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Chapter 45
Spontaneous Theta Rhythm Predicts Insomnia Duration: A Resting-State EEG Study

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Abstract Increased theta power and subjective sleepiness during waking EEG had been found in many researches of sleep deprivation. However, rare studies had ever investigated the theta rhythm in awake and its cortical generators in insomnia disorder (ID). Consequently, based on the scalp EEG signal and its brain cortex distribution reconstructed by a network-based source imaging, we explored the abnormal theta power of insomniacs with different insomnia duration and its cortical generators. Results indicated that, compared to good sleepers, only ID with insomnia duration above 3 years presented sustained decreased theta power in multiple networks. Intriguingly, the theta power of frontoparietal (FPN) and deep structure network (DSN) was negatively correlated with the insomnia duration. These findings suggested that decreased waking theta power in ID may be the electrophysiological correlate of subjective sleepiness deficiency, and the theta power of FPN and DSN was good predictors for the insomnia duration.

Keywords Insomnia disorder · Insomnia duration · Network EEG source imaging · Theta

45.1 Introduction

Insomnia disorder (ID) has been one of the most prevalent and common psychophysiological disorders. Chronic insomnia induced cognitive impairments and increased risks for other psychiatric disorders [1]. Despite its considerable impacts

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on health, the pathophysiological mechanism is still poorly understood, and previous results are controversial.

The increase in theta activity during waking after sleep deprivation was found to be an electroencephalogram markers of homeostatic sleep propensity and subjective sleepiness in both human and rat [2, 3], and this effect was most pronounced in frontal areas. However, it is questionable that whether ID also presents the same pattern. Existing studies were based on the topographic analysis of frontal electrodes; thus, an unsolved problem is its cortex localizations, which may reveal the core regions of dysfunctional sleep homeostasis in patients with insomnia. In addition, the prefrontal cortex and hippocampus were deemed to be the generators of theta oscillation [4, 5], but in insomnia patients the abnormality was consistently found in these areas [6], from which we can infer that insomniacs may also present abnormal theta activity and homeostatic dysregulation during wakefulness.

To achieve these aims, we proposed a method called resting-state cortex rhythms (RECOR) for a detailed localization of cortical sources of resting-state EEG rhythms in a common network parcellation of the human brain function [8]. The main aims of our study were to examine (1) the impact of insomnia disorder on the theta rhythm, and (2) the distribution of abnormal theta rhythm in brain networks, especially in the frontoparietal network (FPN).

45.2 Methods

Thirty-three patients with ID (23 females, age 42.7 ± 9.4 years) and 14 healthy good sleepers (HGS) (6 females, age 41.9 ± 11.7 years) participated in the study. Insomniacs were recruited from Department of Sleep Psychology Center, Daping Hospital, Third Military Medical University, and they were divided into two groups, among which 16 had insomnia duration below 3 years (B3) and 17 above 3 years (A3). All participants completed some questionnaires including Pittsburgh Sleep Quality Index (PSQI), Self-Rating Depression Scale (SDS), and Self-Rating Anxiety Scale (SAS). The diagnosis of the total 33 IDs was evaluated by experienced psychiatrist (author DG and FY) according to the International Classification of Sleep Disorders-3. A written informed consent was obtained after a detailed explanation of the study protocol. The study was approved by the Ethics Committee of Southwest University, and all procedures involved were in accordance with the sixth revision of the Declaration of Helsinki.

Eyes-closed resting-state EEG data was recorded about 5 min from the 64 scalp tin electrodes mounted in an elastic cap (Brain Products, Munich, Germany), with the sampling frequency of 500 Hz around 19:00 to 20:00 in the evening. The impedance of all electrodes was kept below 5 kΩ. The preprocessing was conducted using MATLAB scripts supported by EEGLAB (http://sccn.ucsd.edu/eeglab). The recorded EEG data with ocular, muscular, and other types of artifact were preliminarily identified and excluded. And then, continuous EEG data was filtered with band-pass between 0.1 and 45 Hz and referenced to common average.

