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Alterations of theta oscillation in executive control in temporal lobe epilepsy patients

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ABSTRACT

Attention dysfunction, especially executive control has been investigated within many types of diseases of the central nervous system. The present study aims to clarify alterations of the executive control (EC) network in patients with temporal lobe epilepsy (TLE).

Twenty patients with TLE and 20 matched healthy control subjects participated in the attention network test (ANT), and scalp electroencephalogram (EEG) recordings were set up. The ANT was used to evaluate attention network behavior deficits. Power spectral density (PSD), coherence and correlation were used to detect power and oscillation alterations of attention network in patients with TLE.

The most significant differences in executive control were found between patients with TLE and healthy control subjects. Power spectral density in the theta band, and coherence and correlation in the theta band in the frontal area were decreased in patients with TLE.

Our results indicate that patients with TLE have severe attention dysfunction, especially in executive control. In addition, brain theta oscillation impairment in frontal area might be connected with poor executive control behavior. These findings will provide new insight into diagnosing and treating patients with temporal lobe epilepsy.

1. Introduction

Epilepsy is known as one of the most common chronic neurological disorders, with a diverse range of dysfunctions in cognition, which refers to language, memory and attention (Hommet et al., 2006; Sillanpaa et al., 1998). Cognitive impairments are a critical part of the decline of quality of life in patients with epilepsy (Baker et al., 1997). TLE has the highest morbidity compared with other epilepsy subtypes, and has always been accompanied by severe damage to cognition (Elger et al., 2004). Nevertheless, the precise neurological mechanism of cognition problems that cannot be verified by clinical factors, including biological and psychosocial factors, remains to be clarified.

Cognitive impairments are prevalent among TLE patients (Elger et al., 2004). Attention is the precondition of many advanced cognitive functions (Raz and Buhle, 2006). The first attempt to illustrate attention network activity during the attention process was done by Michael Posner in 1990, and the attention network has been conceptualized as an organ system composed of three functionally and anatomically distinct subsystems known as the alerting network, the orienting network, and the executive control (EC) network (Posner and Petersen, 1990). One convenient paradigm designed by Fan et al., called the attention network test (ANT) has been used to evaluate the efficiency of each of the three components of attention (Fan et al., 2002), and distinct brain oscillations of the attention network have been found in subsequent work (Fan et al., 2007).

Since the original studies by Fan, the ANT has been used as a behavior test to assess cognition and the attention network in many fields (Firbank et al., 2016; Lu et al., 2016; Pauletti et al., 2017; Killgore et al., 2016; Yuan et al., 2014), and functions in orienting and EC have shown deficits in all these subjects. For patients with epilepsy, only a few publications have reported the ANT performance in populations with epilepsy. Tian found that children with idiopathic generalized epilepsy show more reaction time in EC compared with matched healthy subjects (Tian et al., 2010). A series of research toward attention network

Abbreviations: ANT, attention network test; AED, antiepileptic drug; EC, executive control; EEG, electroencephalogram; HC, healthy control; PSD, power spectral density; TLE, temporal lobe epilepsy; RT, reaction time; STFT, short time Fourier transform

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impairment in TLE were done by Zheng and his team (Chen et al., 2015; Li et al., 2016). However, Zheng focused on alertness only, and no significant change in the alerting network among TLE patients was found.

Patients with certain focal brain lesions have been researched in clinical studies performed by clinicians (Fang et al., 2014; Hu et al., 2013), and rough regions have been linked to each of the three subnetworks by using ANT. The conclusion is consistent with former studies from functional magnetic resonance imaging (fMRI) data, which is that the frontal lobe (Visintin et al., 2015), especially for prefrontal and premotor areas (Rinne et al., 2013), plays a key role in modulating EC. In addition, studies conducting theta burst stimulation on healthy people also have been proved to elicit alterations in EC function (He et al., 2013; Xu et al., 2013). A previous study into the nature of focal electrical fields recorded over the midline prefrontal cortex has said that theta oscillation is crucial and should be underlined as the mechanism for evaluating and monitoring in a response task (Luu and Tucker, 2001). Furthermore, event-related potential research found that theta oscillation always accompanied action regulation (Luu et al., 2004) and attention control (Morillas-Romero et al., 2015).

In general, the present study aims to determine alerting, orienting, EC networks' efficiency by ANT testing; to demonstrate whether EC deficiency exists in TLE patients compared with healthy populations; and to clarify whether theta oscillation can be seen in healthy people during the EC period; and, finally, to test the difference in theta oscillation between TLE patients and healthy control subjects.

2. Results

2.1. Results of ANT behavior performance

Effects of alertness, orienting, and EC are listed in Table 2, and showed a general decrease in TLE patients (N = 20 TLE patients, 10 trials averaged in each person) compared with healthy control subjects (N = 20 healthy controls, 10 trials averaged in each person). We discovered significant differences in the EC effect ($t = 4.104$, $P < 0.001$), and orienting ($t = 2.119$, $P = 0.041$). No significant differences were observed in the effects of alerting ($t = 1.922$, $P = 0.062$).

