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Effect of Transcranial Magnetic Stimulation on P300 of Event-Related Potential

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Abstract*— When the odd stimulation is presented, the positive component of electroencephalograph is induced at around 300 ms after the odd stimulation. This positive component is called P300. Many studies suggest that P300 may result from the summation of activity from multiple generators located in widespread cortical and subcortical areas. However, there is still no conclusive indication of the sources of P300. In this paper, we focus on the left supramaginal gyrus as one of the sources of P300. We investigated the temporal aspect of this area using TMS (transcranial magnetic stimulation). We investigated the relationship between the latency of the P300 and an effect of TMS when the left supramarginal gyrus was stimulated by TMS. In our previous study, we reported a method of removing stimulus artifact during TMS with Sample-and-Hold circuit and electroencephalogram (EEG) activity evoked by TMS could be measured successfully. In addition to this method, independent component analysis (ICA) was also applied to recorded EEG data in order to remove the stimulus artifact by off-line analysis. By using these methods, short latency (< 15 ms) EEG responses to TMS could be obtained. We stimulated the left supramarginal gyrus using a figure-eight coil during auditory oddball task. The TMS at 150 ms and 200 ms after the oddball sounds were presented. When the TMS was applied at 200 ms after the oddball stimulation, the peak response of P300 was delayed around 50 ms. Difference of the peak latency between the control measurement and the case of TMS applying at 150 ms was not significant. However, the differences of the peak latency of the control measurement and the peak latency of the measurement in the cases of TMS applying at 200 ms and 250 ms was significant (p<0.05). We considered that this delay was due to inhibiting to recognize the target stimulation.

I. Introduction

TRANSCRANIAL magnetic stimulation allows direct manipulating of cortical activity. Due to successful magnetic stimulation of the human brain [1, 2], TMS has become an important tool for studying the functional organization of the human brain. TMS applied with a figure-eight coil [3] provides a localized and vectorial magnetic stimulation on the cerebral cortex within a 5 mm [4, 5].

The combination of TMS and functional brain imaging techniques such as fMRI (functional magnetic resonance imaging), PET (positron emission tomography) and EEG has become an effective tool for the study of the dynamics of human brain.

It enables manipulating and measuring of cortical activity simultaneously. However, it is difficult to attain high temporal resolution imaging by combined TMS and PET [6, 7] or combined TMS and fMRI [8]. These methods have poor temporal resolution that is over 100 ms resolution. MEG and EEG are useful tools for high temporal resolution imaging. Ilmoniemi and co-workers [9-12] developed a concurrent EEG and TMS measurement system that allowed noninvasive evaluation of the cortical activity and functional connections among different brain areas. TMS-evoked EEG responses can be found to reflect the spread of activation from the cortical sites. The combination of TMS and EEG is an effective method to directly observe how the stimulation of superficial cortex evokes electrophysiological responses and reflect cortical activity. In previous studies, we observed that the alpha wave was suppressed by only cerebellum TMS [13] and developed the EEG measurement system to eliminate the electromagnetic interaction emitted from TMS [14]. There were several studies that revealed the connectivity from the stimulated cortical site to ipsilateral and contralateral cortical areas by the combined method of EEG and TMS [15]-[18].

In this study, we focused on the left supramaginal gyrus as one of the sources of P300 and investigated the relationships between the latency of the P300 and an effect of TMS when the left supramarginal gyrus was stimulated by TMS.

II. Material and Methods

In this study, healthy, right-handed six volunteers were studied as subjects. Subjects were asked to relax and sit on the chair. Subjects were put on the electrode cap with 60 channels. The reference electrode was pasted on the forehead skin and the ground electrodes were pasted on the earlobes. A temporary intercepting the input of the amplifier (sample and hold circuit) was equipped in the electroencephalograph (Nexstim Ltd., Helsinki, Finland), which was controlled by the trigger signal from the magnetic stimulation device. Applying such improved electroencephalograph, it proved that artifact could be removed. And the record of multi channel EEG under TMS can be obtained. EEG data were filtered from 0.1 Hz to 350

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Hz, and the data were sampled at 1450 Hz. About 100 intervals were averaged with the trigger at TMS onset. The data was analyzed from 50 ms pre-stimulus to 600ms post-stimulus. The data were low-pass digital filtered at 200 Hz.

