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Diagnosis Method of Mild Cognitive Impairment Based on Power Variance of EEG

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Abstract— **Mild cognitive impairment (MCI) patients and healthy people were classified by using a "power variance function (PVF)", namely, an index of electroencephalography (EEG) proposed in a previous report. PVF is defined by calculating variance of the power variability of an EEG signal at each frequency of the signal using wavelet transform. After confirming that the distribution of PVFs of the subjects was a normal distribution at each frequency, the distributions of PVFs of 25 MCI patients and those of 57 healthy people were compared in terms of Z-score. The comparison results indicate that for the MCI patients, the PVFs in the θ band are significantly higher in left parieto-occipital area and that those in the β band are lower in the bitemporal area. Multidimensional discriminant analysis using the PVF in the θ-β band recorded only on four electrodes on the left parieto-occipital area could be used to classify MCI patients from healthy people with leave-one-out accuracy of 87.5%. This indicates the possibility of diagnosing MCI by using EEG signals recorded only on a few electrodes.**

I. Introduction

Dementia is one of the most common disorders in the elderly population. Among several subtypes of dementia, the most common is Alzheimer's disease (AD). Although AD is a brain degenerative disorder involving progressive dementia, if it is detected and treated from an early stage, it is possible to slow its progression [1]. Especially, the first stage of AD is known as "Mild Cognitive Impairment (MCI)". Therefore, early diagnosis and effective treatment of MCI are critical issues in the study of dementia.

Recently, functional neuroimaging techniques such as single photon emission computed tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (f-MRI), have been commonly used as methods for diagnosing MCI. Although these techniques are useful for early diagnosis of AD, they are prohibitively expensive and/or require the injection of radioactive tracer compounds. In contrast, electroencephalography (EEG) is inexpensive and non-radioactive; as a result, it has been considerably researched as a diagnostic tool for the early stage of AD.

Spectral analysis of the electroencephalograms of AD patients has been actively performed, and dimensional complexity analysis of such EEG has been undertaken by a few studies [2]. However, according to a broad survey of the relevant literature, the diagnostic accuracy of EEG in AD is currently around 80%, and discriminating MCI was difficult by analysis surveyed.

It has recently been shown that MCI can be classified by analyzing "EEG synchrony," namely, synchronization between each EEG signal recorded on electrodes. It was reported that EEG signals of MCI patients synchronize significantly less than those of healthy people, and classification accuracy of 87.5% for MCI patients was yielded [3]. This value is much higher than that possible by spectral analysis; however, a lot of electrodes are required to analyze EEG synchrony. In consideration of the stress on the subjects, it is better to use as few electrodes as possible in MCI diagnosis.

In this regard, Musha et al. indicated the possibility that MCI could be detected with high sensitivity by evaluating the variance of power of the EEG signals [4], and we analyzed the variance of power of EEG signals at each frequency by our unique index, termed a "Power Variance Function (PVF)" [5] in previous report. A PVF can be calculated from single EEG signal recorded on each electrode. By analyzing PVFs of patients, we found PVFs of MCI patients significantly differ from those of healthy people on some areas of the subjects' heads. This finding indicates the possibility of discriminating MCI by using only a few electrodes (if appropriate electrodes selected).

Here, we show the EEG characteristics of MCI patients as obtained with PVF and the results of discrimination of MCI and Healthy subjects.

II. Power Variance Function

PVF indicates the variance of the power of an EEG signal at each frequency. PVF is calculated as the follows [5]:

$$\mathrm{PVF}(f) = \log \sigma_i^2(f), \tag{1}$$

where,

$$\sigma_i^2(f) = E[(P_i(f,t) - E[P_i(f,t)])^2], \tag{2}$$

$$P_i(f,t) = \left\| \mathrm{CWT}\left[\frac{x_i(t)}{\sqrt{E[x_i^2(t)]}} \right] \right\|^2, \tag{3}$$

and $x_i(t)$ is an EEG signal recorded at electrode i, f is the target frequency to analyze, and $\mathrm{CWT}[x_i(t)]$ shows the continuous wavelet transform (CWT) of $x_i(t)$ [6]. CWT is defined as follows:

$$\begin{aligned} \mathrm{CWT}[x(t)] &= C(a,t) \\ &= \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(\tau)\, \overline{\psi\left(\frac{t-\tau}{a}\right)}\, d\tau, \end{aligned} \tag{4}$$