RECOR (as provided at http://www.leixulab.net/recor.asp) was used to estimate the power of EEG rhythms in the eight large-scale brain networks [7, 8]. It included two steps to calculate the power of EEG rhythms in each brain network. Firstly, network-based source imaging (NESOI) was employed to estimate the cortical sources of EEG theta rhythm (4–8 Hz) [8]. The second step is averaging the solutions of NESOI across all vertices of the eight large-scale brain networks: visual network (VIS), somatomotor network (SOM), dorsal attention network (DAN), ventral attention network (VAN), limbic network (LIM), FPN, default mode network (DMN), and deep brain structure network (DSN).

Statistical analysis was performed by ANOVA, using RECOR solutions of the theta band as dependent variables. ANOVA had one between-participants factor of Group (B3, A3, and HGS) and one within-participants factor of Network, forming a 3×8 mixture design.

45.3 Results

Significant differences were found in PSQI (14.1 ± 2.4, 15.4 ± 2.8, 3.9 ± 1.6, respectively, $F_{[2, 44]} = 95.67$, $p < 0.001$), SAS (55.5 ± 11.9, 52.8 ± 12.5, 31.3 ± 4.3, $F_{[2, 44]} = 23.21$, respectively, $p < 0.001$), and SDS (59.5 ± 11.9, 55.5 ± 13.6, 34.6 ± 6.6, respectively, $F_{[2, 44]} = 20.57$, $p < 0.001$) among the groups of B3, A3, and HGS.

The power of theta rhythm in HGS, B3, and A3 groups was illustrated in Fig. 45.1. Obviously, the theta power in scalp decreased gradually as the disease duration increased (Fig. 45.1a).

We performed a one-way ANOVA among the factor group (HGS, B3, and A3), and the result indicated a significant effect ($F_{[2, 44]} = 3.819$; $p < 0.05$) (Fig. 45.1b). The post hoc testing found a significant lower theta power when A3 (0.914 ± 0.395) was compared with HGS (1.731 ± 1.294, $p < 0.05$) and B3 (1.421 ± 0.655, $p < 0.05$). There is no significant difference between HGS and B3 ($p = 0.43$).

Then we averaged all vertices of a given large-scale brain network; this step may minimize the effects of poor spatial sampling of scalp EEG. We performed an ANOVA between the factors Groups and Networks.

Figure 45.2 illustrated the cortex current density distribution in 3 groups of 8 networks, which evidenced a marginally significant main effect of the factor Group ($F_{[2, 44]} = 2.814$; $p = 0.071$, $\eta P2 = 0.113$ with 95% confidence intervals between 0 and 0.4504) and significant main effect of Network ($F_{[1.247, 54.871]} = 4.841$; $p < 0.05$, $\eta P2 = 0.099$ with 95% confidence intervals between 0 and 0.5345). Interaction effect between Group and Network was not significant.

The post hoc testing showed that, compared to HGS (2.072 ± 0.447), both A3 (1.035 ± 0.089) and B3 (1.195 ± 0.069) groups presented lower power of theta band in DAN ($t = -2.49$, $p = 0.019$ for A3 compared to HGS and $t = -2.069$, $p = 0.048$ for B3 compared to HGS). When compared to A3 in FPN of theta band (1.003 ± 0.069), both the group of HGS (1.537 ± 0.190) and B3 (1.255 ± 0.072)

