Neuromagnetic analysis of the late phase of the readiness field for precise hand movements using magnetoencephalography

Author(s)
Takahashi, M; Watanabe, Y; Haraguchi, T; Kawai, T; Yamane, GY; Abe, S; Sakiyama, K; Hiraide, Y; Lee, WH; Ide, Y; Ishikawa, T

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Original Article

NEUROMAGNETIC ANALYSIS OF THE LATE PHASE OF THE READINESS FIELD FOR PRECISE HAND MOVEMENTS USING MAGNETOEENCEPHALOGRAPHY


Oral Health Science Center, Department of Orthopedic Surgery, Ichikawa General Hospital, Tokyo Dental College, 5-11-13 Sugano, Ichikawa, Chiba 272-8513, Japan
* Department of Oral Medicine, Tokyo Dental College, 5-11-13 Sugano, Ichikawa, Chiba 272-8513, Japan
** Department of Anatomy, Tokyo Dental College, 1-2-2 Masago, Mihama-ku, Chiba 261-8502, Japan
*** Department of Operative Dentistry, Tokyo Dental College, 1-2-2 Masago, Mihama-ku, Chiba 261-8502, Japan

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Abstract

The aim of this study was to elucidate the cortical regulation of precise finger movements by using magnetoencephalography, with particular emphasis on the late phase of the readiness field. Magnetic brain signals were recorded non-invasively by 306 channel magnetoencephalography during the following two tasks. The first task, a simple task, was to bend the right thumb once as quickly as possible. The second task, a precise one, was to alternately oppose the thumb with the index finger and the middle finger of right hand. In this study, we confirmed that the differences between the two tasks were observed in the late phase of the readiness field, especially in the magnetic field 600 ms before the onset of movement. The activity of the magnetic field of the precise movement task was higher than the activity of the simple movement task. There were obvious differences in the spatial and temporal aspects of the left hemisphere. In the simple movement, the premotor area or motor area was activated in the late phase of the time window. The average latency from the EMG onset was 98.6 ± 34.0 ms (n = 5). In the precise movement, the prefrontal area and the SMA were activated in the early and/or middle phases of the time window. The average latency from the EMG onset was 292.0 ± 14.9 ms (n = 3) for the prefrontal cortex and 167.8 ± 38.3 ms (n = 4) for the SMA. The premotor area or motor area was activated in the late stage of the RF. The average latency from the EMG onset was 111.6 ± 61.4 ms (n = 5). Many studies have been performed on the movement-related readiness field. However, the activity of the prefrontal area was higher than the activity of the prefrontal movement task. There were obvious differences in the spatial and temporal aspects of the left hemisphere. In the simple movement, the premotor area or motor area was activated in the late phase of the readiness field. Our study indicated that the prefrontal area and the SMA played important roles immediately before the onset of precise finger movement. The integration of the prefrontal area, the SMA, and the premotor area is important for the onset of precise finger movement.

Key words: Magnetoencephalography—Precision movement—Readiness field—Prefrontal area—Supplementary motor area

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INTRODUCTION

The brain and hand provided humans with the ability to develop science and culture. They have also played important roles in manufacturing and expression. There are no parameters other than deftness and clumsiness for objective evaluations of precise hand movements. A high level of central control is needed to move hands precisely\(^{11,22,28,29}\). Magnetoencephalography (MEG) should make it possible to evaluate such precise movements to some degree. The spatial localization of cerebral cortex activity during finger movements has been examined non-invasively in normal adults using fMRI and PET\(^{1,27,33}\). MEG does not record brain activity due to changes in the blood flow of the brain as fMRI and PET do, but MEG detects the magnetic field, which gives the equivalent current for the cerebral neuron, and thus provides its location image. Using this method, function and information transfer in the neural activity can be observed non-invasively. MEG also provides an excellent temporal resolution in the order of milliseconds against the seconds required for fMRI\(^{13}\). This study clarified the significance of the spatial and temporal progress by comparing and examining activities in the cerebral cortex during the preparatory stage of voluntary extension motions of the human finger.

SUBJECTS AND METHODS

1. Subjects and tasks

The protocol of this study was approved by the Ethical Committee of the Oral Health Science Center at the Tokyo Dental College. Five healthy males (mean age 27 years, range 25–30 years) who gave their informed consents participated in the study. None of the subjects had a history of hand motion problems in terms of subjective or objective symptoms. All of subjects were right-handed as assessed with a modified version of the Edinburgh Inventory\(^{24}\). Each subject was instructed to sit in a relaxed position in a magnetically shield room with his head supported against the helmet-shaped sensor array of the magnetometer. Subjects were instructed to keep their eyes open naturally and gaze at a spot of light illuminated on a screen placed about 1 m in front of them.

