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Somatotopic finger mapping using MEG: Toward an optimal stimulation paradigm

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HIGHLIGHTS

- The somatotopic finger representations in human SI were precisely localized with neuromagnetic steady-state responses to 20-Hz vibrotactile stimuli.
- Cortical sources of adjacent digits were separated significantly in each individual.
- Rapidly alternating the stimulation site overcomes the effects of suppressive interactions in simultaneous digit stimulation and improved source localization accuracy.

ABSTRACT

Objective: In non-invasive somatotopic mapping based on neuromagnetic source analysis, the recording time can be shortened and accuracy improved by applying simultaneously vibrotactile stimuli at different frequencies to multiple body sites and recording multiple steady-state responses. This study compared the reliability of sensory evoked responses, source localization performance, and reproducibility of digit maps for three different stimulation paradigms.
Methods: Vibrotactile stimuli were applied to the fingertip and neuromagnetic steady-state responses were recorded. Index and middle fingers were stimulated either sequentially in separate blocks, simultaneously at different frequencies, or in alternating temporal order within a block.
Results: Response amplitudes were largest and source localization was most accurate between 21 and 23 Hz. Separation of adjacent digits was significant for all paradigms in all participants. Suppressive interactions occurred between simultaneously applied stimuli. However, when frequently alternating between stimulus sites, the higher stimulus novelty resulted in increased amplitudes and superior localization performance.
Conclusions: When receptive fields are strongly overlapping, the alternating stimulation is preferable over recording multiple steady state responses.
Significance: The new paradigm improved the measurement of the distance of somatotopic finger representation in human primary somatosensory cortex, which is an important metric for neuroplastic reorganization after learning and rehabilitation training.

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1. Introduction

The topographic organization of the primary somatosensory cortex (SI) was initially demonstrated using cortical stimulation during neurosurgery (Penfield and Boldrey, 1937). Recently, the representations of body parts in the SI has been mapped using non-invasive imaging modalities such as magnetoencephalography; (MEG) (Biermann et al., 1998; Brenner et al., 1978; Nakamura et al., 1998; Okada et al., 1984) and electroencephalography (EEG) (Giabbiconi et al., 2004; McLaughlin and Kelly, 1993; Noss

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Abbreviations: ANOVA, analysis of variance; CI_{95}, 95% confidence interval; CR_{95}, 95% confidence radius; D1, index finger; D2, middle finger; ECD, equivalent current dipole; EEG, electroencephalography; fMRI, functional magnetic resonance imaging; GOF, goodness of fit; I–S, inferior–superior; ISI, inter-stimulus interval; ITI, inter-train interval; L–M, lateral–medial; MANOVA, multivariate analysis of variance; MEG, magnetoencephalography; P–A, posterior–anterior; PCA, principal component analysis; PSI, pound per square inch; SEF, somatosensory evoked magnetic field; SI, primary somatosensory cortex; SNR, signal-to-noise ratio; SSR, steady-state response; ZPF, Pearson–Filon statistics.

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et al., 1996). Mapping the somatosensory cortex and observing functionally relevant changes within a map are important tools for basic research and clinical applications. For example, MEG studies have demonstrated plastic reorganization of the finger representation after learning (Elbert et al., 1995; Godde et al., 2003; Liu and Ioannides, 2004), peripheral injury (Mogilner et al., 1993; Weiss et al., 2000), and brain lesions (Gallien et al., 2003; Rossini and Dal Forno, 2004; Taub et al., 2002). Furthermore, several studies proposed responsiveness of primary somatosensory cortex in stroke patients as a predictor of recovery (Feys et al., 2000; Forss et al., 1999; Wikström et al., 2000). Spatial maps of the somatotopic organization can be obtained by localizing the sources of the transient somatosensory evoked magnetic field (SEF) following the onset of a stimulus or a change in the stimulus properties (Baumgartner et al., 1991; Brenner et al., 1978; Hari et al., 1993; Okada et al., 1984). Alternatively, the source of the steady-state response (SSR) can be used. A train of rapidly repeated stimuli evokes the SSR as an oscillation that follows the frequency of the stimulus (Nangini et al., 2006; Snyder, 1992; Tobimatsu et al., 1999). The source localization and source-space projection (Robinson and Rose, 1992) provides time courses of cortical activity. The experimental procedure typically requires blocks of stimuli, which are presented to each body part in sequential order. Each block consists of several hundred stimuli, presented with an inter-stimulus interval (ISI) of 0.5–1 s. Such procedure takes about 5–10 min recording time for each body part. Using current techniques, a minimum of two hours may be required to map both left and right hands. For somatotopic organization and mapping to be clinically useful, the procedural timeframe must be shortened significantly.

