31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Research of the Characteristics of Alzheimer's Disease Using EEG

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Abstract— **In this paper, we propose a new method for diagnosing Alzheimer's disease (AD) on the basis of electroencephalograms (EEG). The method, which is termed "Power Variance Function (PVF) method", indicates the variance of the power at each frequency. By using the proposed method, the power of EEG at each frequency was calculated using Wavelet transform, and the corresponding variances were defined as PVF. After the PVF histogram of 42 healthy people was approximated as a Generalized Extreme Value (GEV) distribution, we evaluated the PVF of 10 patients with AD and 10 patients with mild cognitive impairment (MCI). As a result, the values for all AD and MCI subjects were abnormal. In particular, the PVF in the θ band for MCI patients was abnormally high, and the PVF in the α band for AD patients was low.**

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 detected and treated from an early stage, it is possible to slow the progression of AD [1]. Therefore, early diagnosis and effective treatment of AD 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 AD. Although these techniques are useful for the 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 tool, and as a result, there is a considerable amount of research on EEG as a diagnostic method for AD.

Spectral analysis of the electroencephalograms of AD patients has been actively performed, and dimensional complexity and coherence analysis of such electroencephalograms has been undertaken by a few studies [2][3]. However, based on a broad survey of the relevant literature, the diagnostic accuracy of EEG in AD is currently around 80%. Therefore, the most critical issues targeted by EEG studies on AD involve improving the accuracy of the differential diagnosis of AD [4]. In this regard, Musha et al. indicated the possibility that even mild cognitive impairment (MCI) could be detected with high sensitivity by evaluating the variance of power of the EEG [5]. Therefore, it is considered that the variance of power of the EEG is an important index of neuronal abnormality in AD patients.

In this study, we analyzed the variance of power of EEG at each frequency and applied the results to developing a method of early detection of AD. Here, we show the EEG characteristics of AD patients as obtained with the proposed method.

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II. METHOD

A. Variability Characteristics of Each Frequency Component

We calculated the variability characteristics of the power process of each frequency component by applying the Continuance Wavelet Transform (CWT) [6]. CWT is defined as follows:

$$C(a,t) = CWT[x(t)] = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(\tau) \overline{\psi(t)\left(\frac{t-\tau}{a}\right)} d\tau, \qquad (1)$$

where $CWT[x(t)]$ shows the CWT of $x(t)$, $x(t)$ is the target time series, $\psi(t)$ is the mother wavelet, and $\overline{\psi(t)}$ shows the complex conjugate of $\psi(t)$. In this paper, we use the *Gabor wavelet* given by (2) as the mother wavelet.

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

The parameter σ defines the bandwidth of the Gaussian window and f_0 is the central frequency. Here, we use $\sigma = 8$, $f_0 = 1$.

It is known that the real part of $CWT[x(t)]$ shows the variability characteristics of $x(t)$ at frequency $f \simeq \frac{f_0}{a}$. By adapting equation (1) to the EEG signal $x_i(t)$ recorded at electrode j, theoretically it is possible to obtain the characteristics of each frequency component of EEG. However, the amplitude and the signal/noise ratio of EEG generally fluctuate for different individuals. To eliminate individual differences, we introduce the *normalized variability* given by:

$$P_i(f,t) = \left\| CWT\left[\frac{x_i(t)}{\sqrt{< x_i^2(t) >}}\right] \right\|^2, \qquad (3)$$

where $<>$ shows the average of the series [7].

B. Power Variance Function

To evaluate the activity of the EEG variability characteristics, we calculated the variance $\sigma_i^2(f)$ for $P_i(f,t)$:

$$\begin{aligned}\sigma_i^2(f) &= < (P_i(f,t) - < P_i(f,t) >)^2 > \\ &= < P_i^2(f,t) > - < P_i(f,t) >^2 . \end{aligned} \quad (4)$$

This is referred to as *Power Variance Function (PVF)*. The variance of $P_i(f,t)$ as shown above becomes a function $\sigma_i^2(f)$ whose variable is the frequency f. The PVF shows how active the EEG variability is at frequency f.

An example for PVF is shown in Fig. 1, where the PVF is calculated from the electroencephalogram of an AD patient. Each line shows the PVF at each electrode. The peak at 10 Hz indicates that the power variance is particularly high at 10 Hz.

