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An EEG Diagnosis System for Quasi Brain Death Based on Complexity and Energy Analyses*

Jianting Cao, Daishi Watabe, and Liqing Zhang, *Members, IEEE*

***Abstract*— Electroencephalogram (EEG) is often used in confirmatory test for brain death determination in clinical practice. Because the EEG measuring and monitoring is relatively safe and reliable for deep comatose patients, it is believed to be valuable for reducing the risk of diagnosis or prevent mistaken diagnosis of brain death. In this paper, we present EEG complexity analysis and EEG energy analyses for the EEG acquisition of 35 adult patients. In EEG complexity analysis, we firstly report statistically significant differences of quantitative statistics in this clinical study. Next, for the patient-wise case study, we develop a dynamical calculating entropy method to monitor the symptom change of patients. In EEG energy analysis, we firstly accumulate the EEG energy from the extracted components that are related to the brain activities. Then, we evaluate the energy differences between deep comatose patients and brain death. The empirical results reported in this paper suggest some promising directions and valuable clues for clinical practice.**

I. Introduction

The brain death is defined as the cessation and irreversibility of all brain and brain stem functions [1]. Based on this definition, the basic clinical criterion has been established in most countries. For example, the Japanese criterion includes a few major items for brain death determination as follows (see Fig. 1).

• Coma test: motor responses of the limbs to painful stimuli.

• Pupil test: pupils' response to light and pupils dilatation.

• Brainstem reflexes test: e.g., coughing, corneal reflexes, etc.

• Apnea test: patient's capability of spontaneous respiration.

• EEG confirmatory test: no electrical activity occurs above 2 μV.

In the standard process of brain death determination, it often involves certain risks and takes a long time. For example, in order to determine the patient's spontaneous respiration, removing temporarily the respiratory machine is necessary during the apnea test [2]. Moreover, in the EEG confirmatory test, the observation of electrical activities below 2 μV, the recordings should at least 30 minutes, and repeated the same recording after 6 hours. Therefore, in order to reduce the risk and to save the precious time for the medical care in clinical practice, it is desirable to develop a practical yet safe and reliable diagnosis system in the brain death determination.

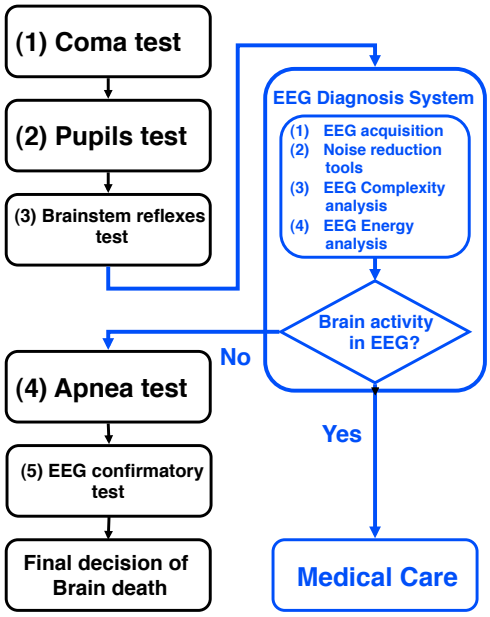

Figure 1. EEG diagnosis system in the brain death determinaton.

We first introduce an EEG diagnosis system into the standard brain death determination process as shown in Fig. 1 [3]. In Fig. 1, after the coma test, pupils test, and brainstem reflexes test conducted for a patient, the EEG diagnosis system comes in at the bedside of patient in the Intensive Care Unit (ICU). The purpose of the EEG diagnosis is to explore advanced signal processing tools to evaluate whether any brain wave activity occurs in the patient's brain. If the decision is positive (i.e., indicating the presence of brain activities), it suggests to side step the further tests of brain death, and go directly to spend more time on the patient's medical care. On the contrary, if the result of EEG diagnosis is negative, the apnea test and EEG confirmatory test will be executed afterwards as in the standard brain death determination procedure. It is worth noting that the EEG preliminary diagnosis is not a substitute of the standard process of brain death determination. Instead, it is our belief that if the EEG diagnosis is reliable and its results are significant, it would provide a simple and risk-free diagnosis tool in the ICU of the hospital without jeopardizing the patient's life.

