Power Spectral Analysis in Lateralized Temporal Lobe Epilepsy: An MEG Study

Yuejun Li1,a, Ting Wu1,2 and Tianzi Jiang1

1Key Laboratory for NeuroInformation of the Ministry of Education, School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu, China

2Department of Magnetoencephalography, Nanjing Brain Hospital, Affiliated to Nanjing Medical University, Nanjing, China

a Corresponding author: liyuejun@std.uestc.edu.cn

Abstract. In clinic, temporal lobe epilepsy (TLE) patients with visually normal MRI findings are more difficult to definitively diagnose than MRI-positive TLE patients. Spectral power can reflect the frequency characteristics of brain activity. In order to find biomarkers for discriminating MRI-negative TLE patients from healthy controls, magnetoencephalograms were recorded for 20 left and 23 right TLE patients with normal MRI results and 22 healthy controls in a no-task, eyes-closed condition. The regional and global powers of the patients and controls in the main frequency bands were analysed. Compared with the healthy controls, the left TLE group presented significantly increased powers in the left temporal region, whereas the right TLE group exhibited significantly increased powers in the right temporal region in the delta and theta bands. In the global power, the right TLE group showed significant increases in the delta and theta bands when compared with the healthy controls. Our results suggest that in the delta and theta bands, regional average powers in the left and right temporal regions can be taken as biomarkers for distinguishing MRI-negative TLE patients from healthy controls.

1. Introduction

Temporal lobe epilepsy (TLE) is the most common drug-resistant focal epilepsy in adults [1]. TLE seizures are traditionally associated with structural abnormalities, such as hippocampal sclerosis, brain tumors, cortical dysplasia, and so on. However, studies have reported that up to 30% of TLE cases have no abnormal findings on MRI [2]. Compared with MRI-positive TLE patients, MRI-negative TLE patients whose MRI findings fail to demonstrate a potential epileptogenic zone are more difficult to definitively diagnose in clinic. In general, further neuroimaging examinations have to be performed, such as positron emission tomography (PET) or intracranial electroencephalography (iEEG). The preoperative assessment of TLE patients with visually normal MRI findings can complicate the presurgical workup. Correct diagnosis for TLE is critical for surgical operation and treatment [3]. Therefore, obtaining insight into the oscillatory brain activity of MRI-negative TLE patients is helpful for the clinical diagnosis and treatment of MRI-negative TLE.

Spectral power can reflect the synchronization mechanism of neuronal activities. Rhythmic oscillations derived from the synchronization of neuronal activities are thought to play a key role in information processing in neuronal networks [4]. Different frequency bands are associated with different networks and functions [5]. In recent decades, magnetoencephalography (MEG), a noninvasive, reliable, and patient-friendly technique, has been applied to studying epileptic disorders...
[6]. MEG may have a higher temporal resolution than functional MRI (fMRI) due to rapid sampling rates and is suitable for investigating the oscillatory brain activity of MRI-negative TLE patients over a broad frequency range. In the current work, we investigate the interictal resting-state brain-background rhythm of MRI-negative TLE patients through their power spectra using MEG. Our aim is twofold: First, we want to determine whether there will be significant differences between MRI-negative TLE patients and healthy controls in terms of spectral power. Second, we seek to find biomarkers for distinguishing MRI-negative TLE patients from healthy controls for the purposes of clinical diagnosis and treatment.

2. Materials and Methods

2.1. Subjects

Twenty left TLE (14 males, age range, 17–41 years, mean ± sd age, 25 ± 7 years) and 23 right TLE (12 males, age range, 20–44 years, mean ± sd age, 28 ± 7 years) patients were recruited from the Nanjing Brain Hospital affiliated with Nanjing Medical University. The classification of epileptic syndromes was based on the criteria defined by the International League Against Epilepsy [7]. The laterality of the TLE was determined using clinical history, video-EEG recordings, neuroimaging, and a comprehensive neurological examination. The TLE patients were selected according to the following criteria: (1) The MRI results of the patient were normal. (2) The clinical diagnosis of TLE was unilateral. (3) The patient was right-handed. And (4) the patient’s age was greater than 17 and less than 45 years. There was no significant difference in epilepsy duration between the left and right TLE groups ($P = .57$, t-test). As a control group, 22 healthy subjects (13 males, age range, 20–41 years, mean ± sd age, 29 ± 6 years) were involved in this study. All the healthy subjects passed neurophysiological examinations and had no history of symptoms related to neurological or psychiatric disorders. There were no significant differences in age or sex between the three groups of subjects. This study was approved by the ethical committee of Nanjing Brain Hospital of Nanjing Medical University. Written consent forms were obtained from all the patients and controls.