Investigation time could be shortened if multiple fingers were stimulated simultaneously. However, the spatial resolution of most neuroimaging techniques is not sufficient to resolve simultaneously activated source, given that distances of only 2–5 mm separate the representations of adjacent fingers (Baumgartner, 1991). While the accuracy for localizing a single dipole with MEG is high, as expressed in confidence limits on the order of a millimeter, simultaneously activated dipole sources can be resolved only if they are separated by several centimeters (Hari et al., 1988). One approach to overcome this limitation is applying vibrotactile stimuli at different frequencies simultaneously to multiple fingers. Spectrum analysis separates the responses in the frequency domain, and source analysis can be performed independently for each Fourier coefficient. A substantial reduction of the required recording time has been proposed for such a simultaneous multiple SSR method (Diesch et al., 2001; Pollok et al., 2002). The advantage of the multiple SSR method may hold true only if the multiple responses are of equal size to the single SSR; yet, reduced amplitudes of multiple SSRs have been found (Biermann et al., 1998; Severens et al., 2010). Given that the source localization accuracy depends on the signal-to-noise ratio (SNR) (Darvas et al., 2005; Ogura and Sekihara, 1993), localization accuracy is likely reduced with multiple SSR because of a smaller SNR, provided similar amounts of background activity. Thus, additional recording time might be necessary for obtaining the same source localization accuracy as with single SSRs. Nonetheless, the multiple steady-state method may be advantageous compared to sequential stimulation because it may overcome the detrimental effects of between block variation in source localization (Jamali and Ross, 2012). Also small head movements affect the simultaneously obtained sources equally and may have a smaller effect on a distance measure than during sequential recording.

The aim of the current study was to investigate accuracy and reliability of the somatotopic map of finger representation in SI obtained with multiple SSRs or equivalent approaches. First, we studied the effect of the stimulation rate on the response amplitude for justifying the best choice of frequencies. Second, we investigated an alternative stimulation approach for simultaneous localization of multiple finger representations, which may cause less interaction and response reduction. We compared the source localization accuracy and cortical waveforms for the various stimulation paradigms.

2. Methods

2.1. Participants

Fifteen healthy right-handed young adults (mean age 22 yrs, range 19–28 yrs, 12 females) without any history of neurological disorders participated in this study. Informed consent was obtained in written form from each participant before engaging in the study, which had been approved by the Research Ethics Boards at the Rotman Research Institute at Baycrest and the University of Toronto.

2.2. Vibrotactile stimuli

Vibrotactile stimuli were delivered to the tip of the finger through a pneumatically driven inflatable circular plastic membrane with diameter of 1 cm (4D-Neuroimaging, San Diego, CA) (Ferris et al., 1993). The membranes were connected via plastic tubes (4 m long, 4 mm inner diameter) and electromagnetic air valves to a supply of compressed air at 70 psi. The in-house built stimulator device, similar to a device described by Wienbruch et al. (2006) was located outside the shielded MEG room and interfaced to a computer via a digital-to-analog conversion card and controlled by customized LabView software (model AT-AO-6, National Instruments, Austin, TX, USA). The valves were activated to periodically inflate the membrane and deliver brief pressure pulses of 10 ms duration to the skin. Trains of pressure pulses were applied for the duration of 3.5 s to the fingertip and induced a flutter sensation. To validate the temporal dynamics and amplitudes of the vibrotactile stimulator, the time-course of the applied oscillating force was measured using a force-sensitive resistor (FSR) (model FSS1500NGR, Honeywell, Canada). The FSR was attached between a plastic probe, simulating the load of finger, and the vibrating membrane. The relations between the time courses of force changes and the pressure pulses are shown for 21-Hz and 23-Hz vibration in Fig. 1A. The inter-train interval (ITI) was set to 1 s. Such vibrotactile stimuli have been shown to evoke a reliable SSR (Jamali and Ross, 2012; Nangini et al., 2006). Any possible mechanical noise produced by the stimulation device was acoustically masked by presenting a white noise sound via insert phones to the participants binaurally at 45 dB above individual sensation threshold.

2.3. Experimental procedures

Two MEG sessions of about one-hour duration were performed. First, we investigated the relation between stimulus frequency and the SSR amplitude for the vibrotactile stimulation in order to find the optimal stimulation frequencies. In the second session, source localization accuracies were compared between three stimulation paradigms, which were sequential recordings of single frequency SSRs, multiple SSRs, and alternating steady-state stimulation of two fingers within the same recording block.

In the first session, we applied vibrotactile stimuli to the index finger of the right hand in seven blocks of 5 min duration. The experimental parameter stimulus frequency was chosen in random order out of the set of 19, 21, 23, 25, 27, 29, and 31 Hz.

In the second session, SSRs were recorded with stimulation of the index finger (D1) and the middle finger (D2) of the right hand for estimating the distance between adjacent finger representations in SI. Three stimulus paradigms were compared. For a fair

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