1. INTRODUCTION

Studies on EEG patterns have proven to be useful for the assessment of clinical pathologies. It has been reported that quantitative frequency analysis of EEG data is useful as a supplement to diagnosis for adult psychiatric diseases [1]. In individuals with mental disorders, abnormalities in EEG have been observed [2].

Among frequency analysis, alpha waves are a popular research topic. Normally, alpha waves have a frequency ranging from 8 to 13.9 Hz, and can be seen the most clearly in healthy individuals in the occipital region of the brain during the closing of the eyes [3,4]. Berger made the unexpected observation that when subjects opened their eyes, the EEG oscillations in the alpha band decreased in amplitude or disappeared completely (the “Berger effect”) [5]. Alpha waves play an important role in cognitive processing. It has been found that alpha peak frequency in posterior regions increases with increasing cognitive demands [6]. Alpha wave activity with high amplitude has been observed in patients with Alzheimer’s disease [7]. This implies that it may be possible that an abnormality in the appearance of alpha waves in the EEG could be an indication of an abnormal EEG. Another study has found that a disruption of electrical oscillations at rest is linearly correlated with neurological deficits. Alpha synchrony is suggested to be a specific biomarker of neurological function in patients with brain lesions [8].

An increased variability of anterior EEG in the alpha band was found to be possibly a characteristic feature for depression, and this could suggest that anterior EEG alpha asymmetry is a trait marker for depression [9]. All of these studies indicate that conducting research on alpha waves is important and useful.

There are cases where alpha waves do not only appear in the occipital region, but also continuously in all regions of the brain. This phenomenon, where alpha waves appear in all or nearly all electrodes, is called the “diffuse alpha pattern”, and is regarded as a type of abnormal EEG [10]. The diffuse alpha pattern has been observed in the EEG of individuals during states of unconsciousness [11], as well as in some individuals suffering from mental disorders.

Research has been carried out that extracts and quantifies the features of the alpha activity and the connectivity between different parts of the brain. It was suggested that mild cognitive impairment patients have a higher degree of functional connectivity between hemispheres and in hemispheres during working memory task [12]. The alpha bandwidth may be the characteristic bandwidth in distinguishing mild cognitive impairment patients from healthy individuals during working memory tasks [13].

In this study, we aimed to investigate the connectivity in the brain of individuals who have the normal alpha pattern, as well as individuals who have the diffuse alpha pattern. We evaluated the alpha activity, and, by using a method called wavelet-crosscorrelation analysis, abstracted how the connectivity in the alpha band between the parts of the brain could be stronger than healthy individuals.
brain is different between individuals with the normal alpha pattern and individuals with the diffuse alpha pattern.

In this research, we wanted to know to what extent the brain works differently in individuals where the diffuse alpha pattern can be observed in the EEG, as compared to individuals whose EEG show the normal alpha pattern. Therefore, we used wavelet-crosscorrelation analysis to visualize the correlation pattern in the brain, and compare the connectivity between the brain of normal alpha pattern individuals and diffuse alpha pattern individuals. It can be hypothesized that the connectivity strength between the parts in the brain might differ between these two groups of subjects.

The novelty of this study is abstracting the alpha band to visualize and investigate the correlation pattern and connectivity strength in the brain. The basis of this study is the use of wavelet-crosscorrelation analysis.

2. METHODS

2.1 Recording of the data
EEGs were recorded from 10 healthy subjects (5 males and 5 females; mean age = 24.40 ± 2.46 years) and 10 individuals suffering from various mental disorders (5 males and 5 females; mean age = 54.80 ± 10.43 years) (Table 1). The healthy individuals were adults whose EEGs showed no abnormalities. Alpha activity could be observed in the occipital area. Abnormalities in the EEGs could be observed in the mental disorder patients. The diffuse alpha pattern appears prominently in all of the 10 patients.

The objective of this study was to investigate and compare the connectivity in the brain of individuals who have the normal alpha pattern, and individuals who have the diffuse alpha pattern. For this reason, we purposely selected 10 healthy subjects whose EEGs did not show the diffuse alpha pattern, and 10 mental disorder patients whose EEG showed the diffuse alpha pattern.

