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EVALUATING THE ENTRAINMENT OF THE ALPHA RHYTHM DURING PHOTIC STIMULATION IN CONTROL SUBJECTS AND PATIENTS WITH ALZHEIMER'S DESEASE

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Abstract: To investigate sequential changes in magnetoencephalograms (MEGs) during photic stimulation (PS), we performed a quantitative MEG analysis of the alpha band (related to stimulus frequency) in 7 patients with Alzheimer's disease and 18 age-matched control subjects. Photic stimulation was at an interval of 0.5 Hz, and the frequency band was from 8 to 10.5 Hz. In each session, the interval lasted ten seconds and was repeated ten times for each frequency. In the topographic study, we assessed the differences between the two groups under two conditions (*i.e.*, during PS and inter-PS). We compared the energy intensity of each site based on international 10/20 derivation. The energy intensity in the patients with Alzheimer's disease was smaller than in the control subjects at each site. The significant changes in effect if photic stimulation could not be observed. These results confirms a widespread loss of functional interactions in the alpha band

Keywords: MEG, entrainment photic stimulation, Alzheimer's disease

. INTRODUCTION

Considering the increasing proportion of the lederly in both developed and developing countries, the increase in the incidence of dementia is an important issue that requires improved methods for diagnosing and treating dementia patients. This is particularly pertinent for preventable dementias, such as Alzheimer's disease (AD).

Magnetic resonance imaging (MRI), single photon-emission computer tomography and positron emission tomography (PET) have been used to diagnose AD clinically. Morphological and functional studies have revealed some common features of dementia, including a high level of atrophy relative to non-demented elderly people. In particular, the hippocampus and temporal lobe are usually the most atrophied areas in the brains of AD patients. In addition, cerebral blood flow and metabolic rate (oxygen consumption) are lower in patients with AD, particularly in the temporal-parietal-occipital are a[1]. Cerebral metabolic rate (glucose consumption) is lower in the temporoparietal area of AD patients. Finally, electroencephalograms (EEG) of AD patients commonly exhibit slow, spontaneous cortical activity, with decreased alpha and beta and increased delta and theta frequencies[2].

Photic stimulation has been used in clinical practice to detect abnormalities associated with mental disorders such as depression and schizophrenia. However, few studies have examined the effects of photic entrainment in dementia patients

Magnetoencephalography (MEG) has been used to evaluate entrainment using photic stimulation. MEG is a non-invasive technique that measures the magnetic fields generated by electrical activity in the brain. MEG has several advantages over other techniques: first, it offers a high degree of spatial resolution due to the combination of a large, fixed array of sensors and the absence of distortion of magnetic fields as they pass through the skull. Second, an MEG field pattern is one-third tighter than an EEG pattern. Finally, the use of the entire head in MEG imaging obviates the labor-intensive application of the many electrodes required for high-resolution EEG. Therefore, MEG is a powerful way to study the physiology of the rapidly spreading electric phase in the encephalon.

The aim of the present study was to investigate the nonlinear dynamic properties of components of MEG imaging in a light-entrainment paradigm.

. METHODOLOGY

A. Experimental setup

All MEG measurements were carried out in a magnetically shielded room at the hospital using a whole-scalp system (PQ1160C, Yokogawa Electric, with 160 coaxial gradiometers [dc SQUID, resolution: 5fT√Hz or less]). The average distance between gradiometers was 25 mm. The total resolution of this system was 10fT√Hz or less. The MEG was recorded at a sampling frequency of 500 Hz. EEGs were recorded simultaneously (NeurofaxEEG-1, Nikhon Koden, Japan), based on the international 10/20 derivation method. Intermittent photic stimulation based on a white LED was

used to stimulate the visual area. The stimulator (flicker, Yokogawa Electric) is a goggle type device with a 20° lateral visual angle and a 15° vertical visual angle. The stimulation intensity and emission time were 3 cd/m^2 and 5 ms ± 10%, respectively. Subjects with their eyes close and in a supine position were stimulated with light flashes (mean intensity: 3 cd/m^2; duration: 5 ms; frequency: 8-10.5 Hz) from light-emitting diodes (LED) mounted in a pair of goggles.. Photic stimulation was carried out for 10 s, followed by a 10-s period in which there was no photic stimulation. This cycle was repeated 10 times for a total trial period of 210 s. We applied six stimulation frequencies (F_{Stim}) from 8 to 10.5 Hz in increments of 0.5 Hz. This cycle was repeated 10 times for a total trial period of 210 s.

