Cortical magnetic activation following voluntary movement and several types of somatosensory stimulation

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Abstract Magnetoencephalography is primarily sensitive to current sources tangential to the skull. Therefore, currents generated in area 3b of the primary somatosensory cortex (S1) and area 4 of primary motor cortex (M1) located on the posterior and anterior banks of the central sulcus, respectively, are easily detected. The movement-related cortical magnetic fields (MRCFs) following voluntary movement and the somatosensory magnetic fields (SEFs) generated by peripheral mixed nerve stimulation (e.g., median nerve) have been widely used to investigate the physiology of normal somatosensory cortical processing. Here, we describe the MRCFs produced by two types of movement (experiment 1) and the SEFs elicited by motor point stimulation (experiment 2), passive movement (experiments 3 and 4), and mechanical stimulation (experiments 5, 6, and 7). In addition, we examined the modulation of these fields.

Keywords: magnetoencephalography, movement-related cortical magnetic fields, somatosensory evoked magnetic fields, MEG, MRCF, SEF

Introduction

Several cortical imaging techniques, such as functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electroencephalography (EEG), and magnetoencephalography (MEG), have provided unequivocal evidence of the brain activity involved in sensorimotor integration. Compared with fMRI and PET, MEG has excellent temporal resolution and has been used to analyze the temporal aspects of cortical sensorimotor information processing. MEG is primarily sensitive to current sources tangential to the skull. Therefore, currents generated in area 3b of primary somatosensory cortex (S1) and area 4 of primary motor cortex (M1) located on the posterior and anterior banks of the central sulcus, respectively, are easily detected.

Cortical activation following voluntary finger movement and motor point stimulation

Many investigators have reported movement-related cortical magnetic fields (MRCFs) following voluntary movement. Neuromagnetic fields, over the hemisphere contralateral to the side of the movement, change im-
such feedback may involve afferent input from muscle spindle receptors monitoring changes in muscle length, sensory organs in joints and tendons, and/or skin receptors activated by the mechanical stretching of the overlying skin. Therefore, we investigated the contribution of sensory feedback from the periphery to the generation of MEF1.

Eight healthy volunteers participated in experiment 1\textsuperscript{(13)}. We recorded MRCFs following two types of finger movement (Task 1 and 2). Task 1 consisted of voluntary finger extension to 40 degrees. In Task 2, an elastic band was placed on the right index fingertip, producing a resistance approximately 1.5-fold higher than the electromyographic activity associated with the voluntary index extension to 40 degrees (Fig. 2). Representative EMG waveforms and isocontour maps for the MF and MEF1 components under these two conditions are shown in Fig. 3. The rectified
and integrated EMG for Task 2 was significantly larger than that for Task 1. The dipole moment at MF in Task 2 was significantly larger than that of Task 1 due to the integrated EMG. On the other hand, there were no significant differences in the dipole moment at MEF1 between Task 1 and Task 2. Fig. 4 shows a representative MRCF waveform detected from one gradiometer in each task and the relationship among EMG, trigger signal, and MEF1 peak in one subject. In Task 2, the electromechanical delay from EMG onset to movement onset was longer than in Task 1. However, the latency from EMG onset to the MEF1 peak in Task 2 did not significantly differ from that of Task 1. The equivalent current dipoles (ECDs) of MEF1 were located significantly medial to that of N20m, and elicited by median nerve stimulation. These findings suggest that the ECD of MEF1 is slightly different from N20m (Brodmann area 3b), and MEF1 is due to muscular contraction and not the onset of joint movement or mechanical stretching of the skin.

In experiment 212), we recorded MRCFs after voluntary index finger extension, and the somatosensory evoked magnetic fields (SEFs) elicited by electrical stimulation of a motor point to investigate the contribution of muscle afferent feedback to the sensorimotor cortex. SEFs were recorded following motor point stimulation of the right extensor indicis muscle using a pair of wire electrodes. MEF1 was observed approximately 36 ms after movement onset (Fig. 5a). The most concentrated SEFs were identified approximately 78 ms (M70) after motor point stimulation, and the onset latency of M70 was 39 ms after motor point stimulation (Fig. 5b). The mean ECD locations of MEF1 and M70 were significantly medial and superior to that of N20m (Fig. 6). The ECD locations and directions of MEF1 and M70 were concordant in the axial, coronal, and sagittal planes. Therefore, MEF1 and M70 may be elicited by muscle afferent feedback following muscle contraction, and these ECDs may be located in area 4.

Cortical activation following passive finger movement

Previous studies investigated the SEF accompanying passive movement using MEG systems14-18. Xiang et al.18) identified four SEF components after the onset of passive finger movement. The peak latencies of these components were 20, 46, 70, and 119 ms after movement onset. Several researchers reported that the large component after passive movement was of long duration with two peaks from 30 to 100 ms after movement onset15-17. The ECDs of these two components were located in area 3b13, area 415, and areas 3b and 417,18. Taken together, two components were observed from 30 to 100 ms after passive
movement, and the magnetic waveforms consisted of two peaks following passive movement that were different from the waveforms consisting of one component following active movement.

