Volumetric Estimation of Functional Brain Regions in Small Children using Spatially Filtered Magnetoencephalography: Differentiating Thumb from Middle Finger

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ABSTRACT

It is difficult to localize the somatosensory cortex in children under 6 years using magneto-encephalography (MEG) with conventional median nerve stimulation. One main reason is that MEG data recorded from small children have poor signal-to-noise ratio due to their small heads and short hands. To find a better approach, this study investigated neuromagnetic activities following finger stimulation using spatially filtered MEG. Four healthy children have been studied with a whole cortex MEG system. Electric stimulation was applied to the thumb and the middle fingers with two Digital Rings. Two trials were recorded for each hand. Focal increases of spectral power were localized using spectrogram and synthetic aperture magnetometry (SAM). A clear response at a latency of 21 ms was identified in 3 children (3/4). Dipole modeling localized the somatosensory cortex in 2 children (2/4). SAM successfully localized the somatosensory cortex in 4 children (4/4). Interestingly, the functional region estimated for the thumb was significantly larger than that of the middle finger ($p < 0.01$). However, it is possible that this effect is due to a larger source amplitude rather than larger source volume. Our results demonstrated that the developed approach could map the somatosensory cortex in children ranging in age from 3 to 6. To our knowledge, this is the first report using non-invasive methods to provide quantitative data indicating that the functional area of the thumb is larger than that of the middle finger in small children.

KEY WORDS

Magnetoencephalography (MEG), Somatosensory evoked field, Children, Middle finger, Thumb, Synthetic aperture magnetometry (SAM), Spectrogram.

INTRODUCTION

MEG measurements can be used to noninvasively localize functional regions of the brain. Somatosensory evoked magnetic field (SEF) is very robust and reproducible, making it very useful for pre-surgical evaluation and functional mapping [Xiang, 2003]. SEF is commonly evoked by electric stimulation applied to the median nerve. However, according to our experience, it is very difficult to localize somatosensory cortex with the median nerve stimulation in small children for the following reasons: (1) Small children under 6 years are generally not cooperative; and it is difficult to find the median nerve. (2) Since small children have smaller heads and shorter hands than those of adults, the MEG data recorded from small children have poor signal-to-noise ratio (S/N). To find a better approach, this study used a new method called SAM to volumetrically localize the somatosensory cortex. Previous studies have demonstrated that the human thumb is functionally and morphologically different from the other digits, enabling capability for a wide range of movements and for precision grasping [Jarvelainen, 2002]. Since SAM has the potential to estimate the three-dimensional extent of a functional region, it is very interesting to find out if SAM can quantitatively differentiate the functional areas responsible for the middle finger and thumb in small children. This is particularly important for MEG study in children ranging in age from 3 to 6 for two main reasons: (1) we may find an objective and quantitative method to investigate the functional development of the brain in children. (2) This will be the first study to quantitatively and non-invasively estimate the functional regions in children.

METHODS

Subjects: Four children (2 girls and 2 boys, aged 3 – 6 years, with a mean age of 4.5 years) were studied. This study has been approved by Research Ethic Board (REB) at our hospital. Consent for the study was obtained from each subject's parents. Inclusion criteria for subjects were: (1) movement and sensation in both hands were normal; (2) child was cooperative.

Stimuli: A Grass electrical stimulation system (Astro-Med Inc., West Warwick, U.S.A) was employed in the current study. The Grass electrical stimulation system had dual outputs (A and B), which allowed us to stimulate the thumb and the middle finger sequentially with a 300 ms difference. The electric stimuli were constant voltage square-wave pulses; their duration was 0.3 ms. Digital Ring Electrodes (Medtronic of Canada Ltd., Mississauga, Canada) were used to stimulate the thumb and the middle fingers. The stimulation intensity was adjusted to a level where children felt itch but not painful.

MEG Recordings: A 151-channel whole cortex CTF OMEGA system was used for recordings (CTF Systems Inc., Port Coquitlam, Canada). Each primary MEG sensor consisted of an axial first-order gradiometer with a 2 cm diameter and 5 cm baseline. Gradiometer to gradiometer distance was approximately 3.2 cm. This system included an array of reference sensors, allowing for environmental noise cancellation up to third-order spatial gradient. MEG measurements were performed in a magnetically shielded room (MSR) with a white noise level of total system below 10 fT/√Hz. The localization of the subject's head relative to the sensor array was measured using three small coils affixed to the nasion and the pre-auricular points. The three coils were simultaneously activated at different frequencies and their positions were determined from their magnetic signals. The system allowed for head localization to an accuracy of 1 mm. Head shape was digitized with Polhemus (Polhemus Inc., Vermont, USA).