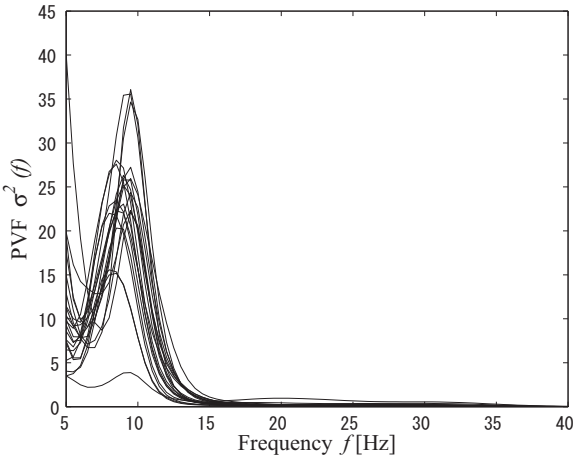


Fig. 1. Calculated PVF of an AD patient: each line shows the PVF at each electrode

C. Approximation to parametric distribution

The PVF of healthy subjects is distributed at each frequency at each electrode. Fig. 2(a) shows a histogram of the PVF at 8.5 [Hz] on F3 for healthy subjects. PVF is distributed over positive values and is shifted to the left.

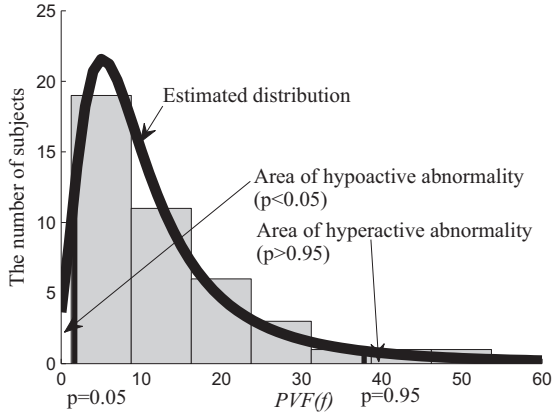
The Generalized Extreme Value (GEV) distribution is a parametric distribution which fits the shape of this histogram well [8]. Here, we approximated the distribution of PVF of healthy subjects to a GEV distribution by applying maximum likelihood estimation, assuming that the PVF is distributed in accordance with the GEV distribution.

GEV distribution is defined as follows:

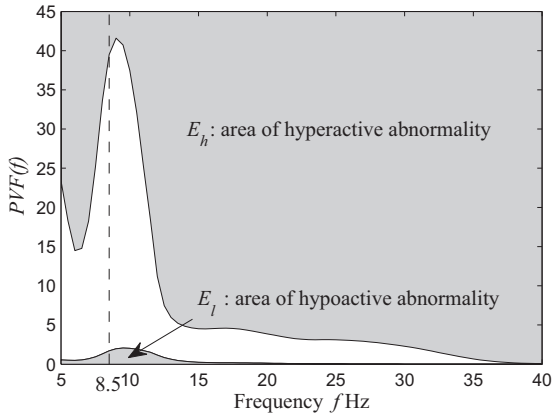
$$\begin{aligned} y &= f(x|\kappa,\mu,\sigma) \\ &= \frac{1}{\sigma} e^{-\left(1+\kappa\frac{x-\mu}{\sigma}\right)^{-\frac{1}{\kappa}}} \left(1+\kappa\frac{x-\mu}{\sigma}\right)^{\left(-1-\frac{1}{\kappa}\right)}, \end{aligned} \quad (5)$$

where κ is a shape parameter, μ is a position parameter, and σ is a scale parameter. This distribution is classified into three types depending on the shape parameter κ: type I or Gunbel distribution when $\kappa = 0$, type II or Fréchet distribution when $\kappa > 0$, and type III or Weibull distribution when $\kappa < 0$. In this research, almost all distributions are type II or Fréchet distributions. In Fig. 2(a), the solid line is the approximated distribution. It significantly matches the histogram.

The distribution as obtained in this way suggests that the upper and the lower 5% of PVF (areas E_l and E_h) can be estimated (cf. Fig. 2(a) and (b)). PVF can be categorized as a *hypoactive* abnormality if it is in E_l or as a *hyperactive* abnormality if it is in E_h.