B. Subjects

Experiments were performed with 7 patients with Alzheimer's disease (2 males [age 76.5 ± 6.0 years] and 5 females [age 77 ± 7.2 years]). For comparison, 18 age-matched healthy subjects (8 males [age78.5 ± 7.2 years] and 10 females [age 76.9 ± 5.0 years]) participated in this study.

This study was approved by the ethics committee of Fujimoto Hayasuzu Hospital, and all of the subjects gave written informed consent before examination.

C. Signal processing

After MEG recordings were done, the 2nd Butterworth low-pass filter was applied to the MEG signals, with a cutoff frequency of 50 Hz. Then, we sampled the signals at a frequency of 100 Hz. We estimated the power spectral densities of the MEG signals during each stimulation or non-stimulation period using FFT and calculated the energy intensity related to the stimulation frequency (F_{Stim}). The low- and high-cutoff frequencies of the energy intensity were F_{Stim}–0.5 Hz and F_{Stim}+0.5 Hz, respectively.

The topographic data were obtained from the 160-ch energy intensities at each stimulation period.

To compare the MEG activities during the stimulation period between the patients with Alzheimer's disease and control subjects, the energy intensities were normalized using those of the first non-stimulation period. The energy intensity ratio (R) was obtained using $R=E_s/E_n$, where E_s and E_n are the energy intensities during the stimulation and first non-stimulation periods, respectively. The comparison and evaluation regions of MEG activity were the same as for the derivation method of the international 10/20 EEG.

The energy intensities of the EEG activity also were calculated and evaluated using the same method applied for the MEG.

The energy intensities of EEG activity were also calculated and evaluated using same method applied to MEG.

.RESULTS

We examined six different stimulation frequencies (F_{Stim}) from 8 to 10.5 Hz to identify the characteristic frequency of the entrainment phenomena in the control and Alzheimer group. We found that different stimulation frequencies produced similar tendencies in each group. Therefore, we observed no significant differences at any particular frequency.

Figure 1 shows a typical example of the topographic data in the patient with Alzheimer's disease.

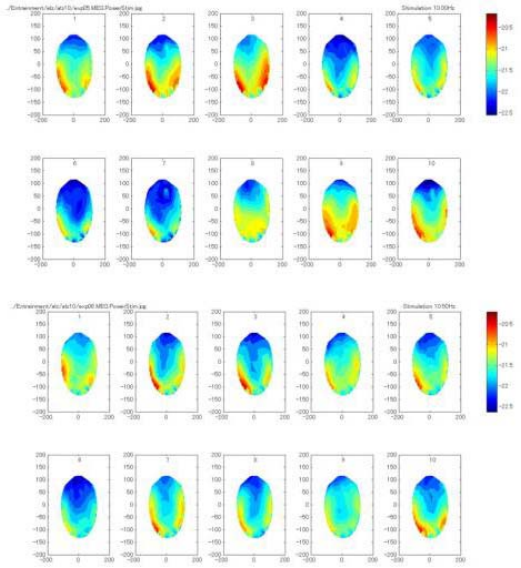

Figure 1 *Typical topographic data* ***during photic stimulation in a patient with*** *Alzheimer's disease by stimulating frequency of 10 (upper half) and 10.5Hz(lower half.)*

During the stimulus, the absolute 8-10.5 Hz band energy of both the control subjects and the patient group was higher at posterior site than at the anterior site throughout the ten-second periods. The total energy intensities were higher in the control group than in the patient group. The signal intensity in posterior has been changes in time and the topographic data show not uniformly activated in posterior site by the stimulated frequency.