Table 1: Patient profile (mean age = 54.80 ± 10.43 years)

| Patient number | Age [years] | Gender | Disorder        |
|----------------|-------------|--------|-----------------|
| 1              | 58          | Female | Schizophrenia   |
| 2              | 40          | Female | Low IQ / Depression |
| 3              | 50          | Male   | Depression      |
| 4              | 55          | Male   | Neurosis        |
| 5              | 56          | Female | Insomnia        |
| 6              | 70          | Male   | Dementia        |
| 7              | 54          | Male   | Depression      |
| 8              | 64          | Female | Schizophrenia   |
| 9              | 66          | Male   | Hypochondria    |
| 10             | 35          | Female | Neurosis / Depression |

Table 1: Patient profile (mean age = 54.80 ± 10.43 years)

The EEGs of all subjects were measured during a state of relaxation while the eyes were closed, and there was no sound at the time of recording. To record the EEG data, the electrodes (19 channels) were placed according to the International 10–20 electrode positions system. The sampling frequency was 500 Hz. For each subject’s measured EEG, five epochs of 2 seconds were selected and analyzed. The number of sampling points was 1000. A bandpass filter was set between 0.53 Hz and 30.00 Hz.

This research was approved by the ethics committee of the Matsumoto clinic and the graduate school of applied informatics of the University of Hyogo. All subjects agreed to be measured and gave written informed consent.

2.2 Analysis methods
Based on wavelet-crosscorrelation analysis (wavelet analysis and crosscorrelation analysis), we were able to analyze non-stationary EEG data in the alpha band, and obtain the correlation pattern and connectivity strength in the brain. We then visualized the correlation patterns in maps, and used statistical analysis to compare the connectivity strength in the brain between healthy individuals and diffuse alpha pattern individuals.

Analyzing low values does not provide a high reliability, therefore low amplitudes were excluded from our analysis.

Wavelet transform
For the first step, we used a method called wavelet transform to obtain 2 second wavelet power spectra in the alpha band in five epochs for each electrode. The wavelet spectra were compared between the healthy subjects and patients. Using this method, it becomes possible to conduct spectrum analysis in a broad frequency range without losing time information [14]. To do time-frequency analysis, it is necessary to choose an appropriate time window. The wavelet transform of a signal can be calculated by projecting the signal onto a basic wavelet. This tiny wave is called the mother wavelet ($g(t)$). A Gaussian wavelet was used as the mother wavelet. The Gabor mother wavelet was chosen because it has one of the lowest values for the time-frequency resolution product. In other words, it has one of the least spreads in the time domain for a given spread in the frequency domain [14, 15].

The length of the Gabor mother wavelet varies according to the frequency, and was therefore set to $m$. The Gabor mother wavelet was employed for the two-second EEG epoch from $-m$ to $1000+m$ (Figure 1). The mother wavelet shifts every two milliseconds along the two-second epoch. The area outside of the epoch was considered zero. Due to convolution of the mother wavelet with the EEG
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epoch, the edge effect occurs, therefore data outside of 2000-m milliseconds was excluded from our next analysis (wavelet-crosscorrelation analysis). In addition, not all data within the 2000-m milliseconds was adopted in the next analysis. Because analyzing low values does not provide high reliability, we set a threshold value for wavelet spectral values. Wavelet spectral values below 10 percent compared to the maximum value of the wavelet power spectrum were also excluded from the next analysis.

By making the mother wavelet expandable and contractable, the time information is saved when conducting frequency analysis. The wavelet transform \( W_x(a,b) \) of a signal \( x(t) \) is calculated in equation 1 [14, 15], where \( a \) is the scaling parameter that changes the flexibility of the mother wavelet, \( b \) is the parameter that shifts the mother wavelet, and \( t \) represents the time. By shifting these parameters on the original signal \( x(t) \), time-frequency analysis becomes possible.

\[
W_x(a,b) = \frac{1}{\sqrt{|a|}} g(\frac{t-b}{a})x(t)dt
\]  

Statistical analysis of wavelet spectra

Using an original program of Matlab R2016b (MathWorks) for each electrode for all epochs of all subjects, we calculated the frequency occurring at the highest wavelet spectral value. We statistically compared the frequencies of the wavelet spectra between the healthy subjects and patients with the diffuse alpha pattern using the Student’s T-test.

