Figure 1

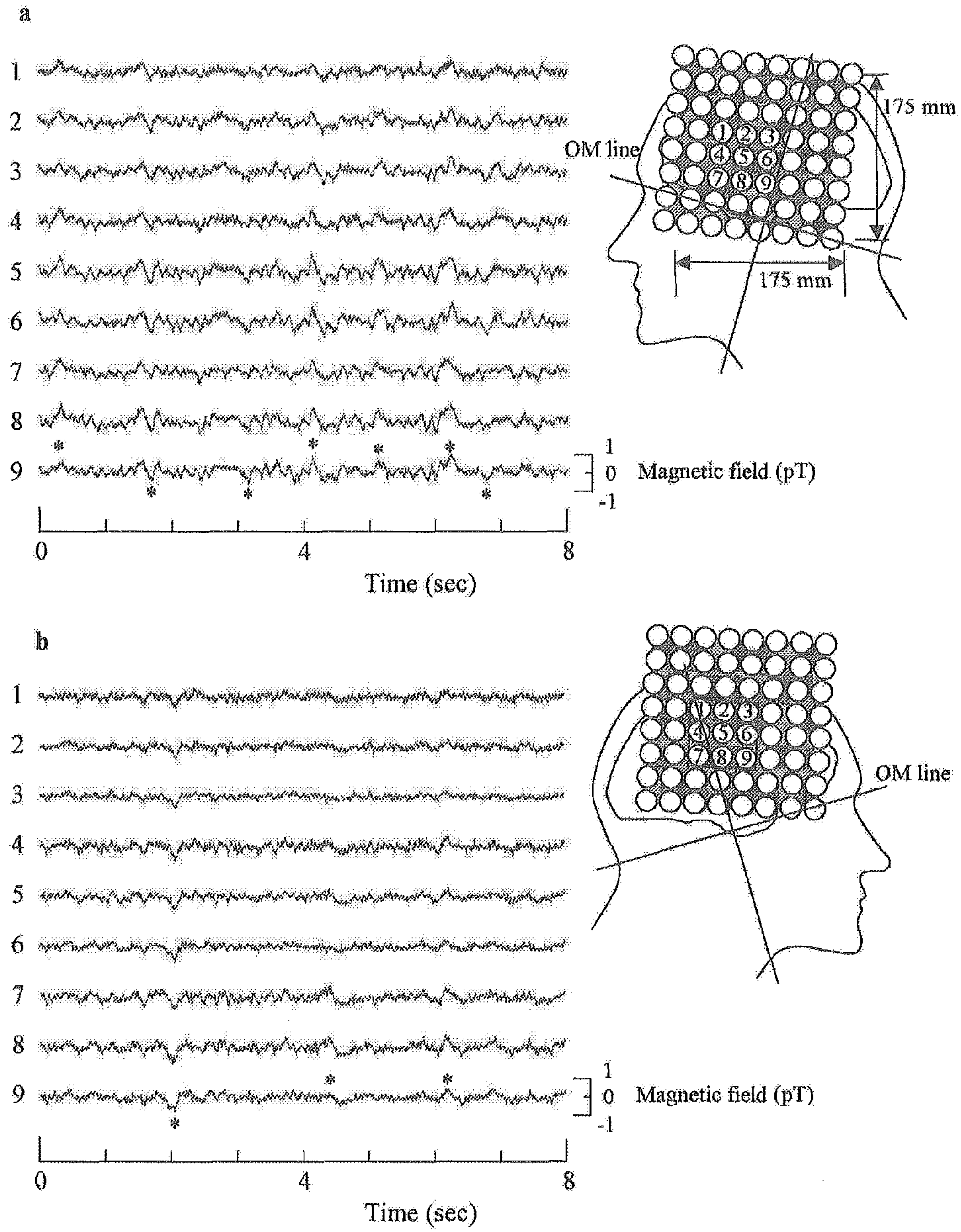
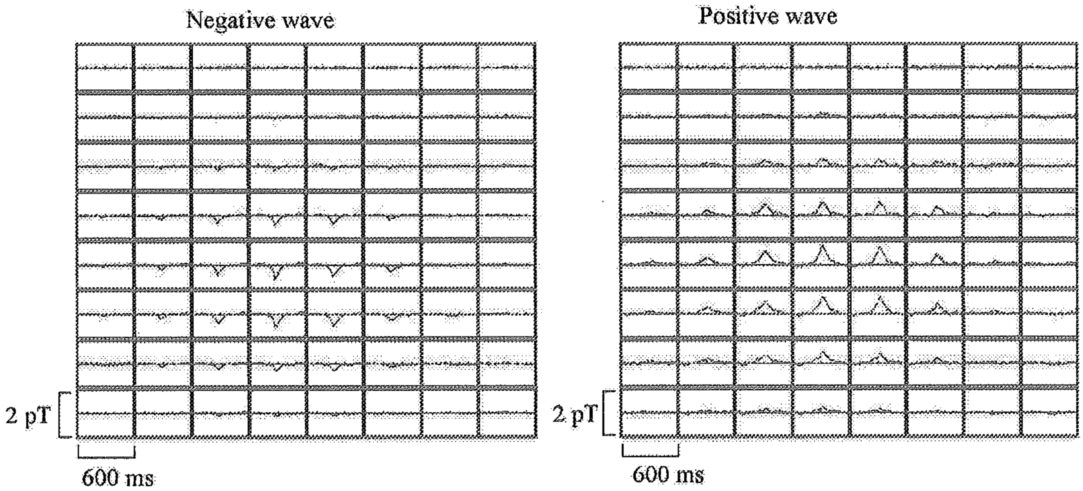