Data were recorded with noise cancellation of third-order gradients. The sampling rate of data acquisition was 1250 Hz. Four hundred trials were recorded for one session; two sessions were recorded for each subject. The analysis window was 50 ms before and 200 ms after the stimulus.

Data analysis: Six frequency bands including 8-15 Hz, 15-30 Hz, 30 – 60 Hz, 60-120 Hz, 120 – 200 Hz and 200 – 300 Hz were analyzed using SAM. The region of interest (ROI) was set to include the whole brain with a 2.5 mm voxel resolution. SAM T values were calculated from the changes in spectral power in each voxel between the active state (after stimulus) and the control states (before stimulus), and normalized by the variance using SAM. The volume of a functional region was calculated by using magnetic source locator (MSL) program [Xiang, 2003]. SAM estimated source activity, as a function of time, by immunizing signal power (variance). The task-related power change was represented by a T value, which was a measurement of the power difference between the active and control conditions normalized by the power of the noise. A SAM voxel with T value higher than 0 (threshold) was considered as an active voxel; a SAM voxel with T value lower or equal to 0 was considered as suppressive voxel or silent voxel, respectively. The active voxels were used to measure the functional region. The volume of a functional region was calculated by multiplying the number of total active voxels with the voxel resolution (2. 5 mm).

RESULTS

The results of waveforms showed that the first deflection (response) was very reproducible; it was evoked by both the thumb and the middle finger stimulations in 3 children (3/4). There was no significant difference between the two sessions in the 3 children. The waveforms following the right and left stimulations were very similar. Two children showed two responses and one child showed three responses. Since the first response was reproducible, this study focused on the first response. The latency of the first response was 21 ± 0.8 ms. There was no significant difference between the thumb and the middle finger in terms of waveform and contour map. Dipole modelling localized the left and the right somatosensory cortex in 2 and 3 subjects, respectively (dipole fitting error < 20%).