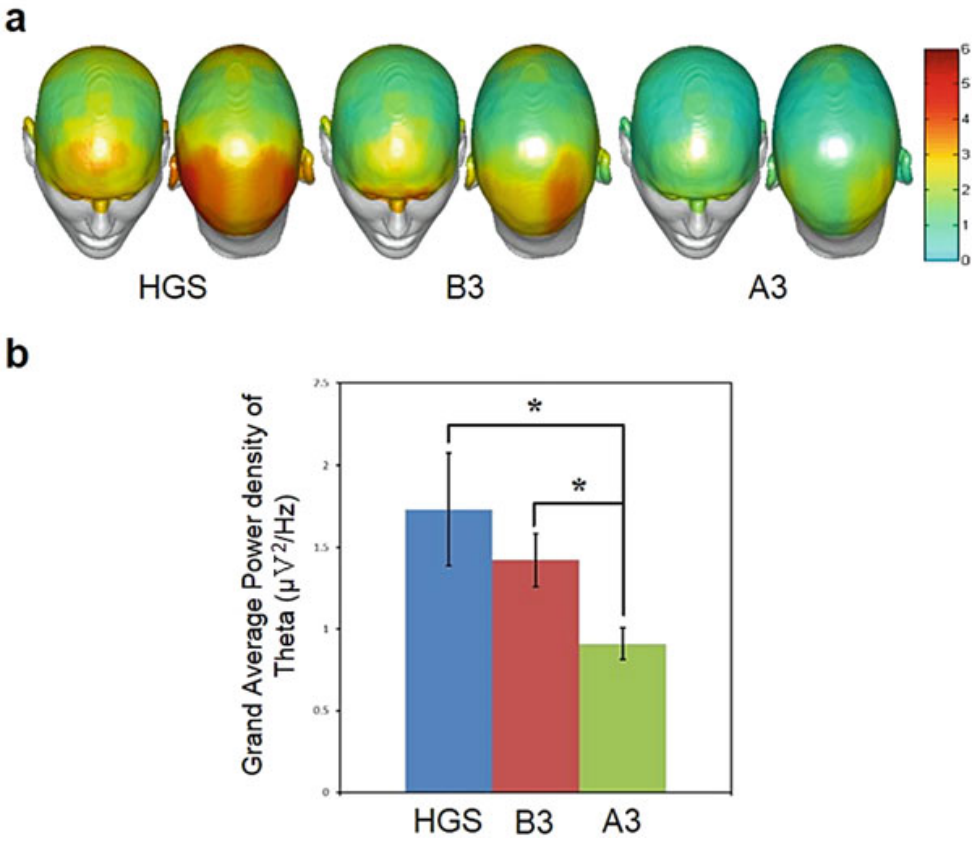

Fig. 45.1 The topography (**a**) and grand average of theta power (**b**) in HGS, B3, and A3 groups. Notice A3 group has significantly lower theta power than HGS. (*) indicate significant difference at $p < 0.05$

presented significant lower power ($t = -2.828$, $p = 0.008$ for A3 compared to HGS and $t = 2.507$, $p = 0.018$ for B3 compared to A3).

When compared to A3 in DSN of theta band (0.935 ± 0.050), both the group of HGS (1.252 ± 0.111) and B3 (1.170 ± 0.065) presented significant lower power ($t = -2.75$, $p = 0.010$ for A3 compared to HGS and $t = 2.890$, $p = 0.007$ for B3 compared to A3). Finally, only HGS (1.412 ± 0.128) and A3 (1.065 ± 0.093) groups showed significant difference in the theta power of SOM ($t = -2.236$, $p = 0.033$).

Pearson partial correlations between the theta power of eight networks and insomnia duration were performed, with age, gender, BMI, and education used as covariates. Results indicated that the insomnia duration negatively correlated with the theta power of FPN ($R = -0.507$, $p = 0.001$) and DSN ($R = -0.406$, $p = 0.007$).

45.4 Discussions

Up to now, the theta rhythm during wakefulness had not been comprehensively researched. Our study not only verified a previous study of decreased theta power during waking EEG [9] but also found that the significant decrease only existed