a
1
2
3
4
5
6
7
8
9
1
0
-1
Magnetic field (pT)
0
4
8
Time (sec)
175 mm
175 mm
OM line
b
1
2
3
4
5
6
7
8
9
1
0
-1
Magnetic field (pT)
0
4
8
Time (sec)
OM line

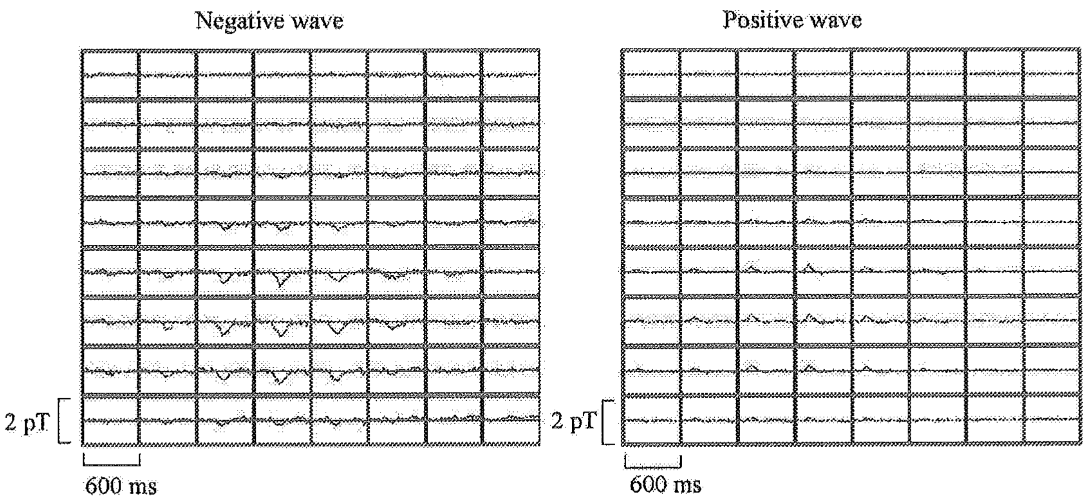
Figure 2

a



Negative wave
Positive wave
2 pT
600 ms
2 pT
600 ms

b



Negative wave
Positive wave
2 pT
600 ms
2 pT
600 ms

Figure 3

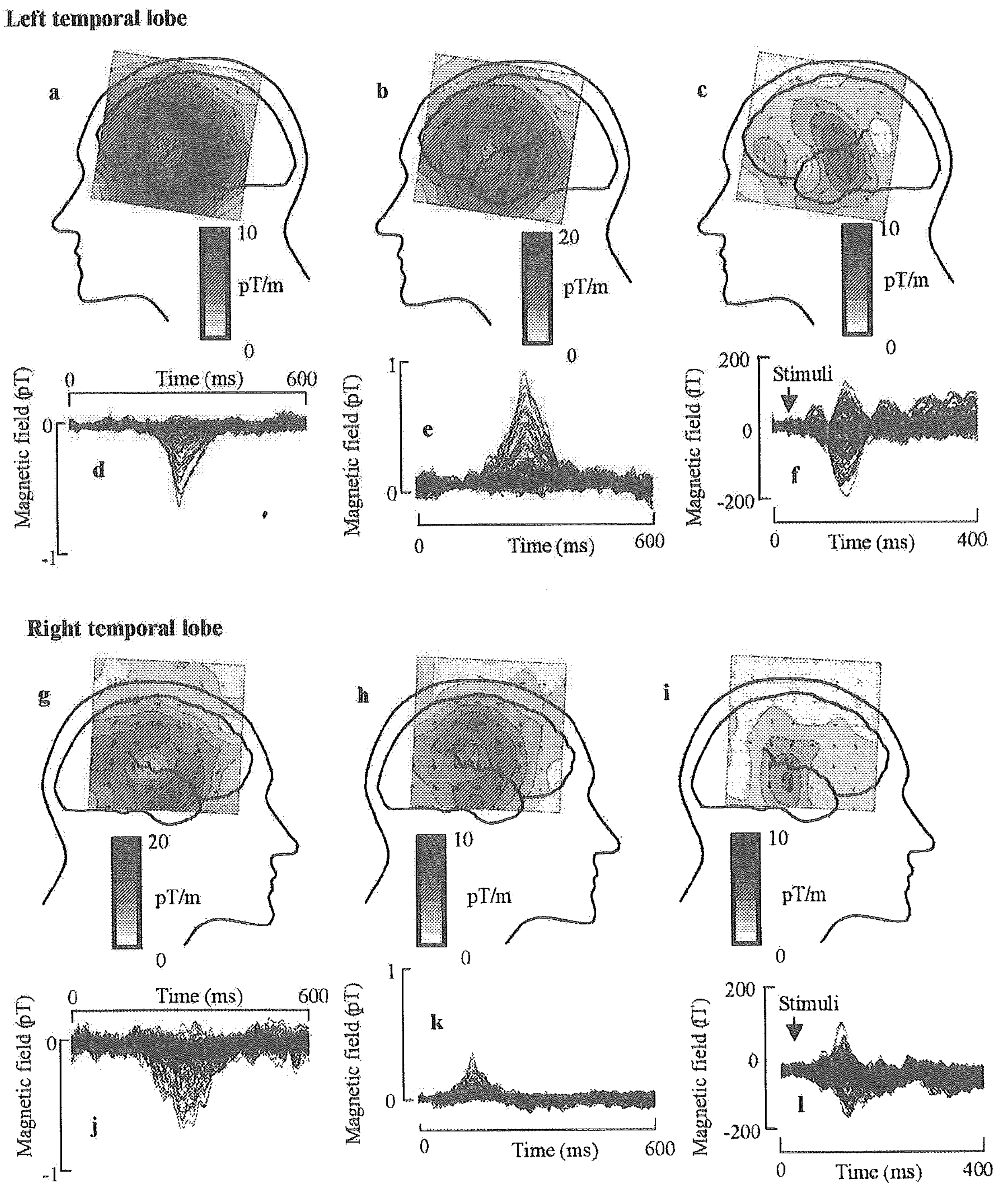

Left temporal lobe
a
b
c
10
pT/m
0
20
pT/m
0
10
pT/m
0
Magnetic field (pT)
0
Time (ms)
600
0
-1
d
1
e
0
Magnetic field (pT)
0
Time (ms)
600
200
Stimuli
0
-200
f
Magnetic field (fT)
0
Time (ms)
400
Right temporal lobe
g
h
i
20
pT/m
0
10
pT/m
0
10
pT/m
0
Magnetic field (pT)
0
Time (ms)
600
0
-1
j
1
k
0
Magnetic field (pT)
0
Time (ms)
600
200
Stimuli
0
-200
l
Magnetic field (fT)
0
Time (ms)
400

