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Abnormal brain activity in fronto-central regions in mental disorders with suicide: An EEG Study

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Abstract— **Suicide is a global health problem, and early and accurate identification of suicide attempt individuals has very important clinical significance. Thus the exploration of neurobiological mechanisms underlying suicidal behavior is crucial for systematically preventing suicide. However, the neurophysiological biomarkers for identifying affective disorders with suicidal attempt are remain unknown. Here, we recruited 28 patients with mental disorders from Tianjin Anding Hospital, and the subjects were divided into suicide attempt group (SA=14) and non suicide attempt group (NSA=14) according to whether they had attempted suicide. We also recruited 14 healthy subjects matched with age and sex ratio as healthy control group (HC=14). By recording the electroencephalogram(EEG) data of 60 electrodes in resting state for eight minutes (four minutes with open eyes and four minutes with close eyes), the absolute power of five frequency bands(delta(0.5-4Hz), theta(4-8Hz), alpha(8-13Hz), beta (13-30Hz), gamma(30-65Hz)) were analyzed to explore the changes of brain rhythm. And then the Modulation index (MI) was calculated to quantify the intensity of phase amplitude coupling (PAC) between different frequency bands in different brain regions, so as to observe the mechanism of neuronal synchronization in different frequency bands. We found that the absolute power of SA group was significantly higher than NSA group and HC group in delta (P<0.05), beta (P<0.05) and gamma (P<0.05) bands. The PAC strength between beta and gamma was calculated and it showed that the PAC strength of SA group was significantly weaker than NSA group in fronto-central regions, indicating that decreased synchronization between neurons could bring about brain function impairment. These findings suggest that the brain electrical activity in the fronto-central regions of the SA group may be damaged, which may lead to an increased suicidal risk in mental disoders. The EEG activity in delta, beta, gamma band and PAC in fronto-central regions may be used as a potential clinical biomarker for preventing suicide.**

I. Introduction

Suicide is a global health problem. According to the World Health Organization (WHO), suicide is the second leading cause of death among adolescents, with an annual death toll of 1 million [1,2]. The number of suicides caused by mental disorders accounts for more than one third of the total number of suicides. Thus, the exploration of neurobiological mechanisms underlying suicidal behavior is crucial for systematically preventing suicide. Suicidal behaviors usually can be divided into three categories: suicidal ideation (SI), suicidal attempt (SA) and complete suicide (SC) [3,4,5]. SI is the precursor of SA, and SA is the main risk factor of suicide behavior. Successful suicide attempt is complete suicide. Therefore, the study of suicide attempt is the most favorable factor to predict suicide behavior.

Unfortunately, the neurophysiological markers that can identify suicidal behavior are unclear, and our ability to identify individuals at risk of suicide is limited. Recently, a study by Benschop and his colleagues, limiting the analysis to female's resting state electroencephalogram(EEG) characteristics only, demonstrated that suicide ideators and suicide attempters showed low frontal beta and gamma activation as compared to low-risk individuals [6]. Furthermore, higher occipital alpha was observed in suicide ideators. Ironically, a recent report by Arikan and his colleagues suggested that suicide ideators exhibited higher gamma, contrasting the previous studies by Benschop [7]. Recently, A resting state of magnetoencephalography (MEG) study of patients with major depression (MDD) by Chattun et al, they found a significantly lower alpha-to-gamma phase amplitude coupling (PAC) between the right caudate and left thalamus in high-risk suicide group compared to both the low-risk suicide group and healthy controls [8].

At present, most of the research on suicide behavior was based on the analysis of behavior, and most of them focused on the normal population, but few studies focused on EEG [9,10,11]. Literature especially lacks studies on patients with suicide attempt. The relationship between EEG and suicidal behavior in patients with mental disorders is still unclear. The important issues related to suicide attempts, including the neurobiological mechanism of suicide attempts and the differences of individual brain activity in the process of suicide attempts, have not been solved. Therefore, early and accurate identification of suicide attempt individuals has very important clinical significance.

