.004$). Furthermore, the interaction between "action condition" × "coil orientation" was significant ($F_{2,56} = 3.330$; $P = 0.043$). The post hoc analyses of the interaction demonstrated that there was no significant difference when comparing the rest condition in PA with AP coil orientation (rest PA, mean = 1.340, SD = 0.683; rest AP, mean = 1.817, SD = 0.863, $P = 0.283$). Conversely, significant difference was found when comparing the precision grip as well as the power grip in PA and AP coil orientation (precision PA, mean = 2.527, SD = 1.190; precision AP, mean = 3.883, SD = 1.236, $P = 0.040$; power PA, mean = 2.112, SD = 1.184; power AP, mean = 3.334, SD = 1.069, $P = 0.042$), indicating greater corticospinal excitability with AP-oriented stimulation. Notably, when comparing precision grip with power grip in AP coil orientation, it was observed a significant increase in MEP amplitude during the execution of the precision grip (precision AP, mean = 3.883, SD = 1.236; power AP, mean = 3.334, SD = 1.069, $P = 0.012$; Fig. 2), whereas there was no significant difference when comparing precision grip with power grip in PA coil orientation (precision PA, mean = 2.527, SD = 1.190; power PA, mean = 2.112, SD = 1.184, $P = 0.106$). We then conducted a two-tailed independent Student's $t$ test, which revealed a significantly shorter latency ($t_{28} = 3.049$, $P = 0.005$) for $MEP_{PA}$ (mean = 0.022 s, SD = 0.002 s) compared with $MEP_{AP}$ (mean = 0.024 s, SD = 0.002 s).

These results demonstrate that corticospinal excitability increases during grasping actions compared with rest and is overall greater with AP than PA coil orientation. Although no differences between coil orientations emerged at rest, significant differences were observed during both precision and power grip, with higher excitability under AP stimulation. Furthermore, within the AP orientation, corticospinal excitability was significantly higher during the precision grip than the power grip, whereas no such difference was found under PA stimulation.

### Short-Interval Afferent Inhibition

***SAI at rest.***

The ANOVA on SAI measured during the rest condition revealed a statistically significant main effect of "ISIs" ($F_{8,224} = 21.077$; $P < 0.001$), but no significant main effect of "current direction" ($F_{1,28} = 1.857$; $P = 0.184$), or in their interaction ($F_{8,224} = 0.493$; $P = 0.86$). The post hoc analysis for the main effect of ISIs confirmed that the peak of inhibition occurred at N20 + 2 ms ($P = 0.008$) and N20 + 3 ms ($P = 0.014$), independent of current direction (Refs. 22 and 35; Fig. 3).

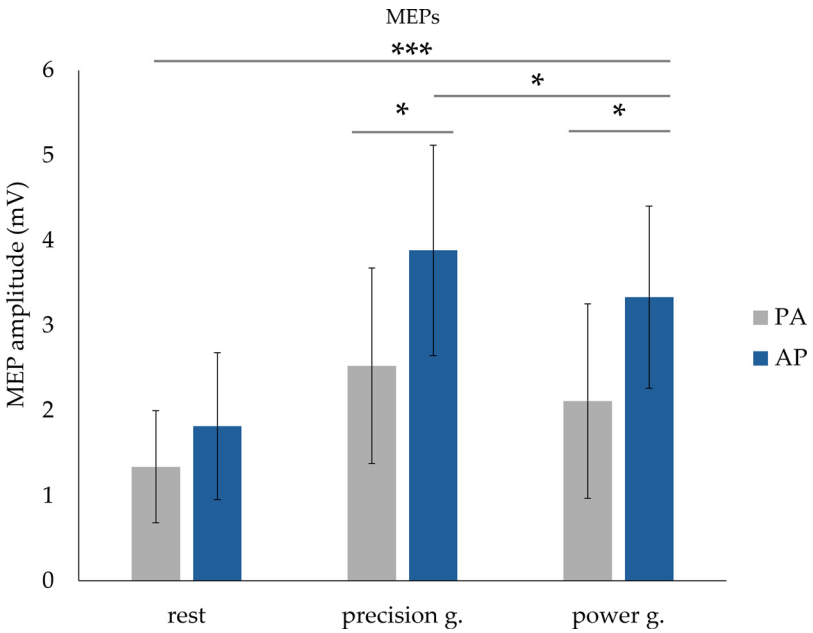


**Figure 2.** Unconditioned motor-evoked potentials (MEPs). The bar plot illustrates the effect of coil orientation (PA, gray bars; AP, blue bars) on unconditioned MEP amplitudes across three conditions: rest, precision grip, and power grip. Significant differences were observed between PA and AP orientations for both precision and power grip. In addition, MEP amplitudes were significantly higher for precision grip compared with power grip under AP orientation. The figure also shows that MEP amplitudes at rest were significantly lower than during both grasping actions. The error bars represent the SD; $^{*}P < 0.05$, $^{***}P < 0.001$.