2.2. Characteristic frequency band

Compared with other frequency bands, the theta band showed significant difference (N = 20 healthy controls, 10 trials averaged in each person) (Fig. 2A), and the theta band becomes the characteristic frequency band with the highest power spectral density (PSD) under the EC condition [θ:δ ($t = 2.392$, $P = 0.027$); θ:α ($t = 2.299$, $P = 0.033$); θ:β ($t = 3.457$, $P = 0.003$); θ:γ ($t = 3.574$, $P = 0.002$),and PSD = $0.092 \pm 0.023\ \mu V^2/Hz$]. Statistical significance has been found in the theta band between healthy control subjects and TLE patients (N = 20 TLE patients, 10 trials averaged in each person), with PSD = $0.026 \pm 0.005\ \mu V^2/Hz$ ($t = 2.739$, $P = 0.012$). In addition, the PSD in TLE patients appears to be decreased compared with the healthy control subjects (Fig. 2B). In the other frequency band, PSD in TLE patients is lower than that in control subjects, but no significant difference has been found.

2.3. Characteristic channel

As seen in Fig. 3, PSD in EC is calculated by PSD in incongruent minus PSD in congruent. Averaged PSD in EC (N = 20 healthy controls, 10 trials averaged in each person) present Fz to be the characteristic channel (PSD = $0.358 \pm 0.132\ \mu V^2/Hz$) among other channels ($P < 0.05$). Base condition while in the resting state is excluded, as base condition exists in both congruent and incongruent conditions. To compare the power variation along with time, time-frequency graphs of the Fz channel were configured and PSD in TLE patents (N = 20 TLE patients, 10 trials averaged in each person) and healthy subjects were compared. Significance was also found between patients and control subjects ($t = 2.157$, $P = 0.044$), with PSD decreased in TLE patients (PSD = $0.070 \pm 0.015\ \mu V^2/Hz$). In addition, averaged time-frequency graphs of Fz show high concentrations of PSD in the period between response onset and 200 ms after response, with PSD = $0.802 \pm 0.164\ \mu V^2/Hz$ in healthy control subjects and PSD = $0.345 \pm 0.067\ \mu V^2/Hz$ in patients, just in the theta band, and these results were significant ($t = -2.584$, $P = 0.014$).

2.4. Coherence and correlation

Averaged coherence and correlation between response onset and 0.2 s after response in HC (N = 20 healthy controls, 10 trials averaged in each person) with averaged value of 0.134 ± 0.007 in coherence and averaged value of 0.124 ± 0.007 in correlation, show significant difference when compared with TLE patients (N = 20 TLE patients, 10 trials averaged in each person), with averaged 0.026 ± 0.004 in coherence ($t = 14.473$, $P < 0.001$) and averaged value 0.020 ± 0.003 in correlation ($t = 13.959$, $P < 0.001$) (Fig. 4).

3. Discussion

We found evidence of the attention network deficit in TLE patients, especially in EC. In healthy subjects, the theta band possessed the highest PSD, and the Fz was found to be a characteristic channel in EC. In our cross-sectional study, a significant reduction of theta power density was found in TLE patients during their executive task. Moreover, the correlation and coherence among Fz and the frontal area were decreased in TLE patients.

EC deficit in the TLE population has been thoroughly investigated in recent years. Zamarian et al. assessed the executive function of 28 TLE patients using the Wisconsin Card Sorting Task (WCST). TLE patients had a worse score in WCST and the score was related to epilepsy duration (Zamarian et al., 2010). In the current study, our result demonstrated a worse executive behavior performance in TLE patients which was in line with the previous literature. Diao et al. found that the inferior executive behavior of TLE patients was related to their lower fractional anisotropy of the uncinate fasciculus, which connects the anterior temporal and frontal lobes (Diao et al., 2015). A recent research demonstrated that a TLE rat model with worse performance in an attention behavior task had neuronal loss in the hippocampus, which is related to learning and choice accuracy (Faure et al., 2014). The accomplishment of executive behavior requires the contribution of the prefrontal cortices (Westlye et al., 2011). The prefrontal lobe is not singly involved in EC behavior, although executive function was often conceptualized as "frontal" neuropsychological measures (Bettcher et al., 2016). Anton (Beer et al., 2013) and colleagues demonstrated a distinct network in the temporal and occipital cortices during multisensory execution, and in keeping with our result, showed a significant reduction of PSD in the occipital area among patients with TLE (details in supplementary material). From the latter linear equation, the reasonable hypothesis was that the temporal lobe participates in the executive circuit and connects compactly with the frontal lobe, with the damage of epilepsy disrupting the executive-related temporal lobe structure, even spreading to the frontal lobe and other executive-related sections.

Accumulative literature has emerged that the prefrontal cortices played a predominant role in the structure of the executive circuit (Bell et al., 2011; Zheng et al., 2015). Theta-band oscillation was demonstrated to be an important electrophysiological activity in the cooperation of executive dominant cortices (Fellrath et al., 2016; Sellers et al., 2016). In our study, we found that the theta band was the dominant frequency band and that the healthy group had the highest theta power density in the prefrontal area during the executive task, which was consistent with previously published work. Moreover, we