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where, a is the scale parameter, $\psi(t)$ is the mother wavelet, and $\overline{\psi(t)}$ shows the complex conjugate of $\psi(t)$. In this paper, the Gabor wavelet [6] as shown below was used as the mother wavelet.

$$\psi(t) = \frac{1}{2\sqrt{\pi}\sigma} e^{-\frac{t^2}{\sigma^2}} e^{-j2\pi f_0 t} \tag{5}$$

where, σ defines the bandwidth of the Gaussian window and f_0 is the central frequency. It is known that the real part of CWT[$x(t)$] shows the variability characteristics of $x(t)$ at frequency $f \approx f_0/a$. Here, we empirically used $\sigma = 8$, $f_0 = 1$.

The variance of $P_i(f, t)$, as shown in (2), becomes a function, $\sigma_i^2(f)$, whose variable is f. The logarithm of $\sigma_i^2(f)$ is calculated and defined as PVF, which indicates how active EEG variability is at f. PVF was defined as simply $\sigma_i^2(f)$ in a previous paper [5], but the distribution of $\sigma_i^2(f)$ was shifted to the left, thereby complicating the multidimensional discriminant analysis of PVFs of subjects. Accordingly, taking the logarithm of $\sigma_i^2(f)$ made it possible to distribute PVF in a normal distribution as described in Section B. For example, Fig. 1(a) shows the histogram of $\sigma_i^2(f)$, and Fig. 1(b) shows that of log $\sigma_i^2(f)$ (i.e., PVF in this study). From these figures, the shape of the distribution approximated to a normal distribution can be found by taking the logarithm of $\sigma_i^2(f)$.

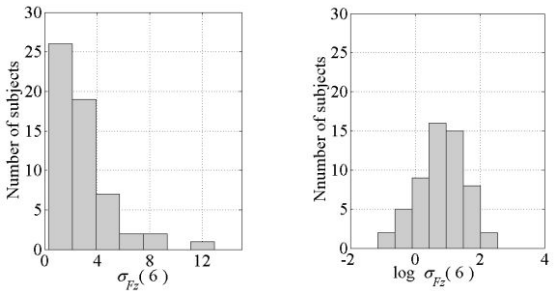
III. Method of Discriminant Analysis

It is to be noticed that using too many values for discriminant analysis degrades the performance and it is necessary to select appropriate values (which differ largely) from all the observed values of the two groups [7]. PVFs of MCI patients and of healthy people (after noise was removed manually from the EEG data) were therefore compared. Discriminant analysis of PVFs of MCI patients and healthy people was then performed.

A. Data Set

EEG signals of 57 healthy subjects (age: 57-89 years), and 25 MCI patients (age: 49-86 years; mini mental state examination (MMSE) was 24-30) were analyzed. The MCI patients were patients who were deemed probable or possible AD patients at 12 or 18 months after their EEG signals were recorded for the first time, and these first EEG signals are used in this paper. All EEG signals were recorded by staff from Brain Functions Laboratory, Inc. and the National Center Hospital of Neurology and Psychiatry [8]. All recordings were made while the patients were at rest with eyes closed for 5 minutes. Twenty-one electrodes were placed over the scalp in accordance with the 10-20 International System, with a right-side auricular reference electrode. The sampling rate was 200 Hz. After the collected data was processed with a bandpass filter with a bandwidth of 2-40 Hz, a wavelet transform was applied. The central frequency of the mother wavelet was varied between 5 and 40 Hz in steps of 0.5 Hz.