Wavelet-crosscorrelation analysis

In order to obtain wavelet-crosscorrelation coefficients (WCC) between all 19 electrodes, we used wavelet-crosscorrelation analysis. Wavelet-crosscorrelation analysis is a method that, while maintaining time information, makes it possible to investigate the correlation between the different parts inside the brain [14, 15]. It is a combination of wavelet transform, crosscorrelation analysis, and correlation analysis. Similar to crosscorrelation analysis, it displays how much the nature and shape of two signals resemble each other at different frequencies.

WCC values range from 0 to 1. The closer the WCC value is to 1, the more the two signals are the same in terms of shape and nature; the closer the value is to 0, the more different the two signals are. As opposed to crosscorrelation analysis, it can also be used for non-stationary data [14, 15]. In other words, signals that have rapidly changing components and transient changes, for example EEGs that have sudden epileptiform discharges, can be analyzed.

By using wavelet-crosscorrelation analysis, it is possible to visualize the connectivity (WCC values) and the propagation (time-lag values) between electrodes at various frequencies, while maintaining the time information [14, 15]. Therefore, it becomes possible to better understand the communication in the brain in function of time [16]. By means of calculating WCC values between freely chosen electrodes, it is possible to know how strong the connectivity is between different parts of the brain for a wide range of frequencies. The wavelet-crosscorrelation function \( WCx,y(a,\tau) \) is defined in equation 2 [14, 15].

\[
WCx,y(a,\tau) = \lim_{T \to \infty} \frac{1}{2T} \int_{-T}^{T} \overline{W_x(b,a)}W_y(b+\tau,a)db
\]  

\( \tau \) is a time-lag in the wavelet space. \( WCx,y(a,\tau) \) is complex-valued and consists of a real part \( RWCx,y(a,\tau) \) and an imaginary part \( IWCx,y(a,\tau) \). \( RWCx,y(a,\tau) \) can be used to express the strength of the correlation between two signals \( x \) and \( y \). \( \overline{W_x(b,a)} \) represents the complex conjugate.

The wavelet-crosscorrelation coefficient \( WRx,y(a,\tau) \) from the real part of the wavelet-crosscorrelation function \( RWCx,y(a,\tau) \) is [16, 17]:

\[
WRx,y(a,\tau) = \frac{RWCx,y(a,\tau)}{\sqrt{RWCx,y(a,0)RWCx,y(a,0)}}
\]

WCC maps

For the next step, we calculated and compared WCC values between the healthy subjects and diffuse alpha pattern individuals. The WCC values were calculated from the numerical EEG data using an original program of Matlab R2016b. We analyzed WCC values of 28 frequencies in the alpha bandwidth. The lowest frequency was 7.94 Hz, and the highest frequency was 13.89 Hz. The WCC value of the average of all 28 frequencies was calculated between all 19 electrodes. We set a threshold
for the WCC values: any values below 0.3 were not included in the analysis. Each WCC value corresponds to a channel pair combination. There were 19 electrode channels, therefore a total of 171 channel pair combinations were possible. We first visualized the WCC values in a brain map, and then compared the brain maps between the individuals with the normal alpha pattern and individuals with the diffuse alpha pattern.

Statistical analysis of WCC

The WCC values of all 171 channel pair combinations were averaged into 1 total WCC value. This total WCC value was statistically compared between the healthy individuals and the patients using the Student’s T-test.

WCC in specific orientations in the brain

In addition, we compared WCC values between the normal alpha pattern subjects and diffuse alpha pattern subjects in specific orientations in the brain: the coronal and sagittal orientations. These were further divided into 2 sub-orientations: the medial coronal and lateral coronal orientations; and the medial sagittal and lateral sagittal orientations. All 4 sub-categories are shown in Figure 2. WCC values were cut out in a specific orientation using an original program of Matlab R2016b. The WCC values were statistically analyzed by using one-way analysis of variance (ANOVA) with Bonferroni corrections.

Phase Locking Value

The Phase Locking Value (PLV) is a method that reveals to what extent the phase difference synchronizes between two signals. In other words, it quantifies the stability of the phase difference between the two signals in a predefined frequency range [18]. A PLV value close to 1 shows that if time elapses, the phase difference between two signals doesn’t change much (strong phase synchrony). When the PLV value is close to 0, the phase difference between two signals changes considerably in function of time (weak phase synchrony). To calculate PLV, it is necessary to first calculate the phase of the signals from the coefficients of their wavelet transform at the chosen frequency. The phase difference between two signals x and y at frequency f and time t can be derived from the angles of their wavelet coefficients (equation 4) [18]:

$$\exp(i(\varphi_x(f,t) - \varphi_y(f,t))) = \frac{\hat{W}_x(f,t)W_y(f,t)}{|\hat{W}_x(f,t)W_y(f,t)|}$$ (4)

where $\varphi$ represents the phase.