Considering the problems mentioned above, this study investigated the resting state EEG to explore the neurophysiological mechanism of suicide attempts in people with mental disorders, and further provide potential neurobiological indicators to predict suicide attempts.

II. Methods

A. Participants

Twenty-eight patients (10 males and 18 females, mean age 38, range 15 to 60 years) were diagnosed as mental disorders that were divided into two groups: non-suicide attempt group (NSA=14) and suicide attempt group (people

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with attempted suicide, SA=14). There was no significant difference in sex ratio and age between the two groups. Meanwhile, fourteen healthy control subjects (HC) matched with age and sex were recruited. The study was approved by the ethics committee of Tianjin Anding Hospital.

B. Electrophysiological Recordings

Subjects were seated in an electrically shielded and light-attenuated room. During EEG recording, the subjects were asked to watch the '+' in the center of the computer screen, and were asked to open or close their eyes every 1 minute according to the voice prompts, while participants were sitting upright, sit as still as possible, not focus on anything in particular and let their mind run free. EEG data were recorded for 8 minutes.

The SynAmps2 electroencephalography system produced by the United States Neuroscan was used in this study. EEG data sets were recorded by 64 Ag/AgCl electrodes that were positioned in compliance with the 10/20 international electrode placement system. The predefined online parameters of data recording were a 1000 Hz sampling rate and 0.01–70 Hz online bandpass filtering. The electrodes M2 and AFZ served as the reference and ground, respectively. For all electrodes, the impedance was kept below 5 KΩ during the EEG recording.

C. Data Pre-processing and Analysis

Pre-processing: The EEG all channels signals were first re-referenced to bilateral mastoid, while down-sampled to 500 Hz and used a band-pass filter range of 0.5 to 65 Hz to reduce DC interference and high-frequency noise. Before analysis, eye or muscle artifacts and other interference were removed using independent component analysis (ICA). Finally, the EEG data were analyzed with two different types of electrophysiological analyses: power spectral density analysis (PSD) and phase amplitude coupling (PAC).

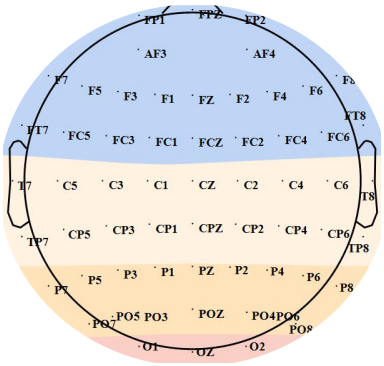

Figure 1. 60 electrodes location shown and four brain regions (Frontal, Central, Parietal, Occipital) division based on standard 10-20 electrode position system.

Power spectral density analysis (PSD): Five frequency bands (delta: 0.5-4 Hz, theta: 4-8 Hz, alpha: 8-13 Hz, beta: 13-30 Hz, gamma:30-65Hz) are extracted by Welch method. The data was segmented in 1s, the sampling frequency was 500 Hz and the sampling points were 500, the overlap length of segmented was 0.5, the Hamming window width was 500. One way ANOVA was used to compare the differences of the absolute power spectral density among the three groups. Furthermore, 60 EEG channels (see Fig. 1) × 3frequency bands(delta(0.5-4Hz), beta(13-30Hz), gamma(30-65Hz)) were analyzed via one-way ANOVA in SPSS. After the data reached normal distribution, one-way ANOVA was performed. Assuming that there was no difference in variance between the two groups, Fisher's LSD test was used for post analysis. The statistical significance level was set as $P<0.05$ for post analysis.

