Analysis of somatosensory cortical responses to different electrotactile stimulations as a method towards an objective definition of artificial sensory feedback stimuli - an MEG pilot study

Jia Liu, Harri Piitulainen, Ivan Vujaklija, *IEEE Member*

Abstract— **Sensory feedback is a critical component in many human-machine interfaces (e.g., bionic limbs) to provide missing sensations. Specifically, electrotactile stimulation is a popular feedback modality able to evoke configurable sensations by modulating pulse amplitude, duration, and frequency of the applied stimuli. However, these sensations coded by electrotactile parameters are thus far predominantly determined by subjective user reports, which leads to heterogeneous and unstable feedback delivery. Thus, a more objective understanding of the impact that different stimulation parameters induce in the brain, is needed. Analysis of cortical responses to electrotactile afference might be an effective method in this regard. In this study, we used magnetoencephalography (MEG) to investigate the somatosensory evoked fields (SEFs) and equivalent current dipoles (ECDs) locations in nine non-invasive electrotactile stimulation conditions (1.2T, 1.5T, 1.8T) × (1 ms, 10 ms, 100 ms) with fixed 1s interval. T is the subject specific sensory threshold of the left index finger. In all conditions, we observed SEFs peaking at ~ 60 ms in the contralateral primary somatosensory cortex. While the amplitudes of the SEFs around 60 ms followed the increase in the stimulation pulse amplitude, the cortical activations were strongest when the stimulus pulse duration was set to 10 ms. These initial results indicate that the somatosensory cortical activations can provide information on the electrotactile parameters of pulse amplitude and duration, and the prosed methodology might be used for an objective interpretation of different artificial sensory feedback arrangements.**

Clinical Relevance—**Analysis of cortical spatiotemporal representations to electrotactile stimulation can potentially be used for tailoring optimal sensory feedback delivery in patients with sensorimotor impairments.**

I. Introduction

Somatosensory cortex is tightly bound together with motor functions and a lack of sensory feedback evidently affects motor functions [1]. Therefore, artificial substitution of motor functions, such as neuroprosthesis, requires both delivery of dexterous motor control capabilities and provision of rich sensory feedback [2] in order to form a high-performance closed-loop human machine interface (HMI). However, it is rather challenging to restore natural feedback because of the complexity of integration of multiple feedback sources. In recent years, several different technologies have been applied to translate artificial sensory feedback, including electrotactile stimulation, vibrotactile stimulation, and mechanotactile stimulation [3]. Particularly, electrotactile stimulation has been deemed advantageous in terms of seamless and responsive implementation, and thus it has been widely used [4]. In electrotactile stimulation, the quality and intensity of tactile sensations can be regulated by modulated stimulation parameters, including pulse amplitude, pulse width or duration, and its frequency. Yet, percutaneous electrotactile sensations are not entirely intuitive, and there is still a lack of objective means to interpret the impact of various stimuli arrangements. In previous magnetoencephalography (MEG) studies, the proprioceptive feedback [5], [7] and electrotactile feedback [1], [6] to the brain have been investigated by analysing cortical activations in the contralateral sensorimotor cortex [7]. In fact, many studies have examined the effects of electrotactile stimulation in the level of cerebral cortex, yet not much is known of the impact that different stimulation parameters to the responses recorded from the somatosensory cortex.

In the present study, we aim to conduct a preliminary investigation into cortical representations of different electrotactile stimulations of the left index finger. We hypothesize that the somatosensory evoked fields (SEFs) will be modulated by different electrotactile stimulation parameters. If proven true, this can be seen as an initial step towards an objective definition of stimulation parameters needed in optimization of artificial sensory feedback. The high density and high temporal-resolution MEG coupled with individual magnetic resonance images (MRIs) were adopted to derive the cortical activations in spatiotemporal domain.

II. Materials and Methods

A. Subject

We studied a right-handed male subject (31 years old) who did not report any history of neuromuscular diseases. Informed consent was obtained from the participant before the pilot study. The study has been approved by the ethical committee of the Aalto University.