When PVF is calculated, a recorded EEG signal is divided into short segments for every constant period and segments with unacceptable noise (e.g. saturation signal, myoelectricity signal, etc.) are manually removed. PVFs are then calculated from the remaining segments, and PVFs near the mean of all the PVFs are chosen. The period of a segment was empirically set to 2.56 s, and 40 PVFs in order of Euclidean distance from the mean of all the PVFs, were chosen. After that, the mean of these 40 PVFs was used as the PVF of a subject.



(a) Distribution of $\sigma_i^2(f)$ (b) Distribution of log $\sigma_i^2(f)$

Figure 1. Comparison between distribution of $\sigma_i^2(f)$ and that of log $\sigma_i^2(f)$; on electrode Fz, f = 6 Hz

B. Comparison of MCI and Healthy

To compare MCI patients and healthy people, the distribution of PVFs was evaluated first. The distributions of PVFs of healthy subjects at each electrode are shown in Fig. 2. The PVFs are distributed at each frequency at each electrode. The color intensity of each graph shows the number of subjects. Chi-square test confirmed that the distribution of PVFs of the subjects is a normal distribution at almost every frequency. Dots along the x axis in each graph mean that the distribution fits a normal one at that frequency. What's more, the PVFs of the MCI patients are similar.

By confirming that the distribution of PVF was a normal one, it was possible to use the "Z-score" to compare PVFs of MCI patients with those of healthy people. Z-score [7] is defined as

$$Z = \frac{E[x] - E[x_c]}{\sqrt{\frac{\sigma}{n} + \frac{\sigma_c}{n_c}}} \tag{6}$$

where, x is an observed value (i.e. PVF(f) of a MCI patient), σ is the variance of x, n is the number of subjects in a group, and subscript c means the values are got from a control group (i.e., healthy people).

The mean Z-scores in δ (5.0-8.0 Hz), α (8.5-13.0 Hz), β (13.5-20.0 Hz), and γ (20.5-35.0 Hz) on each electrode are shown in Fig. 3. Gray areas indicate Z-score of less than 1.65, which means the difference between two groups is not significant when the level of significance p is 0.1. It is clear from Fig. 3 that PVF in the θ band is higher in the left parieto-occipital area and that the β band is lower in the bitemporal area for MCI patients.

C. Discrimination of MCI and Healthy

MCI patients were classified from healthy people by multidimensional discriminant analysis. If a vector **x** consisted of observed values satisfies (7), **x** can be classified as group i.

$$\frac{f_i(\mathbf{x})}{f_j(\mathbf{x})} > \frac{p_j}{p_i} \tag{7}$$

where, p_i is the ratio of **x** in group i, p_j is that in group j (i.e. i means MCI, j means healthy), and $f_i(\mathbf{x})$ is a probability distribution function of multidimensional normal distribution