2.2. Data acquisition

MEG data were acquired using a whole-head CTF 275-channel MEG system (VSM MedTech Systems Inc., Coquitlam, BC, Canada) while the subjects were seated inside a magnetically shielded room with their eyes closed and were instructed to stay awake. At the beginning and end of the recording, the head position relative to the MEG sensor array was recorded by using three small coils attached to the left and right pre-auricular points and the nasion on the subject’s head. The accuracy of the head localization of the system can reach 1 mm. The sampling rate was set to 300 Hz. For technical reasons, two channels (MLT12 and MRT12) had to be omitted leaving 273 channels available. Using a noise cancellation of third-order gradients, the MEG scans for each subject were conducted in a no-task and resting-state condition. Each epoch took 2 minutes and head-position changes less than 5 mm were accepted. For each patient, 15 epochs were recorded, whereas for each control, only two or three epochs were recorded since no epileptiform discharges needed to be excluded.

2.3. Data processing

All the MEG recordings were visually inspected by two experienced epileptologists, who identified the peaks of epileptic spikes and marked them manually. To exclude spike activity, we extracted epochs far (at least 10 s) from recent epileptic spikes. Epochs/segments with eye- or muscle-related artifacts were rejected. Then, artifact-free segments were segmented into 2 s epochs. The minimum and maximum numbers of available 2 s epochs of the subjects were 36 and 127, respectively. For each subject, 30 epochs of 2 s duration were selected. In this study, we focused on the commonly used six frequency bands, including delta ($\delta$: 1–4 Hz), theta ($\theta$: 4–8 Hz), lower alpha ($\alpha_l$: 8–10 Hz), upper alpha ($\alpha_u$: 10–13 Hz), beta ($\beta$: 13–30 Hz), and gamma ($\gamma$: 30–45 Hz). Preprocessing and analysis of the MEG data were performed using the Fieldtrip toolbox, available at
http://www.ru.nl/neuroimaging/fieldtrip [8], running in Matlab (version 8.1 (R2013a) Mathworks Inc.).

For each segment per subject, the absolute power spectral density (PSD) of each channel (time series) was computed over the range of 1–45 Hz with a step size of 1 Hz using the multitaper method based on discrete prolate spheroidal (Slepian) sequences, as implemented in the Fieldtrip toolbox. The spectral smoothing factor was set to 1 Hz. To obtain the average PSDs for each sensor (channel) per subject, the absolute PSDs were averaged across the 30 segments selected. The MEG sensors were grouped into five regions (central, frontal, occipital, parietal, and temporal) for each hemisphere based on the CTF sensor naming system. The eleven midline sensors were not included in any of the partitioned regions. The regional mean PSDs were obtained by averaging the regional PSDs within each partitioned region. Then, the regional band powers were calculated by respectively averaging the regional PSDs within the six frequency bands mentioned above. The global PSDs for each subject were computed by averaging the PSDs across all the sensors of the subject for the individual frequency points. Then, the global band powers were obtained by respectively averaging the global PSDs within the six selected frequency bands.

2.4. Statistical analysis

The statistical analysis was done with Matlab toolbox or SPSS (version 22) for MS-Windows. Between-group differences in spectral power were tested with a nonparametric statistic, the Wilcoxon rank-sum test. Bonferroni correction was applied to control the false discovery rate for multiple comparisons. Corrected \( P \) values < .05 were considered statistically significant.

3. Results

Statistically significant differences in the regional band power were observed between the three groups of subjects (Fig. 1). Contour graphs represent topographical distributions of band power and are expressed as a percentage of power difference between the specified two group. The squares in Fig. 1 indicate that there were significant differences between the patients and the controls in the specified regions using the Wilcoxon rank-sum test (two-tailed) after Bonferroni correction. For the sake of clarity, contour graphs with no significant differences in any regional mean power have been shaded. No significant differences in the regional power were found in the lower alpha, beta, or gamma band between the three groups of subjects.

Compared with the healthy controls, the right TLE group presented significantly increased regional powers in right temporal region (corrected \( P = .011 \)) in the delta band and in the right temporal (corrected \( P = .0058 \)) and frontal (corrected \( P = .018 \)) regions in the theta band, whereas the left TLE group exhibited significantly increased regional powers in left temporal region in the delta (corrected \( P = .036 \)) and theta (corrected \( P = .0071 \)) bands. Between the left and right TLE groups, the right TLE group showed significantly greater regional powers in both left (corrected \( P = .014 \)) and right (corrected \( P = .031 \)) frontal regions in the upper alpha band.
Figure 1. Regional band-power comparisons between the three groups of subjects. RTLEs = right TLEs; LTLEs = left TLEs; HCs = healthy controls; δ = delta; θ = theta; αu = upper alpha; F = frontal; T = temporal.

In the global band power, the right TLE group presented significant increases in the delta (corrected $P = .026$) and theta (corrected $P = .015$) bands when compared with the healthy controls (Fig. 2). No significant differences between the left TLE group and the healthy controls and between the left and right TLE groups in the global band power were found for any selected frequency band.