Phase amplitude coupling (PAC): Modulation index (MI) is an algorithm to calculate PAC proposed by Canolty and Tort et al. [12,13]. It was first applied to the population's cortical electroencephalogram(EoCG) and published in Science in 2006. MI is mainly based on the distribution of amplitude of high frequency rhythm on the phase signal of low frequency rhythm, and then calculates Shannon entropy of the distribution to represent the heterogeneity of the distribution, while the maximum Shannon entropy of uniform distribution is used for normalization. The larger the MI value is, the stronger the phase representing the low frequency rhythm can regulate the amplitude of the high frequency rhythm [14][15]. The calculation process of MI value is shown in Fig. 2.

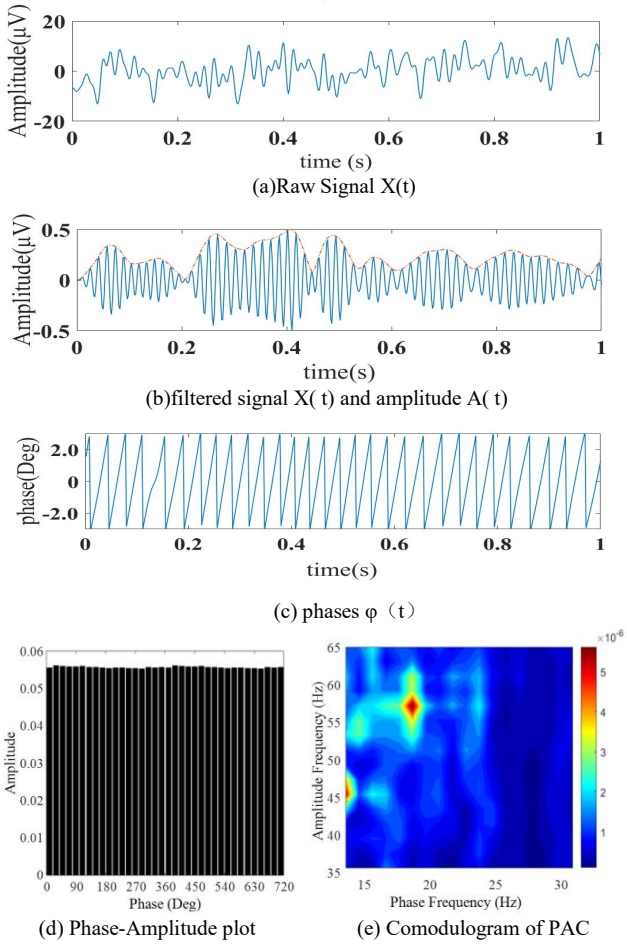

Figure 2. The original signal (a) is filtered in the phase and amplitude frequency range of interest. Then, the Hilbert transform is used to calculate the amplitude (b, red line) and phase time series (c) from the filtered signal. A synthetic phase amplitude time series is constructed and used to obtain the average amplitude distribution (d) on the phase box. (e) It represents the phase amplitude coupling strength.

1) First the time series X (t) (Fig. 2(a)) is filtered at the two frequency ranges under analysis.

2) The Hilbert transform is also applied to X(t) to extract the time series of the amplitude envelope of A(t) (Fig. 2(b,red line)). The time series of the phases of φ(t) (Fig. 2(c)) is also obtained from the standard Hilbert transform of X(t). Then the composite time series is then constructed (Fig. 2(d)), which gives the amplitude of the oscillation at each phase of the rhythm.

3) Next, the phase sequence is divided into N equal length phase segments. In this paper, it is divided into 18 phase segments (from 0 °to 360 °) 20° per segment , and the average amplitude of the sequence on each phase segment is calculated respectively (Fig. 2(d)). The modulation index is represented by the standardized entropy measure H, which is defined as

$$H = -\sum_{j=1}^{N} p_j \log p_j \tag{1}$$

4) N is the number of phase segments, P_j is defined as

$$p_j = \frac{A(fA)_j}{\sum_{j=1}^{N} A(fA)_j} \tag{2}$$

5) When $P_j = \frac{1}{N}$, the maximum possible value of H can be obtained. Through standardization, the modulation index based on entropy can be obtained.

$$MI = \frac{H_{\max} - H}{H_{\max}} \tag{3}$$

III. Results

A. Results of power spectral density

The absolute power of HC group, NSA group and SA group in five bands was revealed in Fig. 3. It was obvious that the SA group exhibited higher absolute power in all bands compared to both the NSA group and HC group, in which delta [f (2,41) = 3.814, P = 0.031], beta [f (2,41) = 3.814, P = 0.031] and gamma [f (2, 41) = 3. 692, P = 0. 027] had statistically significant.