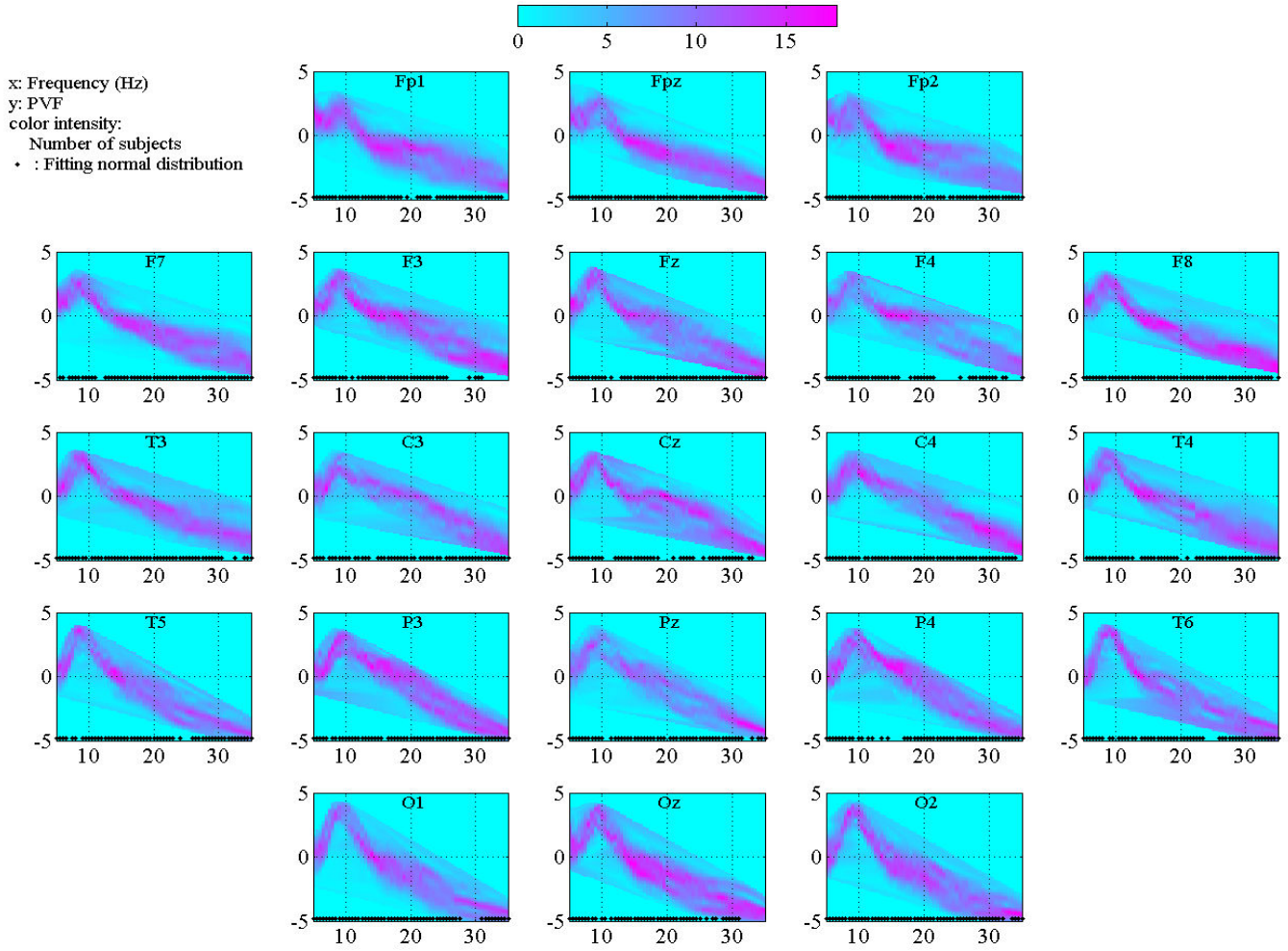
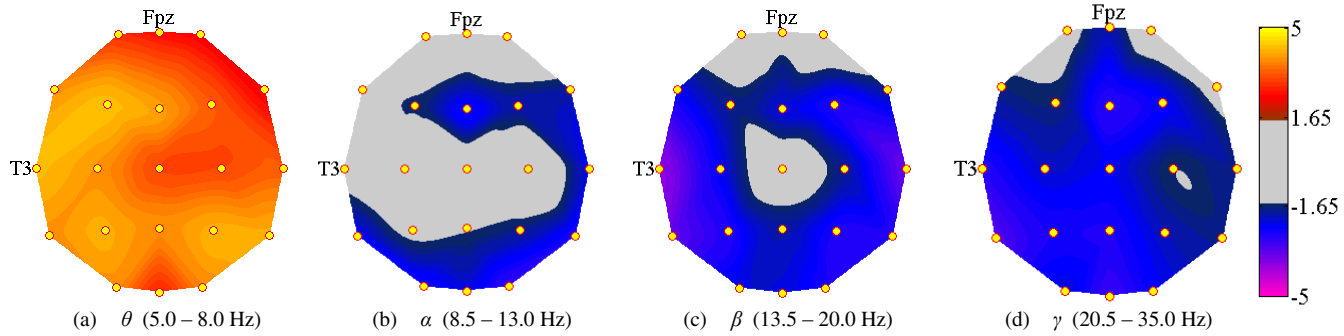


Figure 2. Distribution of PVFs of healthy subjects



(a) θ (5.0 – 8.0 Hz) (b) α (8.5 – 13.0 Hz) (c) β (13.5 – 20.0 Hz) (d) γ (20.5 – 35.0 Hz)