Figure 4

Case 1: after medication

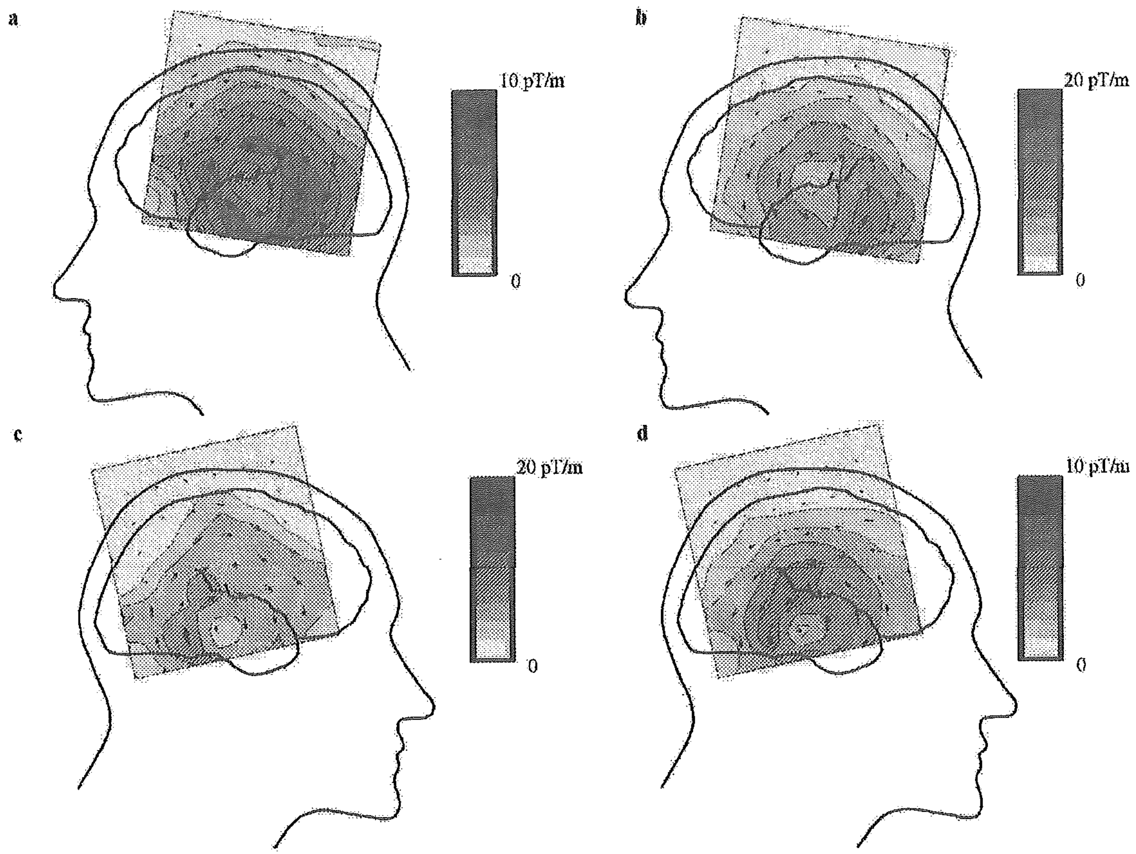
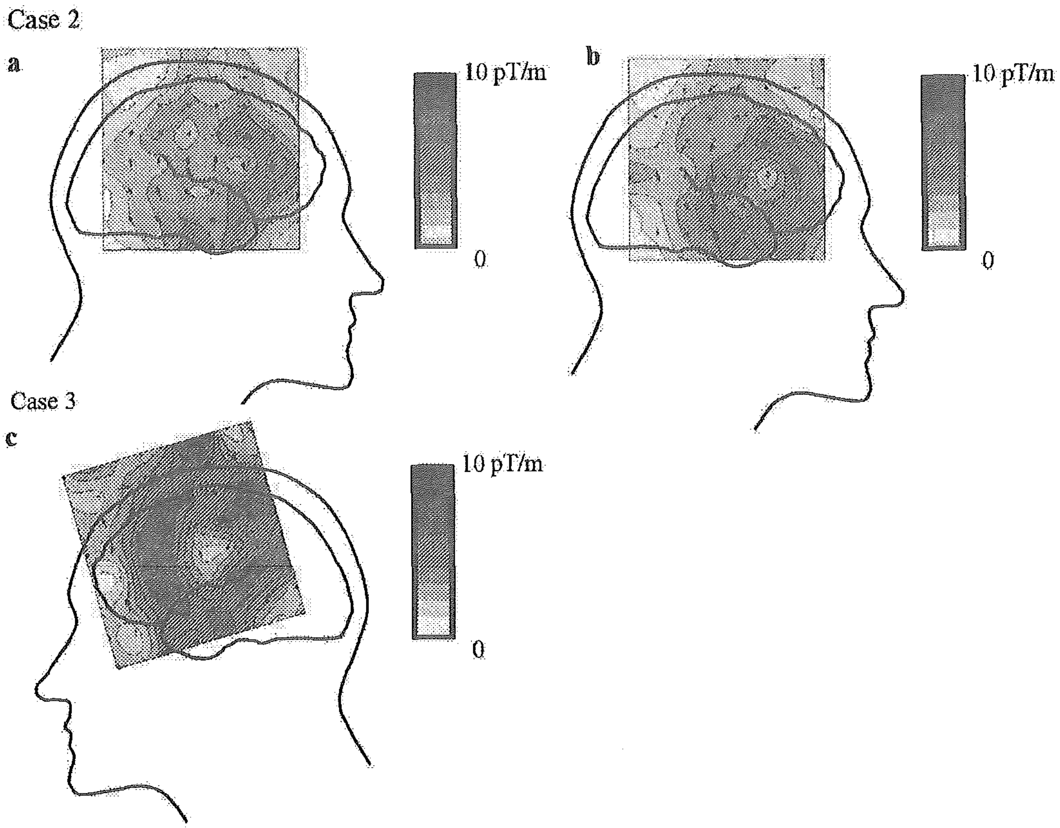