B. Experimental design

A rectangular pulse was delivered as an electrotactile stimuli using a single stimulation channel of a constant current stimulator (Medizin Technik Schwind). The subject was

*Research supported by the Academy of Finland under grants #333149 (Hi-Fi BiNDIng), #296240 and #327228, and "Brain changes across the life-span" profiling funding to University of Jyväskylä under grant #311877.

Jia Liu (corresponding author) and Ivan Vujaklija are with the Department of Electrical Engineering and Automation, Aalto University, 02150, Espoo, Finland (e-mail: jialiu15@foxmail.com, ivan.vujaklija@aalto.fi).

Harri Piitulainen is with the Faculty of Sport and Health Sciences, University of Jyväskylä, 40014, Jyväskylä, Finland (e-mail: harri.t.piitulainen@jyu.fi).

instructed to relax his right hand on a table in front of him and rest his left hand on a pillow. The stimulation electrodes were fixated to the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of the left index finger. The subject was instructed to fix his attention on a back cross in the center of a screen located at a distance of 1.2 m. The subject wore earplugs throughout the whole experiment to reduce the artifacts from any auditory noise. A white paper card with a big rectangle opening was taped to the MEG gantry to prevent the subject from seeing the electrotactile setup.

Prior to MEG recordings, the sensory threshold (T) of the subject was determined by modulating the stimulation pulse amplitude in steps of steps of 0.1 mA. The value of T=4.5 mA was identified. The subject was then exposed to nine electrical stimulation conditions, determined by the combination of three pulse amplitudes of (1.2T, 1.5T, and 1.8T), and three pulse durations of 1 ms, 10 ms, and 100 ms. The single rectangular pulse frequency was fixed at 1 s, consistent with a previous study [8]. Each condition consisted of 100 trials, amounting to a total of 900 stimuli lasting around 15 min. To prevent onset of fatigue or numbness, these were split across 3 separate sessions (5 min/session) with a pseudorandom arrangement. Owing to the manual setup of the pulse amplitude in the stimulator, each session was assigned to a fixed pulse amplitude in random order. Meanwhile, three duration conditions consisting of 300 trials were randomly implemented in each session using a custom-made Presentation (Neurobehavioral Systems, Inc.) script. Each session was followed by a short rest.

C. *Data acquisition*

The MEG data were recorded with a 306-channel (204 planar gradiometers, 102 magnetometers) whole-scalp MEG system (Elekta Neuromag, Elekta Oy, Helsinki, Finland) in a magnetically shielded room (Imedco AG, Hägendorf, Switzerland) at the MEG core, Aalto Neuroimaging, Aalto University. During the measurement, the subject was comfortably seated in an upright position with his head covered by the MEG sensory array. The subject was instructed to keep as still as possible and avoid excessive eye movements. Five indicator coils (three attached to the forehead and one above each ear) were applied to determine the head position with respect to the MEG sensors. Before the MEG measurement, the locations of the five indicator coils and three anatomical landmarks (left and right preauricular points and nasion), as well as more than 100 additional points on the scalp surface were recorded using a 3D digitizer (Fastrak 3SF0002, Polhemus Navigator Sciences, Colchester, VT, USA). The head position was measured in each session and was monitored continuously throughout the whole MEG measurement. The MEG signals were sampled at 1000 Hz and band-pass filtered to 0.1-330 Hz.

Further, the anatomical MRIs were acquired with a 3T whole/body MRI scanner (Magnetom Skyra, Siemens) at the Aalto Neuroimaging Infrastructure center, Aalto University.

D. *Data analysis*

To enable better comparability between experimental conditions, MEG signals were transformed to the same head coordinate system [9], which in our study was the mean position between three sessions. Having the averaged coordinate position as the reference position, we used Maxfilter software (version 2.2; Elekta Oy, Helsinki, Finland) to match the coordinates and compensate for any head movement. Following the coordinate transform, MEG signals were processed with the temporal signal-space separation (tSSS) [10] implemented in Maxfilter software to restrain environment interference.