We stimulated the left supramarginial gyrus using a figure-eight coil. Stimulus intensity of TMS was determined based on the threshold intensity of the muscle movement when the motor area was stimulated. The stimulus intensities were 80 % of motor threshold. A figure-of-eight 70mm coil was used (inner diameter: 53 mm, outer diameter: 73 mm) and was kept tangentially over the scalp by a mechanical holder. The magnetic flux density at the center of each coil was around 1 T (pulse width 0.1 ms, mono phase). Direction of the induced current of TMS was from posterior to the anterior. The TMS at 150 ms, 200 ms, and 250 ms after the oddball sounds were presented. An auditory oddball task was presented with sequences of sounds containing deviant (2 kHz pure tone) and standard (1 kHz pure tone) stimuli. The deviant stimulus occurred in 20 % of all presented sounds. Stimuli were presented with a fixed inter-stimulus interval of 2500 ms.

EEG was recorded in the electric shield room. We removed the TMS artifacts by applying Infomax ICA [19]. The observed random vector X is presented by the mixing matrix A:

$$X=AS$$

where X is the observed vector and vector S contains the independent components. The task is to estimate both the mixing matrix A and the sources S from X. In this study, Infomax ICA was used to estimate independent component S.

III. RESULTS

Fig. 1 shows the EEG of a 60 channels of the whole head with stimulus point. It was possible to measure the evoked EEG after 10 ms of stimulation.

Fig.2 shows the original EEG waveforms that contained artifacts by TMS. Fig.3 shows the calculated independent components by using Infomax ICA. Fig.4 shows EEG waveforms without artifact components.

Fig.5 shows the time sequence of stimulation. The TMS at 150 ms, 200 ms, and 250 ms after the oddball sounds were presented. Fig.6 shows the EEG waveforms of subject A at Cz. Upper figure is the control waveform without TMS and the other figures are the waveforms after TMS stimulation. When the TMS was applied at 200 ms and 250 ms after the oddball stimulation, the peak responses of P300 were delayed around 50 ms and 90 ms. However, in the case of TMS applying at 150 ms the auditory oddball stimulation, this delay was not observed. Fig.7 shows the EEG waveforms of subject B at Cz. In this case, the peak responses of P300 were similar to Fig.6. Fig.8 shows the mean values and the standard deviations of P300 latency in the six subjects. Difference of the peak latency between the control measurement and the case of TMS applying at 150 ms was not significant. However, the differ-

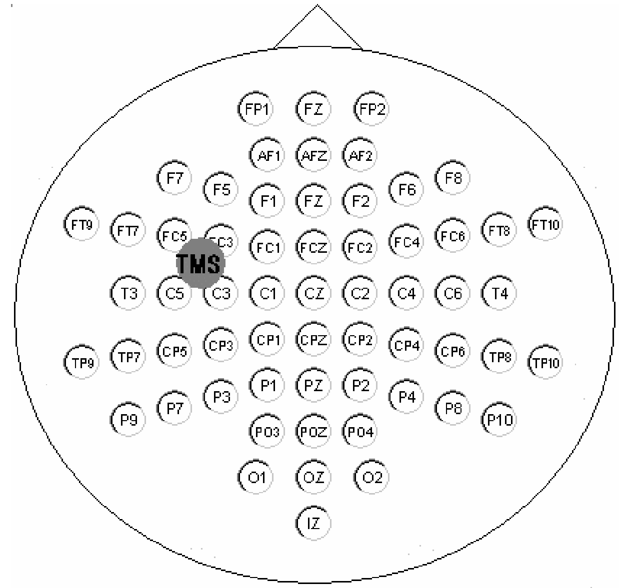

Fig.1 Electrode positions and stimulus point. Stimulus point (gray circle) corresponds to the left supramarginial gyrus.

