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Phase Lag Analysis Scalp Electroencephalography May Predict Seizure Frequencies in Patients with Childhood Epilepsy with Centrotemporal Spikes

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ABSTRACT

Background Childhood epilepsy with centrotemporal spikes (CECTS) is the most common epilepsy syndrome in school-aged children. However, predictors for seizure frequency are yet to be clarified using the phase lag index (PLI) analyses. We investigated PLI of scalp electroencephalography data at onset to identify potential predictive markers for seizure times.

Methods We compared the PLIs of 13 patients with CECTS and 13 age- and sex-matched healthy controls. For the PLI analysis, we used resting-state electroencephalography data (excluding paroxysmal discharges), and analyzed the mean PLIs among all electrodes and between interest electrodes (C3, C4, P3, P4, T3, and T4) and other electrodes. Furthermore, we compared PLIs between CECTS and control data and analyzed the associations between PLIs and total seizure times in CECTS patients.

Results No differences were detected in clinical profiles or visual electroencephalography examinations between patients with CECTS and control participants. In patients with CECTS, the mean PLIs among all electrodes and toward interest electrodes were higher at the theta and alpha bands and lower at the delta and gamma bands than those in control participants. Additionally, the mean PLIs toward interest electrodes in the beta frequency band were negatively associated with seizure times ($P = 0.02$).

Conclusion The resting-state delta, theta, alpha, and gamma band PLIs might reflect an aberrant brain network in patients with CECTS. The resting-state PLI among the selected electrodes of interest in the beta frequency band may be a predictive marker of seizure times in patients with CECTS.

Key words childhood epilepsy; seizure frequency; frequency analysis; phase lag index; predictive marker

Benign epilepsy with centrotemporal spikes, recently renamed childhood epilepsy with centrotemporal spikes (CECTS), is the most common epilepsy syndrome in school-aged children.[1] Patients with CECTS show characteristic seizure semiologies, such as unilateral facial twitching or stiffness and numbness or tingling of the face and throat (the tongue, lips, gums, inner side of the cheek, and teeth), which cause difficulty in speaking (speaking with gurgling noises, speech arrest, drooling, and hypersalivation).[1, 2] CECTS was previously named "benign" epilepsy with centrotemporal spikes; however, some patients require multiple antiepileptic drugs due to frequent and intractable seizure episodes, and some develop cognitive deficits, learning disabilities, and psychiatric or behavioral disorders.[3, 4] These symptoms indicate that ictal and/or interictal epileptic activity affects global brain functions outside of the epileptic regions.

Many researchers have attempted to identify predictive markers for seizure times in patients with CECTS using detailed clinical profiles or electroencephalography (EEG) characteristics.[5, 6] Functional magnetic resonance imaging (MRI) studies have revealed an aberrant brain network during the resting state in patients with CECTS.[7, 8] In EEG frequency analyses, phase lag index (PLI) calculation is a computed analytic method used to estimate connectivity while eliminating volume conduction and is applicable with respect to epileptic and/or global brain function.[4, 9] Using global electrodes, it was observed that the PLI value in the resting state had significantly lower alpha-band connectivity in

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Abbreviations: CECTS, Childhood epilepsy with centrotemporal spikes; EEG, electroencephalography; MEG, Magnetoencephalography; MRI, magnetic resonance imaging; PD, paroxysmal discharge; PLI, phase lag index

patients with CECTS than in control individuals.[10] The lower PLI value for CECTS patients could be related to global dysfunction due to epilepsy or a countermeasure against focal hyperexcitation and hypersynchrony. Some studies on PLI in patients with CECTS have been conducted; however, predictors for seizure frequency are yet to be clarified using PLI analyses.

Therefore, the aim of this study was to reveal the tendency of connectivity changes at each frequency band in patients with CECTS using PLI analyses during scalp EEG records of the resting state and to identify the potential predictive markers among PLIs at each frequency band for seizure times in CECTS using PLI analyses.