All further analyses were then conducted using the scripts in MNE python [11]. First, the continuous MEG data were bandpass filtered between 1 Hz and 40 Hz. Then the fast independent component analysis was used to remove cardiac and eye blinking artifacts. Next, the preprocessed MEG data were segmented into -200 ms to 800 ms epochs relative to the stimulus onset. Epochs exceeding 4 pT for magnetometer channels or 1.5 pT/cm for gradiometer channels were excluded from further analyses. There was an average of 98 trials (ranging from 95 to 100 trials) left in all stimulation conditions. SEFs were obtained by averaging trials in the nine conditions, including 1.2T-1 ms, 1.2T-10 ms, 1.2T-100 ms, 1.5T-1 ms, 1.5T-10 ms, 1.5T-100 ms, 1.8T-1 ms, 1.8T-10 ms, 1.8T-100 ms. For comparison in the sensor level, two orthogonal gradiometer channels were combined using the vector sum, which is implemented in Fieldtrip toolbox [12].

Individual MRIs (2 runs, 176 slice/run) were processed with Freesurfer software [13]. Further, the equivalent current dipoles (ECDs) were used for source localization at 60 ms of the SEFs. A total of fixed 9 sensors consisting of 6 gradiometers and 3 magnetometers over the contralateral somatosensory cortex were selected for the ECDs analysis. Finally, we visualized the ECDs locations on the coregistered individual MRIs.

III. Results

A. *Sensor levels responses*

SEFs were obtained from the subject during nine electrotactile stimulation conditions. Figure 1 depicts the sensor level responses to different electrotactile stimulations delivered to the left index finger. The magnetic field pattern at the main peak of the SEFs, as well as intuitive comparisons in three sets of conditions across two main factors (pulse amplitude × pulse duration) are also shown. We compared the SEFs averaged over the contralateral primary somatosensory (SI) cortex, covering nine channels, in the nine conditions. The main response after the stimulation peaked around 60 ms across all nine conditions. We designated the magnetic response M60, consistent with the way of designation in a previous MEG study [6]. The orientation of the M60 neural current flow was from anterior to posterior (Figure 1, panel B). Similar patterns were observed in all conditions. The clear dipolar field patterns were centered on the right hemispheric sensors near the central sulcus, consistent with the activity generated at the right SI cortex. As can be further seen from the Figure 1 pancel C, the highest and lowest M60 were for 1.8T-10 ms and 1.2T-1 ms, respectively. The strength of M60 increased as a function of pulse amplitude, from the lowest strength at 1.2T to the highest one at 1.8T, irrespective to the pulse duration. When comparing the strength of M60 in relation to the pulse duration, we observed it being the highest for the duration of 10 ms. The amplitude of M60 was slightly higher than when the stimulation duration was set to 100 ms than when it was at 1 ms.