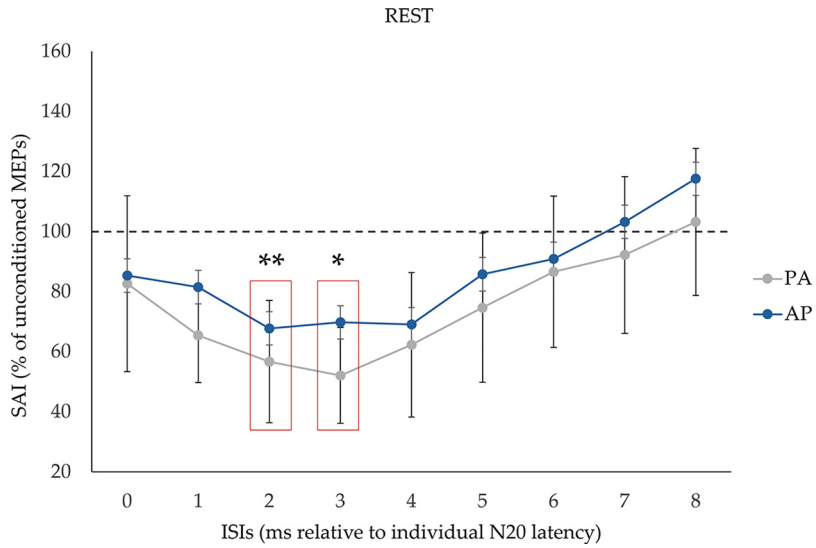


**Figure 3.** Time course of SAI during rest. The ordinate indicates SAI magnitude, calculated as the ratio of conditioned MEP to unconditioned MEP, expressed as a percentage. The abscissa shows interstimulus intervals (ISIs), defined as the delay in milliseconds added to each participant's individual N20 latency (e.g., N20 + 0 ms to N20 + 8 ms). The error bars represent the SD; *$P < 0.05$, **$P < 0.01$, both indicating significance relative to ISI + 0. AP, anterior-posterior (blue); MEP, motor-evoked potential; PA, posterior-anterior (gray); SAI, short afferent inhibition.

These results show that strong inhibition occurs at +2 ms and +3 ms relative to the N20 component, with no significant difference between the AP and PA current directions.

### *ΔSAI: PA versus AP.*

The ANOVA on ΔSAI measured during precision and power grip revealed a significant main effect of "current direction" ($F_{1,28} = 6.429$, $P = 0.017$; Fig. 4), indicating that inhibition was greater for the AP current direction compared with PA, regardless of whether the task involved a precision or power grip. Indeed, no significant main effect was found for "action condition" ($F_{1,28} = 1.115$, $P = 0.3$). A significant main effect of "ISIs" was observed ($F_{8,224} = 2.207$, $P = 0.028$); however, Holm-corrected post hoc tests did not identify signficant pairwise differences. Similarly, the interaction between "action condition" and "ISIs" was significant ($F_{8,224} = 2.487$, $P = 0.013$), but no comparisons remained significant after correction. No significant interactions were found for "action condition × current direction" ($F_{1,28} = 0.384$, $P = 0.541$), "ISIs × current direction" ($F_{8,224} = 0.184$, $P = 0.993$), or the three-way interaction "action condition × ISIs × current direction" ($F_{8,224} = 1.080$, $P = 0.378$). Taken together, these results suggest that the primary factor influencing SAI modulation was the direction of current (Fig. 4), rather than the specific grasp condition or ISI, with more sustained inhibition observed when AP current was applied (Fig. 5).