MATERIALS AND METHODS

Study participants and clinical information

We recruited patients with CECTS whose first scalp EEG data were recorded between January 2005 and December 2015 at Tottori University Hospital. The diagnostic criteria for CECTS were as follows: 1) nocturnal seizures with hemifacial (lip and mouth) clonic movements, laryngeal symptoms, dysarthria, swallowing or chewing movements, and hypersalivation; 2) age at onset between 3 to 14 years; 3) centrotemporal spikes with activation during sleep; and 4) no other neurological abnormalities. We selected 13 age- and sex-matched healthy children for the control group. They developed normally and had no history of CECTS or other central nervous system disorders.

Clinical information and patient classification

We retrospectively reviewed clinical records and extracted the following data: sex, age at disease onset, an ictal manifestation of the first seizure, the total number of seizures, number of seizures before treatment and number of seizures before first EEG, electrodes with paroxysmal discharges (PDs) at the first EEG record, and use of antiepileptic drug treatment.

EEG recordings and visual EEG findings

Scalp EEG was performed before commencing antiepileptic drugs using Neurofax (Nihon-Koden, Tokyo, Japan). Electrodes were placed according to the international 10–20 electrode system with 16 EEG channels (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, and T6). The mean of C3 and C4 was set as the system reference. Signals were digitized at 200 samples per second in all channels using a 60 Hz high-frequency filter and a 0.5 Hz low-frequency filter. The second author (Okazaki T), a certified pediatric neurologist, reviewed the first EEG recordings for centrotemporal spike foci and the presence of tangential dipoles. Tangential dipoles have been previously defined as PDs with frontal positivity and centrotemporal negativity on monopolar montage.[3, 11]

Quantitative EEG analysis: selection of EEG, time window, and electrodes

The second author (Okazaki T) reviewed each EEG recording. Initially, alpha activities during awake eyes-closed resting state were recorded using five artifact-free 2-second epochs, and no PDs within 5 s were selected. For the computed analyses, we used these selected EEG data with referential montages (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, and T6). The mean of C3 and C4 was set as the system reference. The EEG data were analyzed using MATLAB (The MathWorks Inc., Natick, Massachusetts, USA). The frequency bands were classified into delta (0.5–3.9 Hz), theta (4.0–7.9 Hz), alpha (8.0–12.9 Hz), beta (13.0–29.9 Hz), and gamma (30.0–39.9 Hz).

Calculation of the PLI

Before computing the PLI value, we used the bandpass filter to extract each band's signal. Subsequently, we calculated the phase difference between electrodes and extracted the phase difference matrix.

To calculate the PLI of electrodes x and y, we estimated the time series of phase differences across electrodes as:

$$\Delta\phi_{x,y}(t) = \phi_x(t) - \phi_y(t),$$

where $\phi x(t)$ and $\phi y(t)$ indicate the phase values of the x and y electrodes at time t, respectively.[12] We then calculated the functional connectivity as the consistency in the distribution of instantaneous phase differences $\Delta\phi_{x,y}(t)$ defined as:

$$PLI = \left| \frac{1}{n} \sum_{t=1}^{n} sign(\Delta\phi_{x,y}(t)) \right|,$$

where the consistency of the phase difference of n segments was examined.[12, 13]

The PLI ranges between 0 and 1. If the PLI is 0, the two signals are either not coupled or are coupled with a phase difference centered at approximately 0 mod π. If the PLI is 1, the two signals are perfectly phase-locked at a value of $\Delta\phi$, which is different from 0 mod π. When this non-zero phase locking is strong, the PLI is large. However, it is worth noting that PLI does not indicate which of the two signals is leading in the phase.[14]