The EEG diagnosis system (Fig. 1) includes a portable EEG acquisition device and the EEG-oriented signal

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Jianting Cao is with the Saitama Institute of Technology, Fusaiji 1690, Fukaya-shi, Saitama 369-0293, Japan, and also with the Laboratory for Advanced Brain Signal Processing, RIKEN Brain Science Institute, Saitama 351-0198, Japan (E-mail: cao@sit.ac.jp).

Daishi Watabe is with the Saitama Institute of Technology, Fusaiji 1690, Fukaya-shi, Saitama 369-0293, Japan (E-mail: dw@sit.ac.jp).

Liqing Zhang is with the Shanghai Jiao Tong University, #800, Dongchuan Road, Shanghai, China (E-mail: zhang-lq@cs.sjtu.edu.cn).

processing tools such as noise reduction, source separation, feature extraction, complexity and energy analysis. The noise reduction and the source separation, followed by the Fourier and time-frequency analysis tools have been developed in [4, 5]. This paper will focus on EEG complexity analysis and EEG energy analyses to evaluate the differences between deep comatose patients and brain deaths.

II. EEG Data Recording

The EEG measurements were recorded at the bedside of patients in a university hospital ICU (Shanghai, China), where the level of environmental noise could be fairly high. The EEG recording machine was a portable *NeuroScan ESI-32* system (El Paso, TX). In the system, a total of nine electrodes were placed on the forehead of the patient lying on the bed, which mainly cover the non- or least hairy area of the scalp. Specifically, six channels are placed at Fp1, Fp2, F3, F4, C3, C4, according to the standard 10/20 system; two electrodes that connect the two ears are used as reference, namely (A1+A2)/2; the addition channel, GND, serves as the ground (Fig. 2). The sampling rate of EEG was 1 *kHz*, and the resistances of electrodes were set under 8 *kΩ*. During the clinical measurements, no gel or any other conductive pastes was used during all sessions of EEG recording.

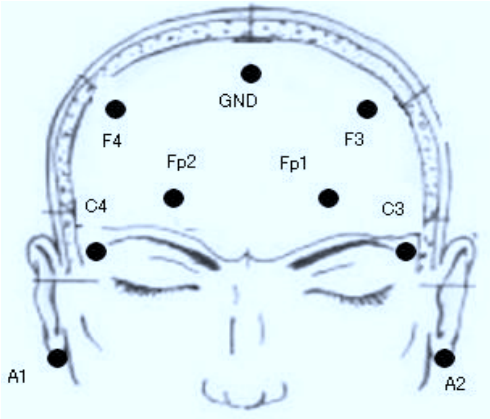

Figure 2. The layout of electrodes.

35 adult patients have been examined using EEG from June 2004 to March 2006, with age range from 17 to 85 years old. All patients were in deep comatose or brain death before the EEG recordings. Patients were all lying down in the bed with eyes closed during the EEG measurements. Correspondingly, no ocular or muscle artifacts were observed. However, sometimes the heart beat rhythm can be observed from specific patients. In China, there was still no legal regulation or instructions regarding to the brain death diagnosis at the time of data collection. In our case, the medical classification between comatose and brain death was pre-determined by two experienced physicians based on continuous monitoring and several typical tests. The EEG recordings were supervised by one physician and operated by either medical doctor or medical staff. In some cases the determination results were further confirmed later on based on extra evidence.

The experimental protocol was approved by the local ethics committee of the hospital, and all recorded data were used with permission of patients' family. Because the health conditions of patients varied, each patient might have different number of recorded data sessions at the same or different day. Finally, a total of 64 sessions' recordings from 35 patients were used in this paper.

