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## Maintained volitional activation of the muscle alters the cortical processing of proprioceptive afference from the ankle joint

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### ABSTRACT

Cortical proprioceptive processing of intermittent, passive movements can be assessed by extracting evoked and induced electroencephalographic (EEG) responses to somatosensory stimuli. Although the existent prior research on somatosensory stimulations, it remains unknown to what extent ongoing volitional muscle activation modulates the proprioceptive cortical processing of passive ankle-joint rotations.

Twenty-five healthy volunteers ( $28.8 \pm 7$  yr, 14 males) underwent a total of 100 right ankle-joint passive rotations ( $4^\circ$  dorsiflexions,  $4 \pm 0.25$  s inter-stimulus interval,  $30^\circ/\text{s}$  peak angular velocity) evoked by a movement actuator during *passive* condition with relaxed ankle and *active* condition with a constant plantarflexion torque of  $5 \pm 2.5$  Nm. Simultaneously, EEG, electromyographic (EMG) and kinematic signals were collected. Spatiotemporal features of evoked and induced EEG responses to the stimuli were extracted to estimate the modulation of the cortical proprioceptive processing between the *active* and *passive* conditions.

Proprioceptive stimuli during the *active* condition elicited robustly  $\sim 26\%$  larger evoked response and  $\sim 38\%$  larger beta suppression amplitudes, but  $\sim 42\%$  weaker beta rebound amplitude over the primary sensorimotor cortex than the *passive* condition, with no differences in terms of response latencies.

These findings indicate that the *active* volitional motor task during naturalistic proprioceptive stimulation of the ankle joint enhances related cortical activation and reduces related cortical inhibition with respect to the *passive* condition. Possible factors explaining these results include mechanisms occurring at several levels of the proprioceptive processing from the peripheral muscle (i.e. mechanical, muscle spindle status, etc.) to the different central (i.e. spinal, sub-cortical and cortical) levels.

### Introduction

The conscious sense of movement and posture of the body is referred to as proprioception (Proske and Gandevia, 2012). It is part of the somatosensory system that connects the periphery to the central nervous system through afferent pathways, mainly involving the dorsal column medial lemniscus pathway (Tuthill and Azim, 2018). Proprioceptors are mechanoreceptors located in the muscles and tendons (e.g. muscle spindles and Golgi tendon organs), joints (e.g. Golgi endings) and skin (e.g. Ruffini endings) (Taylor, 2009) sensitive to mechanical forces produced by the body or acting on it (Proske and Gandevia, 2012; Purves et al., 2018; Tuthill and Azim, 2018). Therefore, proprioceptors

inform the brain about the state of the locomotor system. Changes in this state modulate the firing rate of the proprioceptors which is then transmitted to spinal cord, brainstem nuclei, cerebellum, thalamic nuclei and the cortex. The cortical target is wide spread, but most dense to the primary sensorimotor cortex (SM1), following specific topographic arrangements according to the modality and somatotopy (Purves et al., 2018). The role of proprioception is crucial in numerous every-day scenarios ranging from quiet standing (Gatev et al., 1999), locomotion (Farris and Sawicki, 2012) or efficient movement execution through an appropriate motor planning (Richardson et al., 2014). Therefore, impaired or improved proprioception has significant implications in training, ageing or motor diseases (Dietz, 2002; Ferlinc et al.,

**Abbreviations:** EEG, Electroencephalography; MEG, Magnetoencephalography; EMG, Electromyographic; ICA, Independent Component Analysis; EOG, Electrooculograms; RMS, Root Mean Square; TFR, Time-frequency representation; SM1, Primary somatosensory cortex.

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2019; Han et al., 2016).

The quantification of the cortical processing of the proprioceptive input can provide tools to enhance the understanding in how the afferent information is integrated into movement control. To this purpose, neurophysiological recordings such as magnetoencephalography (MEG) and electroencephalography (EEG), have been used in combination with neuroimaging compatible movement actuators capable to produce accurate passive joint rotations (i.e. proprioceptive stimuli) (Piitulainen et al., 2018, 2020; Piitulainen et al., 2015a). The joint rotation stimulates the respective peripheral proprioceptors activating the cortical areas according to the stimulated limb (Nurmi et al., 2023; Piitulainen et al., 2015a). The study of the cortical response to these movements regarded the assessment of evoked (Alary et al., 1998; Piitulainen et al., 2015a; Smeds et al., 2017) and induced (Illman et al., 2023; Mujunen et al., 2022) responses to the proprioceptive afference. The former somatosensory evoked responses reflect the cortical excitation as a result of the sensory information travelling along the dorsal column pathway (Yamada, 2014). In contrast, the latter responses quantify the modulation of the SM1 cortex beta-band power (~14–32 Hz) to the proprioceptive stimulation and they have been proposed as measure of the degree of cortical inhibition-excitation. Specifically, the early reduction of the beta power over SM1 cortex (*suppression*, or event-related desynchronization) reflects cortical activation because of the somatosensory afference, and the delayed increase of the beta power (*rebound*, or event-related synchronization) likely represents intra- or intercortical inhibition phenomena (Barone and Rossiter, 2021; Engel and Fries, 2010; Salmelin and Hari, 1994; Tan et al., 2016).

It has been demonstrated that the SM1 proprioceptive processing is modulated as an effect of muscle activation in response to somatosensory stimulation during dynamic movement planning, execution, and visualization (Cebolla and Cheron, 2015; Cheron and Borenstein, 1987, 1992; Sugawara et al., 2016). The way in which cortical responses to somatosensory stimuli are modulated has been shown to be largely dependent on the experimental design including movement characteristics and context (Collins et al., 1998; Gantchev et al., 1994; Jiang et al., 1991; Mouchnino et al., 2015). Somatosensory evoked cortical responses are most often suppressed when the concurrent sensory input with motor processing is irrelevant to the motor task, and thus the disturbing information is inhibited to prioritize smooth or appropriate motor output (sensory gating phenomenon) (Morales-Muñoz et al., 2016; Morita et al., 1998; Rushton et al., 1981). On the contrary, the cortical response can be facilitated when the movement-related afferent information is relevant to the ongoing motor task (Misiaszek et al., 1997; Staines et al., 2000, 2002). Movement-related modulations of somatosensory inflow have been widely investigated in the upper limb during active, dynamic movements (Cheron and Borenstein, 1987; Huttunen and Lauronen, 2012; Kakigi et al., 1995) and only to a lesser extent in the lower limbs (Asanuma et al., 2003; Staines et al., 1998; Tinazzi et al., 1997). Furthermore, the previous studies exclusively relied on the use of electrical stimulation eliciting early cortical potentials, while little is known on the cortical responses to naturalistic proprioceptive stimulations during active conditions. Indeed, actuator-based joint rotation allows to stimulate peripheral proprioceptors in a more naturalistic way (i.e. triggering their firings similarly to a voluntary movement) and thus not necessarily initiating the same afferent mechanisms elicited by electrical stimulation (Abbruzzese et al., 1985; Mima et al., 1996; Piitulainen et al., 2013; Piitulainen et al., 2015a).

To the best of our knowledge, there is no prior study investigating the modulation of the cortical proprioceptive processing to naturalistic proprioceptive ankle-joint stimulation during active conditions. Therefore, the purpose of the present study was to quantify whether the steady volitional activation of the ankle plantar-flexor muscles affects the cortical processing of naturalistic proprioceptive afference arising from the respective muscles and joint. We aimed for close to real-world-naturalistic stimulation condition to obtain further insight into the role of the proprioception to motor control. We expected: (i) enhanced

cortical activation (i.e. stronger evoked responses and beta power suppression) and (ii) reduced cortical inhibition to the proprioceptive stimuli during *active* than *passive* condition. We hypothesised that the *active* functional state affects the neuronal processing of the proprioceptive afference at all possible levels from the muscular (i.e. receptor level) to the spinal and brain (i.e. subcortical and cortical) levels, and the respective net effect would be detectable from the cortical responses. The results would guide the future studies investigating the role of cortical proprioception in motor performance and adaptation in, e.g., ageing, rehabilitation, training and neurological or developmental diseases.