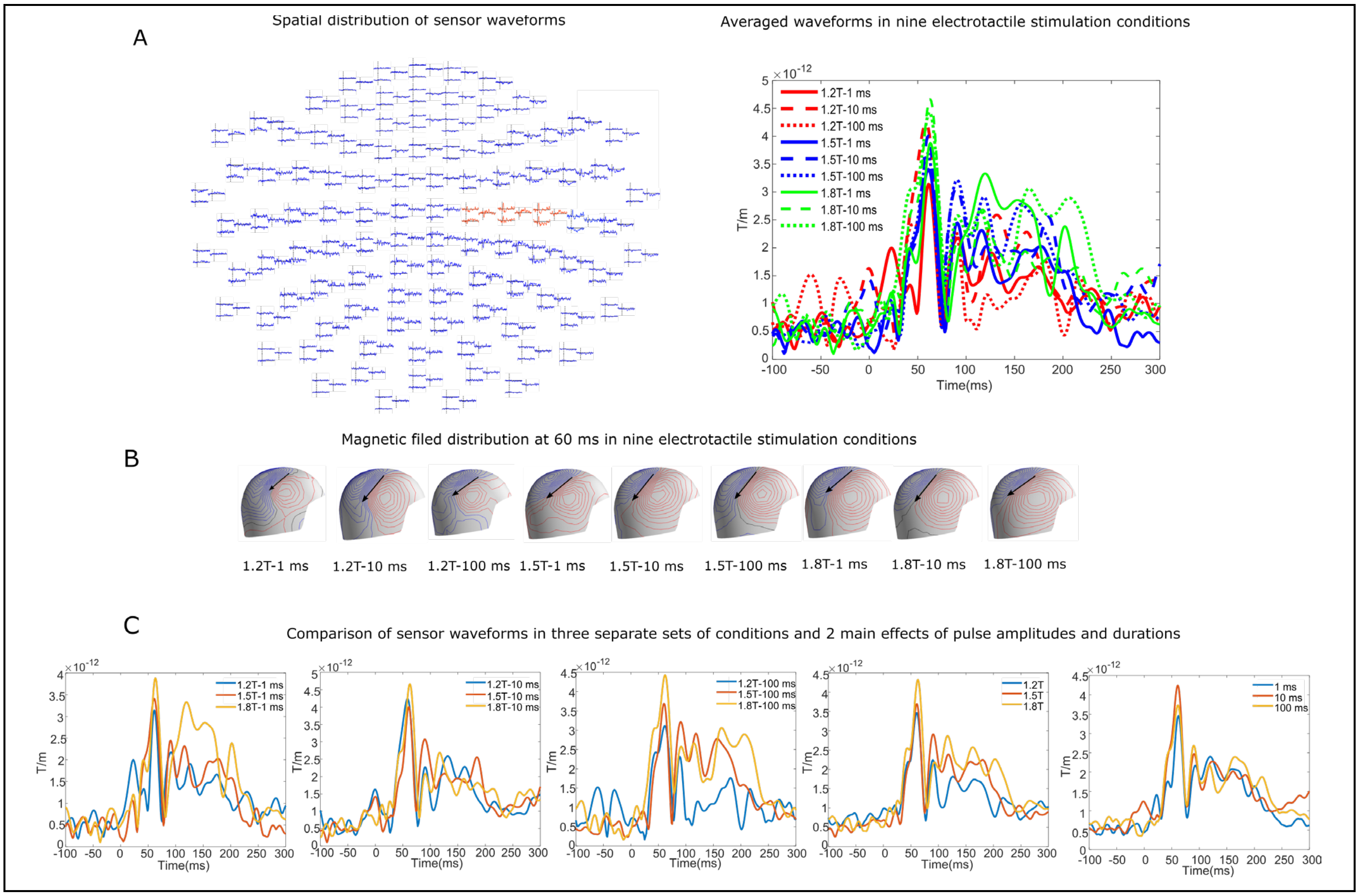

Figure 1. Differences in SEFs to electrotactile stimulation between nine conditions. (A) left shows the 2D sensory array of evoked responses. The red channels, with the vector sum of gradiometers, are selected for sensor level comparison. (A) right displays SEFs across nine stimulation conditions. (B) visualizes the field pattern of ECDs at the main response peak of 60 ms. The blue and red isocontour lines indicate magnetic flux into and out of the skull, respectively. The black arrow denotes the surface projection of ECDs. (C) compares the SEFs obtained from nine conditions in three separate sets of conditions and two main effects.

B. Cortical sources

Figure 2 illustrates the source locations superimposed on the MRI of the subject across all nine stimulation conditions. The source coordinates at the specific time points and goodness-of-fits (GoF) for all ECDs are shown in TABLE I. GoFs seem high and stable, indicating adequate explanation by the dipole fitting. The sources of nine conditions were similarly located the right SI cortex, slightly posterior from the central sulcus [14], corresponding to the right SI cortex. The biggest deviation was evoked by the 1.2T-100 ms condition, where the sources seem to be located slightly anterior of the central sulcus (blue circle, Figure 2). In general, the sources corresponding to the weakest stimulation amplitude (1.2T) appear to originate more towards the superior of the brain (circles, Figure 2).

TABLE I. ECDS RESULTS TO ELECTROTACTILE STIMULATION

Condition	***time/ms***	***x/mm***	***y/mm***	***z/mm***	***GoF/%***
1.2T-1 ms	61	51	-26	54	96.6
1.2T-10 ms	59	50	-26	49	78.6
1.2T-100 ms	61	42	-15	57	78.3
1.5T-1 ms	59	50	-27	48	86.7
1.5T-10 ms	60	49	-28	48	81.8
1.5T-100 ms	62	49	-29	45	88.9
1.8T-1 ms	61	47	-27	48	77.9
1.8T-10 ms	61	50	-28	48	99.5
1.8T-100 ms	62	50	-31	45	99.4
Mean	60.7	48.7	-26.3	49.1	87.5
SD	1.1	2.7	4.5	4.0	9.1