Previous PET and fMRI studies proposed that passive movement activates an extensive cortical sensorimotor area, e.g., the contralateral primary sensorimotor area, supplementary motor area (SMA), posterior parietal cortex (PPC), and bilateral secondary somatosensory areas (cortices) (S2)\textsuperscript{19-24}. However, the time course of activities in these cortical areas has not been clarified because PET and fMRI do not have the temporal resolution of MEG. Furthermore, many MEG studies have not shown evidence for activities in motor-related cortical areas outside the primary sensory and motor areas following passive movements\textsuperscript{14-18}.

Therefore, we recorded MRCFs following voluntary finger movement and SEFs following passive finger movement to examine the detailed time course of cortical activities and source localizations following passive finger movement. We analyzed these signals with a multiple dipole analysis system in experiment 3\textsuperscript{25}. The most
prominent movement-evoked magnetic field (MEF1) following voluntary movement was obtained approximately 35 ms after movement onset, and the ECD was estimated to be in M1 (Brodmann area 4). Similar to previous studies, the two peaks of the MEG response associated with passive movement were recorded between 30 and 100 ms after movement onset\textsuperscript{15,18}. The earliest component (PM1) peaked at approximately 36 ms, and the second component (PM2) peaked approximately 86 ms after movement onset. The peak latency and ECD localization of PM1, which was estimated to be in area 4, were the same as those of MEF1 after voluntary movement. The ECDs of PM2 were estimated to be in area 4, the supplementary motor area (SMA) and posterior parietal cortex (PPC) over the hemisphere contralateral to the movement, and in the secondary somatosensory cortex (S2) of both hemispheres (Fig. 7). The peak latency of each source activity was obtained between 54-109 ms in the SMA, 64-114 ms in the PPC, and 84-184 ms in the S2 (Fig. 8). Our results suggest that the magnetic waveforms with middle latency (50-100 ms) after passive movement are different from those after voluntary movement, and these waveforms are generated by the activities of several cortical areas, i.e., area 4, SMA, PPC, and S2. In this study, the time courses

![Fig. 7](image)

Fig. 7 The ECDs following passive movement were overlaid on the inflated brain of a representative subject. The ECDs were estimated at the primary sensorimotor area (red dipole), SMA (green dipole), PPC (purple dipole), and cS2 (blue dipole) in this subject. (Onishi et al., 2012\textsuperscript{25})

![Fig. 8](image)

Fig. 8 Time course of each source activity, and the location of each source using BESA analysis following active and passive finger movements. (a) Time course of each source activity for all subjects. (b) Time course of the averaged activity for each source. (c) Schematic presentation of the locations of all dipoles following passive movement. 1, area 4; 2, supplementary motor area (SMA); 3, posterior parietal cortex (PPC); 4, contralateral secondary somatosensory cortex (cS2); and 5, ipsilateral secondary somatosensory cortex (iS2). (Onishi et al., 2012\textsuperscript{25})
The SEFs elicited by electrical stimulation of the peripheral nerves or skin have been investigated in detail. When the median nerve is electrically stimulated, SEFs are clearly observed over the sensorimotor cortex contralateral to the stimulated side. It is generally accepted that the peak latencies of prominent deflections occur at approximately 20 ms (N20m), 35 ms (P35m), and 60 ms (P60m) after median nerve stimulation at the wrist (Fig. 11).

There have been several SEF studies using mechanical stimuli (MS), e.g., air puffs (pneumatic stimulation), brushes, plastic pieces driven by airflow, and vibration buzzers. Pneumatic stimulation is a useful tool to investigate the activities in the SMA, PPC, and S2 accompanying passive movement in humans. We also examined the effect of the range and angular velocity of passive movement on SEFs following passive movement in experiment 4. We recorded SEFs following passive movement under three conditions, including normal range - normal velocity (NN), small range - normal velocity (SN), and small range - slow velocity (SS), while varying the movement range and angular velocity. We calculated the amplitude, and ECD locations and strength of each component. After passive movement, clear SEF deflections of PM1, PM2, and a third component (PM3) were observed in the hemisphere contralateral to the movement. The PM1 amplitude was larger under NN and SN conditions (Fig. 10), and the mean ECD location for PM1 was at M1. The PM3 amplitude was larger under the SN condition (Fig. 10), and the mean ECD location for PM3 under the SS condition was at S1. The durations of passive movement under NN and SS conditions were 166 ms and extended into the period when PM3 was observed. Thus, the amplitude of PM3 deceased under NN and SS conditions because the muscle spindle-dependent activity of M1 overlapped with the activity of S1 caused by cutaneous input. The activity of S1 following cutaneous input became easy to detect under SN conditions, and the amplitude of PM3 appeared to increase. The PM1 amplitude was dependent on the angular velocity of passive movement, suggesting that PM1 reflects afferent input from muscle spindles, whereas the ECD for PM3 was located in the S1, suggesting that PM3 reflects cutaneous input.