Figure 5



厚生科学研究費補助金（21 世紀型医療開拓推進研究事業）

分担研究報告書

脳磁図を用いた高齢者平衡機能障害の診断と機序解明および転倒防止に関する研究（痴呆・骨折分野）

Specific evaluating method and therapeutic approach for chronic dizzy sensation

Hiroshi Oe, M.D., Hiroaki Naritomi, M.D.,

Department of Cerebrovascular Medicine,

National Cardiovascular Center

Abstract

Objective: Paroxysmal dizziness or vertigo is very common symptom with various neurological and psychological disorders, and continuous and chronic dizzy or floating sensation (chronic dizziness, CD) is also popular symptom. However, effective treatment of such chronic dizziness is not determined because of the lack of objective method for evaluating this sensation. We had found the specific evaluating method and therapeutic approach to the chronic dizzy sensation.

Method: On the basis of assumption that CD may be attributable partly to cortical functional abnormality, we attempted to estimate the cortical vestibular function by measurements of auditory-evoked magnetic fields (AEFs). Magnetic field signals in the parieto-temporal cortex were evoked by 1,000 Hz tone-burst with 90 dB normal hearing level (nHL) sounds in using magnetoencephalography (MEG), which are known to stimulate the vestibular system, and 100-msec (N100m) waveforms were analysed as electrical current arrows in normal subjects (n=9) and patients with CD patients (n=14).

Results: In normal subjects, the currents direction of N100m always headed toward one direction on the superior temporal lobe, on the other, in the patients with CD, the currents direction of N100m always appeared rotational pattern over the temporoparietal lobe. Such spinning current-arrows pattern disappeared in four of our patients with amelioration of dizzy sensation following an anti-epileptic drug.

Conclusions: We successfully detected the spinning electrical currents of the N100m in AEFs on the patients with CD in MEG. This method is useful for evaluating dizzy sensation and anti-epileptic medication is effective to the amelioration of CD.

(Presented in BIOMAG2002)

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1. Introduction

Treatment and management of acute or paroxysmal vertigo or dizziness has been examined in detail [1]. On the other, there are also patients who are suffering from continuous and long-standing dizzy, floating sensation all day long. In spite of efforts to assign a detecting of such chronic dizzy sensation, objective evaluating method and treatment has not been studied yet. The disequilibrium implies a mismatch among inputs from the multisensory systems subserving static-dynamic spatial orientation, postural, vestibular, visual and somatosensory systems [2]. We assumed that the dysfunction of cortical vestibular center might play a role in the manifestation of chronic dizziness (CD). We, therefore, attempted to estimate the functional abnormality of cortical vestibular center

(CD). We, therefore, attempted to estimate the functional abnormality of cortical vestibular center using electrophysiological methods in the subjects complaining CD. We previously reported that magnetoencephalography (MEG) could successfully demonstrate cortical functional abnormality of patients with temporal lobe epilepsy (TEL) by analyzing electrical neuronal signals as current arrows on a current-arrow map [3]. In the present study, we measured cortical neuronal electrical currents calculated by auditory evoked magnetic fields (AEFs) by 1,000Hz tone-burst with the intensity of 90 dB normal hearing level (nHL) to evaluate subjective CD. Because such sound could stimulate saccular in the inner ear and lateral vestibular (Deiter's) nucleus in the brain-stem on the pathways of the vestibular system [4].

2. Subjects and Methods

2.1. Subjects

We defined CD as abnormal anytime feelings of long-lasting floating, swaying and/or dizzy nonrotatory sensations for 6 months or more. Clinically, there were no positive neurological findings about hemiparesis, disequilibrium and truncal-limb ataxia, such as coordinative and gait tests. We excluded the patients with abnormal findings of the otorhinologic examinations, caloric test and auditory brain-stem response. We measured AEFs in eleven healthy normal subjects without history of acoustic problem (4 males and 7 females with 67 ± 4.9 years) and fourteen patients with CD (6 males and 8 females with 68 ± 8.4 years).

2.2. Methods

2.2.1 Measurement Instruments and Acoustic Stimuli

To measure AEFs, we used the superconducting quantum interference device (SQUID) system (MC-6400, Hitachi Ltd.,) with 64 co-axial gradiometer (8x8 matrix) in a two-dimensional plane [3]. The acoustic stimuli consisted of a 1,000 Hz tone-burst with the intensity of 90 dBnHL. The stimuli intervals were varied 25% randomly at the center frequency of 0.3 Hz.