Figure 2 shows the energy intensity of Alzheimer female patients and age matched female control subjects.

In females, the patients with Alzheimer's disease had lower MEG energies in all region compared to the control subjects, but no significant values even in the P and O regions, are obtained (P<0.05).

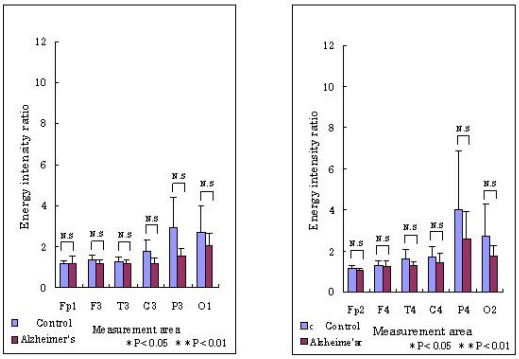

Figure 2. MEG energy intensity in female control (light bars) and subjects with Alzheimer's disease (dark bars)

Figure 3 shows the energy intensity of Alzheimer male patients and age matched female control subjects.
There were no significant differences of energy between the controls and Alzheimer subjects in all regions.

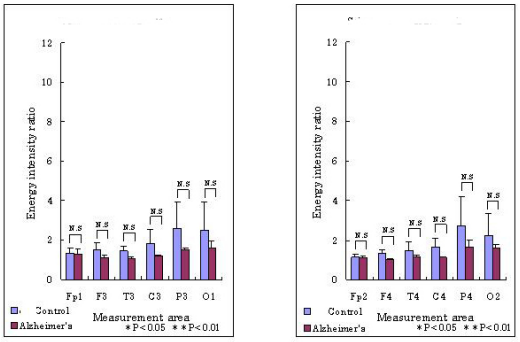

Figure 3. EEG energy in male control (light bar) and Alzheimer patient (dark bar)

The EEG energies showed similar tendencies in the male and female groups. Although small number of patients performed in this experiment, no significant gender differences were observed in the Alzheimer group. In addition, we saw no major change in the topography of the MEG energy based on visual observation in terms of number of trail.

. DISCUSSION

We estimated the energy intensity on photic stimulation in both control and patient with Alzheimer's disease. We focused on the comparison of the EEG and MEG, gender differences, and the influence of patients with Alzheimer's disease.

The EEG and MEG signals were similar. However, photic stimulation induced activation of the visual cortex (O region) in the EEG, while the MEG signal was activated in both the O and P regions.

Various studies have reported gender differences in EEG entrainment phenomena [3,4,5]. Females generally have a higher amplitude in the resting EEG than males, with significant differences in the delta, theta, alpha 2, and beta bands at limited electrode sites. The gender differences were more pronounced in EEG activity during photic stimulation, and females had a higher EEG amplitude in the frequency band identically or harmonically related to the stimulus frequency. These findings provide further evidence of gender differences in EEG activity in both stimulus and non-stimulus conditions. However, there are no significant difference in both EEG and MEG in control subjects in the elder control subjects..

The mechanism for the alpha rhythm in EEG and MEG has been studied extensively [6,7,8,9]. These studies suggested that the synchronization of alpha band is decreased in the patients with Alzheimer's disease. Our study confirmed energy intensity was lower in Alzheimer patients in the alpha band.

Furthermore, we must consider the influence of medication. In general, these antipsychotic medicines reinforce photic excitation reaction [4]. Although the subjects gained photic excitation reaction, their MEG energy related to the stimulation frequency decreased. Therefore, we suspect that the Alzheimer's disease caused the decrease in energy and loss of complex nonlinear interactions occurs between visual input and ongoing MEG activity.

.CONCLUSION

We measured spatio-temporal changes in higher brain function using MEG, focusing on the alpha wave. The patients with Alzheimer's disease show fewer changes in alpha activity during stimulus and this may reflect a widespread loss of functional interactions in the alpha band throughout the PS.

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