## Materials and Methods

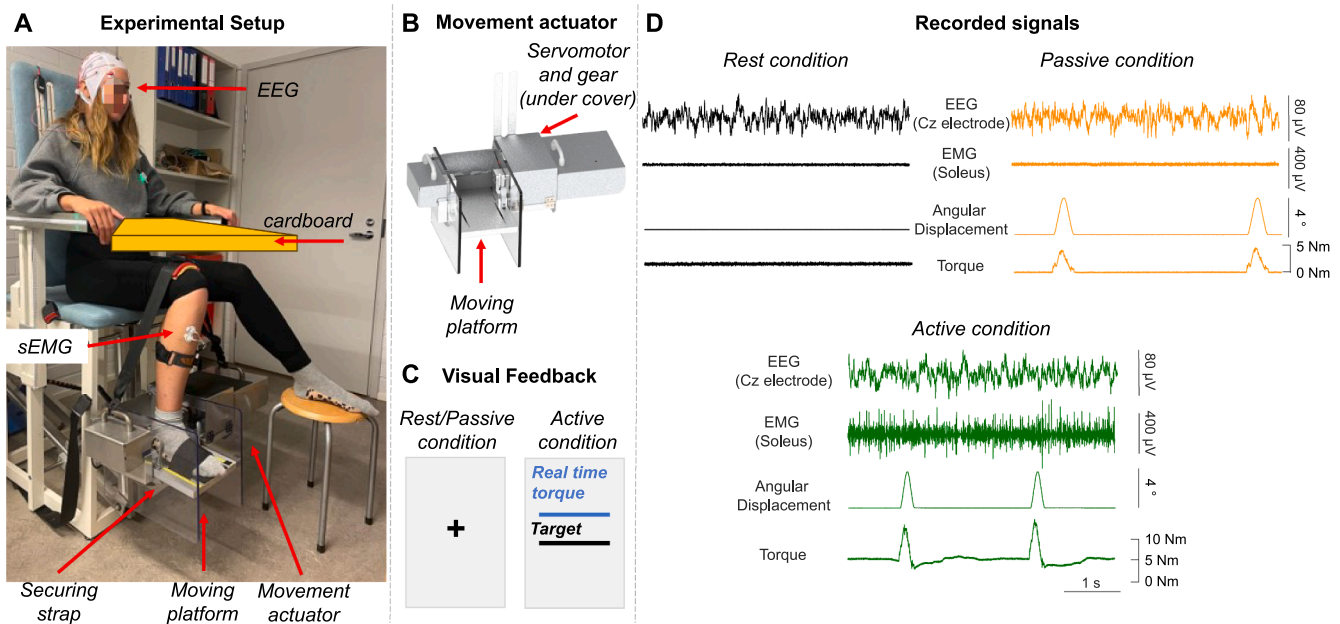
### Participants

We studied 25 young participants recruited through active advertisements by means of social media, university student and staff mailing lists and leafleting within the University of Jyväskylä campus (14 males, mean  $\pm$  SD, age =  $28.8 \pm 7$  years, height =  $1.71 \pm 0.8$  m, mass =  $71.6 \pm 12.4$  kg). Participants did not report any movement disorder or neuropsychiatric disease. Their Waterloo footedness inventory score was  $42 \pm 32$  on a scale from  $-100$  to  $100$  (van Melick et al., 2017) indicating a predominance of right-footed volunteers (23 out of 25 participants). All the participants received a thorough explanation of the study protocol before being asked to sign the informed consent. Prior to the measurements, the study received the approval from the University of Jyväskylä's Ethics Committee in accordance with the Declaration of Helsinki (approval number: 369/13.00.04.00/2020). The recruited group of volunteers underwent the data collection of the current study and the one described in our recent work (Giangrande et al., 2024) on the same day.

### Experimental procedure and measurements

The measurements were carried out at the Faculty of Sport and Health Sciences in the University of Jyväskylä, Jyväskylä, Finland. We stimulated participants' right ankle-joint by delivering intermittent rotations in the dorsiflexion direction through a custom-made movement actuator. Two conditions were tested: with volitional plantarflexion at a constant isometric force (*active* condition) and while the ankle joint was relaxed (*passive* condition). Each condition was measured twice in two different 4-min trials, thus a total of four trials were performed by each participant.

**Experimental setup.** Fig. 1A shows the experimental setup adopted for the study. Participants sat in a chair equipped with a silent motorized ankle-movement actuator detailed in Fig. 1B. The actuator was constituted by two parts: a rotating platform for the foot and a control and automation section. Movements were generated by a servomotor controlled by a programmable logic controller. The rotating platform comes with the measurements of angular velocity and applied torque. Technical characteristics: maximum angular speed  $200^\circ/\text{s}$ , maximum torque 100 Nm. The same actuator was previously used in (Piitulainen et al., 2022). Participants placed the right foot on the rotating platform, maintaining the  $90^\circ$  position in both ankle and knee joint. The anatomical rotation axis of the talocrural ankle joint was identified according to Isman et al. (Isman and Inman, 1969), and it was aligned with the axis of the rotating platform. Participants wore shielded earplugs (ER-3C, 50 Ohm, Etymotic Research) to mask the low auditory noise produced by the ankle movement actuator. The vision of the moving foot was also blocked by using a brown cardboard in the line of sight. A screen was placed at 1.5 m in front of the participant to provide visual feedback in accordance with the experimental condition (Fig. 1C). The real-time data visualization as well as the stimulation pattern delivery was handled by a custom-made Graphical User Interface (Matlab R2022b, MathWorks Inc, Natick, MA, USA) properly configured for the



**Fig. 1.** Experimental Setup and measurements. A) Participant's right foot was placed on the rotating platform with knee and ankle joints at  $90^\circ$ . 30 EEG, 2 EOG channels and EMG from right soleus and tibialis anterior were recorded. B) Detail of the used movement actuator. C) Visual feedback varied between the conditions. A fixation cross was shown during the passive condition, and the real-time torque with 5 Nm target level during the active condition. D) Example of pre-processed signals (6 s) from a representative subject during active, passive and rest conditions. From top to bottom of each condition: EEG from Cz electrode, EMG from Soleus muscle, angular displacement and torque applied on the pedal are represented.

specific movement actuator through a data acquisition I/O board (USB-6216 CE-board, National Instrument Austin, 14 Texas, United States). During the experiment, EEG and electromyographic (EMG) signals as well as ankle-joint torque and foot angular displacement from the rotating platform were recorded.

**Measurements.** 30-EEG signals and two electro-oculograms (EOG) were recorded by means of a wireless EEG amplifier – MEACS, ReC Bioengineering Laboratories and LISIN, Turin, Italy (Cerone et al., 2019, 2022; Cerone and Gazzoni, 2018). We used a cap with 30 Ag/AgCl electrodes embedded into the fabric following the international 10–20 system (EasyCap GmbH, Gliching, Germany). To optimize the skin-electrode contact, each electrode site was carefully cleaned with an abrasive paste (NuPrep, Weaver and Company, Aurora, USA) and then filled with a conductive gel (NeurGel, SPES MEDICA, Genova, Italy). The EOGs were acquired using surface electrodes ( $\varnothing$  24 mm Ambu s.r.l., Denmark) positioned in the up-left and down-right corners of the eye region to monitor eye movements and blinks. The raw EEG and EOG signals were collected using a monopolar derivation with the FCz electrode of the cap taken as a reference and were sampled at 2048 Hz with 0.1–500-Hz bandpass. EMG signals were recorded synchronously with EEG.