(a) Histogram of PVF and estimated distribution on F3 at 8.5[Hz]

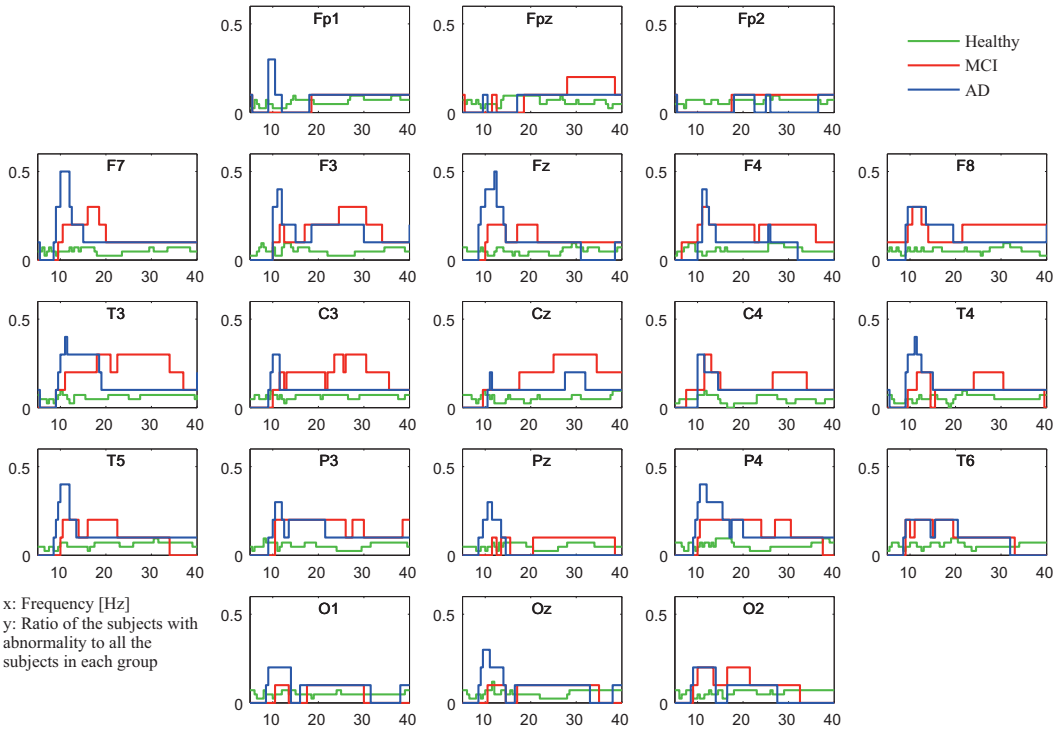


(b) Area of abnormality in F3

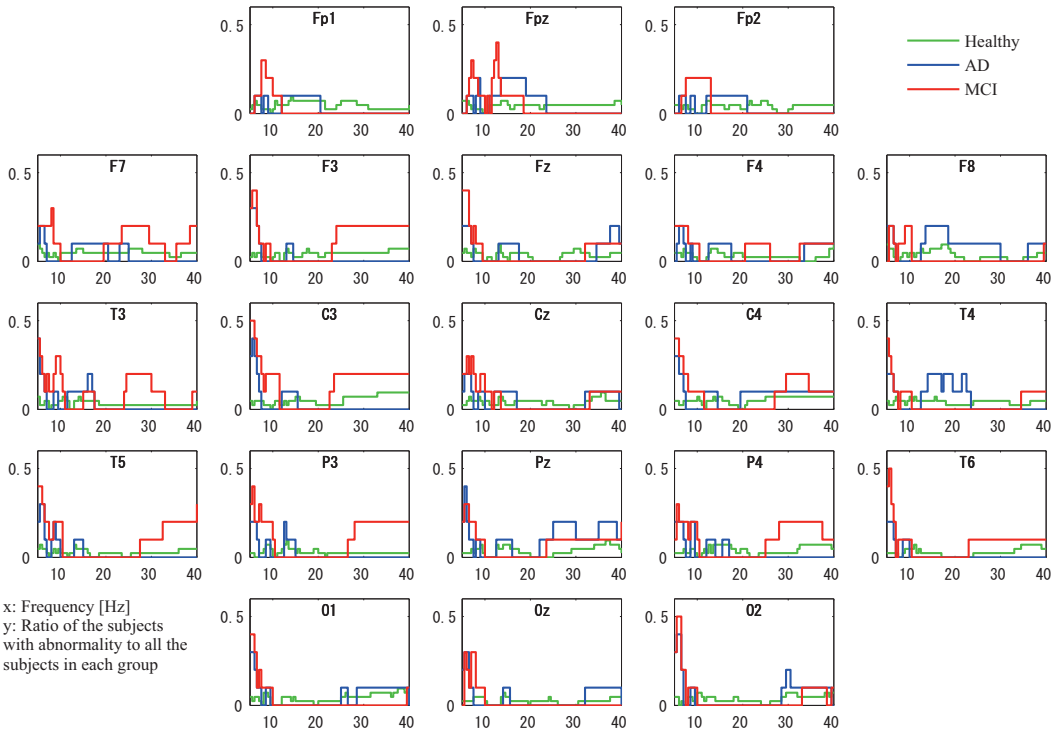
Fig. 2. Approximation to a general extreme distribution