2.2.2. Recording of AEFs and Producing Current-arrow Map

In AEFs, the magnetic counterpart of the auditory evoked highest–amplitude potential wave is called N100m. We tried to detect the auditory evoked cortical electrical currents of N100m by evoked magnetic fields. The current-arrow map can be produced from the derivatives of the normal component (Bz) of the AEF signals as $x=dBz/dy$ and $y=-dBz/dx$. This method was developed by Hosaka and Cohen [5], and the derivatives of the normal component (Bz) of the magnetic field have been directly measured by Hämälinen et al [6]. However, these methods did not visualize the current-arrow distribution. Our method can produce a counter map of the magnitude of the current arrows ($I = [Ix^2+Iy^2]^{-1/2}$, pT/m) in the same figure as the electrical current arrows. In this way, the current-arrow map of N100m can indicate the direction, distribution and magnitude of cortical neuronal electrical currents based on the maximum response of N100m generator.

2.2.3. Quantitative evaluation of directions in the current-arrow map

The magnitude of neuronal electrical currents in the current-arrow map could be indicated in pT/m as quantitative evaluation. On the other, to evaluation of the electrical directions of current-arrows on the map quantitatively, direction of the pathway is defined counter-clockwise. The difference (*d I rot*)value can be defined from the difference between maximum plus value and minimum minus value. In this way, we calculated *d I rot* value as the quantitative value and compared with mean± SD *d I rot* values of two groups statistically.

2.2.4. Approach to the treatment

The results of AEFs measurements provided us an important clue for understanding the mechanisms of CD manifestation and for exploring novel therapeutic approach. Accordingly, we treated 8 patients associated with moderate and/or severe dizziness among 14 CD patients with anti-convulsants (valproic acid 400-800 mg/day) for one month or more. Serial AEFs measurements were performed in 4 of them to find the relationship between clinical effects and changes in AEFs results.

3. Results

Typical current-arrow maps and 64 AEFs waveforms obtained at the left temporoparietal area in a normal subject (Fig. A). The current-arrow map (Fig. B) is produced from 64 N100m peak waveforms. The current-arrows always headed toward one direction indicating single dipole pattern over the superior temporal lobe. On the other, in all the patients with the CD, the direction of current-arrows showed a clockwise or counter-clockwise spinning pattern over the unilateral or bilateral temporoparietal areas (Fig. D), which were produced by 64 AEFs waveforms (Fig. C). In order to evaluate quantitatively such spinning pattern, we calculated the *d I rot* value as quantitative factor of spinning current arrows and analyzed them statistically. The mean±SD *d I rot* value in the normal subjects indicated 1.59±0.46 (range from 1.01 to 2.07) and that in the CD indicated 3.34±1.42 (1.92 to 5.66). There was significant difference (p<0.001) between the mean±SD *d I rot* values in the normal subjects and the CD .

Eight patients who had abnormally high *d I rot* values were treated with valproic acid 400-800 mg/day. After the administration, 6 patients showed a remarkable amelioration of dizzy sensation, while the other 2 exhibited no improvement of dizziness. In all the 4 patients, the rotational abnormality of current arrows disappeared completely or showed the tendency toward disappearance, and *d I rot* values were markedly reduced.

4. Discussions

We have reported the current-arrows of interictal discharges in the patients with the TEL in using MEG [3]. Our results showed that the pattern of patient with the TEL indicated the same spinning pattern with those of the CD patient. We speculated that the manifestation of spinning current-arrows showed cortical electric discharges resulting from neuronal electric hypersensitivity, such as epileptic phenomenon. We experienced four patients with CD whose dizzy sensation markedly ameliorated, improved the dizziness and began to walk without aid following an anti-epileptic treatment. The administration of anti-convulsants may inhibit abnormal electrical discharges in the cortical vestibular center and hence may be effective for improving the dizzy sensation.

Acknowledgments

We thank Dr. S. Ohira, Dr. Y. Nagakane, Dr. K. Saitou, Ms. N. Ohno and Ms. M. Minagawa for the technical helps. This study was supported by a Grant-in-Aid for Scientific Research No.13072601, Supported by the Ministry of Health, Welfare and Labor of Japan.