The stability of the phase difference across the epochs is quantified by a Phase Locking Value (PLV) in equation 5 [18]:

$$PLV(f,t)=\frac{1}{N_{\text{epoch}}} \sum_{\text{epoch}=1}^{N_{\text{epoch}}} \exp(i(\varphi_x, \text{epoch}(f,t) - \varphi_y, \text{epoch}(f,t)))$$ (5)

where $N$ shows the number of epochs of one subject.

The PLV derived from each subject was computed in the alpha band and averaged using an original program of MATLAB 2016b. PLV was calculated and averaged between all 171 channel pair combinations. Because phase synchrony could be prominent in the medial areas in the brain, PLV was in addition calculated and averaged along the medial coronal and medial sagittal orientations. PLV is considered to reflect the connectivity between brain regions [18].

Statistical analysis of PLV

The PLV values of all 171 channel pair combinations were averaged into 1 total value. This total PLV value was statistically compared between all healthy subjects and all patients using the Student’s T-test. The statistical analysis of PLV was performed between all electrodes, and in the medial coronal and medial sagittal orientations. In addition to the T-test, we used the Rayleigh test to analyze the circular dispersion of the phase in the brain. The Rayleigh test can be used to statistically analyze whether or not samples are drawn from a uniform distribution [19]. The test was performed between all epochs of the healthy subjects, and between all epochs of the patients.

3. RESULTS

3.1 EEGs

Figure 3 shows the EEG of a healthy subject (Figure 3a), and a patient with the diffuse alpha pattern (Figure 3b). In the healthy subject’s EEG, alpha waves mainly appear in the occipital region of the brain (electrodes O1 and O2) during eyes closed. This is the normal alpha pattern. In the patient’s EEG, alpha waves appear in many regions of the brain (almost all electrodes). This is the diffuse alpha pattern.
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3.2 Wavelet spectra

Figure 4 shows the wavelet spectra of a representative example of a healthy subject with the normal pattern (Figure 4a) and a patient with the diffuse alpha pattern (Figure 4b). The wavelet spectra are shown at all 19 electrodes, according to the International 10–20 electrode positions system. In the healthy subject, high alpha wave activity mainly appears in O1 and O2. In the patient, high alpha wave activity widely appears in electrodes Fp1, Fp2, F3, Fz, F4, C3, Cz, C4, T3, and T4.

Figure 5a shows the wavelet power spectra at O2 of a representative example of a healthy subject, and Figure 5b shows the wavelet power spectra at O2 of a representative example of a patient with the diffuse alpha pattern. The peak of the wavelet spectra in the alpha bandwidth at O2 in the healthy individual is at a higher frequency than in the patient.

Figure 6 shows the average frequency value at the peak of the wavelet power spectra in the alpha band. The ordinate shows the total average frequency value of all 19 electrodes. The highest wavelet power spectra in the alpha band of the patients with the diffuse alpha pattern occur at a lower frequency than the highest wavelet spectra in the alpha band of healthy individuals with the normal alpha pattern (P < 0.001).

3.3 WCC comparison

Figure 7 shows brain maps that plot the average WCC values of all healthy subjects (Figure 7a) and of all patients with the diffuse alpha pattern (Figure 7b) in

Figure 3: EEG of an epoch of a healthy subject (a), and a patient with the diffuse alpha pattern (b). In the healthy subject’s EEG, alpha waves appear only in O1 and O2 (normal pattern); in the patient’s EEG, alpha waves appear in many electrodes (diffuse alpha).

Figure 4: Wavelet spectra at all electrodes of a healthy subject with the normal alpha pattern (a) and a patient with the diffuse alpha pattern (b). The abscissa shows the time in seconds, and the ordinate shows the frequency in Hz. The color bar on the right of the figure represents the lowest and the highest spectral value for all 19 electrodes.