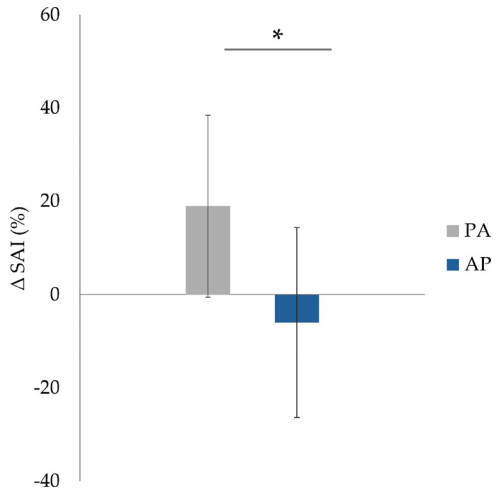


**Figure 4.** Percentage change in short-latency afferent inhibition (ΔSAI%) as a function of current direction (PA and AP), collapsed across action conditions (precision grip and power grip). ΔSAI% was computed as the difference between SAI in the precision or power grip and rest conditions, expressed as a percentage. The error bars represent the SD; *$P < 0.05$. AP, anterior-posterior; PA, posterior-anterior.

To further explore whether the stronger SAI observed in the AP condition could be influenced by larger unconditioned MEP amplitudes, we conducted correlation analyses focused on the AP group. For each participant, we computed the mean unconditioned MEP amplitude by averaging across Precision and Power conditions. These values were then correlated with *1*) the mean SAI ratio (conditioned/unconditioned MEP) and *2*) the ΔSAI values averaged across all ISIs. No significant correlations were found (SAI ratio: $r = -0.254$, $P = 0.161$; ΔSAI: $r = -0.012$, $P = 0.947$), indicating that differences in unconditioned MEP amplitudes do not explain the stronger SAI modulation with AP current direction.

## DISCUSSION

Motor control relies on the dynamic interplay of excitatory and inhibitory influences that shape sensorimotor integration. To assess motor and somatosensory temporal interactions, we measured SAI at multiple interstimulus intervals (0–8 ms), using individualized N20 somatosensory evoked potential (SEP) components, to comprehensively explore these dynamics during isometric grasp execution (precision vs. power grip) compared with rest, under two different TMS stimulation protocols (PA vs. AP coil orientation). Our results reveal greater SAI in the antero-posterior (AP) current direction during execution of both actions and a significant increase in corticospinal excitability during precision grip as compared with power grip when tested using AP coil orientation. These findings suggest that distinct cortical circuits are differentially engaged depending on current direction and grasp type, providing new insights into the mechanisms underlying sensorimotor control in hand grasping behaviors.