Figure 3. Z-score of PVF of MCI patients

calculated from reference data from group i. Multidimensional normal distribution is defined as

$$f_i(\mathbf{x}) = N(\mathbf{x}; \boldsymbol{\mu}_i, \boldsymbol{\Sigma}_i) = \frac{1}{(2\pi)^{n/2}|\boldsymbol{\Sigma}_i|}\exp\left[\frac{1}{2}(\mathbf{x}-\boldsymbol{\mu}_i)^T\boldsymbol{\Sigma}_i^{-1}(\mathbf{x}-\boldsymbol{\mu}_i)\right] \quad (8)$$

where,

$$\mathbf{x} = \{x_1, x_2, \dots, x_n\}^T \quad (9)$$

$$\boldsymbol{\mu} = \{\mu_1, \mu_2, \dots, \mu_n\}^T \quad (10)$$

$$\boldsymbol{\Sigma} = \begin{bmatrix} \sigma_{11} & \cdots & \sigma_{1n} \\ \vdots & \ddots & \vdots \\ \sigma_{n1} & \cdots & \sigma_{nn} \end{bmatrix} \quad (11)$$

$$\sigma_{pq} = E\left[(x_p - \mu_p)(x_q - \mu_q)\right], \quad p, q = 1, 2, \dots, n \quad (12)$$

and x is a observed value, n is the number of observed value, μ is the mean of x, and σ_{pq} is the covariance between x_p and x_q.

According to the results of section B, electrodes in left parieto-occipital and bitemporal area were selected, and were placed in a symmetrical arrangement or in a continuous line in consideration of convenience of putting electrodes on pa-

tients' heads. PVFs in δ-β band (5.0-17.5 Hz) were selected except frequency where distribution of PVFs wasn't normal distribution.

The same number of subjects (24, including reference and target) were selected at random from the MCI patients and healthy people because of clarity in evaluation of accuracy. Then, we used the 40 PVFs calculated from a subject in section A as reference data, because samples more than the observed values are required as reference data for multidimensional discriminant analysis.

IV. Results

The results of discriminant analysis on the MCI and healthy patients are listed in Table I. Specificity refers to the percentage of subjects who are classified as healthy among a group of healthy people and sensitivity refers to that of ones who are classified as MCI among a group of MCI patients. Accuracy refers to the percentage of subjects who are classified correctly among all subjects. These percentages were evaluated by leave-one-out cross validation, so a target subject was classified using reference data except 40 PVFs of the target subject. Bold text indicates the results are larger than 80%

When electrodes T4 and T6 were used, the specificity was highest (i.e., 91.7%) but sensitivity was comparatively low.

The specificity tends to be higher than sensitivity when T4 is used. On the other hand, the sensitivity was higher than 80% when electrode T3 was used, and it was higher than specificity in all cases. The highest accuracy, 87.5% was achieved by using T3, T5, O1, and Oz. In this case, both specificity and sensitivity were also 87.5%. The second highest accuracy 84.6% was obtained by using T3, T5, and O1.

V. Discussion

Comparison of MCI and healthy patients showed that PVF in the θ band is higher in the left area of the brain. This result seems to be valid because it is well known that the left brain is supposed to control logical, objective, and analytic thinking, so it is natural for MCI patients to show abnormality in the left area of brain. Moreover, PVF of MCI patients in the θ band was also higher in the parieto-occipital area. This area is located right above posterior cingulate cortex, which is verified as the first area damaged by Alzheimer's disease by many researches using PET [9]. On the other hand, PVF in the β band was lower in the bitemporal area for MCI patients, and this matches results of many researches using spectral analysis. These results indicate PVF can include both characteristics of spectral analysis and neuro-imaging analysis such as PET.