The EMG activity of two antagonist muscles of the leg (soleus and tibialis anterior) was measured. Prior to electrode positioning, the skin over the muscles of interest was treated with an abrasive paste (NuPrep, Weaver and Company, Aurora, USA). Afterwards, a pair of Ag/AgCl electrodes ( $\varnothing$  24 mm Kendall, Covidien, Dublin, Ireland) was positioned on the right soleus medialis and tibialis anterior muscles 2-cm apart in accordance with the electrode placement guidelines of (Merletti and Cerone, 2020; Stegeman and Hermens, 2007). EMGs were recorded in bipolar derivation through a wireless amplifier (DuePro, OT Bioelettronica, Turin, Italy) with a sampling frequency of 2048 Hz in the frequency range of 10–500 Hz.

Ankle-joint torque and foot angular displacement from the rotating platform were recorded through the data acquisition unit with a sampling frequency of 1 kHz (output signal range: 0–5 V).

Data were then offline synchronized with EMG by means of a common external trigger introduced in (Cerone et al., 2022).

**Proprioceptive stimulation.** After EEG and EMG preparation, we recorded 30-s resting baseline data while participants sat in the armchair, and instructed to relax and gaze at a black fixation cross on a grey background displayed in the screen in front of them. Then, we delivered the proprioceptive stimuli every  $4 \pm 0.25$  s (i.e.  $4^\circ$  ankle joint dorsiflexions) during the *active* and *passive* conditions. The peak angular velocity of the rotation was  $30^\circ/\text{s}$  starting with an ankle joint angle of  $90^\circ$  (Toledo et al., 2016). During the *passive* condition, participants were asked to relax their lower limbs and gaze at the fixation cross. During the *active* condition, participants were requested to apply a constant plantarflexion torque of  $5 \pm 2.5$  Nm (i.e. opposite to the direction of the stimulation) throughout the duration of the stimulation. To this end, they were provided with visual feedback showing the target force level and the applied torque filtered with a 100-ms moving average (Fig. 1C). To avoid any visual contamination in the EEG responses caused by the brisk changes of the visual feedback due to the concurrent stimulation, the torque feedback line was kept constant for 800 ms after each stimulus onset. During this 800-ms window, the displayed torque was set to the average torque over 100-ms interval preceding the stimulus onset. A total of 100 stimulations were delivered separately for *active* and *passive* condition in four 50 repetition trials (two per condition) in pseudo-random order, balancing the starting condition among all participants.

### Signal analysis

Data were processed using MNE-Python software (Gramfort et al., 2013) and Matlab R2022b (MathWorks Inc, Natick, MA, USA). Foot angular displacement signals were resampled from 1000 Hz to a common sampling frequency of 2048 Hz and then synchronized to EEG and EMG data by offline aligning them according to a common external trigger sent at the beginning of each measurement trial.

**EEG preprocessing.** First, a visual inspection on EEG signals was carried out to identify the channels characterized by poor contact. Second, a bandpass 4th order Butterworth filter at 0.1–95 Hz was applied to EEG signals. Third, 30 EEG components were isolated through the Independent Component Analysis function to identify and discard the components associated with artifacts such as eye blinks, saccade

movements or neck, temporal, mastoids muscular activity contamination. Fourth, bad channels were interpolated by replacing them with the average of their neighbors. Finally, all EEG signals were offline referenced by applying a common average reference (McFarland et al., 1997).

**EMG preprocessing.** First, the EMG signals were bandpass filtered at 20–400 Hz with a 4th order Butterworth filter. To quantify the degree of muscular activation during *active* and *passive* conditions, root-mean square of EMG was computed for the whole stimulation duration separately for soleus and tibialis anterior. The root-mean square value of the initial 30-s period of resting without stimulation was used as a reference value.

**Evoked-EEG responses.** EEG signals were epoched from –200 to 1000 ms with respect to the stimulus onset occurring at 0 s. The epochs of the two trials of the same condition were concatenated together. Then, the epochs were averaged separately for each EEG channel and condition. The peak amplitude and latency of the most prominent negative (N1) and positive (P2) deflection, and their respective peak-to-peak amplitude were determined for each EEG channel separately. The EEG channel showing the strongest evoked response was identified and used in the final analysis to examine differences between the conditions. Finally, the grand average evoked responses were obtained by averaging the responses across all the participants to visualize topographic scalp distribution of the evoked responses in terms of quality and location.

**Induced-EEG responses.** Induced responses (i.e. ~ 20-Hz beta-band modulation) were quantified by means of the temporal spectral evolution method introduced by Salmelin and Hari (1994) (Salmelin and Hari, 1994). Preprocessed EEG signals were divided into epochs from –1 to 3 s with respect to the stimulus onset and evoked responses were subtracted from the data as suggested by David et al. (David et al., 2006). Average time–frequency representation (TFR) plots of the epochs were yielded on frequencies in the range 1–40 Hz (in 1-Hz steps) using Morlet wavelets (number of cycles = frequency/2) (Mujunen et al., 2022). TFR of the channel showing the highest peak to peak amplitude of the evoked responses was visually inspected to evaluate participants' individual beta bandwidth. Then, EEG data was filtered according to the specific beta bandwidth through a 4th order Butterworth filter (high-pass cut-off at  $19 \pm 5$  Hz; low-pass cut-off at  $28 \pm 4$  Hz). Next, EEG signals were rectified and averaged with respect to the stimulus onset and the signal envelope was extracted using the Hilbert function. A baseline correction (from –1000 to 0 ms) was applied to the averaged induced responses separately per condition. Participants who did not show beta modulations exceeding the noise level were excluded from the analysis, where the noise level was defined as three standard deviations of the EEG signal amplitude in the 1-s pre-stimulus baseline period. Similarly to evoked response analysis, we considered merged trials for those participants showing beta modulations and we averaged the epochs according to the EEG electrode site. The response at each EEG electrode site was characterized in terms of negative and positive (i.e. beta suppression and rebound respectively) peak amplitude and latency. Moreover, for both conditions we evaluated the area under the curve of the beta rebound (Akrawi et al., 1996) to estimate the differences between *active* and *passive* conditions in terms of beta recovery. Finally, the grand average induced response was obtained by averaging the individual responses across participants showing beta modulations above the noise level. Peak amplitudes of the grand average responses were used to obtain a topographic distribution of the response over the scalp and to determine the electrode site showing the largest and more robust positive and negative deflections to be used in the final analyses.

### Statistical analysis

All results are given as mean  $\pm$  SE (standard errors). Statistical tests were performed in Matlab R2022b (Mathwork Inc, Natick, MA, USA). A Shapiro-Wilk test was used on the data to test the hypothesis of normality of its distribution which was rejected ( $p < 0.05$ ). Additionally,

we calculated the effect size in the Wilcoxon test based on the z value and interpreting the result according to Cohen et al. where the effect size r is considered to be small ( $r \leq 0.1$ ), medium ( $0.1 < r < 0.5$ ) or large ( $r \geq 0.5$ ) (Cohen, 1988).

**Degree of muscle activation among conditions.** A non-parametric Wilcoxon signed rank test was adopted to identify statistically significant differences on the degree of muscular activity among rest, *active* and *passive* conditions. Bonferroni's method correction was further applied to adjust the significance level correcting for multiple comparisons.

**Effect of volitional muscle activation on EEG responses.** We tested the effect of volitional muscle activation on peak amplitude and latencies of the evoked and induced responses using Wilcoxon signed rank test (conditions: *active* vs. *passive*). For beta rebound, the area under curve parameter was also tested between the conditions.