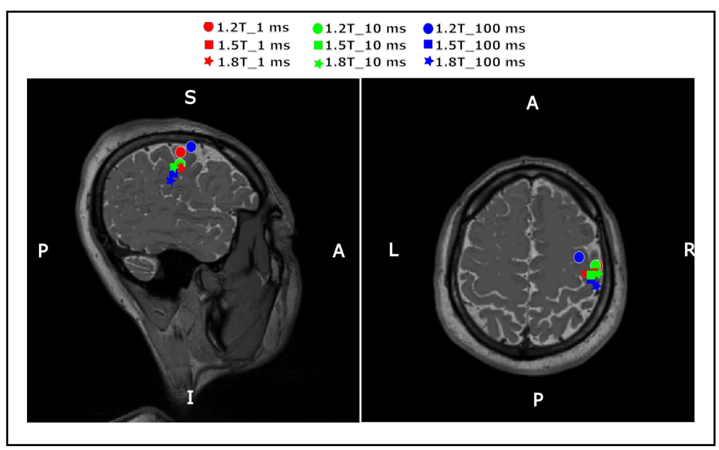

Figure 2. The source locations of the subject in sagittal (left) and axial (right) planes across nine stimulation conditions. The sources were computed from the SEFs in the time window of 55-65 ms that correspond to the highest GoF. Note: L is left, R is right, A is anterior, P is posterior, S is superior, I is inferior.

IV. Discussion

The present study used MEG to characterize somatosensory evoked brain activations and together with the individual MRI to localize the cortical sources during different electrotactile stimulations of the left index finger. We detected the SEFs in the contralateral SI cortex peaking around 60 ms, and found this M60 localized to the posterior bank of the central sulcus or postcentral gyrus in all nine stimulation conditions. By comparing these results in nine stimulation conditions, we identified similar patterns of current flow and magnetic field distribution, as well as approximate anatomical MRI coordinates. Most importantly, we revealed that the amplitude of M60 SI response increased along with the rise of electrotactile stimulation pulse amplitude. At the same time, M60's amplitude was the highest for the stimulation pulse duration of 10 ms.

In line with an pervious SEFs study [8], the cortical responses to electrotactile stimulation of the left index finger was maximum at about 60-70 ms located at the contralateral SI cortex. Similarly, the contralateral SI response M60 has also been detected after the median nerve electrical stimulation in newborns [1]. In all stimulation conditions, the magnetic field patterns were adequately (GoF > 77%) explained by a fitted dipole in the contralateral SI cortex. In agreement with previous two M60 studies [1], [8], the ECDs of M60 were located around the finger area of the SI cortex with a posterior orientation of the current flow. A prior study [15] has verified that afferent signals through cutaneous fibers reach area 3b in the SI cortex. In agreement with an earlier study [1], our results indicate that the M60 is likely originating from the 3b, 3, or 2 areas in the SI cortex. Further, the sources of the responses to all electrotactile stimulation conditions seem to be located slightly posterior of the central sulcus.

To our knowledge, this is the first MEG study that specifically investigates the relationship between somatosensory cortical responses and the amplitude and the duration of the electrotactile stimulus delivered percutaneously at the distal portion of a limb. By comparing the SI responses M60 at the sensor level across nine conditions, we observed that there are stronger SI cortical activations generated from posterior of the central sulcus along with the increase of the stimulation pulse amplitude from 1.2T to 1.8T. Meanwhile, the depths of sources during 1.5T and 1.8T electrotactile stimulation condition were deeper than those in 1.2T. Once the pulse durations have been increased from 1ms to 10 ms and then to 100 ms, the strongest SI response M60 was detected for the stimulus duration of 10 ms, followed by the durations of 100 ms and 10 ms. Given the limited study population, it is too early to speculate the consistency and mechanism of these observations. Nevertheless, this study indicates that the applied methodology can have merits in the efforts towards providing objective means for defining optimal stimulation parameters for artificial sensory feedback based on brain responses.