Table 1. Clinical information of patients with CECTS

Patient No.	Sex	Age at onset, (years, months)	Ictal manifestation of first seizure	Total number of seizures	Electrodes with paroxysmal discharges at the first EEG record	Dipole
1	M	6, 0	IR, 2G, OP	3	Lt-mT	+
2	F	7, 0	IR, Cl, HS	3	Lt-pT, mT, C, P	+
3	M	7, 1	Cl, 2G, HS	1	Rt-C	+
4	F	7, 9	IR, HF, Cl, HS	2	Lt-C,P, mT Rt-P, pT	+
5	F	8, 1	IR, OP, HS	4	Lt-mT, C	+
6	M	8, 7	G or 2G	3	Rt-mT	+
7	F	5, 10	IR, OP, HS	37	Lt-C Rt-P, mT, P,	+
8	M	10	Cl, HS	13	Lt-C	-
9	M	7, 0	OP	13	No paroxysmal discharges	N/A
10	M	3, 7	IR, OP	20	Lt-mT	+
11	M	5, 10	HF, OP	20	Lt-mT	+
12	M	5, 5	IR, Cl	8	Rt-C	N/A
13	M	5, 7	IR, Cl	5	Lt-mT, F Rt-C	N/A

Mean PLIs among all electrodes and mean PLIs toward interest electrodes

Using the above method, we compared the mean PLIs among all electrode pairs (mean PLI among all electrodes) between patients with CECTS and control participants. Subsequently, we calculated the mean PLIs between the electrodes of interest and the other electrodes in each patient (mean PLI toward interest electrodes) because the special connectivity changes in epilepsy are predicted to be more prominent in the electrodes with epileptic discharges. We calculated the mean PLIs of all pairs between the interest electrodes, including C3, C4, P3, P4, T3, and T4 electrodes and other electrodes. Finally, we compared the mean PLIs toward interest electrodes between patients with CECTS and control participants.

Statistical analyses

Statistical analysis was performed using SPSS statistics software (version 27.0, IBM Corp., Armonk, NY). Categorical variables, including sex, age at onset of the seizure, seizure times, seizure type, spike foci side and tangential dipole, and the number of antiepileptic drugs used, were compared using the chi-square test. Statistical significance was set at a p-value of < 0.05.

Subsequently, the mean PLIs among all electrodes and towards interest electrodes in each frequency band were compared between patients with CECTS and control participants using Welch's t-test. Because of the repetitive analyses, statistical significance was set at a p-value of < 0.01.

Lastly, multivariate linear regression analysis was used to identify significant correlations between seizure times and the PLIs in each frequency band. Statistical significance was set at a p-value of < 0.05.

Ethics

This study was conducted in accordance with the Declaration of Helsinki, and Tottori University Hospital Institutional Review Board approved the protocol (approval number: 18A072). Written informed consent to participate in this study was obtained from the participant's legal guardian or their next of kin.

RESULTS

Clinical characteristics of CECTS patients and control participants

This study included 13 (4 female and 9 male) patients who met the inclusion criteria. The patients' clinical characteristics are shown in Table 1. The total number of seizures ranged from 1 to 37 (mean: 10, range: 1–37). At the first EEG recording, there were only six electrodes with PDs on the left, three on the right, and three on both sides. Dipole appeared in nine patients.

Mean PLIs among all electrodes between CECTS patients and control participants

Fig. 1 shows the heat map of a matrix plot of band-specific mean PLIs of all pairs of electrodes in each group (Fig. 1). The CECTS group showed significantly lower mean PLIs among all electrodes at the delta and gamma bands than the control group (P < 0.001). In contrast, the CECTS group had significantly higher means of the mean PLIs among electrodes at the theta and alpha bands than the control group (P < 0.001) (Table 2).

Mean PLIs toward interest electrodes between CECTS patients and control participants

Fig. 2 shows pairs of electrodes with significant differences of connectivity between patients with CECTS and control participants. At the delta and gamma bands, the CECTS group had significantly lower mean PLIs toward the interest electrodes than the control group (blue lines, P < 0.001). In contrast, the CECTS group had significantly higher mean PLIs toward the interest electrodes at the theta and alpha bands than the control group (red lines, P = 0.006 and P < 0.001, respectively) (Table 3).