The first work was a simple movement task, bending the right thumb once as quickly as possible while the right arm and the right four fingers were fixed in the rest position by a regin splint and bandage. The second task was a precise movement task, alternately opposing the thumb with the index finger and the middle finger of the right hand under the same conditions. After each task, subject was instructed to return the thumb to the rest position to be ready for the next movement. The mean time of each movement was about 5 s (shown in Fig. 1). More than 50 single epochs were recorded with a five minutes break for each of the two tasks. Each subject took part in at least two sessions with pauses.

2. Data recording

Magnetic brain signals were recorded non-invasively with 102 pairs of gradiometers from 102 loci in the cerebral cortex using a MEG (Vectorview, Neuromag Co., Helsinki, Finland). To monitor eye movements, an electro-oculogram (EOG) was recorded using a pair of electrodes placed on the upper and lower orbital regions. Electromyograms (EMGs) were recorded using a pair of surface electrodes attached to the right flexor pollicis longus muscles. During the recording session, subjects were instructed to concentrate on performing these above-mentioned two tasks. EOG, EMG, and MEG signals were monitored throughout the session with a computer display in an operating room. The behavior of the subject was also monitored from the operating room using a video camera. Raw data were stored on a CD-ROM disk for off-line analyses. All signals were digitized at 401 Hz and were band pass filtered (0.03–15 Hz for MEG and EOG and 100–200 Hz for EMG).

In order to localize magnetic sources due to the task on MR image, the locations of
three anatomical landmarks (the nasion and the bilateral preauricular points) and of four head position indicator (HPI) coils attached to both sides of the lateral upper borders of the forehead and mastoid processes were determined with a three-dimensional digitizer (Isotrak, Polhemus Inc., VT). The exact locations and orientations of the sensors with respect to the head were determined by measuring the magnetic fields produced by currents leading to the HPI coils. We measured the position of the head before and after the experiments. When the head movement did not exceed 1 cm between sessions, we were advanced to the analysis. MRIs of all subjects were acquired with a 1.5-T Siemens Magnetom TM system. The reference points were marked in the MRI, and MEG/MRI coordinate systems were aligned using these marked points with the locations of the digital anatomical landmarks.

The MEG signal trace recorded for 3,000 ms in duration, starting 2,500 ms before the EMG onset and 500 ms after the EMG onset during the two tasks. The onset was determined by the time when the EMG of the right flexor pollicis longus muscles exceeded a certain level (17.5 ± 1.7 μV: the finger movement task). Before averaging, the spontaneous signals were reviewed in off-line to exclude inadequate triggering signals so that epochs containing eye motion artifacts, ambiguous EMG bursts, or other artifacts were omitted from the analysis. The mean number of remaining artifact-free trials in one session was 50 (range 50–56). One hundred epochs, added from two sessions of each task, were averaged for each task. Isocontour maps were constructed from the measured data at selected time points by the method of minimum-norm estimates. To identify the sources of movement-related magnetic fields, the signals were divided into several periods. During each period, one equivalent current dipole (ECD) was first determined by a least-squares search for a subset of channels over the areas where movement-related magnetic fields were visually detected. Only ECDs attaining more than 85% of the goodness-of-fit (gof) and less than 268 mm³ of 95%-confidence-volume were accepted for analysis, in which the entire time period and all the channels were taken into account for computing the parameters of a time-varying
multidipole model®. The ECDs were then superimposed on the subject’s MRIs to show the source locations with respect to anatomical structure.

RESULTS

1. Signal configuration

The magnetic components of brain mag-
netic activities in all five subjects during the two tasks are shown in Fig. 2. Each trace contains 102 lines for 3,000 ms of magnetic force recorded by 204 sets of sensors aligned over the head. These contrasted magnetic waves confirmed the previous differences between the two tasks. In four of the five subjects, the precise movement-related activities were distributed for 600 ms before the EMG onset. The simple movement-related activity is evoked in the late stage of the recording window.

Figure 3 illustrated the value of root mean square (RMS) of the magnetic field strength taken from 204 sensors during two tasks of subject 4, starting 700 ms before the EMG onset and ending 300 ms after the EMG onset. In the simple movement, the activity of the RF (readiness field) was indistinct before the EMG onset. The peak of the movement-evoked field (MEF) I, the MEF II, and the MEF III was identified after the EMG onset. The latencies of MEF I, MEF II, and MEF III were about 70, 170, and 250 ms, respectively, after the EMG onset.