TABLE 1. The results of discriminant analysis

Electrode	Specificity (%)	Sensitivity (%)	Accuracy (%)
T3	66.7	**83.3**	75.0
T4	79.2	75.0	77.1
T3, T4	66.7	**83.3**	75.0
T3, T5	71.1	**83.3**	77.1
T5, T6	75.0	75.0	75.0
T4, T6	**91.7**	75.0	**83.3**
T3, T5, O1	**83.3**	**87.5**	**84.6**
T4, T6, O2	**83.3**	75.0	79.2
T3, T4, T5, T6	70.8	**87.5**	79.2
T3, T5, O1, Oz	**87.5**	**87.5**	**87.5**
T4, T6, O2, Oz	**83.3**	75.0	79.2

In discrimination of MCI patients and healthy people, the sensitivity was higher than 80% when electrode T3 was used, and accuracy increased as electrodes were added on left-occipital area. This indicates that abnormality on left-temporal lobe (i.e., T3) appears in both of MCI patients and healthy people, but abnormality on wide area of left-occipital lobe appears in only MCI patients. The highest accuracy was 87.5% when four electrodes were used, T3, T5, O1, and Oz. This value is as high as that of discrimination by EEG synchrony; however, the electrodes in this study were arranged symmetrically or in a continuous line, and all combinations of electrodes were not evaluated. It is therefore possible to obtain higher accuracy if other electrode arrangements were evaluated simply to aim at high accuracy.

Though high accuracy was yielded by PVF, the number of subjects is not enough to confirm its practicality, and there is little medical or neurological evidence that PVF is related to neuronal abnormality. Accordingly, to develop the method as a tool for diagnosis of MCI, more patients must be surveyed and opinions must be exchanged with medical intellectuals.

VI. Conclusions and Future Works

PVF is a very sensitive index of neuronal disorder. It can be used to classify MCI patients from healthy people with accuracy higher than 80% by obtaining PVFs with a few electrodes. We will survey more patients to develop proposed method as a tool for diagnosis for MCI.

References

[1] H. Matsuda and T. Asada, *Diagnostic Imaging Learned by Watiching and Diagnosis*. Nagai Shoten Co., Ltd., Osaka, 2004

[2] C. Besthorn, H. Sattel, C. Geiger-Kabisch, R. Zerfass, and H. Förstl, "Parameters of EEG dimensional complexity in Alzheimer's disease," *Electroencephalography and Clinical Neurophysiology*, vol. 95, no. 2, pp. 84–89, 1995.

[3] J. Dauwels, F. Vialatte, C. Latchoumane, J. Jeong, and A. Cichocki, "EEG Synchrony Analysis for Early Diagnosis of Alzheimer's Disease: Study with Several Synchrony Measures and EEG Data Sets," 31st Annual International Conference of the IEEE EMBS, pp. 2224–2227. Minneapolis, Minnesota, USA, Sep, 2009,

[4] H. Matsuzaki and T. Musha, "A new tool for estimating abnormal neuronal activity of Alzheimer's disease," *Clinical Neurophysiology,* Volume 119, Issue 6 , pp. e89-e90, June, 2008.

[5] T. Ueda, T. Musha, T. Yagi, "Research on the characteristics of Alzheimer's disease using EEG," *The transactions of the Institute of Electrical Engineers of Japan.C*, vol. 130, no. 10, pp. 1827-1832, Oct. 2010.

[6] C. Torrence and G. Compo, "A practical guide to wavelet analysis," *Bulletin of the American Meteorological Society*, vol. 79, no. 1, pp. 61–78, 1998.

[7] PA. Lachenbruch and M. Goldstein, "Discriminant Analysis," *Biometrics*, Vol. 35, No. 1, pp. 69-85, 1979.

[8] T. Musha, T. Asada, F. Yamashita, T. Kinoshita, Z. Chen, H. Matsuda, M. Uno, and W.R. Shankle, "A new EEG method for estimating cortical neuronal impairment that is sensitive to early stage Alzheimer's disease," Clinical Neurophysiology, Vol. 113, no. 7, pp. 1052-1058, 2002

[9] Satoshi Minoshima, Norman L Foster, David E Kuhl, "Posterior cingulate cortex in Alzheimer's disease," *Lancet*, no. 344, pp. 895-895, 1994