Correlation between seizure times and PLIs in CECTS patients

We performed a multivariate linear regression analysis to clarify the correlation between seizure times and PLIs in patients with CECTS. No significant correlation between seizure times and PLIs among all electrodes was observed. However, mean PLIs towards interest electrodes on the beta frequency band were negatively associated with total seizure times (P = 0.020) (Table 4, Fig. 3).

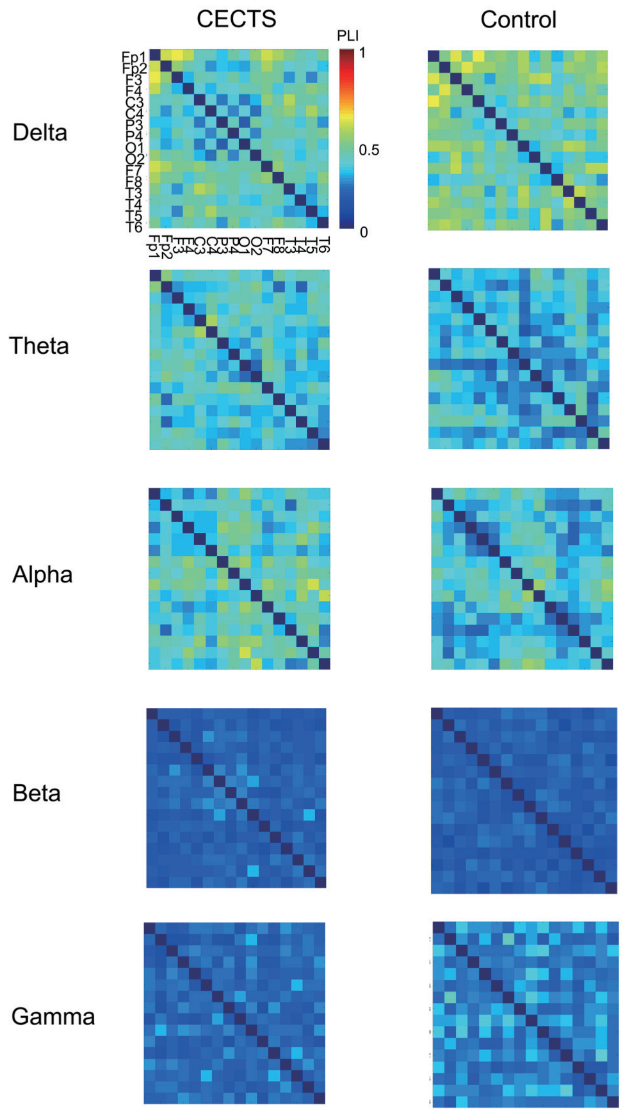

Fig. 1. Heat map of a matrix plot of band-specific mean phase lag index (PLI) among all pairs of electrodes in each group. The heat map shows connectivity in the delta, theta, alpha, and beta frequency bands with different color scales for each band. The closer the PLI is to 1 and the closer it is to red, the more the phases are aligned. On the contrary, the closer the PLI is to 0 and the closer it is to blue, the more the phases are out of alignment. CECTS, childhood epilepsy with centrotemporal spikes.

DISCUSSION

We analyzed PLIs using scalp EEG data during the resting state and discovered that the mean PLIs among all electrodes and the mean PLIs toward interest electrodes (C3, C4, P3, P4, T3, and T4) were higher in the theta and alpha frequency bands and lower in the delta and gamma frequency bands in patients with CECTS than in control participants. In patients with CECTS, the mean PLIs toward interest electrodes in the beta band were negatively associated with seizure times. Hyposynchronization of the beta frequency band may occur in patients with CECTS and may be associated with the degree of epileptic excitation in these patients.