III. EEG Complexity Analysis for Patients

In the literature, many complexity measures have been proposed or developed for characterizing neurophysiological signals (e.g., [6-12]). In our complexity analysis, four types of complexity measures are under investigation:

1) The approximate entropy (ApEn) [10], which is a quantity that measures the regularity or predictability of a random signal or time series.

2) The time delay-embedded normalized singular spectrum entropy (NSSE) [11], which is a complexity measure arisen from calculating the singular spectrum of a delay-embedded time series.

3) The C_0 complexity [8], which is a complexity measure based on simple Fourier analysis.

4) The *α-exponent* based on detrended fluctuation analysis (DFA) [12], which estimates the fractal scaling exponent.

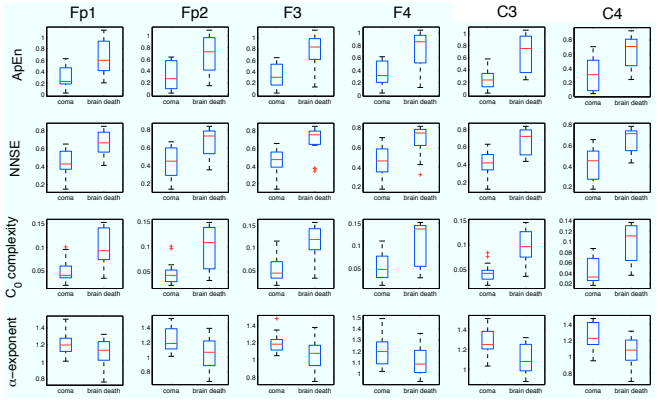

Figure 3. Box plot statistics of four complexity analysis for 6 channels between comatose group and brain death group. The maximum, minimum and average values are displayed.

Notably, all these measures are strictly invariant to the scaling of the signal (hence independent of the signal's power). The parameter setup in our experiment is selected upon literature recommendation and tested by trial and error. In Fig.3, as a quantitative study, we find the statistical differences between the comatose patient group and brain death group by used four EEG complexity analysis methods within the total of 35 patients.

In the patient-wise case study, we will focus on the development of a dynamic ApEn algorithm for observing the symptom variation of each individual patient.

The standard ApEn algorithm [10] is computed by

$$ApEn(N,m,r) = \phi^{m,r} - \phi^{m+1,r}, \qquad (1)$$

where N is the length of a time series, m is the length of a sample vectors, and ϕ is a natural logarithmic average over a sample vector. The index r is the so-called tolerance parameter.

By introducing a time window with width t' (see Fig. 4), we can compute ApEn for *i-th* window by

$$ApEn(t',m',r)_i = \phi_i^{m',r} - \phi_i^{m'+1,r}, \quad (2)$$

where $i = 1,2,\cdots,N$ Moving the window with a steady sample, we can obtain a vector of ApEn as

$$\mathbf{DApEn} = \left[ApEn(t',m',r)_1,\cdots,ApEn(t',m',r)_N \right]. \quad (3)$$

Consequently, when computing ApEn, we can only obtain a scalar, however, by computing **DApEn**, we can obtain a vector in which it involves dynamic complexity information.

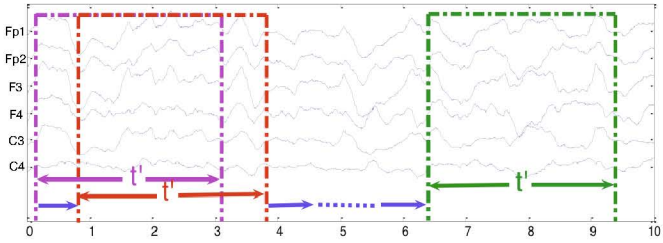

Figure 4. The diagram of dynamic complexity analysis, moving time window with width t'.