III. RESULT

We analyzed the electroencephalograms of 42 healthy subjects (The age wes 57-89 years), 10 AD patients (The age was 68-88 years, Mini-Mental Status Exam (MMSE) score was 6-23), and 10 MCI patients (The age was 49-86 years, MMSE was 24-30). The MCI patients were patients who were deemed probable or possible AD patients at 12 or 18 months after their electroencephalograms were recorded for the first time, and these first electroencephalograms are used in this paper. All electroencephalograms were recorded by staff from Brain Functions Laboratory, Inc. and the National Center Hospital of Neurology and Psychiatry. All recordings were made while the patients were at rest with eyes closed for 5 minutes. Twenty-one electrodes were placed over the scalp



(a) Ratio of subjects with *hypoactive* abnormality ($p < 0.05$) to all subjects in each group



(b) Ratio of subjects with *hyperactive* abnormality ($p > 0.95$) to all subjects in each group

Fig. 3. Ratio of subjects with abnormality to all subjects in each group on the each electrode

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].

Fig. 3(a) shows the ratio of subjects with *hypoactive* abnormality to all subjects in each group (Healthy, AD, and MCI). From this figure, it is seen that AD patients tend to have abnormaly in the 10-13 [Hz] band. This is remarkably clear in the left temporal area (F7, F3, T3, C3), Fz, T4 and P4, where the ratio of AD subjects with abnormality to all AD subjects is larger than 0.4. MCI subjects often had abnormaly in the 15-30 [Hz] band in the left temporal area (F7, F3, T3, C3) and Cz, where the ratio of MCI subjects with abnormality to all MCI subjects is larger than 0.3.

Fig. 3(b) shows the ratio of subjects with *hyperactive* abnormality to all subjects in each group. From this figure, MCI patients overall tend to have abnormality in the 5-10 [Hz] band. The ratio of MCI subjects with abnormality to all MCI subjects is larger than 0.5 in the right posterior area (T6, 02) and C3, and larger than 0.4 for many of the other electrodes. The electrodes are T3, C3, Pz, and O2 where the ratio of AD patients with abnormality to all AD subjects are larger than 0.4.

Combining the *hypoactive* and the *hyperactive* values, all AD and MCI subjects exhibited abnormal values for some of the electrodes. Besides the ratio of healthy subjects with abnormality to all healthy subjects is smaller than 0.1 on the whole electrodes in the each abnormality.

IV. Discussion

A number of other studies have reported that slowing on EEG is prominent in the left temporal area of AD patients [9][10]. We also observed hypoactive abnormality in the temporal area in this study. Considering this fact, it appears that PVF includes spectral information. The power variance becomes zero when the signals fluctuate with a constant amplitude, and therefore PVF can be a solid indicator against steady noise. In addition, smooth lines can be drawn for PVF by using the Wavelet transform in order to perceive the overall tendencies for each bandwidth.

It should be pointed out that MCI patients exhibited abnormally high PVF in the θ band and AD patients exhibited low PVF in the α band. The electrodes for which abnormal values were taken were different depending on whether subjects exhibited *hyperactive* or *hypoactive* abnormality. Therefore, it might be possible to develop a method for diagnosing MCI in the pre-clinical stage by applying this result.

Although all AD and MCI subjects exhibited abnormal values, 10% of the healthy subjects also exhibited abnormal values in some frequency bands at some electrodes, and this might result in decreased accuracy in distinguishing between MCI subjects and healthy subjects. The estimated GEV distribution often did not match significantly with the distribution of the observed PVF in the left temporal area above 25 [Hz] since the number of healthy subjects was insufficient and the PVF histograms were not sufficiently smooth. In future studies, it will be necessary to obtain a larger number of samples from healthy subjects and to calculate proper distributions.

Based on the present results, in order to develop a sensitive algorithm for diagnosis of MCI in future work, we will select the proper electrodes and frequency bands and will consider whether they indicate *hypoactive* or *hyperactive* abnormality.

V. Conclusions and Future Works

It is possible to use PVF to calculate the variance of each frequency component from the electroencephalograms of AD-MCI subjects. The method proposed here indicates that MCI patients exhibit abnormally high PVF in the θ band and AD patients exhibit low PVF in the α band, and it might be possible to develop a diagnostic method for MCI for use in the pre-clinical stage by applying these findings. In the future, we will apply our method in the development of a sensitive algorithm for the diagnosis of MCI.

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