In previous research on patients with CECTS, clinical findings showed no correlations between seizure times and sex or seizure semiology.[5] Several studies have indicated a correlation between early seizure onset age and frequent seizure episodes[12, 13]; however, a similar correlation was not found in the present study. This may be due to the insufficient sample size in our study to identify a significant correlation.

Some studies have identified factors predictive of frequent seizures in patients with CECTS using visual EEG examination. For example, Gregory and Wong described frontal positivity and centrotemporal negativity as the tangential dipole associated with connectivity

Table 2. The mean phase lag index among all electrodes in patients with CECTS and control participants in each frequency band

Frequency band	Patients with CECTS (*n* = 13)		Control participants (*n* = 13)	*P*-value
Delta	0.36 ± 0.24	<	0.40 ± 0.25	< 0.001*
Theta	0.32 ± 0.23	>	0.28 ± 0.21	< 0.001*
Alpha	0.34 ± 0.24	>	0.30 ± 0.21	< 0.001*
Beta	0.17 ± 0.13		0.16 ± 0.12	0.081
Gamma	0.19 ± 0.14	<	0.23 ± 0.16	< 0.001*

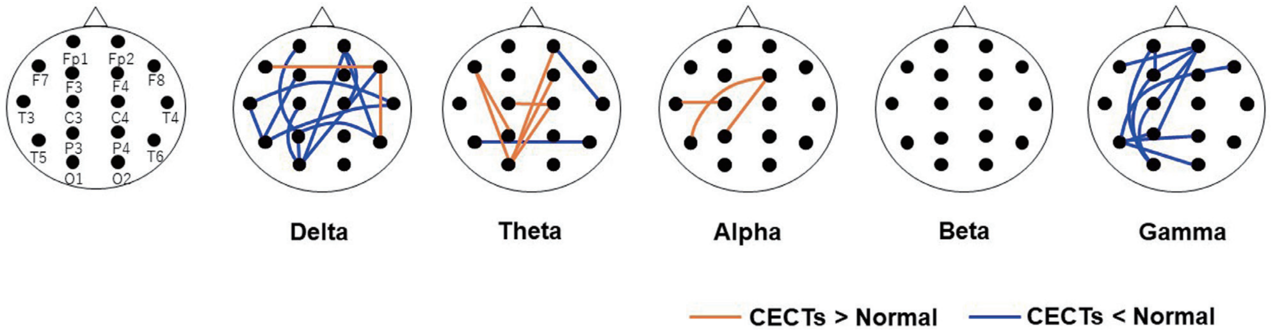

Fig. 2. Pairs of electrodes with significantly higher (red) or lower (blue) connectivity in patients with CECTS than in control participants. The pairs with significant differences tended to include interest electrodes (C3, C4, P3, P4, T3, and T4) in the delta and theta bands. CECTS, childhood epilepsy with centrotemporal spikes.

of frontal and central or temporal activity.[11] They concluded that patients with tangential dipole spikes had a lower incidence of clinical abnormalities and seizure times than patients without tangential dipole spikes. Vinayan et al. also described patients with CECTS with these tangential dipole spikes as having better educational results.[3]

Recent research has described other predictive markers on visual EEG examination; the frontal focus, bilateral asynchrony, and frequency of PDs have been described as frequent seizure markers.[15, 16] Conversely, other researchers could not detect predictive markers on EEG recordings for seizure times in patients with CECTS.[5, 12] No correlation has been established between visual EEG and seizure outcomes in patients with CECTS.