In the precise movement, the activity of the RF was distinct before the EMG onset. The slow readiness field evoked the MF (motor field). Then, a large magnetic activity was evoked for about 300 ms after the EMG onset. The three peaks of the MEF I, MEF II, and MEF III were indistinct.

2. Spatial and temporal aspects of the cortical loci of current source in the simple and precise finger movements

Spatial and temporal aspects of the cortical loci of the current source estimated by the simple and precise finger movement-related MEG signals are shown in Fig. 4. The cortical loci of the current source estimated by the MEG signals 400 ms in duration, starting 400 ms before the EMG onset and ending at the EMG onset, were plotted successively in time sequence at the cortical loci of the prefrontal area, the SMA, and the premotor area. Examples of the current source on MR images in the prefrontal area, the SMA, and the premotor area estimated from MEG recordings are shown on the right side of the graph. (The right side of MRI: the right side of the head. The left side of MRI: the left side of the head.) Graph: The closed circles indicate the spatio-temporal aspect of the current sources for each subject in the precise movement task. Open squares indicate the spatio-temporal aspect of the current sources for each subject in the simple movement task. The current sources were registered at the prefrontal area in three of the five subjects and at the SMA in four of the five subjects in the precise movement task. At the premotor area, the current sources were registered at the premotor area in all subjects in both tasks. The mean latency and S.D. at each locus are shown in the left most side of this figure (*: precise movement task, **: simple movement task).
before the EMG onset are plotted successively in time sequence at the prefrontal cortex (Broadman’s area (BA) 8, 9, 10, 11, 12, 13, 44, 45, 46), the supplementary motor area (SMA) (BA 6), the premotor area (BA 6). In the two tasks, the estimated ECDs fitted the standard values (see Methods).

In the simple movement, the premotor area or motor area was activated in the late phase of the time window. The average latency from the EMG onset was $-98.6 \pm 34.0 \text{ms} (n=5)$. In the precise movement, the prefrontal area and the SMA were activated in the early and/or middle phases of the time window. The average latency from the EMG onset was $-292.0 \pm 14.9 \text{ms} (n=3)$ for the prefrontal cortex and $-167.8 \pm 38.3 \text{ms} (n=4)$ for the SMA. The premotor area or motor area was activated in the late stage of the RF. The average latency from the EMG onset was $-111.6 \pm 61.4 \text{ms} (n=5)$. In the two tasks, the activation loci estimated (prefrontal area, the SMA, and the premotor area) were lateralized to only the left hemisphere. Thus, this study showed only the contralateral activation of the cerebral cortex preceding the movement.

**DISCUSSION**

Cortical magnetic fields accompanied by voluntary finger movements generally include slow magnetic fields preceding the movement [5,6,12,21]. This study showed a difference between the magnetic field activities of the two tasks before the EMG onset. The ECDs were estimated with more than 85% of the field variance and less than $268 \text{mm}^3$ of 95% confidence-volume. In this study, we examined slow magnetic fields preceding the finger movement. Erdler et al. [7] classified the slow cortical magnetic fields preceding voluntary finger movements into two components: the Bereitschafts fields (BF) 1 and BF 2, which emerge 1.9–1.7 s and about 0.5 s before the onset of the movement, respectively. The current sources producing the former were localized in the SMA, while those producing the latter were located in the primary motor area. Transcranial magnetic stimulation of the human brain revealed that the excitability of pyramidal tract motoneurons started to elevate 80–120 ms before the onset of voluntary finger movements [4,10,30], indicating that the readiness field (RF) starts earlier than the activation of pyramidal tract motoneurons, which are directly involved in the execution of movements. The changes in the magnetic field could be analyzed in only one subject performing the task of the single thumb movement (shown in Fig. 3). We believe that brain cortex activity at a low level is induced during weak voluntary movement such as simple thumb bending. In the task of alternately opposing the thumbs with the index finger and the middle finger on the same side, the activity of the SMA and the premotor area was induced in all five subjects in the preparatory stage of the motion from about 600 ms before the onset of movement (shown in Fig. 3). In the next section, we discuss the confirmed activities of the prefrontal area, the SMA, and the premotor area.

1. **Prefrontal area**

The prefrontal area includes a large region; BA 8, BA 9, BA 10, BA 12, BA 13, BA 44, and BA 46. In three of the five subjects in this study, activities of the prefrontal area were estimated in BA 9 or BA 46 (shown in Fig. 4). No previous studies analyzing activities in the prefrontal area using MEG have been published. A clinical study reported that damage to the prefrontal area hindered complicated movements [18,19]. The prefrontal area contains a number of neurons which are activated by flexion and extension of the wrist. The prefrontal area is not involved in the functions of kinesthesia or accepting direction of movements. Therefore, it has been considered that the prefrontal area regulates spatial recognition and movements and is involved in higher motor functions [14,20]. The prefrontal area plans a series of movements, executes the movement plan, and then assesses whether the movement has been carried properly or not.