Figure 5: Wavelet spectra at the O2 electrode of a subject with the normal alpha pattern (a) and a subject with the diffuse alpha pattern (b). The abscissa shows the time in seconds, and the ordinate shows the frequency in Hz. The highest alpha wave activity is shown at the upper right of the color bar.
the alpha bandwidth. Blue displays $0.85 \leq WCC < 0.88$, green displays $0.88 \leq WCC < 0.91$, and red displays $0.91 \leq WCC \leq 1.00$.

Figure 8 shows the total average of the WCC values between all electrodes of all 10 healthy subjects (normal alpha pattern) with all 10 patients (diffuse alpha pattern) in the alpha bandwidth. The total average of the WCC value in the patients with the diffuse alpha pattern is significantly higher than the total WCC value in the brain of healthy individuals with the normal alpha pattern ($P < 0.001$).

Figure 9 shows the brain maps of the coronal and sagittal orientations of the brain of the healthy subjects (upper row, N=10) and patients with diffuse alpha pattern (lower row, N=10). (a) represents the WCC of the medial coronal orientation, (b) is the lateral coronal orientation, (c) is the medial sagittal orientation, and (d) represents the lateral sagittal orientation of the brain. For the coronal orientation, blue displays $0.88 \leq WCC < 0.91$, green displays $0.91 \leq WCC < 0.94$, and red displays $0.94 \leq WCC \leq 1.00$; for the sagittal orientation, blue displays $0.80 \leq WCC < 0.85$, green displays $0.85 \leq WCC < 0.90$, and red displays $0.90 \leq WCC \leq 1.00$. The total average of the WCC value in the patients with the diffuse alpha pattern is significantly higher than the total WCC value in the brain of healthy individuals with the normal alpha pattern ($P < 0.001$).
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lateral sagittal orientation of the brain in (d). For the coronal orientation, blue displays $0.88 \leq \text{WCC} < 0.91$, green displays $0.91 \leq \text{WCC} < 0.94$, and red displays $0.94 \leq \text{WCC} \leq 1.00$; for the sagittal orientation, blue displays $0.80 \leq \text{WCC} < 0.85$, green displays $0.85 \leq \text{WCC} < 0.90$, and red displays $0.90 \leq \text{WCC} \leq 1.00$. For both the coronal and sagittal orientations, it can be observed that the WCC values of the patients are higher than the WCC values of the healthy individuals.

Figure 10 shows the average of the WCC values of all 10 healthy subjects (normal alpha pattern), and the average of the WCC values of all 10 patients (diffuse alpha pattern) for 4 different orientations in the brain: the medial coronal, the lateral coronal, the medial sagittal, and the lateral sagittal orientations. The WCC values represent the average value between the electrodes in each of these four orientations.

For the coronal orientation, blue displays $0.88 \leq \text{WCC} < 0.91$, green displays $0.91 \leq \text{WCC} < 0.94$, and red displays $0.94 \leq \text{WCC} \leq 1.00$; for the sagittal orientation, blue displays $0.80 \leq \text{WCC} < 0.85$, green displays $0.85 \leq \text{WCC} < 0.90$, and red displays $0.90 \leq \text{WCC} \leq 1.00$. For both the coronal and sagittal orientations, it can be observed that the WCC values of the patients with the diffuse alpha pattern are significantly higher than the WCC values of the healthy individuals.

3.4 PLV comparison

Figure 11 shows the total average of the PLV between all 19 electrodes, the medial coronal, and the medial sagittal of all 10 healthy subjects (normal alpha pattern), and all 10 patients (diffuse alpha pattern) in the alpha bandwidth. The abscissa shows the orientation, the ordinate shows the PLV values. The upper line bars and asterisks show the results of the T-test; the asterisks just above the bar graphs show the results of the Rayleigh test. We can observe that in all three cases, the average PLV values of the subjects with the diffuse alpha pattern is higher than the average PLV values of the healthy individuals. These results are significant between all electrodes ($P < 0.01$), and along the medial sagittal orientation ($P < 0.001$). In the patients, between all electrodes and along the medial sagittal orientation, the dispersion of the phase is polarized ($P < 0.05$).