In this study, we initially analyzed the mean of global connectivity (mean PLIs among all electrodes). We then analyzed the connectivity between the electrodes on peri-Rolandic areas and other areas (mean PLIs toward interest electrodes), as the epileptogenic areas develop aberrant networks with other areas in patients with focal-onset epilepsy.[17]

The two analyses showed similar tendencies in the connectivity changes: increasing on theta and alpha bands and decreasing on delta and gamma bands. These tendencies were also observed in a previous magnetoencephalography (MEG) study, which found decreased connectivity of the delta frequency band in study in patients with CECTS,[18] as well as enhanced functional connectivity of the alpha frequency band between anterior and posterior cerebral regions and less connectivity of the gamma frequency band at EEG than in the MEG post-treatment study.[18] Another study observed increased connectivity of the theta frequency band of EEG data at the onset of epilepsies with variable etiologies.[19] This tendency was partially obvious on the network via the peri-Rolandic area.[18] The same tendencies of increasing and decreasing connectives at each frequency band between the analyses for global and interest electrodes might indicate that the aberrant networks develop via the epileptogenic cortical regions in patients with CECTS.

An association between connectivity and seizure times or frequency in CECTS patients is yet to be confirmed. This study revealed that a low PLI toward interest electrodes in the beta frequency band might be a risk factor for frequent seizures times in CECTS patients. The PLI analysis at the beta frequency band using scalp EEG data might be applicable for estimating the seizure

Table 3. Mean PLIs in the pairs between the interest electrodes (C3, C4, P3, P4, T3, and T4) and the other electrodes (mean PLIs toward PD electrodes) in patients with CECTS and control participants in each frequency band

Frequency band	Patients with CECTS (n = 13)		Control participants (n = 13)	P-value
Delta	0.34 ± 0.23	<	0.39 ± 0.25	< 0.001*
Theta	0.31 ± 0.22	>	0.29 ± 0.21	0.006*
Alpha	0.34 ± 0.25	>	0.30 ± 0.22	< 0.001*
Beta	0.17 ± 0.13		0.16 ± 0.12	0.029
Gamma	0.19 ± 0.14	<	0.22 ± 0.16	< 0.001*

Table 4. The results of multivariate regression analysis between seizure times and PLIs with electrodes toward interest electrodes in each frequency band

Frequency band	B	β	95% CI of B		VIF	P-value
			Lower	Upper		
Delta	–0.76	–0.02	–3.53	2.02	1.01	0.59
Theta	0.12	0.00	–2.72	2.95	1.00	0.94
Alpha	1.45	0.04	–1.12	4.02	1.01	0.27
Beta	–5.63	–0.07	–10.39	–0.88	1.01	0.02*
Gamma	1.86	0.03	–2.69	6.42	1.00	0.42

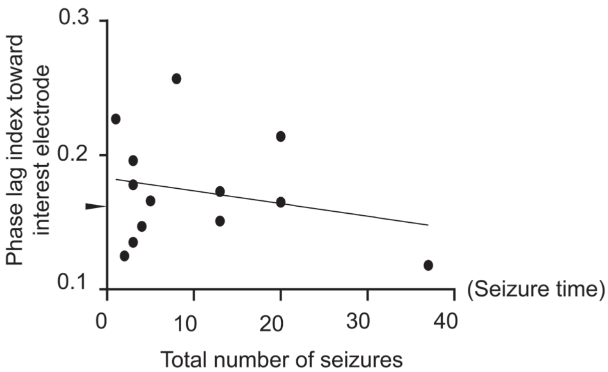

Fig. 3. Association between mean phase lag index (PLI) toward interest electrodes at the beta frequency band on the scalp EEG recordings and total seizure times of each patient with CECTS. The arrowhead indicates PLIs toward interest electrodes in control participants (0.16). PLIs toward PD electrodes were negatively associated with the seizure times that were significant.

frequency and determining antiseizure medication at the onset timing in patients with CECTS.