In this study, the activities in the prefrontal area were not observed during simple move-
ments but rather during precise movements before the SMA or the premotor area were activated (shown in Fig. 4). These findings suggest that the activities in the prefrontal area are essential for complicated behaviors such as precise movements. The prefrontal area carries out higher functions than the SMA or the premotor area.

2. **Supplementary motor area (SMA)**

When the SMA is damaged, tension of the proximal muscle increases\(^{31}\). When the SMA is stimulated, the proximal muscle is activated\(^{25}\), thus suggesting that the SMA controls the proximal muscle. Brinkman and Porter\(^{2}\) have been reported that the SMA was activated during finger movements. The SMA is associated closely with spontaneous movements\(^{15}\), especially activated strongly during memory-based intrinsic movements\(^{23}\). In a study of piano players, the amount of blood flow in the posterior side of the SMA increased when the subjects played songs that they had memorized, but blood flow in the anterior side of the SMA increased when they played songs which were unfamiliar\(^{26}\). In this study, SMA activities were observed in four of the five subjects (shown in Fig. 4). These activities were observed in three of these subjects in the anterior area. When compared to the simple movement, alternatively touching the index and middle fingers with the thumb is more complicated.

Erdler et al.\(^{7}\) used whole-head MEG to measure SMA activities while instructing their test subjects to place their thumbs on each of the other four fingers, one by one. They reported that SMA activities began 1.9–1.7 s before the movement onset (shown in Fig. 4). In this study, we were able to estimate the active site of SMA using time-varying multi-dipole analysis. The task in our study was spontaneous, instantaneous, and intermittent, not continuous. As a result, the latency of SMA activity was longer than the result by Erdler et al.\(^{5}\).

3. **Premotor area**

The premotor area is a region anterior to the motor area that corresponds to BA 6. BA 6 is divided into the above-mentioned SMA and the premotor area. Anatomically, it is generally accepted that the premotor area closely correlates to the cerebellum and that it is involved in induced movements. When compared to the motor area, the ratio of neurons that are active during the preparation period for motoneurons becomes higher\(^{20}\). A clinical study indicated that a lesion in the premotor area hindered contralateral skill movements\(^{8}\). During forelimb movements in animals, two types of information, spatial and body-part information, are integrated in the premotor area\(^{10}\). In our study, each subject was required to alternatively touch the index and the middle fingers using the thumb as the precise movement. When compared to the simple movement, more integration of spatial and body-part information was clearly required. In the regulation of this movement, the premotor area was activated following the excitation of the prefrontal area and the SMA (shown in Fig. 4).

4. **Concerning latency**

In the past, numerous studies have been made on the RF in humans. In most of them, the BF was evoked 1,000–2,000 ms before the movement onset, but it was only 600 ms in ours (shown in Fig. 3). It is unclear whether the BF was shortened or the prefrontal or SMA activities were added to the BF \(^2\). However, the sequence of activities from the SMA to the premotor area was maintained. Therefore, the BF was considered to be shortened. It is possible that an instruction such as “move as quickly as possible” affects the BF shortening. Libet et al.\(^{17}\) has suggested that recognizing the intention to perform a voluntary movement is faster than a movement accompanied with consciousness. This occurs about 200 ms before the start of the EMG. Furthermore, they concluded that the start of a voluntary movement is performed unconsciously. The voluntary control of a movement does not mean the start of a voluntary movement, but rather means the selection and control of that movement. The voluntary movement is
determined by the neurological processes for execution or termination of movement that start unconsciously. Our study indicates that the brain emphasizes conscious activities for controlling voluntary movements (shown in Fig. 4).

This hypothesis needs to be verified by instructing subjects to perform other tasks. The activity of the prefrontal area and the SMA occurred early, showing that these areas are closely related to the central regulation for precise movements. In the future, we will devise different tasks to measure the magnetic fields of precise movements of the fingers that require more voluntary control and compare our new data with the present results. Our intention is to reveal the central regulation of voluntary movements and precise movements.

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REFERENCES


NEUROMAGNETIC ANALYSIS OF PRECISE MOVEMENT


Reprint requests to:
Dr. Masanori Takahashi
Department of Orthopedic Surgery,
Ichikawa General Hospital,
Tokyo Dental College,
5-11-13 Sugano, Ichikawa,
Chiba 272-8513, Japan
E-mail: mtkhs@tdc.ac.jp