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Neural correlates of somatosensory paired-pulse suppression: A MEG study using distributed source modeling and dynamic spectral power analysis

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ABSTRACT

Paired-pulse stimulation has been used previously to evaluate cortical excitability and sensory gating. To help elucidate the neural network involved in paired-pulse suppression of somatosensory cortical processing, magnetoencephalographic (MEG) responses to paired-pulse electrical stimulation of the left median nerve of the wrists of 13 healthy males were recorded using an intra-pair interstimulus interval (ISI) of 500 ms and an inter-pair ISI of 8 s. Minimum norm estimates showed the presence of cortical activation in the bilateral primary somatosensory cortex, the post-central sulcus and the supplementary motor areas. Compared with the responses to the first stimulation, the responses to the second stimulation were attenuated in these areas with gating ratios (the amplitude ratios of the second response to the first response) of 0.54–0.69. By spectral power dynamic analysis, beta frequency oscillations were found to be associated with an early-latency (30–36 ms) gating process in the contralateral primary somatosensory cortex and post-central sulcus, whereas theta and alpha oscillations were correlated with paired-pulse suppression of activations at 98–136 ms in the ipsilateral primary somatosensory cortex, the bilateral post-central sulcus and the supplementary motor areas. In summary, it can be concluded that differential oscillatory activities are involved in the pair-pulse suppression in various somatosensory regions in response to repetitive external stimulations.

Introduction

Cortical responses to paired-pulse stimuli have been used to examine sensory gating phenomenon (Freedman et al., 1991). When there is correct short stimulus onset asynchrony, the second response is typically suppressed in a normal brain (Freedman et al., 1991). The presence of a relatively preserved magnitude of the second response suggests that there is either an overall increase in cortical excitability or the presence of a deficit in sensory gating. Alteration in sensory gating for various sensory modalities, such as auditory, somatosensory, and visual stimuli, has been reported in schizophrenia (Arnfred and Chen, 2004; Brockhaus-Dumke et al., 2008; Edgar et al., 2005; Thoma et al., 2007; Williams et al., 2011), epilepsy with hippocampal sclerosis (Rosburg et al., 2008), migraine (Hoffken et al., 2009), and aging (Lenz et al., 2012).

A gating deficit in the primary somatosensory cortex (SI) or secondary somatosensory cortex (SII) of schizophrenia patients has been reported by previous electroencephalographic (EEG) (Arnfred and Chen, 2004; Arnfred et al., 2001a,b; Lenz et al., 2012) and magnetoencephalographic (MEG) studies (Edgar et al., 2005; Thoma et al., 2007). One recent EEG and fMRI study has identified the hippocampus and claustrum as possible neural correlates with the inhibitory processes underlying somatosensory P50 suppression (Bak et al., 2011). SI activation is not easily identified in fMRI studies, therefore the role of the somatosensory cortices in sensory gating remains uncertain.

Brain activity consists of an ensemble of sources that generate rhythmic activities in several frequency ranges. In response to external sensory input, these sources are coherently coupled and, when activated, there are subsequent alterations in brain rhythms for the sake of processing sensory perception and to allow integration (Adler et al., 1982; Hsiao et al., 2006, 2008; Schicatano and Blumenthal, 1995). Accumulated evidence has suggested the involvement of beta activity in auditory-sensory or somatosensory gating (Hong et al., 2008; Kisley and Cornwell, 2006). A reduction after first stimulus onset in the beta phase

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(Rosburg et al., 2009) and lowering of alpha phase and theta phase locking activities (Brockhaus-Dumke et al., 2008) have been found in schizophrenia patients. However, it remains unknown as to what is the exact source localizations of the oscillatory generators engaged in the sensory gating mechanism (Hong et al., 2008).

With excellent temporal resolution and allowing non-invasive brain imaging recording, magnetoencephalography (MEG) is able to elucidate the dynamic spatiotemporal characteristics of somatosensory cortical activation (Lin et al., 2006b). Minimum norm estimate (MNE) is a MEG visualization method that utilizes distributed source modeling with additional *a priori* constraints and can represent a number of local or distributed sources, even when they overlap in time (Hamalainen and Ilmoniemi, 1994). As a result, MNE has been suggested to be the preferred method when analyzing multi-source somatosensory evoked activations compared to other inverse approaches (Lin et al., 2006a). Furthermore, it provides source-based spatiotemporal imaging of the cortical oscillations (Lin et al., 2004).

This study characterizes the spatiotemporal activation patterns of the neural networks associated with somatosensory gating using MEG recording together with MNE and spectral power dynamic analysis. The specific aims were: (a) to obtain the distributed somatosensory gating network with respect to cortical localizations, time intervals of significance between two responses, and gating ratios; (b) to explore the gating-related cortical oscillations derived from the current strength waveforms of the cortical sources; and (c) to examine the correlations between cortical oscillatory power and gating ratios.