The tendency was not observed in the analysis using global electrodes. In a previous study of EEG connectivity for patients with epilepsy, the connectivity of the beta frequency band among sensorimotor areas decreased.[20] A study using functional MRI in patients with CECTS indicated the connectivity between sensorimotor areas and other cortices, and the connectivity between sensorimotor areas and the inferior motor area, decreased during the resting state.[21] The centrotemporal spikes interrupt the connections between sensorimotor and other areas, including language areas, inferior frontal areas, and the caudate.[22] Using scalp EEG, our study revealed more disrupted connectivity from sensorimotor areas toward other areas in CECTS patients with more frequent seizures.

Interestingly, the PLIs toward the PD electrodes on the beta frequency band did not differ between patients with CECTS and control participants (Table 3). Compared with those in the control participants, the PLIs toward PD electrodes in patients with CECTS were high among patients with infrequent seizures and low in patients with frequent seizures. The inversion phenomenon among the different seizure frequencies was similar to the network analysis results in children on the autism spectrum.[23] This resulted in no differences in PLIs between all patients with CECTS and control participants in this study.

In conclusion, the mean PLIs using all electrodes and toward PD electrodes in patients with CECTS increased at theta and alpha frequency bands and decreased at delta and gamma frequency bands compared with those of the control participants. The mean PLIs toward PD electrodes at the beta frequency band were negatively associated with seizure times in patients with CECTS. This difference in the resting-state EEG connectivity may be a predictive marker for seizure times in patients with CECTS.

Limitations

Our study had some limitations. The seizure times were modified using medical treatment. The tendency of low PLIs toward interest electrodes in patients with frequent seizures was not prominent enough to provide a cut-off value for predicting the frequent seizure cases; a study with more patients is required to provide this.

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DATA AVAILABILITY STATEMENT

The data presented in this study are available upon request from the corresponding author. The data are not publicly available due to the inclusion of personal information.

AUTHOR CONTRIBUTIONS

Conceptualization, M.O, T.O and T.O; methodology, T.O and M.O; software, M.O and M.N; validation, M.O and T.O; formal analysis, T.O; investigation, T.O, S.K and H.Y; resources, T.O; data curation, T.O and T.O; writing—original draft preparation, T.O and M.O; writing—review and editing, T.O, K.O, and T.H; visualization, M.O; supervision, Y.M; project administration, A.F; funding acquisition, M.O. All authors have read and agreed to the published version of the manuscript.

The authors declare no conflict of interest.

