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Research paper

The temporal stability and variability across frequency bands in neural synchrony between primary and secondary somatosensory areas following somatosensory stimulation

Jun-ichi Uemura [a,*], Minoru Hoshiyama [a,b]

[a] *Department of Rehabilitation Sciences, School of Health Sciences, Nagoya University, 1-1-20 Daiko-Minami, Higashi-ku, Nagoya 461-8673, Japan*
[b] *Brain and Mind Research Center, Nagoya University, 1-1-20 Daiko-Minami, Higashi-ku, Nagoya 461-8673, Japan*

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ABSTRACT

Objectives: To examine the temporal stability and variability of neuronal synchronization among the contralateral primary somatosensory cortex (cSI) and contralateral (cSII) and ipsilateral secondary somatosensory cortex (iSII) in response to median nerve stimulation.
Methods: Both the spontaneous magnetoencephalography (MEG) signals as the pre-stimulus condition and somatosensory evoked magnetic-fields (SEF) were recorded in eleven healthy subjects. We calculated a phase-locking value (PLV) between two areas among cSI, cSII, and iSII in five frequency bands (theta: 5–7 Hz, alpha: 8–12 Hz, beta: 15–29 Hz, gamma-1: 30–59 Hz, and gamma-2: 60–90 Hz), and compared the PLV among in pre-stimulus and stimulus conditions.
Results: The PLV between cSI and cSII for the theta band activity varied within 2 s from the stimulus onset. On the other hand, the PLV between cSI and iSII for the alpha band did not vary within 2 s.
Conclusion: The fluctuation of neuronal synchrony among sensory-related cortices in response to median nerve stimulation depends on the induced frequency band and inter-region.
Significance: This study is the first to report the temporal characteristic of stimulus-driven neural synchrony following somatosensory stimulation.

1. Introduction

Recently, neural networks among brain areas have been of marked interest. There have been mainly two methodological approaches: functional magnetic resonance imaging (f-MRI) and magnetoencephalography (MEG), to investigate the neural networks, recordings of the resting state, and task-related brain activities. The resting state brain activity includes activities of resting state networks (RSNs), in which widely distributed brain areas function with temporal coherences at rest (Biswal et al., 1995; Brookes et al., 2011a; Brookes et al., 2011b; de Pasquale et al., 2010; Fox and Raichle, 2007; Liu et al., 2010;). For the somatosensory neural system, MEG (de Pasquale et al., 2010; Yuan et al., 2012) and f-MRI (Biswal et al., 1995; Brookes et al., 2011b) studies have shown a sensorimotor network at rest as well as other RSNs, such as a default mode network and dorsal attentional network. Furthermore, a stimulus-driven neuronal network among sensory-related cortices has been identified (Bardouille and Boe, 2012; Brookes et al., 2011a; Kujala et al., 2007). Neuronal synchrony from the alpha to gamma frequency bands was observed between the primary (SI) and secondary (SII) somatosensory cortices until 200–500 ms following median nerve stimulation (Hagiwara et al., 2010; Simões et al., 2003).

Following the identification of the neural network between spatially separate brain regions, some studies exploring the temporal and spectral evolution of coupling regions in a resting state suggested that temporally and spectrally variable neuronal dynamics underlie the resting state networks detected (Britz et al., 2010; Brookes et al., 2014; Hillebrand et al., 2012; Smith et al., 2009). Concerning the stimulus-driven neural network between somatosensory-related cortices, the characterizing phase locking between SI and SII in the early-stage somatosensory processing following electrical stimulation has been investigated, but the temporal variability across frequency bands remains unknown. Given the temporal and spectral non-stationarity in resting state networks, it is hypothesized that dynamic neural synchronization across frequency bands contributes to the stimulus-driven neural network between SI and SII following median nerve stimulation. To assess the temporal instability in the stimulus-driven neural network,

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* Corresponding author.
E-mail address: uemura@met.nagoya-u.ac.jp (J.-i. Uemura).

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we applied MEG, which shows significant advantages with excellent time resolution in characterizing temporal non-stationarity, and the phase-locking value (PLV) approach (Lachaux et al., 1999). It was reported that the PLV does not rely on stationarity, unlike spectral coherence, and it enables the accurate estimation of synchronization among networks (Lowet et al., 2016). In this study, we traced the neural synchrony of the MEG signals among the contralateral SI (cSI), contralateral SII (cSII), and ipsilateral SII (iSII) until 2 s following median nerve stimulation as well as the spontaneous signals under the non-stimulus condition. We estimated the PLV using source-reconstructed MEG signals, which yielded more information based on the brain anatomy than the sensor-level signals. Then, we compared the PLV between stimulus and non-stimulus conditions. This paper focuses on the temporal variability across frequency bands in the stimulus-driven neural network between SI and SII. Assessing the temporal instability in the stimulus-driven neural network can provide valuable insights into the interaction between the resting state and stimulus-driven neural networks.

2. Materials and methods

2.1. Participants

Eleven healthy volunteers (2 males and 9 females, mean age: 21.0 years, range: 20–22 years) participated in the experiment. All subjects showed right-hand dominancy based on the Edinburgh Handedness Questionnaire (Oldfield, 1971), and they had no history of neurological or psychiatric disease. Each participant gave informed consent for the study and experimental protocol prior to its commencement. This study was approved by the ethical committee of the Faculty of Medicine, Nagoya University.