### Results

Fig. 1 D shows a representative example of continuous pre-processed signals for rest, *passive* and *active* conditions. On average,  $2 \pm 3$  independent components related to artifacts due to eye movements or muscular neck activity were rejected to reconstruct EEG signals. The signals were overall of good quality. Indeed, in the 68 % of cases no channels replacement was performed as all the channels were considered of good quality, whereas a single channel was replaced in the 20 % of the tested population and only the 12 % of cases reported 3 bad channels to be interpolated prior running the EEG data analysis. The most frequently replaced channels were Iz, Tp9 and Tp10 and it was not surprising because of their location particularly dependent on the individual subject scalp anatomy, likely resulting in a poor contact. The number of stimuli was fixed to 98 for both conditions, this was the minimum number of good quality EEG epochs across conditions and participants, i.e., 2 % of the stimuli were excluded.

**Degree of muscle activation among conditions.** Fig. 2 shows the soleus and tibialis anterior EMG-RMS amplitude during rest, *active* and *passive* conditions. As expected, the EMG-RMS was significantly higher ( $p < 0.01$ ) for soleus (i.e. agonist) muscle during the *active* than both the rest and *passive* conditions (*active*  $12.02 \pm 1.41$   $\mu$ V, *passive*  $1.98 \pm 0.09$   $\mu$ V, rest  $1.81 \pm 0.11$   $\mu$ V). EMG-RMS amplitude during the *passive* condition did not differ from the rest condition. Similarly, the EMG amplitude of the tibialis anterior (i.e. antagonist) muscle during rest showed statistically significant differences ( $p < 0.01$ ) only when compared to the *active* condition (*active*  $4.46 \pm 0.73$   $\mu$ V, *passive*  $2.39 \pm 0.34$   $\mu$ V, rest  $2.37 \pm 0.32$   $\mu$ V). The EMG-RMS values found during rest and the *passive* condition are within the range for typical EMG-RMS noise value when

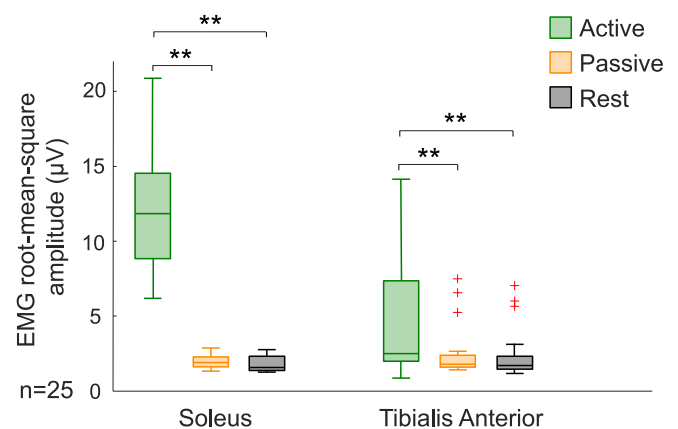


Fig. 2. Boxplots showing the muscular activation level ( $\mu$ V) of soleus and tibialis anterior muscles during trials for active, passive and 30-s rest conditions ( $n = 25$  participants). Statistical analysis by Wilcoxon signed-rank test,  $**p < 0.01$ .

measured using Ag/AgCl electrode pairs (Piervirgili et al., 2014).

**Evoked-EEG responses.** Fig. 3 shows the evoked-EEG responses for both conditions. All participants showed a prominent evoked-EEG response peaking at the Cz electrode placed at the vertex (i.e., over the lower limb area of SM1 cortex). In accordance with the literature, we found N1 component at  $\sim 100$  ms followed with a positive P2 component at  $\sim 200$  ms with respect to the stimulus onset. Peak response characteristics for both conditions are shown in Table 1. Qualitatively, the evoked response shape in the peak response channel and spatial distribution across all EEG channels were similar for *active* and *passive* conditions for both N1 and P2. However, the peak-to-peak amplitude was 26 % larger for the *active* ( $14.51 \pm 1.41 \mu\text{V}$ ) than *passive* ( $11.3 \pm 1.04 \mu\text{V}$ ) condition ( $p < 0.001$ ) with a large effect ( $r = 0.68$ ). The latencies of N1 and P2 peaks did not show statistically significant differences between the conditions ( $p > 0.05$ ).

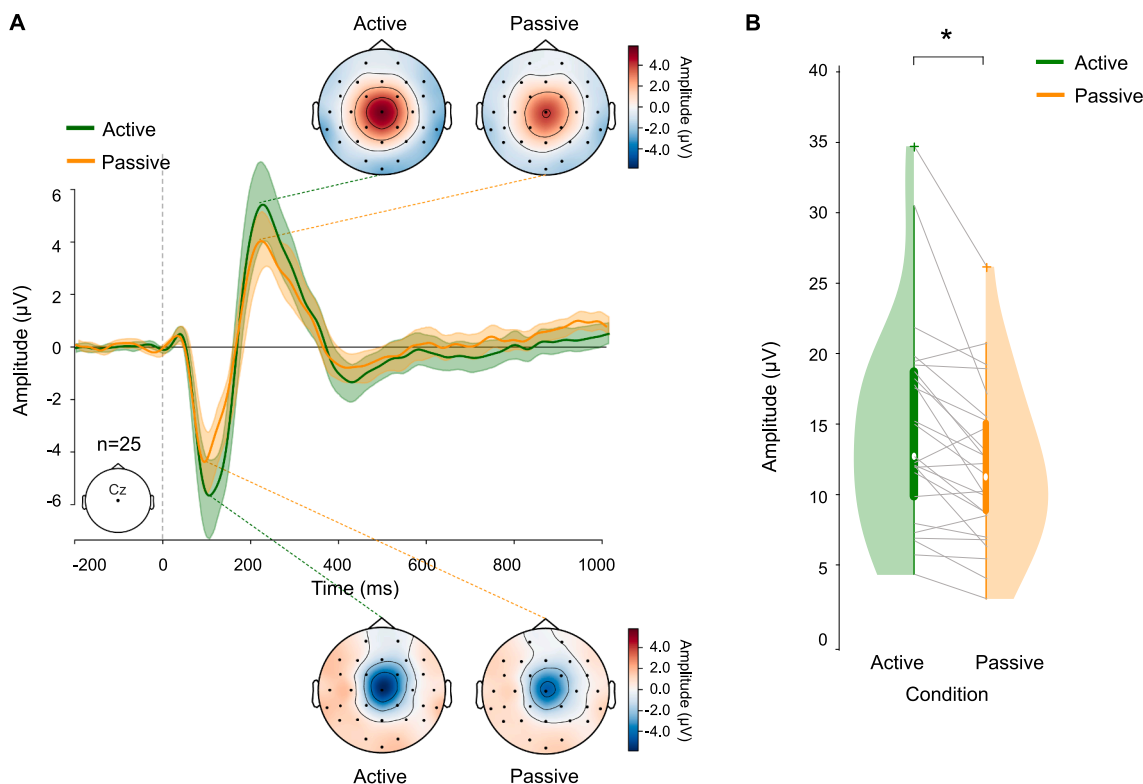
**Induced-EEG responses.** Table 1 shows the beta suppression, rebound strength and respective latencies. 19 out of 25 participants showed significant beta modulations at the Cz electrode located over the foot area of SM1 cortex. Fig. 4 shows group level time–frequency representations and scalp topographies for suppression and rebound of the beta power for both conditions. The spatial distribution was similar with apparent difference in the peak suppression and rebound amplitudes. The time–frequency representations in Fig. 4 show typical evolution of beta power with early suppression followed with rebound. Fig. 5 shows the group level temporal–spectral evolution of beta power at  $\sim 25$  Hz, and individual amplitudes for the beta suppression and rebound. Despite a noticeable inter-individual variation, the peak beta suppression was stronger ( $p < 0.01$ ) and rebound weaker ( $p < 0.05$ ) for *active* than *passive* condition, with a large effect ( $r = 0.67$ ,  $r = 0.57$  respectively for beta rebound and suppression amplitudes). Furthermore, the *passive* condition appeared to have a more prolonged rebound recovery than the *active* condition, and thus significantly larger area- We under-the-curve