V. Conclusion

Our results suggest that electrotactile stimulation parameters have an impact on the evoked SI cortex responses. We demonstrate that contralateral M60 SI cortex response, originated posterior to the central sulcus, is evoked across all nine stimulation conditions. The amplitude of M60 increase following the rise of stimulation pulse amplitude, whereas the M60 response was the strongest for the stimulation pulse duration of 10 ms. This pilot study provides the feasibility for providing the definition of electrotactile feedback stimuli. The cortical mapping of somatosensory feedback is promising for the restoration of sensory feedback in a closed-loop HMI.

Acknowledgment

The study was supported by Mia Illman for MEG collection, Ivan Zubarev and Yongjie Zhu for MEG data analysis, Dennis Yeung for improving the experiment, as well Aalto Neuroimaging center and MEG core.

References

[1] N. Forss and V. Jousmäki, "Sensorimotor integration in human primary and secondary somatosensory cortices," *Brain Res.*, vol. 781, no. 1–2, pp. 259–267, 1998.

[2] D. Farina *et al.*, "Toward higher-performance bionic limbs for wider clinical use," *Nat. Biomed. Eng.*, 2021.

[3] S. Dosen, C. Prahm, S. Amsüss, I. Vujaklija, and D. Farina, "Prosthetic Feedback Systems," in *Bionic Limb Reconstruction*, Cham: Springer International Publishing, 2021, pp. 147–167.

[4] K. Li, Y. Fang, Y. Zhou, and H. Liu, "Non-Invasive Stimulation-Based Tactile Sensation for Upper-Extremity Prosthesis: A Review," *IEEE Sens. J.*, vol. 17, no. 9, pp. 2625–2635, 2017.

[5] M. Bourguignon, H. Piitulainen, X. De Tiège, V. Jousmäki, and R. Hari, "Corticokinematic coherence mainly reflects movement-induced proprioceptive feedback," *Neuroimage*, vol. 106, pp. 382–390, 2015.

[6] L. Lauronen, P. Nevalainen, H. Wikström, L. Parkkonen, Y. Okada, and E. Pihko, "Immaturity of somatosensory cortical processing in human newborns," *Neuroimage*, vol. 33, no. 1, pp. 195–203, 2006.

[7] H. Piitulainen, M. Bourguignon, R. Hari, and V. Jousmäki, "MEG-compatible pneumatic stimulator to elicit passive finger and toe movements," *Neuroimage*, vol. 112, pp. 310–317, 2015.

[8] J. Xiang *et al.*, "Somatosensory evoked magnetic fields following passive finger movement," *Cogn. Brain Res.*, vol. 6, no. 2, pp. 73–82, 1997.

[9] M. Illman, K. Laaksonen, M. Liljeström, V. Jousmäki, H. Piitulainen, and N. Forss, "Comparing MEG and EEG in detecting the ~20-Hz rhythm modulation to tactile and proprioceptive stimulation," *Neuroimage*, vol. 215, no. March, 2020.

[10] S. Taulu and J. Simola, "Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements," *Phys. Med. Biol.*, vol. 51, no. 7, pp. 1759–1768, 2006.

[11] A. Gramfort *et al.*, "MNE software for processing MEG and EEG data," *Neuroimage*, vol. 86, pp. 446–460, 2014.

[12] R. Oostenveld, P. Fries, E. Maris, and J. M. Schoffelen, "FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data," *Comput. Intell. Neurosci.*, vol. 2011, 2011.

[13] B. Fischl, "FreeSurfer," *Neuroimage*, vol. 62, no. 2, pp. 774–781, 2012.

[14] E. Smeds, H. Piitulainen, M. Bourguignon, V. Jousmäki, and R. Hari, "Effect of interstimulus interval on cortical proprioceptive responses to passive finger movements," *Eur. J. Neurosci.*, vol. 45, no. 2, pp. 290–298, 2017.

[15] T. Allison, G. McCarthy, C. C. Wood, P. D. Williamson, and D. D. Spencer, "Human cortical potentials evoked by stimulation of the median nerve. II. Cytoarchitectonic areas generating long-latency activity," *J. Neurophysiol.*, vol. 62, no. 3, pp. 711–722, 1989.