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Age-related changes across the primary and secondary somatosensory areas: An analysis of neuromagnetic oscillatory activities

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HIGHLIGHTS

- We recorded somatosensory evoked magnetic fields with oscillatory activity indices to evaluate the effects of aging on the primary (SI) and secondary (SII) somatosensory areas.
- The oscillatory activities well depicted the age-related cortical disinhibition across SI and SII.
- Our data provide the first evidence for age-related changes in cortical synchrony in SII.

ABSTRACT

Objective: Age-related changes are well documented in the primary somatosensory cortex (SI). Based on previous somatosensory evoked potential studies, the amplitude of N20 typically increases with age probably due to cortical disinhibition. However, less is known about age-related change in the secondary somatosensory cortex (SII). The current study quantified age-related changes across SI and SII mainly based on oscillatory activity indices measured with magnetoencephalography.
Methods: We recorded somatosensory evoked magnetic fields (SEFs) to right median nerve stimulation in healthy young and old subjects and assessed major SEF components. Then, we evaluated the phase-locking factor (PLF) for local field synchrony on neural oscillations and the weighted phase-lag index (wPLI) for cortico-cortical synchrony between SI and SII.
Results: PLF was significantly increased in SI along with the increased amplitude of N20m in the old subjects. PLF was also increased in SII associated with a shortened peak latency of SEFs. wPLI analysis revealed the increased coherent activity between SI and SII.
Conclusions: Our results suggest that the functional coupling between SI and SII is influenced by the cortical disinhibition due to normal aging.
Significance: We provide the first electrophysiological evidence for age-related changes in oscillatory neural activities across the somatosensory areas.

1. Introduction

Age-related changes in the primary somatosensory area (SI) have been reported by a number of studies on somatosensory evoked potentials (SEPs). The most notable finding of SEPs in normal aging is the increased amplitude of the N20 component, which is the initial cortical response following electrical stimulation of the median nerve or fingers (Desmedt and Cheron, 1980, 1981; Drechsler, 1978; Tanosaki et al., 1999). The age-related electrophysiological changes in SI were also confirmed by magnetoencephalographic (MEG) studies, which demonstrated that the N20m component, an MEG counterpart of the N20 component (Wood et al., 1985), exhibited increased amplitude in the old (Huttunen et al., 1999; Stephen et al., 2006). Although the precise physiological mechanism has not been fully elucidated, the increased amplitude is probably caused by cortical disinhibition in the old (Drechsler, 1978; Huttunen et al., 1999; Stephen et al., 2006). In addition to the amplitude difference, the N20 latency is also prolonged in the old because of the slowing of conduction velocity in the peripheral nerves and spinal cord (Desmedt and

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Cheron, 1980; Dorfman and Bosley, 1979). Thus, the age-related electrophysiological changes, up to the level of SI, have been well established.

Since somatosensory evoked magnetic fields (SEFs) can easily detect activity of the secondary somatosensory area (SII), many studies adopted SEFs to investigate the functional significance of SII. In contrast to SI, SII possesses higher cortical functions, such as sensorimotor integration, tactile discrimination, attention, perception of unified body image, and nociceptive information processing (for reviews, see Hari and Forss, 1999; Kakigi et al., 2000; Lin and Forss, 2002). In addition, it has been suggested that SII is unique in having dual afferent pathways. Several neurophysiological and anatomical studies have reported that SII receives input from SI as well as the thalamus (Karhu and Tesche, 1999; Lin and Forss, 2002; Raij et al., 2008; Zhang et al., 1996, 2001a, 2001b). A previous SEF study demonstrated an age-related reduction in source-wave amplitudes of SII using multi-dipole analysis (Stephen et al., 2006). However, a large number of averaging in their study was likely to have caused habituation, and the SII response did not appear for a relatively large number of subjects, which makes the results less conclusive. To our knowledge, there have been no ensuing studies conducted for assessing age-related changes in SII. Therefore, unlike the accumulating evidence on the age-related changes of SI, aging effects on SII have not been fully understood.

In the present study, we focused on oscillatory activities to evaluate the age-related changes across the somatosensory areas. We used two indices for synchronous neural oscillations: the phase-locking factor (PLF) and weighted phase-lag index (wPLI). PLF measures local phase synchrony with respect to incoming stimuli (Palva et al., 2005; Sinkkonen et al., 1995), whereas wPLI measures the consistency of the phase relationship between signals in separate areas while diminishing the effect of volume conduction (Vinck et al., 2011). A benefit of using these oscillatory activity indices is that both indices assess only the phase of the signals and are independent of amplitude (Sinkkonen et al., 1995; Vinck et al., 2011). We employed PLF as an index for local field synchrony in each somatosensory area (i.e., SI and SII), and wPLI as an index for functional connectivity between the two cortical areas. Here we consolidate the presence of aging effects on SII by utilizing those oscillatory activity indices in conjunction with the SEF analysis.