**Table 1**

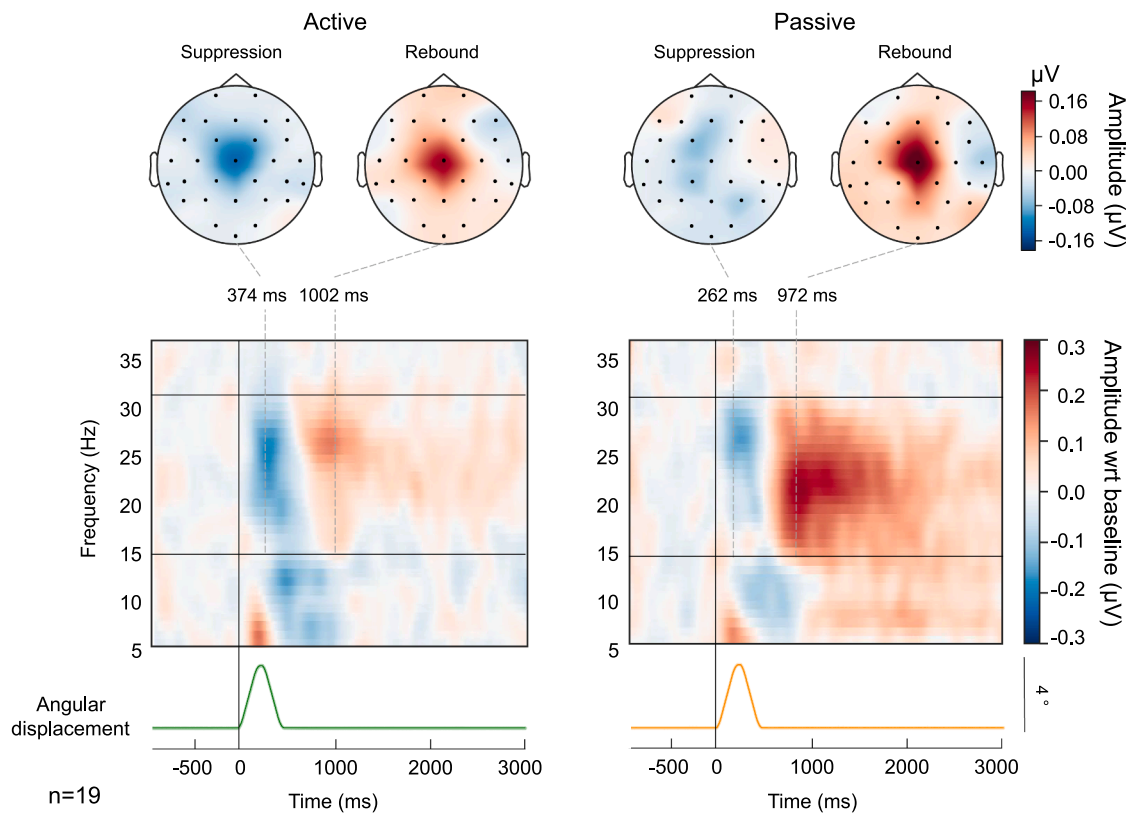
Evoked and induced responses characteristics (peak amplitudes and latencies, mean  $\pm$  SE) for passive and active conditions. Additionally, the P-value is shown to highlight the statistically significant differences between the two conditions (Statistical analysis by Wilcoxon signed-rank test, \* $p < 0.05$ , \*\*\* $p < 0.001$ ).

	Active condition	Passive condition	p-value
<b>Evoked responses – N1</b>			
Peak amplitude ( $\mu\text{V}$ )	$-7.20 \pm 0.74$	$-5.66 \pm 0.59$	$0.001$ (*)
Latency (ms)	$119.5 \pm 13.0$	$104.2 \pm 2.6$	0.129
<b>Evoked responses – P2</b>			
Peak amplitude ( $\mu\text{V}$ )	$6.84 \pm 0.38$	$5.47 \pm 0.66$	$0.009$ (**)
Latency (ms)	$232.6 \pm 7.2$	$285.5 \pm 3.2$	0.138
<b>Evoked responses – Peak-to-peak</b>			
Amplitude ( $\mu\text{V}$ )	$14.04 \pm 1.47$	$11.14 \pm 1.12$	$0.0006$ (***)
<b>Induced responses – Suppression</b>			
Strength ( $\mu\text{V}$ )	$-0.43 \pm 0.91$	$-0.31 \pm 0.03$	$0.003$ (*)
Latency (ms)	$374.1 \pm 6.2$	$262.3 \pm 4.0$	0.259
<b>Induced responses – Rebound</b>			
Strength ( $\mu\text{V}$ )	$0.51 \pm 0.07$	$0.88 \pm 0.14$	$0.012$ (*)
Latency (ms)	$922.6 \pm 3.48$	$1028.6 \pm 4.9$	0.055
Area under curve ( $\mu\text{V}\cdot\text{s}$ )	$-0.0013 \pm 0.0002$	$-0.0020 \pm 0.0003$	$0.0004$ (***)

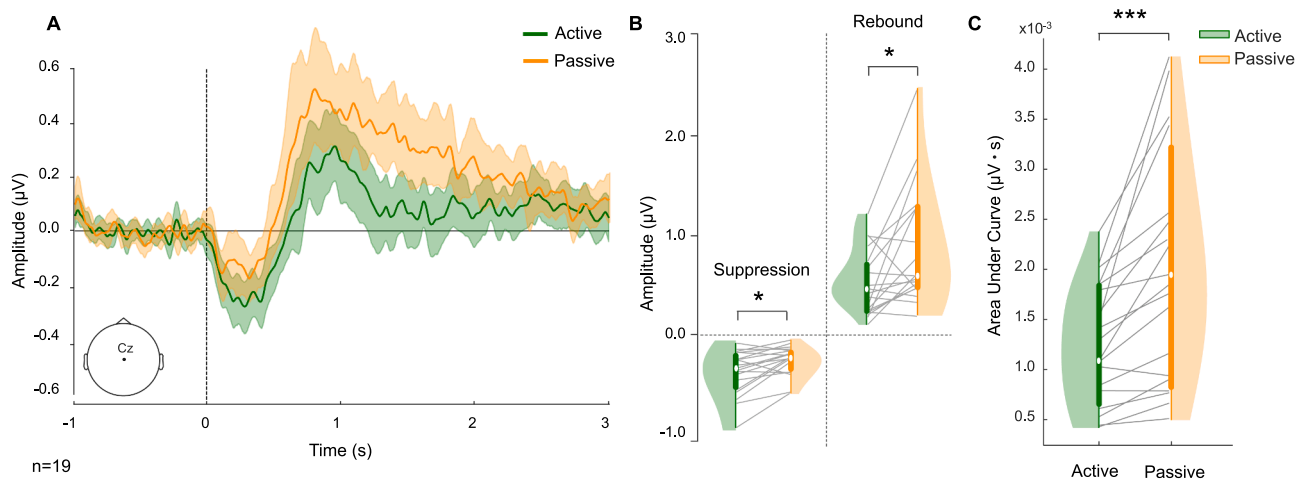
of the rebound ( $p < 0.001$ , Fig. 5 C) with a large effect ( $r = 0.61$ ). No differences were found in the peak-response latencies between conditions ( $p > 0.05$ ). Finally, the baseline beta power did not differ ( $p > 0.05$ ) between *active* ( $2.0 \pm 0.2 \mu\text{V}$ ) and *passive* ( $2.1 \pm 0.2 \mu\text{V}$ ) conditions.



**Fig. 3.** Evoked response results. A) Grand average of evoked responses across participants for active (green) and passive (orange) conditions at Cz electrode level ( $n = 25$  participants). Shaded areas correspond to the standard deviations across participants. Topographies at the most prominent peaks are represented for both conditions. B) Violin plots of peak-to-peak amplitude of evoked responses for both active (green) and passive (orange) conditions. Solid grey lines indicate individual values of peak-to-peak amplitude (Statistical analysis by Wilcoxon signed-rank test, \* $p < 0.05$ ).