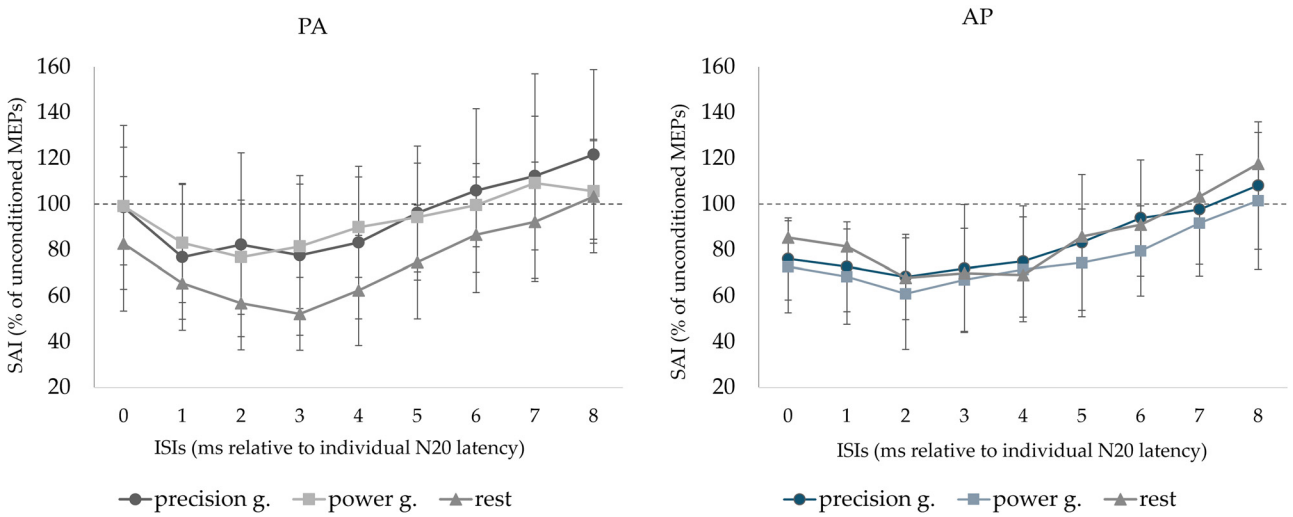


**Figure 5.** Time course of SAI during the three action conditions. The ordinate indicates SAI magnitude, calculated as the ratio of conditioned MEP to unconditioned MEP, expressed as a percentage. The abscissa indicates interstimulus intervals (ISIs) relative to the N20 latency. The error bars represent the SD. The figure displays non-normalized SAI values over time, before delta computation. AP, anterior-posterior (blue); MEP, motor-evoked potential; PA, posterior-anterior (gray); SAI, short afferent inhibition.

### Corticospinal Excitability during Grasping

A key result of our study is the significant increase in corticospinal excitability during precision grip compared with power grip when AP currents were applied, with no such difference observed under PA stimulation. This finding supports the idea that more superficial M1 populations—preferentially engaged by AP stimulation—may play a crucial role in executing precision grip, which demands greater dexterity and fine-tuning of movements (38). These results align with the previous evidence suggesting a partial dissociation in the circuits targeted by different coil orientations (28, 31, 35, 43) with distinct subsets of M1 neurons differentially involved in precision versus power grip (11). In contrast, PA stimulation, which primarily targets deeper layers of M1, may obscure the contribution of superficial neuronal populations and thus provides a more generalized assessment of corticospinal activity (38).

### Short-Latency Afferent Inhibition during Grasping

The ability to extract relevant sensory information from the environment to shape motor output is essential for daily activities, particularly in relation to hand configurations. To investigate this, we assessed the time course of short-afferent inhibition (SAI), an inhibitory phenomenon elicited when peripheral nerve stimulation precedes a TMS pulse over M1, leading to a reduction in motor-evoked potential (MEP) amplitude. Typically observed at short interstimulus intervals (ISIs) of 20–25 ms (22, 44), SAI provides insight into the inhibitory influence of sensory afferent signals—whose arrival in S1 is marked by the N20 component (45–47)—on corticospinal output. To our knowledge, no studies have characterized the interaction between afferent somatosensory volleys on corticospinal excitability using SAI with 1-ms resolution in both precision and power grip, comparing AP and PA current directions.

At rest, our results revealed that the peak of inhibition occurred at ISIs of 2 and 3 ms relative to the individualized N20 component, aligning with previous studies that reported maximal SAI at similar intervals (22, 35). Notably, no significant difference was observed between AP and PA current directions. This contrasts with the findings of Ni et al. (35), who reported SAI differences based on coil orientation at rest. In contrast, during both grasping actions, our findings reveal a significant effect of current direction on SAI, with greater inhibition observed in the AP orientation.

### Action State Dependency

The functional connections within the parieto-premotor brain network responsible for action control are dynamic and their temporary state (i.e., state-dependency) certainly plays a crucial role in shaping the impact that brain and peripheral nerve stimulation (PNS) has on corticospinal excitability (48–50). Our results suggest that, at rest, the distinct neural populations recruited by the two current directions respond to afferent input in a similar manner. Conversely, during the voluntary generation of a descending command, the inhibitory effect of SAI remains sustained in M1 neuronal populations engaged by AP, whereas it drops in M1 neuronal populations engaged by PA coil orientation. In fact, AP stimulation recruits more superficial cortical layers which are known to receive a larger proportion of interareal connectivity (6, 51) and thus might supposedly be more actively involved in sensorimotor integration.