Due to space constraint, let's present one specific patient case (the consciousness state changes from deep comatose to brain death). The patient was a 17-year-old female with the virus encephalitis. This patient suffered from the difficulty of breathing, and the respiratory machine was used in the ICU right since her admittance to the hospital on October 14, 2005. On October 18, 2005, the patient was in a deep comatose state with dilated pupils, but was found to have a very weak visual response. On the same day, the EEG was recorded about 3 minutes at the patient's bedside. Next day, on October 19, 2005, the patient further suffered from apnea, and her pupils lost the light response. Two clinical doctors preliminarily diagnosed the patient as a brain death. On the same day, the EEG was recorded in 4 minutes.

In total, the EEG recordings from 2 days have the durations about 7 minutes. Here, we apply the developed **DApEn** presented in Eqs. (2), (3) to 2 days recorded EEG signals, the results are obtained in Fig. 5.

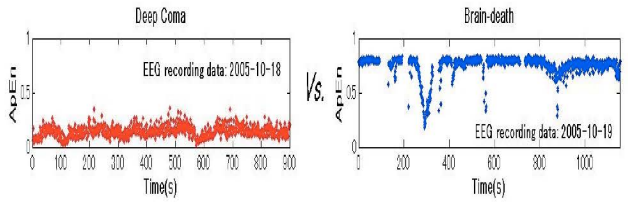

Figure 5. Dynamic complexity analysis (**DApEn**) for a patient with two consciousness states. The ApEn value of comatose state was close to zero, and brain death was close to one.

As shown in the Fig, 5, we can clearly observe a mode shift (transition from deep comatose to brain death) between these two days. This data analysis result is completely identical to the result given by clinical doctors. From this result we know that the live brain with rhythm activities have a high regularity, it produces a low ApEn value. Contrarily, a random signal such as noise (without brain activities) with a low regularity, it produces a greater ApEn value.

IV. EEG Energy Analysis for Patients

Let us firstly define the EEG energy using the power spectrum within the frequency band multiply by recorded EEG time. Specially, when the recorded EEG time is equal to one second, the EEG energy is equal to the power spectrum. Since the energy or the power of spontaneous activities in a live brain is usually higher than that of non-activity components, therefore, we can use the EEG energy analysis to evaluate the energy (or the power spectrum) of the extracted activities differences between comatose patients and brain deaths.

The energy of brain activities can be computed by using empirical mode decomposition (EMD) proposed in [13]. This method is used to decompose the data into several oscillatory components called intrinsic mode function (IMF). The IMF components are usually expressed as the standard Hilbert transforms, from which the instantaneous frequencies can be calculated. The local energy and the instantaneous frequency derived from the IMF components through the Hilbert transform can be given a full energy frequency time distribution of the data. Moreover, in order to extract brain activity features from multi-channel EEG simultaneously, we can use recently developed multivariate empirical mode decomposition (MEMD) method [14].

Here, we firstly demonstrate an example applying MEMD to a patient's EEG. The patient is an 18-year-old male with a primary cerebral disease, who was admitted to the hospital on May 20, 2004. After a month hospitalization, on June 22, 2004, the patient lost his consciousness and remained in a deep coma state. On the EEG examining day, his pupils were dilated, and the respiratory machine was used. The patient was completely unresponsive to external visual, auditory, and tactile stimuli, and was incapable of any communication. The symptom of patient was very similar to a brain death case. Applying MEMD to this patients' EEG, we can obtain the results shown in Fig. 6.

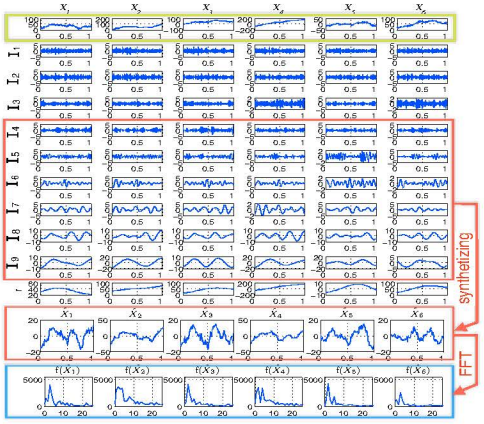

Figure 6. The EEG energy analysis for a comatose patient. Top row (X_1 to X_6) were the recorded EEG in one second, I_1 to I_9 are decomposed 9 *IMF* components, and r is a residual component. The estimated $\hat{x}_1$ to $\hat{x}_6$ are brain activities in time domain, and bottom row are the estimated brain activities in frequency domain.