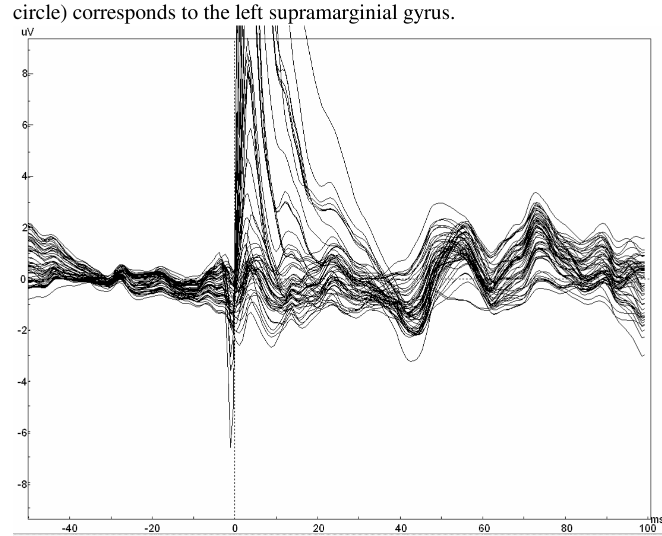

Fig.2 Original waveforms that contained artifacts by TMS

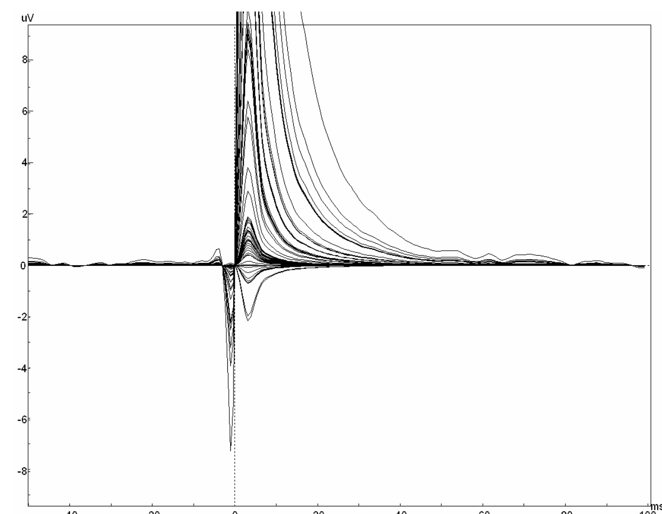

Fig.3 Artifacts that were evoked by TMS

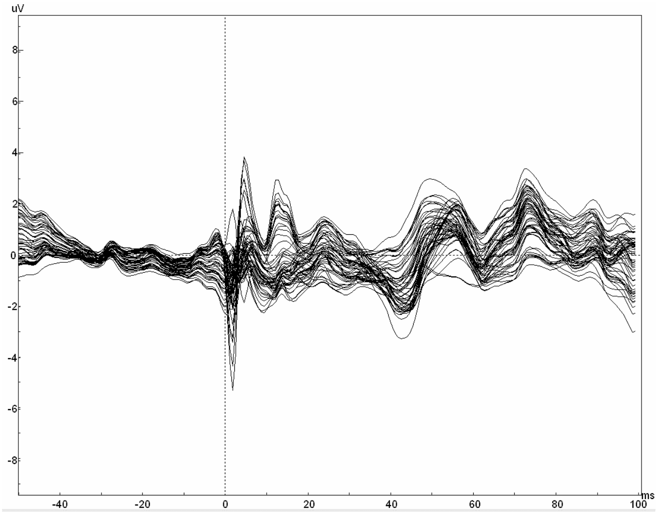

Fig.4 Processed EEG waveforms without artifact components

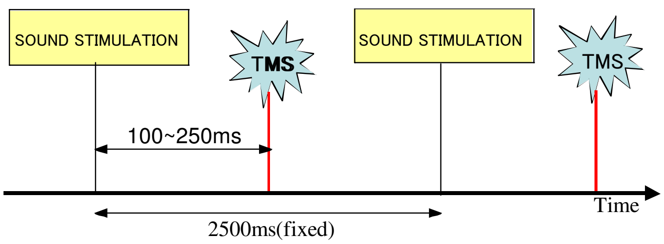

Fig.5 Time sequence of stimulation

ences of the peak latency of the control measurement and the peak latency of the measurement in the cases of TMS applying at 200 ms and 250 ms was significant ($p<0.05$).