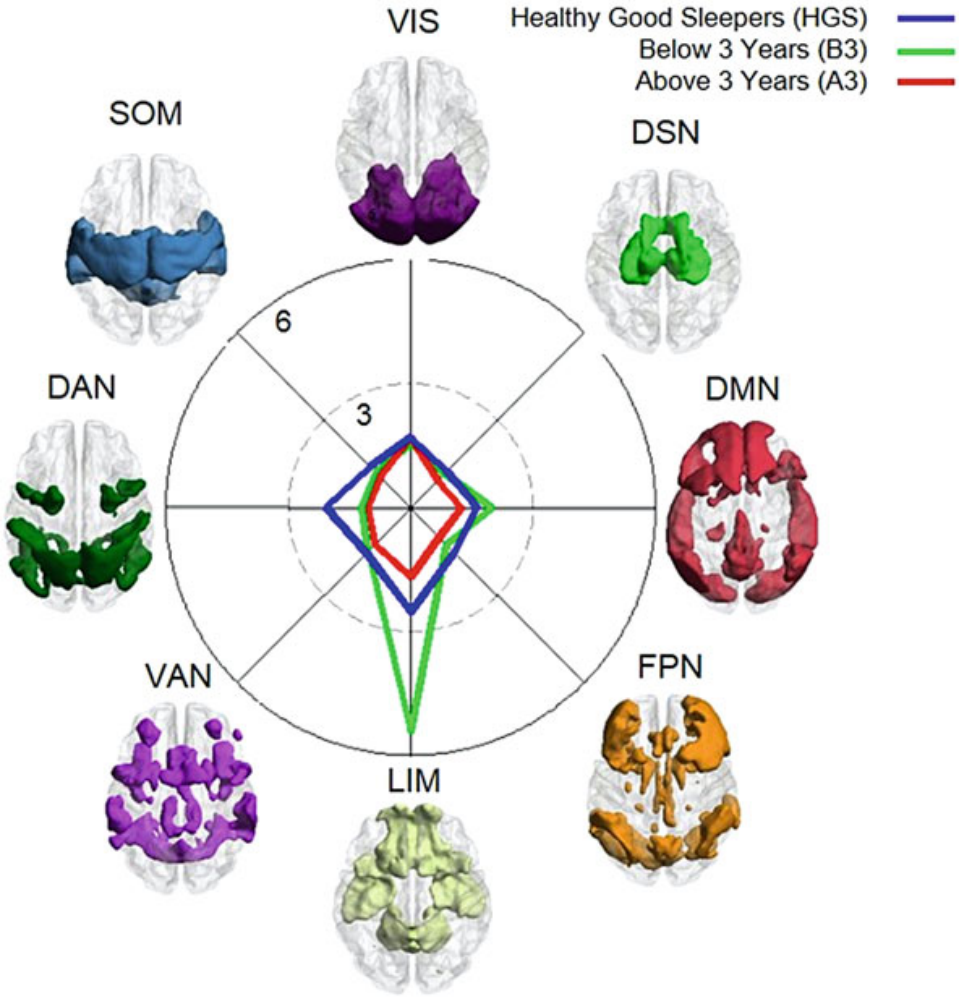

Fig. 45.2 Network normalized electroencephalographic (EEG) spectral power density distribution in eight Networks of theta band. A statistical ANOVA interaction was performed among the factors Groups (HGS, B3, and A3) and Networks (VIS, SOM, DAN, VAN, LIM, FPN, DMN, and DSN)

in the patients with longer insomnia duration. Indirect evidences from sleep deprivation demonstrated that theta activity in waking was seen as a marker of homeostatic sleep propensity [2]. Besides, the prefrontal cortex and hippocampus were deemed to be the generators of theta oscillation [4, 5], but insomnia was characterized by abnormal morphometry in the frontal cortex and hippocampus [6]. Accordingly, the decreased theta power in A3 group may be the reflection of decreased homeostatic sleep propensity or subjective sleepiness deficiency in patients with insomnia and correlate with their impaired brain structures. Obviously, insomnia duration was a key factor affecting the patients' theta power in waking and leading this homeostatic dysregulation.

What are the corresponding brain networks of the decreased theta power in ID? To answer this question, cortical sources of theta rhythm were compared among groups of B3, A3, and HGS. Our results revealed that the decrease was not widely distributed throughout the brain but concentrated on the networks of SOM, DAN,

FPN, and DSN. Additionally, we also found that the decrease of theta power in FPN and DSN negatively correlated with insomnia duration. It suggested that insomnia duration could be predicted by spontaneous theta activity in FPN and DSN.

In conclusion, by using the network-based source imaging of resting-state EEG theta rhythm, this study characterized insomniacs with different insomnia duration. Results indicated that the decreased theta power didn't exist in all insomniacs; only the chronic insomniacs with longer insomnia duration presented the most obvious decrease. The insomnia duration-related decreased theta power may be the reflection of decreased sleep propensity and abnormal brain morphometry in the frontal cortex and hippocampus. In addition, the networks of FPN, DAN, SOM, and DSN were the cortical sources of decreased theta power. However, only FPN and DSN in theta band presented negative correlations with insomnia duration, which may correlate with the atrophy of core regions in two networks and represent gradually dysfunctional cognitive control and disrupted sleep homeostasis in patients with different insomnia duration. These results motivated future researchers and clinicians to regard the insomnia duration as a highly pathogenic factor, and source localization technique of RECOR also may be an effective and convenient method to explore the neurodegenerative characteristics in insomnia disorder.

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