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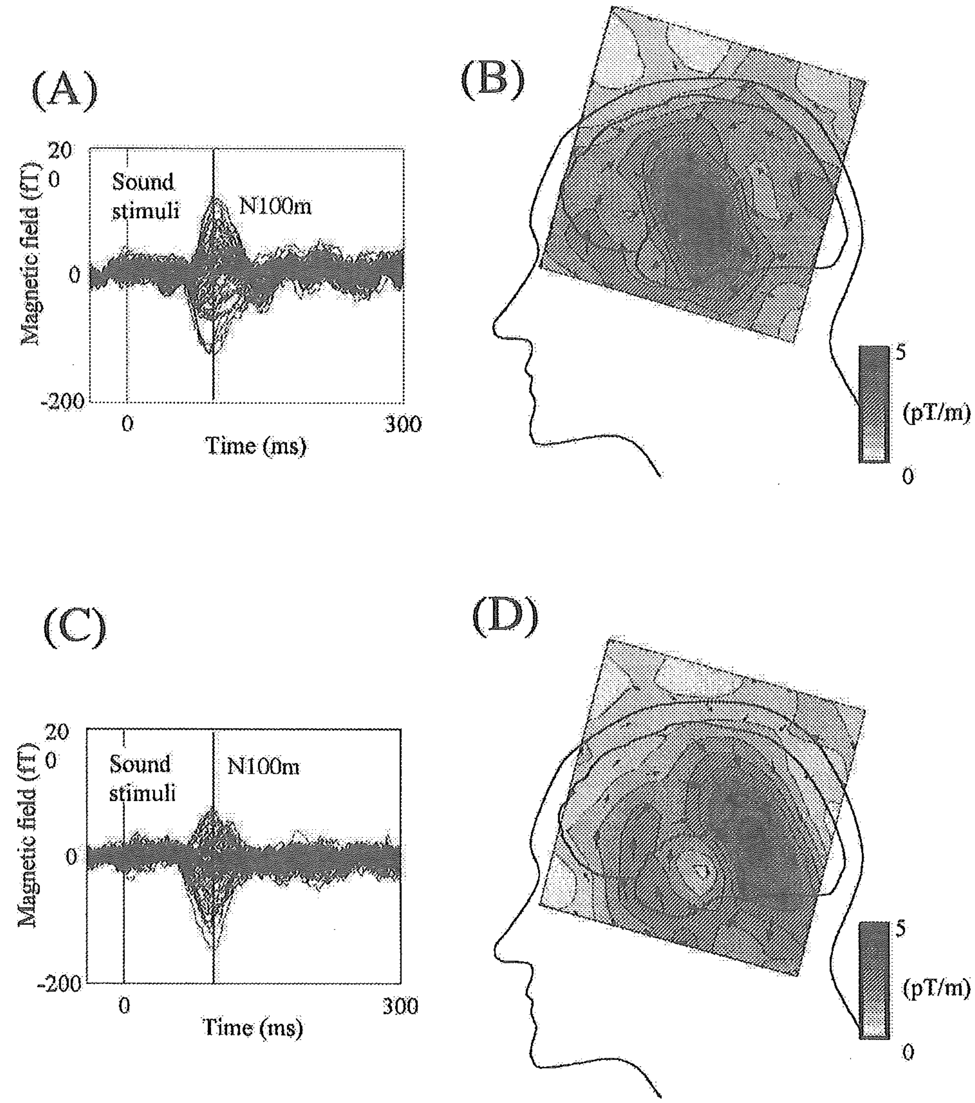

Fig. N100m waveforms and current-arrow maps of a normal subject and a patient with chronic dizziness

厚生科学研究費補助金（21 世紀型医療開拓推進研究事業）

分担研究報告書

Propagation analysis of epileptic discharge in temporal epilepsy patients using magnetoencephalogram

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[2]Department of Cerebrovascular Medicine, National Cardiovascular Center

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Abstract

Objective: Our aim of this study is to analyze the propagation of epileptic discharge.

Methods: We used two processes, i.e., the subtraction of magnetocardiogram signals and a time-averaging process, to obtain a clear epileptic waveform. With these methods, we obtained a current arrow map of MEG signals with which the epileptic discharge could be visualized. We also measured an auditory-evoked magnetic field to obtain a landmark of brain position.

Results: A large current distribution appeared in the limbic structure of each temporal lobe, and large current orientation in opposite directions was observed.

Conclusions: Current-arrow map has a potential to detect propagation current in the brain. Thus, epileptic activation, which can not be estimated by one dipole model, may be analyzed in detail by using current-arrow map method.

(Presented in BIOMAG2002)

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1 Introduction

In the case of temporal lobe epilepsy, only 50% [1] or 20% [2] localization has been defined because of interictal complex spikes. To address this issue, we have visualized the epileptic discharge by using a current arrow map [5]. In the report, we have investigated the large spatial distribution, i.e. the transference phenomenon in the kindling effect, in interictal epileptic discharges in temporal epilepsy patients [5].