Cortical activation following mechanical stimulation

The SEFs elicited by electrical stimulation of the peripheral nerves or skin have been investigated in detail. When the median nerve is electrically stimulated, SEFs are clearly observed over the sensorimotor cortex contralateral to the stimulated side. It is generally accepted that the peak latencies of prominent deflections occur at approximately 20 ms (N20m), 35 ms (P35m), and 60 ms (P60m) after median nerve stimulation at the wrist (Fig. 11).

There have been several SEF studies using mechanical stimuli (MS), e.g., air puffs (pneumatic stimulation), brushes, plastic pieces driven by airflow, and vibration buzzers. Pneumatic stimulation is a useful tool to...
record SEFs in response to face or lip stimulation. However, the rise time for pneumatic stimulation is relatively long (greater than 10 ms); thus, the early cortical activity cannot be measured as clearly as the responses generated by electrical stimulation. Jousmäki et al.\textsuperscript{(53)} presented a novel solution for the use of tactile stimuli on various parts of the body in MEG studies; however, the stimulus intensity of their device is unclear. In contrast, the rise time of mechanical pins driven by piezoelectric actuators is less than 1 ms, and the stimulus is precise and consistent. Therefore, this devise is useful for investigating the early phase of cortical activity following life-like tactile sensation, tactile-off responses, and response to multiple stimuli distributed over a region for sensory paradigms, such as two-point discrimination.

We investigated the cortical activation following tactile-on and tactile-off stimulations in experiment\textsuperscript{58).} We used a mechanical stimulator driven by a piezoelectric actuator (Fig. 12a and b). MS were applied to the tip of the right index finger. The interstimulus interval was set at 2000 ms, including a constant stimulus of 1000 ms duration (Fig. 12c). Prominent SEFs were recorded from the hemisphere contralateral to the stimulated side approximately 57 ms and 133 ms after the onset of tactile-on
The source activities for P50m and P100m significantly increased concurrently with the number of pins used for MS (Fig. 15). However, the increased ratios for the source activities according to the increase in the number of pins were significantly smaller than that induced by electrical stimulation (Fig. 16). When the number of the pins doubled from 1-pin to 2-pins, from 2-pins to 4-pins, and from 4-pins to 8-pins, S1 activities increased by only 130%.

In addition, two pins were used in experiment 7 to examine the effect of the inter-pin distance on SEFs. The pin diameter and protrusion height were the same as those used in experiment 6. The distances between two pins were set to 2.4, 4.8, and 7.2 mm (Fig. 14c). Three types of MS (with inter-pin distances of 2.4, 4.8, and 7.2 mm) with 1 ms duration of protrusion were applied to the tip of the right index finger at 2 Hz. The source activities significantly increased when the inter-pin distance was increased from 2.4 to 7.2 mm. The source activities for both P50m and N100m elicited by MS with an inter-pin dis-
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(a) Sequence of the pins used in experiment 6. Two arrays of four tiny pins (1-, 2-, 3-, 4-, or 8-pins) were used. The distance between pins was set at 2.4 mm. (b) Pattern example of the mechanical stimulus in experiment 6. The interstimulus interval was set at 500 ms, including 1 ms for stimulus duration. (c) Sequence of the pins used in experiment 7. Two tiny pins were used and the inter-pin distances were set at 2.4, 4.8, and 7.2 mm. (Onishi et al., 2013)

Fig. 14 (a) Sequence of the pins used in experiment 6. Two arrays of four tiny pins (1-, 2-, 3-, 4-, or 8-pins) were used. The distance between pins was set at 2.4 mm. (b) Pattern example of the mechanical stimulus in experiment 6. The interstimulus interval was set at 500 ms, including 1 ms for stimulus duration. (c) Sequence of the pins used in experiment 7. Two tiny pins were used and the inter-pin distances were set at 2.4, 4.8, and 7.2 mm. (Onishi et al., 2013)

(b) Above 1000 stimuli

(c) 2.4 mm 4.8 mm 7.2 mm

Fig. 15 (a) Grand averaged source waveforms across subjects elicited by each set of pins used for mechanical stimulation. (b) The mean source activities of each component were summarized to compare the source activities among the pin numbers for mechanical stimulation. (Onishi et al., 2013)

*1: P50m: 8-pins > 4-pins (p < 0.01), 3-pins (p < 0.01), 2-pins (p < 0.01), 1-pin (p < 0.01)
*2: P50m: 4-pins > 2-pins (p < 0.05), 1-pin (p < 0.01)
*3: N100m: 8-pins > 4-pins (p < 0.05), 3-pins (p < 0.01), 2-pins (p < 0.01), 1-pin (p < 0.01)
*4: N100m: 4-pins > 1-pin (p < 0.05)
tance of 7.2 mm were significantly larger than those elicited by MS with an inter-pin distance of 2.4 mm (Fig. 17). The number of stimulated receptors appeared to increase as the inter-pin distance and the number of pins increased. These findings clarified the effect of the number of pins and inter-pin distance for MS on SEFs.

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this article.

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