2. Methods

2.1. Subjects

Fifteen young volunteers (5 females; age, 29.0 ± 4.1 years; height, 171.0 ± 8.9 cm) and fifteen old volunteers (5 females; age, 63.7 ± 3.7 years; height, 162.0 ± 8.7 cm) participated in this study. All were right-handed and had no past medical history of neurological conditions. Prior to data collection, all participants gave written informed consent. This study was approved by the local ethics committee at Kyushu University.

2.2. Recording of neuromagnetic activity

The right median nerve was electrically stimulated at the wrist with constant current pulses of 0.2-ms duration. Intensity of the stimuli was adjusted above the motor threshold to produce slight contraction of the abductor pollicis brevis muscle. The interstimulus interval was pseudo-randomized (mean = 3 s). During the stimulation, continuous MEG signals were recorded using a whole-head 306-channel sensor array (Elekta, Neuromag) with 102 identical triple-sensor elements. Each triple-sensor element is composed of two orthogonally-oriented planar-type gradiometers and one magnetometer. Prior to recording, four head-position-indicator coils were attached to the subjects' head. Anatomical landmarks (nasion and bilateral preauricular points) and scalp shape were then digitized to construct a three-dimensional head coordinate system. At the beginning of the recording session, the subjects' head position was measured with respect to the center of the sensor array. The recording was performed while subjects lay in a supine position with their head positioned inside the helmet-shaped sensor array. During the recording, the subjects kept their eyes open, and their vigilance was monitored by MEG signals and a video camera positioned inside the shield room. Sampling rate was 5 kHz, with a 0.1–1500 Hz recording bandpass filter. A spatiotemporal signal space separation (tSSS) method (Taulu and Simola, 2006) was applied offline to the data to reduce external artifact signals. The data was downsampled to 1 kHz prior to the time–frequency analysis.

2.3. Data analysis

2.3.1. SEF analysis

SEFs were obtained by averaging approximately 100 responses offline. Trials exceeding 3000 fT/cm in amplitude were excluded before averaging. Root mean square (RMS) waveforms were reconstructed using each orthogonally-oriented pair of gradiometers (Hagiwara et al., 2010; Kida et al., 2006, 2007), and latencies and amplitudes were evaluated at sensors with maximal amplitude. Dipole moment was not assessed in this study because MRI was not obtained for all subjects. The waveforms were filtered at 0.3–150 Hz, and mean amplitude during the 50-ms pre-stimulus period was set as a baseline. We focused on the N20m component for the analysis of the SI response. With regard to SII, major components with bitemporal distribution peaking at around 70–120 ms (cSII for the contralateral response, and iSII for the ipsilateral one) were analyzed. The cSII response was reassured after subtracting the SI response using a signal space projection so that the waveform and isocontour map of cSII can be isolated (Hagiwara et al., 2010). Age-related differences for latencies were evaluated by an analysis of variance with age groups and height as covariate factors, and amplitudes were assessed by unpaired Student's *t*-test with respect to the age groups. In principle, this part of the analysis was conducted to determine sensors of interest for the following analysis of oscillatory activities in SI and SII.

2.3.2. Assessment of oscillatory activities within the somatosensory areas

Prior to this part of the analysis, we calculated vector sum signals from the raw data sets at each gradiometer pair, followed by continuous wavelet transformation for each single-trial data using complex Morlet to extract the time–frequency domain of the signals. The data at each time–frequency point was obtained at 1-Hz frequency resolution and 5-ms time resolution. We calculated two indices of neural synchrony: the phase-locking factor (PLF), which represents phase synchronization with respect to the stimuli, and the weighted phase-lag index (wPLI), which represents inter-areal phase synchrony.

To calculate PLF, we used the same computation method described by previous studies (Palva et al., 2005; Sinkkonen et al., 1995). Briefly, PLF was given by the following equation:

$$\mathrm{PLF} = \left| \frac{1}{N} \sum_{n=1}^{N} \frac{w_n(f,t)}{|w_n(f,t)|} \right|$$

where $w_n(f,t)$ represents the amplitude as well as the phase of a specific frequency f at a timepoint t, and N denotes the total epoch number. As seen in the equation, PLF yields only the phase of the signal whilst being unaffected by its amplitude. We used PLF as a measure to evaluate local field synchrony in SI and SII, which were represented by those at the sensors determined from the SEF analysis.