IV. Discussion

The combination of TMS with EEG represents a powerful tool to study the effects of TMS-induced cortical reactions, thus providing useful information about the neurophysiological processes underlying TMS.

When the auditory oddball stimulation is presented, the positive component of EEG is induced at around 300 ms after the stimulation. Many studies suggest that P300 may result from the summation of activity from multiple generators located in widespread cortical and subcortical areas [20]. There are dorsolateral prefrontal, supramaginal gyrus, and cingulated gyrus as the P3a generators. There are ventrolateral prefrontal, superior temporal sulcus, and medial temporal as the P3b generators. However, there is still no conclusive indication of the sources of P300. In this paper, we focused on the left supramaginal gyrus as one of the sources of P300 because of easy stimulating. The main finding of this study is the delay of P300 in the case of TMS applying at several hundred ms after the auditory oddball stimulation.

About the delay of P300 latency in the case of TMS applying at 200 ms and 250 ms after the oddball sound stimulation, we considered that this delay was due to inhibiting to recognize the target stimulation. These results suggest that the left supramarginal gyrus contributes the generating P300 component at around 200 ms after oddball stimulation.

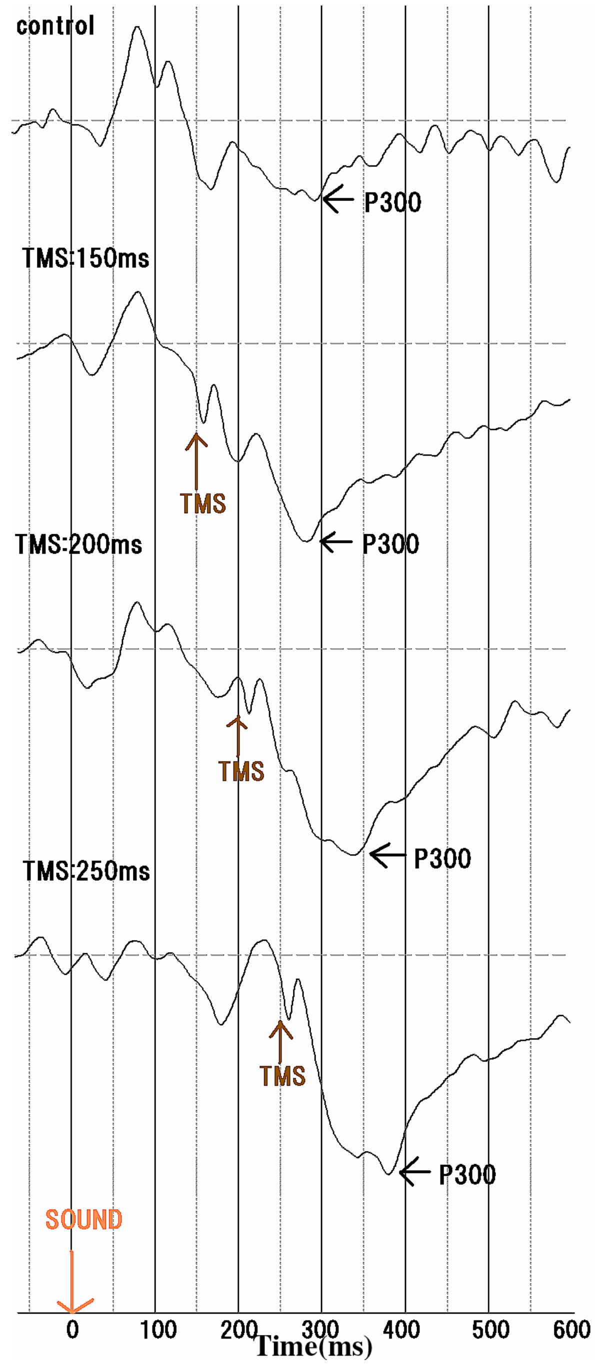

Fig.6 EEG waveforms of subject A at Cz. Upper figure is the control waveform without TMS and the other figures are the waveforms after TMS stimulation. When the TMS was applied at 200 ms and 250 ms after the oddball stimulation, the peak responses of P300 were delayed around 50 ms and 90 ms. However, in the case of TMS applying at 150 ms the auditory oddball stimulation, this delay was not observed.

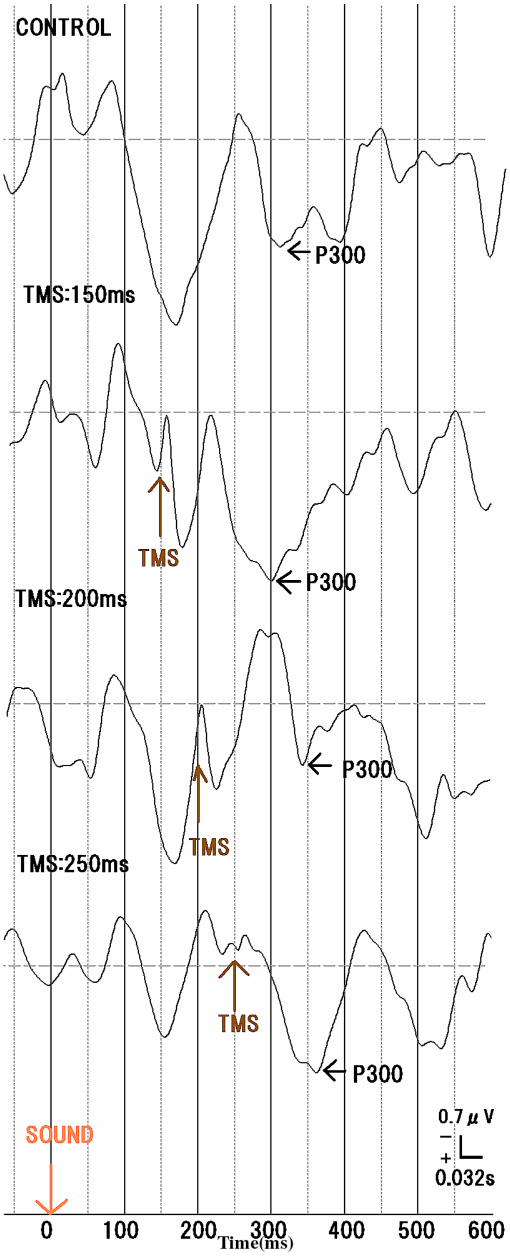

Fig.7 EEG waveforms of subject B at Cz. The peak responses of P300 were similar to Fig.6.

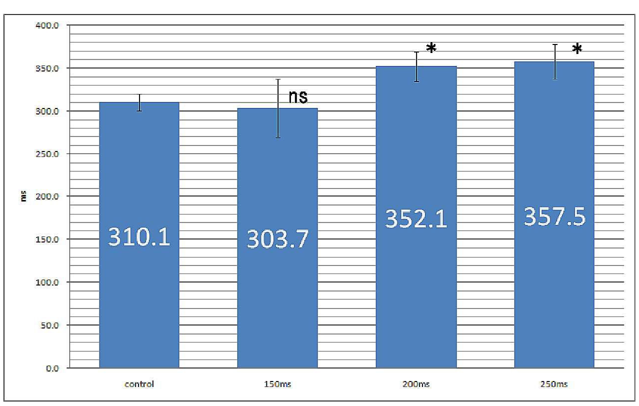

Fig.8 Mean values and standard deviations of P300 latency in the six subjects. ns : not significant. * : significant (p<0.05).

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