Figure 2. Global band-power comparisons between the three groups of subjects. Error bars denote standard deviations of global power. Asterisks indicate that there was a significant difference between the specified two groups using the Wilcoxon rank-sum test (two-tailed) after Bonferroni correction. δ = delta; θ = theta; αl = lower alpha; αu = upper alpha; β = beta; γ = gamma.

4. Discussion
The significant differences between the left or right TLE group and the control group in the regional band power were found in the delta and theta bands. The left and right TLE patients respectively presented significantly increased powers in the temporal region ipsilateral to their epileptogenic focus when compared with the healthy controls. These significant changes can be associated with the lateralization effect of TLE, indicating that the relatively lower frequency activity (delta and theta) of TLE patients enhanced in the temporal region on the side of the epileptogenic focus even in the interictal period. Tao et al. (2011) investigated the functional brain networks of TLE patients using EEG and suggested that interictal regional delta slowing can be taken as a network marker of TLE patients [9]. Quraan et al. (2013) analysed the spectral power of left TLE patients using EEG. Their results showed that compared with healthy controls, left TLE patients presented increased power in the left temporal region in the delta band for both eyes closed and eyes open conditions, and in the bilateral temporo-parietal regions in the theta band for the eyes closed condition [10]. In the delta band,
their results are in line with our results. In the theta band, besides the increased power in the ipsilateral temporal region, as can be seen from Fig. 1, the left TLE patients exhibit an increased but nonsignificant power in the right temporal region partly coinciding with their results. Of note, the majority of their patients have had left medial temporal sclerosis that may make a contribution to their results. In contrast, our patients have no structural abnormalities and the changes in spectral power are likely to be more representative of the pathophysiological mechanism of TLE per se.

For the left TLE group versus the right TLE group, significant increases in the regional power were found in the bilateral frontal regions in the upper alpha band. The right TLE group presented stronger upper alpha activity than the left TLE group in the left and right frontal regions, though compared with the healthy controls, both the TLE groups showed no significant changes in any partitioned region. In the theta band, the right TLE group also exhibited significantly increased power in the ipsilateral frontal region compared with the healthy controls. These increased activity in frontal regions in the right TLE group can reflect a compensatory mechanism. All the patients in this study are right handed and the left hemisphere is predominant. In rhythmic brain oscillations, the left TLE group showed a better preservation than the right TLE group. Preservation in spectral power in left TLE can also be observed in the global power in Fig. 2. Compared with the healthy controls, the right TLE group presented significantly increased global powers in the delta and theta bands, whereas no significant differences between the left TLE group and the healthy controls in the global power were found in any selected frequency band.

5. Conclusion
In this study, we examined the lateralization effect of TLE on spectral power. In the delta and theta bands, compared with the healthy controls, the left and right TLE groups showed different alterations in the regional and global powers, which can be attributed to the effect of lateralization of TLE. The left TLE group showed a better preservation in spectral power than the right TLE group possibly reflecting a compensatory mechanism and an ipsilateral predominance. Our results suggest that in the delta and theta bands, alterations in spectral power in the ipsilateral temporal region can be treated as a biomarker that can distinguish MRI-negative TLE patients from healthy controls for the purposes of clinical diagnosis and treatment.

Acknowledgments
This work was partially supported by the National Key Research and Development Program of China (Grant No. 2017YFB1002502), National Natural Science Foundation of China (Grant No. 81501550, and No. 81871398).

References
[1] S.S. Keller, G.R. Glenn, B. Weber, B.A.K. Kreilkamp, J.H. Jensen, J.A. Helpern, et al., Brain, 140, 15 (2017)
[2] W. Muhlhofer, Y.L. Tan, S.G. Mueller, R. Knowlton, Epilepsia, 58, 16 (2017)
[3] T. Wu, D. Chen, Q. Chen, R. Zhang, W. Zhang, Y. Li, et al., Complexity, 2018, 10 (2018)
[4] V. Kitchigina, I. Popova, V. Sinelnikova, A. Malkov, E. Astasheva, L. Shubina, et al., Exp Neurol, 247, 14 (2013)
[5] E. Basar, C. Basar-Eroglu, S. Karakas, M. Schurmann, Int J Psychophysiol, 39, 8 (2001)
[6] E. Foley, A. Cerquiglini, A. Cavanna, M.A. Nakubulwa, P.L. Furlong, C. Witton, et al., Epilepsy Behav, 30, 6 (2014)
[7] ILAE, Epilepsia, 30 (4), 11 (1989)
[8] R. Oostenveld, P. Fries, E. Maris, J.M. Schoffelen, Comput Intell Neurosci, 2011, 10 (2011)
[9] J.X. Tao, X.J. Chen, M. Baldwin, I. Yung, S. Rose, D. Frim, et al., Epilepsia, 52, 10 (2011)
[10] M.A. Quraan, C. McCormick, M. Cohn, T.A. Valiante, M.P. McAndrews, PLoS One, 8, 14 (2013)