Methods

Subjects

Thirteen healthy right-handed men (20–34 years old, mean age 24.4 years) participated in this study. All of them were undergraduate or graduate students in National Yang-Ming University. The experimenter CHC interviewed the subjects about their medical history and personal habits. None had histories of neurological diseases and alcohol or drug abuse. There was no history of psychiatric disorders in the subjects and their first-degree relatives. One subject smoked 1–2 cigarettes per day, and six subjects were low-caffeine users (less than 100 mg/day) (Schicatano and Blumenthal, 1995). To minimize the influence of nicotine and caffeine, they were asked to withhold from having coffee and cigarette before recording on the test day. Informed consent was obtained from the participant prior to the MEG recordings.

Somatosensory stimulation and MEG recordings

Each subject received electrical stimulation of the left median nerve of the wrist by an electrical stimulator (Konstant-Strom Stimulator) using the paired-pulse paradigm. Each pulse of the paired stimulations was 0.2-ms constant-current square-wave with an interstimulus interval (ISI) of 500 ms, and with the inter-pair interval fixed at 8 s. The ISI of 500 ms was used because it elicited robust sensory gating phenomena in comparison with shorter or longer ISIs in the previous studies (Adler et al., 1982; Bak et al., 2011), and could be applied in studies for differentiation between certain diseased and normal states (Edgar et al., 2005; Thoma et al., 2007). A recent MEG study has demonstrated a significant gating ratio of the early somatosensory deflection (P35m) with 500 ms ISI (Stevenson et al., 2012). In the present study, the stimulus intensity was set 20% above the motor threshold required to elicit a visible twitch of the abductor pollicis brevis muscle (mean intensity: 4.2 ± 0.12 mA).

Somatosensory evoked fields (SEFs) were recorded using a whole-scalp 306-channel neuromagnetometer (VectorviewTM, Elekta Neuromag, Helsinki, Finland) composed of 102 identical triple sensor elements. Each sensor element consisted of one magnetometer and two orthogonal planar gradiometers. The planar gradiometers of this device detect the largest signal directly above the activated cerebral areas (Hämäläinen et al., 1993). The exact position of the head with respect to the sensors was obtained by measuring magnetic signals produced by current leads to four head indicator coils at known sites on the scalp. Individual Cartesian coordinates were determined using a 3-D digitizer. The x-axis passed through the preauricular points from

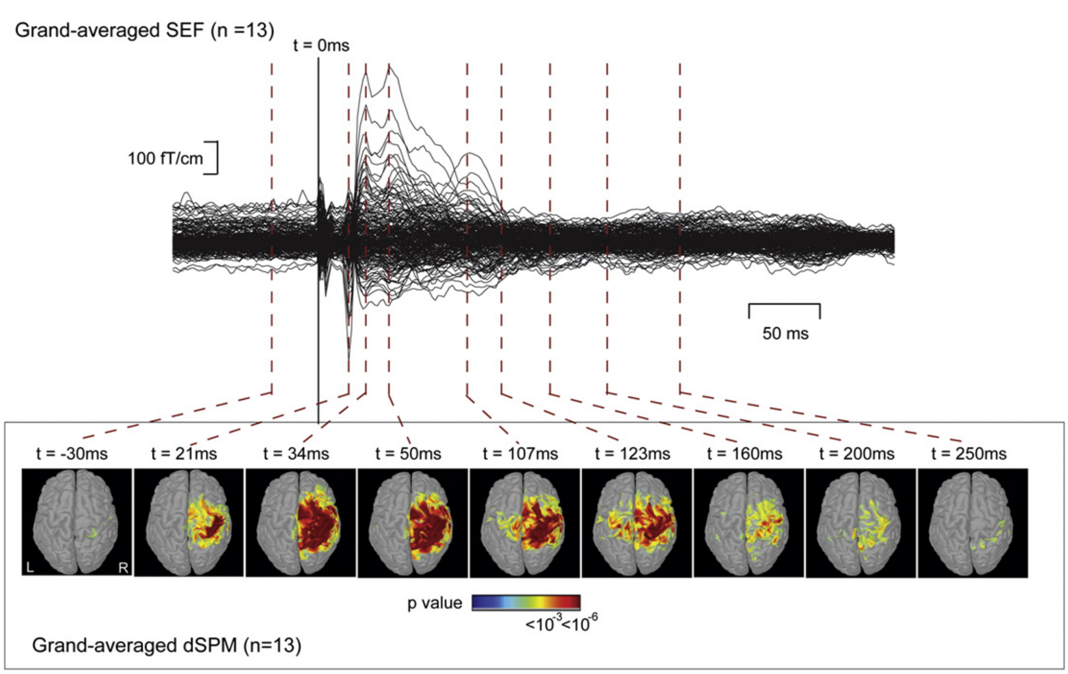

Fig. 1. Top: Averaged and superimposed evoked magnetic activities caused by median nerve electrical stimulation from 204 gradiometers across the subjects; Bottom: Spatiotemporal activation of the averaged dynamic statistical parametric maps from −100 to 400 ms. These maps are shown on the Colin27 surface. The significance level of the cortical maps is color-coded with significance being denoted by red.