**Fig. 4.** Group average topography and time–frequency representations of active and passive conditions for those subjects showing induced responses ( $n = 19$ ). Top panel shows topographies of time frequency representation within individual beta frequency band ( $n = 19$ ) at peak suppression and rebound. Middle panel shows time frequency representations. Data is presented based on z-score transformations (baseline normalization: 1 s before the movement onset). Horizontal black lines indicate the lower and upper range of the individually chosen frequency bands. The vertical line at 0 s represents movement onset, whereas the dashed lines represent the group average latencies of peak suppression and rebound. Bottom panel shows the grand average of the angular displacement among participants.



**Fig. 5.** Induced responses results ( $n = 19$  participants). A) Grand average of induced responses at  $\sim 23$  Hz across participants for active (green) and passive (orange) conditions at Cz electrode level. Shaded areas correspond to the standard deviations across participants. B) Violin plots of beta suppression and rebound peak amplitudes for both active (green) and passive (orange) conditions. C) Violin plots of the area under the rebound curve values for both active (green) and passive (orange) conditions. Solid grey lines indicate individual values (Statistical analysis by Wilcoxon signed-rank test,  $*p < 0.05$ ,  $***p < 0.001$ ).

**Discussion**

We examined the effect of volitional muscle activation on evoked and induced somatosensory EEG responses during proprioceptive stimulation of the ankle joint and we observed that the ‘active’ state of the sensorimotor system modulates the cortical processing of proprioceptive afference. In line with our hypothesis, we found that the cortex was

more strongly activated by the stimulation during the *active* than *passive* condition. This result suggests intensified proprioceptive processing in the SM1 cortex during the *active* condition. We monitored EMG signals and the ankle-joint torque to ensure the *active* condition from the *passive* one, but our observations about the proprioceptive processing are limited to the cortical level only. Specifically, the *active* condition was accompanied with weaker beta-rebound amplitude than the *passive*

condition, suggesting weaker cortical inhibition when the motor cortex is in the ‘active’ state. There are several potential mechanisms for our observations. Firstly, volitional muscle activation is accompanied with efferent gamma motor neuron input to intrafusal fibers of the muscle spindles sensitizing them (Ellaway et al., 2015; Macefield and Knellwolf, 2018; Purves et al., 2018). This sensitization may lead to more synchronized afferent proprioceptive volleys to the SM1 cortex, enhancing the amplitude of the cortical responses. Secondly, the muscle–tendon units in the rotated joint naturally become mechanically more resistant to the rotational stimulus due to reduction in the muscle and tendon slack and increased muscle stiffness from a resting to the *active* condition. The increased stiffness will likely also enhance the activation and synchrony of the proprioceptors. Thirdly, the functional state of the SM1 cortex differs between *active* volitional and resting *passive* states and thus may influence the intra and intercortical processing of the proprioceptive stimulation. Moreover, subcortical and spinal modulations cannot be excluded as contributing to affect the overall sensorimotor processing (Fitzpatrick and McCloskey, 1994; McChesney and Woollacott, 2000; Nakamura et al., 2023; S.R. et al., 1994; Toledo and Barela, 2014). Finally, attentional and cognitive factors cannot be excluded as contributing mechanisms eliciting the observed differences in the cortical responses. These consistent results suggest that the currently used measures of cortical proprioception (i.e. evoked and induced EEG responses) show high potential as neurophysiological markers to investigate mechanisms and adaptations of cortical proprioceptive processing in other research and clinical contexts.

#### Effect of volitional muscle activation on evoked-EEG responses.

The characteristics of evoked N1 and P2 components were in line with the descriptions of other colleagues investigating evoked responses of proprioceptive ankle-joint stimulations in young healthy adults (Toledo et al., 2016). The grand average responses revealed a stronger peak-to-peak amplitude of the evoked responses (N1 and P2) elicited during *active* than *passive* condition, while no clear differences appeared to be in the early P50 response, representing the earliest cortical processing of the proprioceptive afference. We did not investigate the early component at the individual level, since it was not robust enough to be quantified. Earlier components can be, indeed, quantified using electrical stimulation of the peripheral nerves, activating all afferents simultaneously (Allison et al., 1991; Halonen et al., 1988). However, in case of naturalistic ankle rotation stimulus, the proprioceptors are activated asynchronously (i.e. with varying timings of several milliseconds differences) at slightly different phases of the evoked movement. Therefore, the temporal spread of the afferents might result in a lower signal-to-noise ratio, thus “blurring” the earliest peak of the response (Piitulainen et al., 2015a).

The observed differences between the *active* and *passive* conditions might be influenced by attentional or cognitive factors. Indeed, the attention level of the participants could affect the amplitude of the cortical responses (Arnfred, 2005; Eimer and Driver, 2000; Eimer and Van Velzen, 2002; Gherri and Eimer, 2008; Hötting et al., 2003; Piitulainen et al., 2021; Quant et al., 2004). The attention was directed more to the foot during the *active* than the *passive* task, since participants had to actively maintain a constant torque through visual feedback. On the contrary, during the *passive* condition participants were instructed to be completely relaxed and to focus on the fixation cross on the feedback screen. Thus, it is reasonable to suggest that the cortical responses were amplified partly due to directed attention to the proprioceptive afference and the *active* task itself. Our group has previously shown that directed attention to the proprioceptive stimulation alone may enhance the SM1 cortex evoked-field amplitude to proprioceptive stimulation of the hand (Piitulainen et al., 2021).

Nevertheless, important mechanical and neuronal mechanisms at different levels of the proprioceptive processing pathway (i.e. from the muscle to the brain level) may explain the stronger cortical response during *active* than *passive* condition. Indeed, N1 has been shown to mainly reflect the somatosensory processing with proprioceptive

emphasis (Toledo et al., 2016), whereas the P2 response in the SM1 cortex might be more affected by the wider top-down and other reciprocal processes of the sensorimotor integration in the brain. Anaesthetic studies have indicated that N1 response has been associated to the feedback from the muscle spindles (Abbruzzese et al., 1985; Starr and Cohen, 1985), with less contribution from the cutaneous tactile and joint mechanoreceptors. Thus, the mechanical and neuronal status of the peripheral proprioceptors between *active* and *passive* conditions might enhance especially the N1 response. In our case, the active muscle contraction increases the tension in the muscle–tendon unit, and thus increases the tissue stiffness and removes the muscle–tendon unit “slack” more evident in the *passive* condition. Therefore, the proprioceptors are more readily activated, and likely fire in better synchrony in occurrence of an external perturbation. The better synchrony of somatosensory afference would naturally be reflected as stronger cortical response, even in case of identical “amount” of the afference, as EEG is fundamentally a measure of synchrony among a large population of neurons. Thus, the better synchrony would in turn increase the EEG signal-to-noise ratio. On the other hand, it is hard to estimate how effective the ~ 5-Nm ankle-joint torque was to mechanically sensitize the proprioceptors. For example, the muscle spindles are extremely sensitive to tiny length changes (as low as 5 µm during vibration) of their parent muscle (Brown et al., 1967), and Pacinian corpuscles are capable to detect even 10 nm skin motions (Brisben et al., 1999). Possibly because of the high sensitivity of the proprioceptors, the evoked and induced SM1 cortex responses to proprioceptive stimuli are shown to be invariant to mechanical factors, such as the range of the movement stimulation (Nurmi et al., 2023).