4. DISCUSSION

We compared the normal alpha pattern with the diffuse alpha pattern, and investigated how the connectivity in the brain differs between these 2 patterns. We found that the connectivity in the brain of individuals with the diffuse alpha pattern is stronger than in individuals without the diffuse alpha pattern. We could explain this finding by hypothesizing that the connectivity in the brain in individuals with the diffuse alpha pattern needs to be stronger in order for the communication in the brain to work sufficiently.

It is common that alpha waves in healthy individuals have the highest alpha wave activity (the highest volt-
age) in the occipital region of the brain. Previous research reported that in some individuals, alpha activity in the brain increases with age [4]. In addition, there have been reports that alpha activity occurs at a higher frequency in healthy individuals, and occurs at a lower frequency in elderly people [10]. In this research, the distribution of the alpha activity and the frequency in the alpha band of the wavelet spectra was different between the individuals with the normal alpha pattern and the individuals with the diffuse alpha pattern. Observing a map of wavelet spectra could be helpful for doctors to intuitively understand the distribution and frequency in the alpha band.

The results in our study statistically confirm that the WCC values between all the electrodes at all frequencies were significantly higher in the individuals with the diffuse pattern than the WCC values of the healthy subjects. In previous research, it was found that wavelet-crosscorrelation analysis can help reveal and visualize the dynamic changes of brain conditions [14, 15]. Calculating WCC values allows to visualize the connectivity in the human brain, as well as the communication between the brain regions which cannot be seen by means of EEG alone. It allows easy comparison of the brain function between individuals with the normal alpha pattern and individuals with the diffuse alpha pattern. Investigating the connectivity in the brain can be useful to diagnose mental diseases.

Several studies have been carried out on the connectivity in the brain of people with abnormal EEG and mental diseases. There is evidence that individuals suffering from dementia such as Alzheimer’s disease, might have altered functional brain connectivity patterns when compared to healthy individuals [17]. Another study revealed that in people with Alzheimer disease, the connectivity in the brain, as well as the small world property of the brain is altered [20]. The study suggests that there is a disrupted organization of functional brain networks in people suffering from Alzheimer’s disease. It has been reported that depression is a mental illness that presents alterations in functional brain connectivity [21]. In addition, another study revealed that there may be an increase in brain functional connectivity in individuals suffering from depression [22]. A relation can be found between dementia and depression: some dementia patients have symptoms of depression [23].

Our results suggest that in healthy individuals, communication may occur either in only the occipital area; or either in only the frontal area of the brain. In the patients with the diffuse alpha pattern, it could be the case that communication in the brain is only possible if all regions of the brain are actively involved [24]. This might be due to inefficiency in the connectivity in the brain of the patients. In the brain of healthy individuals, it could be that communication in the brain occurs at a relatively low level of connectivity. Communication in the brain of healthy individuals may be more efficient than patients with the diffuse alpha pattern.

Studies about connectivity between specific brain regions have also been conducted. Auditory connectivity via the corpus callosum has been reported to be responsible for the interplay of right and left speech-relevant brain regions [25]. It appears that there is a significantly increased effective connectivity in the gamma band from the right to the left secondary auditory cortex during conscious perception of left ear stimuli [25]. However, it remains unknown in which direction the interhemispheric communication is realized. Another study has reported that the functional connectivity of the human brain changes in several regions in the brain of individuals suffering from mesial temporal lobe epilepsy. An increased functional connectivity was found in the medial temporal lobe, the frontal lobe, and between the parietal and frontal lobes [26]. Another study has suggested that in cognitive impairment patients, the connectivity between hemispheres is stronger than the intra-hemispheric connectivity [13]. The study also revealed that these patients display greater connectivity than healthy individuals, and suggests that the patients mobilize a compensatory mechanism to maintain the processing effectiveness while the processing efficiency is reduced [13].

In our study, it was observed that along the sagittal orientation, the functional connectivity between the occipital and the frontal areas of the brain in the patients is strong, especially in the medial area. Along the coronal orientation, the functional connectivity between the right and left hemispheres of the brain was strong in the medial area. A similar trend of inefficiency may be concluded for the communication between the frontal and occipital areas of the brain via the parietal area.

Our results are in line with previous studies revealing altered connectivity in people with abnormalities and diseases in their brain. The increased connectivity found in our results suggest that in mental disorder patients with the diffuse alpha pattern, the communication in the brain in general, as well as the communication between the left and right hemispheres via the parietal area may not be efficient.
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