As shown in Fig. 3(b-f), post-hoc comparisons using Fisher's LSD test displayed that the delta absolute power was significantly increased in the SA group compared to that in the HC group($p<0.05$) and NSA group($p<0.05$). Moreover, the SA group showed higher beta power than the HC group ($P<0.05$). The SA group also exhibited significantly higher gamma power than in the HC group($P<0.05$).

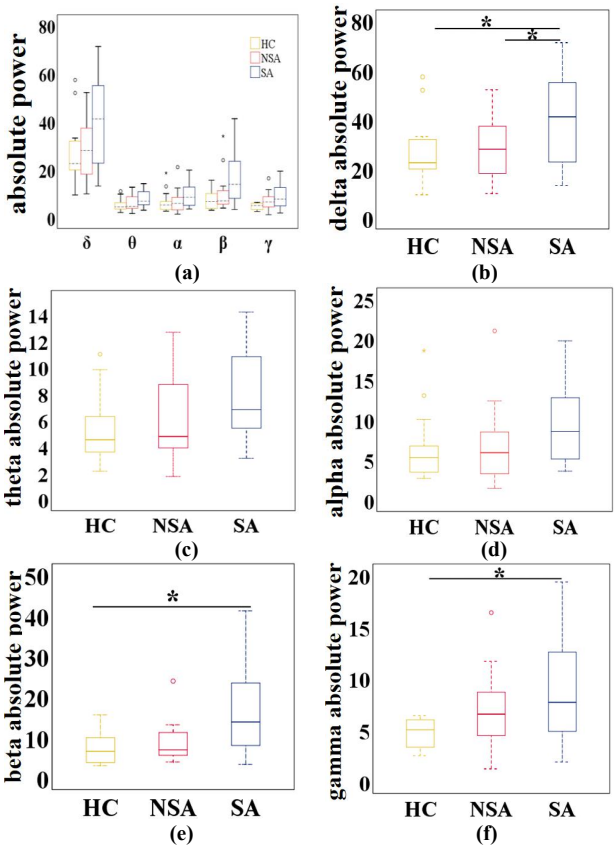

Figure 3. The absolute power averaged over whole brain in delta, theta, alpha, beta and gamma bands among the three groups.

Furthermore, to compare the difference of SA group with the NSA group and HC group in the EEG power spectral density at 60 electrodes, we charted the difference of EEG power spectral density topographic maps to compared the SA group with HC group and the SA group with NSA group in the delta, beta, gamma bands, respectively shown in Fig. 4. The results showed SA group exhibited increased power spectral density for the Frontal and Central brain regions in the delta, beta and gamma bands.

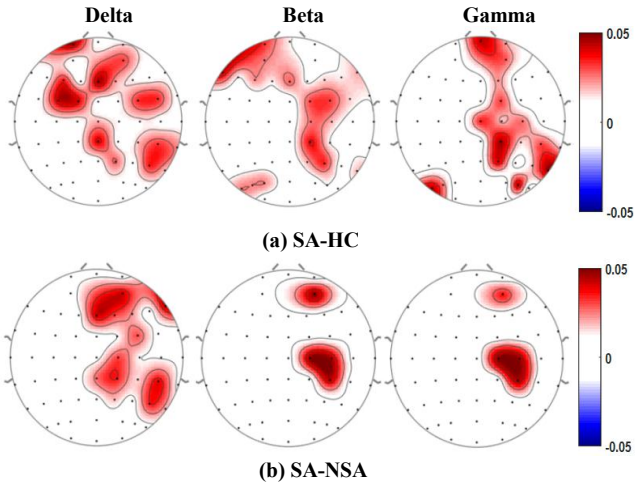

Figure 4. (a) The difference of the EEG power spectral density at 60 electrodes between SA group and HC group(SA-HC). (b) The difference of the EEG power spectral density at 60 electrodes between SA group and NSA group(SA-NSA).