2.2. Experimental design

Each participant lay down on a bed in a magnetically shielded room during the recording. The right median nerve was stimulated at the wrist with 0.5-ms constant-current square-wave pulses by an electrical stimulator (S-2727B, Nihon-Koden, Japan), at an intensity 20% above the motor threshold (44.2 ± 6.3 V) with an inter-stimulus interval of 2 s. (If cortical activity were being recorded from SII, an inter-stimulus interval of 2 s may be short. However, this study investigated the temporal stability and variability in neural synchrony focused on the phase between brain areas, and not the amplitude of cortical activity. Further, the PLV can be calculated from a spontaneous condition, it is therefore likely that there is little effect of the inter-stimulus interval on the results.) Participants were asked to ignore the stimuli, keeping their attention on a silent video projected on a screen 30 cm in front of them.

2.3. Data acquisition

We used a whole-head MEG system (PQ1160C, Yokogawa Electric Co., Japan) with 160 axial-type first-order gradiometers and a 50-mm-long baseline detection coil. The initial bandpass filter was between 0.3 to 500 Hz, at a sampling rate of 2000 Hz, with a notch filter at 60 Hz. An electro-ocular gram (EOG) with a pair of disk electrodes placed on the lateral canthus and 2 cm below the infra-orbicular edge of the right eye, and electrocardio gram (ECG) with a pair of electrodes on both sides just beneath the clavicle, were recorded for artifact rejection at the pre-processing stage, as described below.

Firstly, spontaneous signals were recorded as the pre-stimulus condition with no stimulus (NS) for three minutes in a dark and noise-shielded room. The participants were instructed to stay awake with their eyes open and relax. Somatosensory evoked fields (SEF) were recorded following right median nerve stimulation. MEG signals were continuously collected for 400 s during the administration of 200 stimuli.

Prior to the MEG recording in each participant, his/her scalp shape was digitally traced using a 3D digitizer (SR system-R, YOKOGAWA, Japan), which enabled us to fit the MEG coordinates to those of the standardized brain, as described below.

2.4. Data analysis

All data analyses including the preprocessing, source imaging, and calculation of PLV were performed with the software Brainstorm (Tadel et al., 2011), which is open-source software (http://neuroimage.usc.edu/brainstorm/). All implementation details are therefore readily documented and can be verified in Brainstorm.

Firstly, using the EOG and ECG data, artifacts caused by the heart-beat and eye movement/blinking were attenuated by designing signal-space projections from selected segments of data about each artifact event (Nolte and Curio, 1999). Furthermore, segments with residual artifacts of extra-cephalic origin were rejected by visual inspection from datasets before further analysis.

For the spontaneous MEG data, epochs for 1 s were segmented and collected (Pre-stim). For the SEF data, epochs from the stimulus onset to 1 s after the stimulus (Seg-1) and from 1 to 2 s after the stimulus (Seg-2) were separately collected. Over 160 epochs (NS: 173.0 ± 4.6, SEF (Seg-1 and -2): 173.6 ± 5.7 trials) were used to estimate source activities. In Brainstorm, the depth-weighted minimum norm model (Hämäläinen and Ilmoniemi, 1994) was used with the default parameter settings, including a set of elementary current dipoles, up to 7500 dipoles, distributed over the individual cortical envelope. Each individual cortical envelope projecting the source activities was created from Brainstorm's default anatomy, Colin 27, which is the Montreal Neurological Institute (MNI) brain template, based on each individual scalp shape digitized. We manually selected three regions of interest (ROIs) on the cortex with 15 vertices (mean size: 3.47 cm^2): the contralateral primary somatosensory cortex (cSI) and contralateral (cSII) and ipsilateral (iSII) secondary somatosensory cortex (Fig. 1).

The PLV between two areas among the three cortical areas in five frequency bands (theta: 5–7 Hz, alpha: 8–12 Hz, beta: 15–29 Hz, gamma-1: 30–59 Hz, and gamma-2: 60–90 Hz) was calculated for each epoch of Pre-stim, Seg-1, and Seg-2 source time-series. The PLV, ranging from 0 to 1, estimates the variability of phase differences between two brain areas. In each participant, the calculated PLV was averaged in Pre-stim, Seg-1, and Seg-2, respectively. To remove the influence of individual differences, the PLV ratio was calculated by dividing values of the three conditions by the value of Pre-stim for each participant. The PLV ratio in each frequency band was statistically analyzed among the conditions using one-way repeated measures ANOVA with post hoc multiple comparison tests (Bonferroni correction). All statistical analyses were performed with the SPSS statistical package (version 22). *P*-values of <0.05 were set as significant.

3. Results

In all participants, SEF were clearly identified until approximately 200 ms, and were included in Seg-1 (Fig. 2). On the other hand, there was no prominent SEF component in Seg-2. The regional field power in cSI, cSII, and iSII lasted until 300 ms after stimulus onset (Fig. 1 lower panel).

The PLV between cSI and cSII in the theta band significantly varied among conditions (F (2, 20) = 9.387, p = 0.001). Multiple