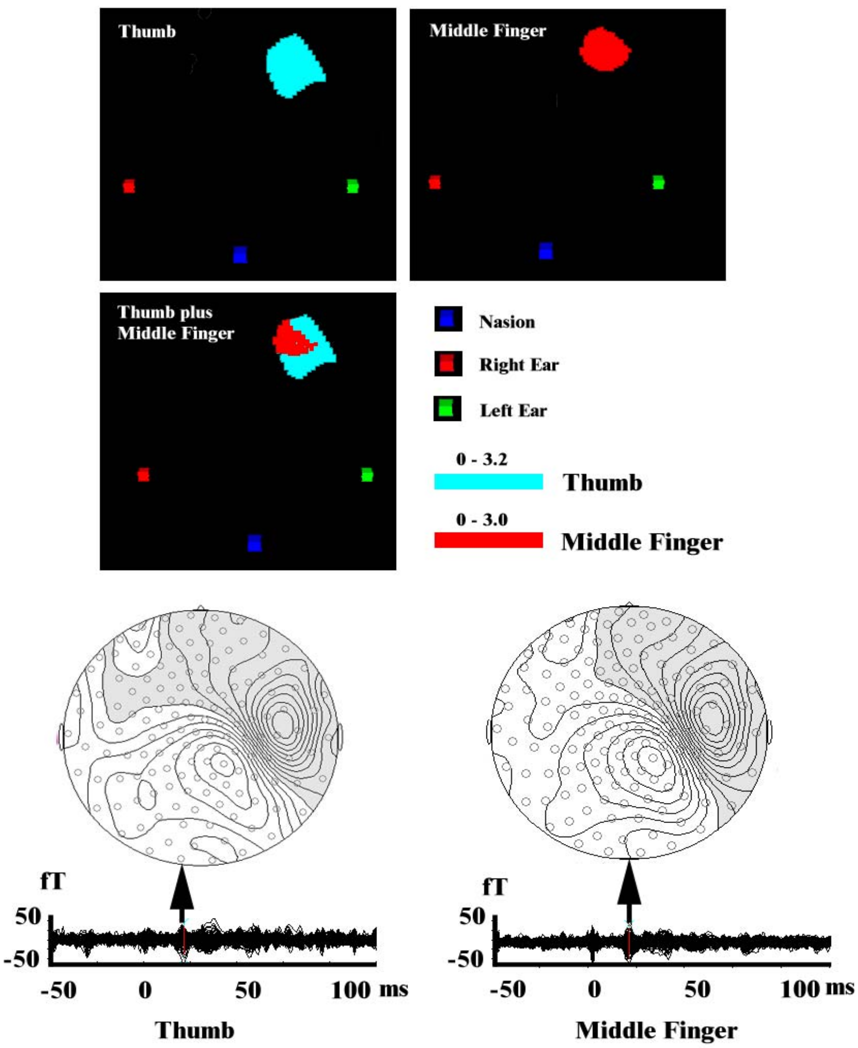

Figure 1. Waveforms, contour maps and SAM images from a representative child following electric stimulation applied to the thumb and the middle finger. The values indicated above the red and blue bars corresponding to the thumb and middle finger activations stand for SAM Student-T values, respectively. There is no significant difference between the thumb and the middle finger in terms of waveform and contour map. However, the extent of the reconstructed functional region of the thumb is significantly larger than that of the middle finger.

The results of SAM analysis demonstrated that the spectral distributions in the frequency bands of 8-15 Hz, 15-30 Hz, 120-200 Hz, and 200-300 Hz varied among subjects. In contrast, the spectral distributions in the frequency bands of 30-60 Hz and 60-120 Hz were reproducible and robust. One focal increase of spectral power (activation) was clearly identified in the left and right somatosensory cortices in 4 children (100%, 4/4). The most striking finding in this study was that the functional region estimated for the thumb was significantly larger than that of the middle finger ($p < 0.01$) in 60-120 Hz bands for both the left and right hemispheres. The volume measured for the right thumb and middle finger were 2344 ± 126 mm^3 and 1782 ± 122 mm^3, respectively. The volume measured for the left thumb and middle finger were 2385 ± 111 mm^3 and 1654 ± 197 mm^3, respectively.

DISCUSSION

This study has developed an approach to map the somatosensory cortex in children ranging in age from 3 to 6. In comparison with the conventional median nerve stimulation, finger stimulation is much easier to set up and is more acceptable to small children. The results of this study have demonstrated that electric stimulation of finger combined with SAM analysis can accurately localize the somatosensory cortex in small children, even when the conventional dipole based source localization failed. According to our experience, it is very difficult to record somatosensory evoked magnetic fields to electric stimulation applied to median nerve from children ranging in age from 3 to 6 years due to the fact that the small child cannot tolerate and/or keep still while his or her median nerve is stimulated. To solve this problem, we tried finger stimulation using digital ring electrode. Our results have demonstrated that the newly developed approach could clearly localize and delineate the somatosensory cortex corresponding to the thumb and the middle finger. We consider this result is very important for clinical application of MEG in functional brain mapping in paediatrics.

Quantitatively measuring brain functional areas corresponding to the thumb and the middle finger have not been reported, particularly in children ranging in age from 3 to 6 years. To reach our goal, we introduced a new software package, MSL, which allowed us to volumetrically estimate functional region by quantitatively measuring SAM voxels and/or T values for a selected 3D region. The most important finding in this study is the extent of the reconstructed functional region of the thumb and the middle fingers. The neuromagnetic difference between the thumb and the middle finger has been noted in adults [Jarvelainen, 2002]. Jarvelainen and colleagues have found that the somatosensory 20-ms responses differs for thumb and middle finger. The present study is the first volumetric study of the neuromagenetic activation in the somatosensory cortex in small children. This study used a systematic approach in visualizing and quantitatively measuring the three-dimensional neuromagnetic activation (Fig. 1). The results are interesting and important for two main reasons: (1) this study has gone beyond using MEG for merely localizing functional areas and our data have demonstrated that the methods could quantitatively describe the volumetric characteristics of two functional regions. (2) To our knowledge, this is the first non-invasive study showing the volumetric differences between the thumb and the middle finger in children ranging in age from 3 to 6 using MEG. Therefore, we consider this study has provided a new approach to investigate the development of the functional regions in children. However, caution is necessary in terms interpreting the volumetric results since the volume measure can be confounded by a change in the source amplitude.

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