However, this effect was not specific to the type of grasp, as both precision and power grips showed similar modulation over time compared with rest. Although one previous study (27) reported increased SAI during precision grip compared with power grip with AP currents, this discrepancy may be attributed to methodological differences. In that case, the assessment of SAI was not tailored to the individual N20 latency and was used a single ISI of 20 ms, with the test stimulus (TS) set to elicit a 1.5-mV MEP amplitude during both precision and power grips. Given that differences in stimulation intensity can influence the detection of subtle differences (32), these methodological variations may account for the

limited overlap between our findings and those of Davis et al. (27). In addition to these methodological considerations, the specific neural dynamics of S1 during prehension may further explain our results. In fact, S1 neurons exhibit marked fluctuations in firing rates across different stages of prehension (12, 52). During the hold phase, when force is maintained rather than actively modulated, neuronal firing is at its lowest, suggesting a reduced encoding of grip-specific sensory input. As a consequence, it is reasonable to imagine that our results represent only a specific phase of prehension behavior, during which these populations exhibit similar sensitivity to both types of grasps within the context of an isometric contraction. Therefore, it is possible that somatosensory afferents exert a similar level of inhibition over corticospinal excitability during action, which is not sufficiently detailed to distinguish between the two types of grasps. In this context, SAI may serve as a measure that provides a more generalized assessment of the somato-motor interplay. Although SAI captures the different sensorimotor dynamics between rest and action, it may lack the sensitivity to differentiate the specific sensorimotor demands of precision and power grips.

However, it should be considered that execution of a grasping action engages a complex parietofrontal network, in which S1-M1 connections represent only one of the critical nodes. In this network, another fundamental hub is represented by the premotor cortices, particularly the ventral premotor cortex (PMv), which plays a crucial role in transforming object-related visual properties into suitable motor plans (53–57). Previous studies on PMv-M1 connectivity have shown that PMv exerts a significant influence on M1 during various grasping movements (39, 53, 54). Moreover, recent findings suggest that the more superficial M1 neuronal populations targeted by PMv input are preferentially involved in the execution of precision grip rather than power grip (38). It is reasonable to propose that the differentiation between these two types of grips may emerge at the level of PMv. Due to its critical involvement in motor planning, PMv may play a more prominent role than S1 in disentangling between precision and power grips.

In addition, the role of cholinergic modulation in shaping both sensory afferent processing and motor output may further contribute to this effect. SAI is believed to be linked to central cholinergic activity, as it can be reduced or abolished by muscarinic antagonists (58) and is known to be modulated by acetylcholine (59, 60). Acetylcholine regulates thalamocortical transmission, influencing both the gain and the spatiotemporal properties of sensory processing. Afferent information from the thalamus is distributed broadly across the cortex, following pathways characterized by lower spatial (61–63) and temporal (64, 65) resolution. This widespread projection pattern, combined with phase-dependent afferent sensitivity, may reduce the specificity of responses to different grasp types, leading to a less selective modulation in terms of both temporal dynamics (ISIs) and spatial encoding (precision vs. power grip).

### Future Studies

To further explore the modulation of SAI, future studies may investigate its dynamics across different phases of prehension (i.e., preparation vs. execution). Although previous research has examined movement-related modulation of SAI (32, 36), no studies have systematically assessed how it evolves across the distinct phases of prehension, particularly with respect to the differences between power and precision grip. A key objective will be to determine the most effective methodological approaches—such as optimizing ISI selection and TMS intensity—which may help enhance the sensitivity of SAI measures in detecting subtle differences between these two types of grips. In addition, pharmacological interventions targeting the cholinergic system might provide valuable insights into how these widespread cortical projections influence sensorimotor processing during prehension, further elucidating the neural mechanisms underlying grip-specific modulation of afferent inhibition. Moreover, it may be of interest to extend the investigation to other brain areas potentially involved in grip-specific control, such as PMv, given its known role in object-related action planning and its functional connectivity with M1.

### Conclusions

At rest, no differences in SAI were observed between AP and PA current directions. However, during action execution, SAI was greater with AP stimulation, and corticospinal excitability increased during precision compared with power grip when using the AP orientation. These results indicate that distinct cortical circuits are differentially engaged depending on current direction and grasp type, providing new insights into the neural mechanisms underlying sensorimotor control in human hand movements.

## DATA AVAILABILITY

The dataset supporting the conclusions of this study is available on Figshare: https://doi.org/10.6084/m9.figshare.29505413.v1.

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## DISCLOSURES

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

## AUTHOR CONTRIBUTIONS

K.B., E.D., A.C., G.K., and A.D. conceived and designed research; K.B. and E.D. performed experiments; K.B. analyzed data; K.B., G.K., and A.D. interpreted results of experiments; K.B. prepared figures; K.B. drafted manuscript; K.B., E.D., A.C., G.K., A.D., and L.F. edited and revised manuscript; K.B., E.D., A.C., G.K., A.D., and L.F. approved final version of manuscript.

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