The primary Ia-afferents of the muscle spindle are suggested to be the primary source for the somatosensory evoked EEG responses to joint stimulation (Drews et al., 1998; Mima et al., 1996). During the voluntary movement, the muscle spindles are further neuronally sensitized through a gamma motor-neuron input to their intrafusal muscle fibers occurring simultaneously with alpha motor-neuron input to the skeletal muscle fibers (Prochazka, 2015). The contraction of the intrafusal fibers of the muscle spindle will then contract the spindle together with the muscle, which may increase the overall Ia-afferent firing rate. When the motor task requires precision in the muscle force production, as was the case in the current *active* task, the baseline activity of the gamma motor neuron is further increased, increasing also the spindle responsiveness (Purves et al., 2018). Together, the mechanical and neuronal factors affecting the peripheral proprioceptors may intensify or alter the nature of the proprioceptive afference, that is then seen as stronger evoked-EEG response in the SM1 cortex.

In addition to the enhanced sensitivity of the proprioceptors, we cannot exclude that also the cutaneous tactile mechanoreceptors in the sole of the forefoot were sensitized during the *active* condition. However, the contribution of tactile afferents has shown to be weak. Indeed, there is prior evidence that even when the cutaneous and joint afferents of the hand and wrist were blocked using peripheral ischemic anaesthesia, while muscle afferents were left intact, the evoked early EEG potentials were not altered (Mima et al., 1996). Nevertheless, the effect of tactile afferents on the late cortical responses evoked by naturalistic stimuli to the lower limbs has not yet been explored in the literature. Thus, we did not rule out the contribution (albeit weak) of the cutaneous afference of the sole on the examined naturalistic phenomenon as the tactile input is an important part of proprioception and sensorimotor integration. However, it is worth mentioning that both the proprioceptors and tactile mechanoreceptors are very sensitive, and thus are likely partially activated even during the passive condition by the passive resistance of the tissues to the evoked movement.

Additionally, the neuronal mechanisms at the spinal and cortical very likely contributed to the differences in cortical activation to the proprioceptive stimulation between the *active* and *passive* conditions. The somatosensory afference from the peripheral receptors to the SM1 cortex is modulated along its pathway in spinal, medullary and thalamic



circuits, and actually, the brain can modify this feedback as well (McIlroy et al., 2003). For example, there is evidence from rodent models showing that the status of the cortex may facilitate or enhance the thalamic signalling towards the cortex through cortico-thalamic feedback loops (Alitto and Usrey, 2003; Briggs and Usrey, 2008; Soo-Hyun et al., 2008). Indeed, during voluntary muscle actions, the somatosensory receptor input to the spinal cord converges in the spinal circuits which are also under control by the efferent motor output from the brain (Seki et al., 2003). Thus, the cortical motor output may affect the proprioceptive afference at subcortical levels of the central nervous system before it reaches the cortex. This active multi-level peripheral mechanism may partly explain the currently observed differences in the cortical responses between the *active* and *passive* conditions.

The “state” of the sensorimotor cortices is fundamentally different between the *active* and *passive* condition. In both tasks, the cortical *status quo* is maintained, either by keeping the steady isometric plantarflexion or to remaining passive/relaxed. However, the *active* condition was associated with active motor output and directed attention towards the visuomotor force precision task. Thus, the active engagement of various cortices (motor, visual, etc.) and related sensorimotor integration, might have an effect also on the cortical sensorimotor processing with respect to the *passive* condition. We observed that the processing of the proprioceptive afference was intensified (i.e. stronger response) during the *active* task. Similar observation of facilitated cortical response has been observed before if the somatosensory afference has been relevant for the ongoing motor task (Gantchev et al., 1994; Staines et al., 2002). The ankle joint rotation was indeed very relevant, although distracting, for the current motor task. It is also possible that the stronger somatosensory potentials reflect a higher cortical activation which is more strongly pronounced during the active task due to active inhibition of the distracting joint rotation stimulus, disturbing the *status quo*. Active inhibition has been shown to be associated with emphasized SM1 cortex activation (i.e. beta-power suppression) to stabilize motor output against visual presentation of distracting dynamic hand actions when participants were attempting to maintain steady isometric pinch force (Hari et al., 2014). The authors suggested that the mechanism was likely related to activation of the mirror neuron system, but similar active inhibition, or “self-mirroring” could be present also for proprioceptive afference.

Our observations contrasted with some previous studies showing reduced somatosensory evoked responses to electrical peripheral nerve stimulation (Asanuma et al., 2003; Rushton et al., 1981; Takahara et al., 2020). Electrical stimulation activates the somatosensory afferents with high synchrony allowing, e.g., accurate detection of the earliest N20 peak for the upper limb (Huttunen and Lauronen, 2012; Kakigi et al., 1995), which is not possible to elicit for more time varying naturalistic proprioceptive stimuli of lower limb joints rotations. Indeed, “naturalistic” somatosensory stimulation such as ankle rotation, may activate the neuronal networks in a more purposeful manner and thus the previously observed inhibitory gating effect to peripheral electrical stimulation might be dampened. Furthermore, it might be that the cortical sensorimotor processing varies between upper (fine motor) and lower (gross-motor locomotion) limbs (Staines et al., 1998). There might be more direct cortico-motoneuronal connections from the motor cortex to the upper limb spinal lower motoneurons than to the lower limb ones (Lemon, 2021), suggesting that spinal level circuits could be more “independent” in the control of stereotyped gross-motor actions like gait.

Finally, the peak response latencies did not differ between the conditions. This finding was not surprising since we expect little to no changes in the conduction velocity and central processing times of the proprioceptive afference to fixed proprioceptive stimuli, and considering that we tested a population of young, healthy adults (Toledo et al., 2016).

**Effect of volitional muscle activation on induced EEG-responses.** The beta modulation was too weak to be quantified reliably in 27 % of the currently studied population, both for beta suppression and

rebound. This result is typical, and it was in line with recent similar studies. Induced response amplitude is typically characterized by substantial inter-individual variation (Illman et al., 2022; Mujunen et al., 2022), and it is likely associated to differences in the individual functional anatomy. Thus, the source location and orientation may be more or less optimal, which can dramatically affect the beta power signal and thus its modulation amplitude. This issue is present even when using magnetoencephalographic (MEG) recordings, which has higher signal-to-noise ratio with respect to EEG, and thus allows more robust induced responses (Illman et al., 2022). Additionally, some other factors have been observed to affect the beta power modulation, such as variations in the circadian individual rhythm (Wilson et al., 2014). Nevertheless, the obtained induced responses agreed in spatiotemporal and spectral features with what has been previously shown by other colleagues investigating the cortical proprioceptive processing related to passive ankle joint stimulations (Toledo et al., 2016). For the first time, we showed clear differences in induced response amplitudes between *active* from *passive* conditions for somatosensory stimulus. The *active* condition elicited stronger beta suppression and weaker rebound compared to the *passive* condition. These findings are likely attributable to the stronger activation of the SM1 cortex and/or the active processes related to ongoing motor control that is much less emphasized in the *passive* condition. Induced responses reflect the dynamics of the brain oscillations driven by beta-burst activity in the SM1 cortex (Barone and Rossiter, 2021). Specifically, the beta suppression (i.e. reduction in the beta power) is thought to reflect the activation of the SM1 cortex and it has been found to occur, e.g., in response to active and passive movements, motor imagery, and action observation (Barone and Rossiter, 2021; Engel and Fries, 2010; Tan et al., 2016). Whereas the delayed beta rebound (i.e. increase in the beta power) has been attributed to the cortical inhibition or motor cortical deactivation and it has been thought to be an indicator of the movement outcome processing (Baker, 2007; Barone and Rossiter, 2021; Parkkonen et al., 2015; Pfurtscheller, 1992).