2 Method

2.1 MEG measurement

We measured spontaneous MEGs and auditory evoked magnetic fields (AEMFs) of three patients with temporal epilepsy by using a SQUID (superconducting quantum interference device) system (MC-6400, Hitachi, Ltd.) with a 64-coaxial gradiometer [3,6]. This system was installed in a magnetically shielded room (MSR) with a double mumetal layer. The sensor array in the system is an 8x8 matrix on a flat plane with a pitch of 25 mm. Each sensor incorporates a first-order gradiometer that includes an 18-mm-diameter bobbin with a 50-mm-long baseline. The magnetic field sensitivities of all channels are below 20 fT $Hz^{-1/2}$. The spontaneous MEG and AEMF were measured twice each for both hemispheres. The anatomical head position was adjusted by using four-coil indicators on an orbitomeatal basal (OM) line. After passing through a bandpass filter (0.1-50 Hz), notch filter (50 Hz), and amplifier circuit, the spontaneous MEG signals (2 minutes) were digitized at 1 kHz and the AEMF signals (8 minutes) were digitized at 250 Hz by a computer. Although we could not measure both hemispheres at the same time because of the flat measurement plane, it was sufficient to detect signals from the temporal lobe, which could be fitted by the flat plane.

2.2 Signal analysis [5]

To detect only the epileptic waveform, we subtracted the magnetocardiogram signals deriving from the patients' hearts from the spontaneous MEG signals. Then, in the same manner as for EEG epilepticform analysis, we manually averaged the epileptic sharp waves to obtain a clear signal. We then compared the raw epileptic waveforms and the averaged waveforms to eliminate the influence of waveform distortion. To visualize the epileptic discharge current inside the brain two-dimensionally, we produced current-arrow maps by deriving the normal component (Bz) of the magnetic field. Such current maps are useful for reviewing neural networks directly and topographically without dipole estimation, although the head sphere shape affects the current-arrow pattern. By using a current-arrow pattern with each epileptic discharge waveform, the averaged discharge could be visualized. For these measurements, informed consent was obtained from all patients.

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3 Results

Figure 1 shows the temporal epileptic waveforms, which were averaged as a trigger of peak waveform, in left temporal lobe. Left figure is negative wave pattern and right figure is positive wave pattern. In both figures, there are peak waveforms in center of temporal lobe [5].

Figure 2 shows the current-arrow maps in both temporal heads. In each hemisphere, current direction of circular pattern is opposite. Especially, in left temporal lobe, the current-arrow pattern.

4 Conclusions

This indicates that our topographical visualisation method creates the possibility of developing a new diagnosis method for temporal epilepsy patients.

Acknowledgment

This study was supported by a Grant-in-Aid for Scientific Research No.13072601, Supported by the Ministry of Health, Welfare and Labor of Japan.

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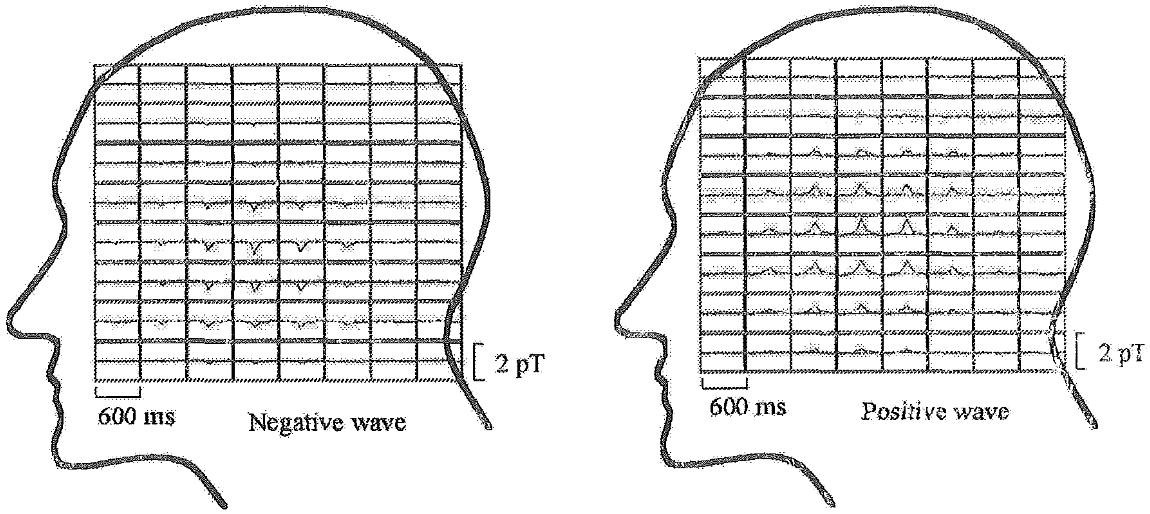

Fig. 1 Averaged negative and positive waveforms for left temporal lobe