B. *Results of phase amplitude coupling*

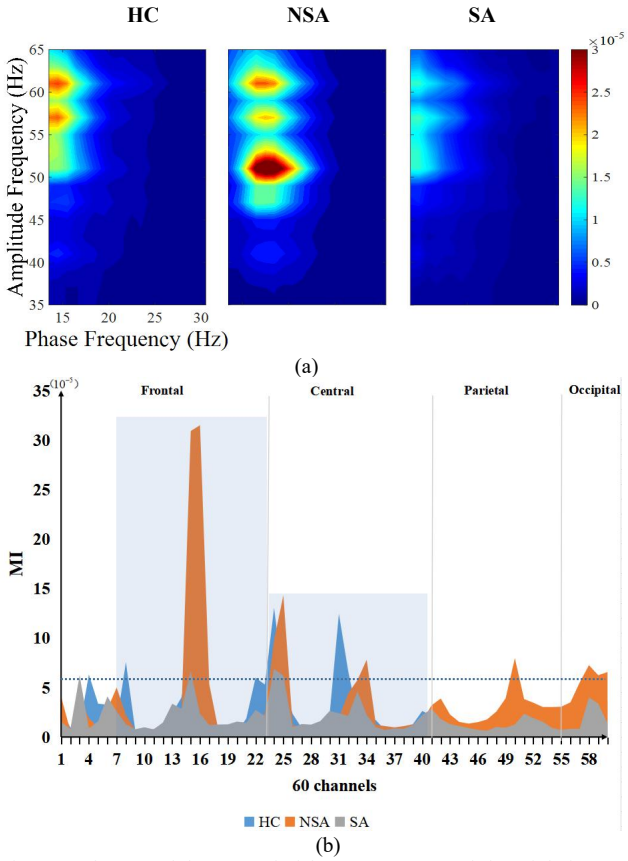

Figure 5. The comodulograms of of three groups. From left to right is HC group, NSA group and SA group(a). Obviously, the coupling strength of SA group is less than other groups in fronto-central regions. (b) the MI of beta-to-gamma PAC of the three groups.

To research the mechanism of neuronal synchronization between different frequency bands in the three groups, we plotted the comodulograms and calculated the MI of beta to gamma PAC in three groups. The comodulograms of beta to gamma PAC was shown in Fig. 5(a), it was found that the PAC at beta(13-20Hz) to gamma(45-60Hz) of SA group was weaker than HC group and NSA group. As shown in Fig. 5 (b), SA group exhibited lower MI than the HC group and NSA group in fronto-central regions.

IV. CONCLUSION

In this work, we demonstrated that SA group showed significantly higher delta, beta and gamma activation(see Fig. 3), and it also had a significantly lower PAC strength between beta and gamma (see Fig. 5(a)) as compared to both the NSA group and HC group in the frontal-central regions. From the Fig. 5(b), the SA group exhibited lower MI than the NSA group in Frontal and Central regions.

In conclusion, in mental disorders, people with suicidal behavior showed increased delta, beta and gamma activation and decreased PAC strength between beta and gamma compared to the people without suicidal behavior in fronto-central regions. A lower PAC strength between beta and gamma frequency bands implied a weaker neuronal synchronization. Thus, these findings indicated that patients with suicidal behavior have weaker neuronal synchronization in fronto-central regions, and the impairment between the Frontal and Central was prominent in patients with suicidal behavior. The EEG activity in delta, beta and gamma band and the PAC in fronto-central regions may be used as a potential clinical biomarker for preventing suicide.

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