As seeing from Fig. 6, the recorded 6 channels EEG are decomposed into 9 *IMF* components (I_1 *to* I_9) and a residual component (r) from high frequency to low frequency simultaneously by MEMD. Since the brain activity of the consciousness lost patient are usually below 40 Hz, therefore, we can remove the high frequency IMF components I_1 to I_3 (refer to electrical interference or other noise from environment that contains in the recorded EEG), and a residual component (r). We then synthetize the suitable components from I_4 to I_9 to the estimated components (the denoised components), and transfer them to frequency domain by fast Fourier transform (FFT). Finally, we can compute the power spectrum of each decomposed component. In this case, the total of the power spectrum (EEG energy) is about 2800 (see Fig. 7, C_1 means the first comatose patient). This result of EEG energy analysis indicated that the patient still had physiological brain activity.

Applying the same EEG energy analysis method to the total of 35 patients' EEG, we obtained the EEG energy patterns shown in Fig. 7.

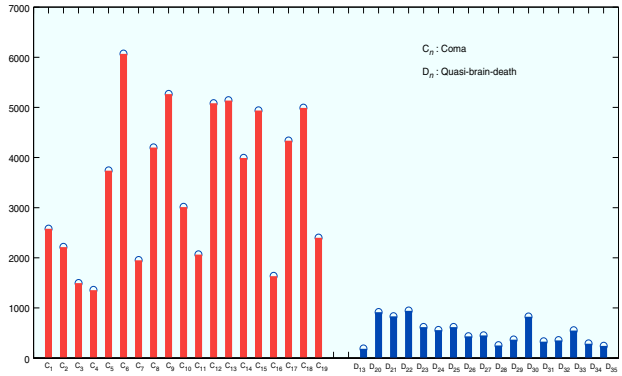

Figure 7. The EEG energy brain distribution of 35 patients. C_1 to C_{19} are 19 comatose patients, and D_{20} to D_{35} are 16 brain deaths. D_{13} is the same patient as C_{13}.

As can be seen in Fig. 7, among 19 comatose patients (C_1 to C_{19}), the maximum value of power spectrum goes up over 6000, and their averaged value is above 2000. It illustrates that the comatose patients' brain activities are exist. Contrary to this, in the case of 16 brain deaths (D_{20} to D_{35}), there is no spectral power over 1000. That implied the absence of brain activities in brain deaths except for some kinds of noise. C_{13} and D_{13} is the same patient who has two consciousness states changes from comatose to brain death (the same result that we already obtained by using the EEG complexity analysis shown in Fig. 5.) Based on the experimental results, we can conclude that the EEG energy analysis method can be used to evaluate the comatose patient and brain death in the clinical practice.

V. Conclusion

In this paper, we have proposed EEG complexity analysis and EEG energy analyses methods in the EEG diagnosis system for the determination of brain death. In the EEG complexity analysis, we found that the statistically significant differences between the group of comatose patient and brain death. Moreover, the developed dynamic calculating entropy method can be used to monitor the symptom change of patients. In EEG energy analysis, we can evaluate the EEG energy differences between deep comatose patients and brain death. In terms of the clinical utility, we believe that the real-field analysis of the EEG recordings would provide the medical doctor with valuable cues of the ongoing activities of the brain. Hence, our proposed method can be potentially used as a diagnostic and prognostic tool in clinical practice.

In the future study, we are planning to collect more real-field EEG data for more in-depth data analysis such as the low-frequency component decomposition, and pattern classification. In conclusion, we believe that the developed tools for EEG analysis would shed a light on the real-time medical diagnosis in clinical practice, and it might open a challenging research direction in biomedical engineering.

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