The EEG signal is primarily caused by the synchronous activity of large group of neurons, likely belonging to several different neuronal populations (Schutter and Hortensius, 2011). Therefore, a stronger cortical activation can be related to the increased synchrony of neuronal activity or to the larger number of neurons involved in the synchronous activity. In the current study, we indeed observed stronger beta suppression to the proprioceptive stimulation during *active* than *passive* condition. This observation thus suggests that the proprioceptive processing in the SM1 cortex was intensified due to the volitional muscle activation in line with what found by Heinrichs et al. (Heinrichs-Graham and Wilson, 2016) who demonstrated a significant positive correlation between the amplitude of beta suppression and spontaneous activity of the motor cortices (Heinrichs-Graham and Wilson, 2016). It is possible that the ongoing motor control in the SM1 cortex activated more strongly the cortical proprioceptive and/or sensorimotor integration neuronal network(s), thus intensifying the cortical proprioceptive processing. The stronger beta suppression of the *active* condition may also reflect the activation of early cortical inhibitory neuronal networks in favour of the continuous readjustments to maintain the *status quo* of the cortex throughout the task (Hari et al., 2014; Piitulainen et al., 2015b). This hypothesis is reinforced by TMS studies suggesting that the somatosensory afference to the SM1 cortex activates the cortical inhibitory neuronal networks as demonstrated by a reduction of the cortical motor output ~ 50 ms after the arrival of the somatosensory afference to the cortex (Bailey et al., 2016; Tokimura et al., 2000).

The cortical inhibition is partly controlled by sub cortical (e.g. thalamic and sub thalamic) structures, which are important in timing and pausing the motor output sequences. These structures regulate the activity of basal ganglia that further inhibit the thalamus to suppress the thalamic facilitation of the motor cortices, and thus help to suppress the activation of competing motor programs in the motor cortex (Brittain et al. 2012). A marker of the reduced cortical excitability or inhibition of the thalamo-cortical circuitry is the enhancement of the post-movement

beta power (Pfurtscheller and Neuper, 1994). In the current study, the SM1 cortex after the stimulus was not at “rest” during the *active* condition, but more so during the *passive* one. Therefore, there was less room for post-movement beta modulation in the cortex, shown by weaker beta rebound amplitude (i.e. weaker cortical inhibition) during the *active* than *passive* condition, probably reflecting some higher-level mechanisms such as sensorimotor integration and directed attention to maintain the steady precision force output task. This suggestion is further reinforced by the faster rate of beta recovery (i.e. inhibition recovery) of the *active* condition with respect to the *passive* one, highlighted by the smaller area under the rebound curve. In fact, the beta rebound obtained during the *passive* condition not only showed a higher amplitude but it took longer to recover back to the baseline when compared to the one obtained from the *active* condition. These findings are in line with prior observations of Cassim et al. where a larger and longer beta rebound was found for brief movements with respect to sustained ones (Cassim et al., 2000).

Finally, also for induced responses motor imagery and attentional effects can potentially partly explain the obtained results. Specifically, motor imagery has been shown to induce beta power modulation, with initial beta suppression followed with a rebound in similar manner as observed after active volitional movements (Neuper and Pfurtscheller, 2001). In addition, our group has shown earlier that beta power is suppressed when attention is directed, to the proprioceptive stimulation of the hand (Piitulainen et al., 2021). We designed the experimental protocol to minimize possible effects of the motor imagery by not instructing the participants to focus on the movement stimuli. However, we cannot completely rule out that the motor imagery or attentional effects on the induced response amplitudes.

### Study limitations and future perspectives

Although clear evoked and induced EEG responses were obtained in the present study for both *active* and *passive* conditions, caution must be taken when interpreting the results. Indeed, in addition to the mechanical and sensorimotor neuronal mechanisms, motor imagery and attentional effects cannot be excluded as possible contribution to the observed differences between *active* and *passive* condition. In this view, the contribution of attention and motor imagery should be quantified in the future studies to comprehensively understand the multi-mechanistic nature of the cortical processes related to proprioception during *active* and *passive* conditions. There are some further methodological enhancements that should be considered in future experiments to confirm the current observations, e.g.: (i) use of high-density EEG for better identification of the cortical proprioceptive sources, (ii) use of individual anatomical magnetic resonance images of the participants' head to confirm the results also in the source level, (iii) experimentally account for the influence of alpha-gamma coactivation by, e.g., repeating the experiment with a progressive increase of voluntary contraction (Watanabe and Hirayama, 1976), (iv) incorporate spinal (e.g. through H-reflex measures) and spindle (e.g. through microneurography) sensitivity measurements to quantify the differences at peripheral and spinal levels between conditions and further clarify the related proprioceptive mechanisms. Finally, the obtained results are not necessarily extendable to upper extremities or other muscular groups/activations. We cannot exclude that different mechanisms regarding the proprioceptive processing could take part when investigating other joints or limbs. Indeed, different cortical neuronal populations are involved when a different part of the body is stimulated with somatosensory stimuli, evidenced with distinct frequency bands for the beta rebound in the sensorimotor cortex (i.e. lower frequencies for the hand than for the foot stimulations) (Pfurtscheller and Neuper, 1994; Salmelin et al., 1995). Therefore, specific studies focusing on the upper extremities or performing movements in different directions should be separately performed to further investigate this aspect.

Owing to the importance of proprioception during development,

aging, sport and motor disorders, understanding how the sensorimotor information is gathered within the cortical neuronal networks appears of paramount importance. Our findings showed that cortical responses are modulated by volitional muscular activation, thus contributing to the understanding of the neurophysiological mechanisms of proprioception, which are still poorly described. We proved that EEG-based variables can robustly track changes in the integration between the afferent-efferent pathways. However, although the use of EEG/MEG variables as biomarker of sensorimotor cortical function has already been demonstrated in recent studies on developmental diseases (Illman et al., 2023; Piitulainen et al., 2020), post-stroke patients (Keser et al., 2022; Parkkonen et al., 2015) and elderly (Walker et al., 2020), the effect of voluntary muscle contraction on cortical proprioceptive processing in motor disorders has not yet been assessed. Proprioceptive responses can be quantified in reproducible manner using EEG (Illman et al., 2022) and the proprioceptive stimuli can be repeated identically using a motorized-movement actuator. Therefore, longitudinal studies on patient groups are needed to track the effects of rehabilitation, ageing or neurological diseases on cortical proprioception.

### Conclusion

Our study was the first one evaluating the effect of volitional muscular activation on the processing of proprioceptive afference in the SM1 cortex for the ankle-joint rotation stimuli using EEG. We demonstrated a stronger cortical activation and weaker inhibition in response to naturalistic proprioceptive stimulation of the ankle joint during *active* steady volitional motor task when compared to *passive* condition. These changes in SM1 cortex processing and integration of proprioceptive afference may find an explanation at different levels of the proprioceptive processing occurring both at peripheral (i.e. proprioceptors) and central (i.e. cortical, sub-cortical and spinal) levels. When compared to the *passive* condition, the *active* task is accompanied with a mechanical and neuronal sensitization of the peripheral proprioceptors, and active alterations in the neuronal interactions occurring at spinal, subcortical and cortical levels. We demonstrated that evoked and induced EEG responses can robustly track the effects of the active motor control and are thus feasible markers to study human cortical sensorimotor integration, allowing the examination of the cortical proprioceptive processing during *active* and *passive* tasks in both healthy and likely also in pathological populations. This would enable a greater insight about the role of proprioception which holds a non-negligible relevance in numerous scenarios ranging from quiet standing, locomotion or efficient movement execution.

### Patient Consent Statement

Prior to measurements, all participants signed a written informed consent.

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### Ethical Approval

The study conformed to the Declaration of Helsinki and all the experiments were approved by the ethics committee of University of Jyväskylä.

## Credit authorship contribution statement

**Alessandra Giangrande:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation. **Toni Mujunen:** Writing – original draft, Methodology. **Giacinto Luigi Cerone:** Software, Resources, Methodology. **Alberto Botter:** Writing – original draft, Supervision, Resources, Methodology, Formal analysis, Data curation. **Harri Piitulainen:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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