REFERENCES

1. Amrutkar C, Riel-Romero RM. Rolandic Epilepsy Seizure. In: StatPearls [Internet]. Treasure Island (Florida): StatPearls Publishing [updated 2022 Jun 12; cited 2022 Jun 30]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534845/
2. Guerrini R, Pellacani S. Benign childhood focal epilepsies. Epilepsia. 2012;53(suppl 4):9-18. DOI: 10.1111/j.1528-1167.2012.03609.x, PMID: 22946717
3. Vinayan KP, Biji V, Thomas SV. Educational problems with underlying neuropsychological impairment are common in children with Benign Epilepsy of Childhood with Centrotemporal Spikes (BECTS). Seizure. 2005;14:207-12. DOI: 10.1016/j.seizure.2005.01.009, PMID: 15797356
4. Oguri M, Okanishi T, Kanai S, Baba S, Nishimura M, Ogo K, et al. Phase Lag Analyses on Ictal Scalp Electroencephalography May Predict Outcomes of Corpus Callosotomy for Epileptic Spasms. Front Neurol. 2020;11:576087. DOI: 10.3389/fneur.2020.576087, PMID: 33424739
5. Watemberg N, Afunevitz S, Ganelin-Cohen E, Mahajnah M. Clinical Features at the Time of Diagnosis of Benign Epilepsy With Centrotemporal Spikes Do Not Predict Subsequent Seizures. Pediatr Neurol. 2018;88:36-9. DOI: 10.1016/j.pediatrneurol.2018.08.024, PMID: 30337131
6. Xiao F, An D, Chen S, Ren J, Zhou D. Clinical and Electroencephalographic (EEG) Features Associated With Refractoriness in Benign Childhood Epilepsy With Centrotemporal Spikes. J Child Neurol. 2015;30:1591-7. DOI: 10.1177/0883073815575367, PMID: 25792427
7. Chen S, Fang J, An D, Xiao F, Chen D, Chen T, et al. The focal alteration and causal connectivity in children with new-onset benign epilepsy with centrotemporal spikes. Sci Rep. 2018;8:5689. DOI: 10.1038/s41598-018-23336-z, PMID: 29632387
8. Tan G, Xiao F, Chen S, Wang H, Chen D, Zhu L, et al. Frequency-specific alterations in the amplitude and synchronization of resting-state spontaneous low-frequency oscillations in benign childhood epilepsy with centrotemporal spikes. Epilepsy Res. 2018;145:178-84. DOI: 10.1016/j.eplepsyres.2018.07.007, PMID: 30048931
9. Ueda R, Takeichi H, Kaga Y, Oguri M, Saito Y, Nakagawa E, et al. Atypical gamma functional connectivity pattern during light sleep in children with attention deficit hyperactivity disorder. Brain Dev. 2020;42:129-39. DOI: 10.1016/j.braindev.2019.11.001, PMID: 31761311
10. Choi HS, Chung YG, Choi SA, Ahn S, Kim H, Yoon S, et al. Electroencephalographic Resting-State Functional Connectivity of Benign Epilepsy with Centrotemporal Spikes. J Clin Neurol. 2019;15:211-20. DOI: 10.3988/jcn.2019.15.2.211, PMID: 30938108
11. Gregory DL, Wong PKH. Clinical relevance of a dipole field in rolandic spikes. Epilepsia. 1992;33:36-44. DOI: 10.1111/j.1528-1157.1992.tb02280.x, PMID: 1370800
12. Zhang J, Dong X, Wang L, Zhao L, Weng Z, Zhang T, et al. Gender Differences in Global Functional Connectivity During Facial Emotion Processing: A Visual MMN Study. Front Behav Neurosci. 2018;12:220. DOI: 10.3389/fnbeh.2018.00220, PMID: 30319370
13. Lee EH, You SJ. Factors associated with electroencephalographic and clinical remission of benign childhood epilepsy with centrotemporal spikes. Brain Dev. 2019;41:158-62. DOI: 10.1016/j.braindev.2018.08.011, PMID: 30205923
14. You SJ, Kim DS, Ko TS. Benign childhood epilepsy with centro-temporal spikes (BCECTS): early onset of seizures is associated with poorer response to initial treatment. Epileptic Disord. 2006;8:285-8. PMID: 17150442
15. Arhan E, Serdaroglu A, Ozturk Z, Aydın K, Hırfanoglu T. Serial changes in the paroxysmal discharges in rolandic epilepsy may predict seizure recurrence: A retrospective 3-year follow-up study. Epilepsy Behav. 2018;82:150-4. DOI: 10.1016/j.yebeh.2018.03.014, PMID: 29625366
16. Tang H, Wang Y, Hua Y, Wang J, Jing M, Hu X. Analysis of serial electroencephalographic predictors of seizure recurrence in Rolandic epilepsy. Childs Nerv Syst. 2019;35:1579-83. DOI: 10.1007/s00381-019-04275-0, PMID: 31267183

17 Alexander H, Govindan RB, Anwar T, Chirumamilla VC, Fayed I, Keating RF, et al. Global and intertuberal epileptic networks in tuberous sclerosis based on stereoelectroencephalographic (sEEG) findings: a quantitative EEG analysis in pediatric subjects and surgical implications. Childs Nerv Syst. 2022;38:407-19. DOI: 10.1007/s00381-021-05342-1, PMID: 34455445
18 Niu K, Li Y, Zhang T, Sun J, Sun Y, Shu M, et al. Impact of Antiepileptic Drugs on Cognition and Neuromagnetic Activity in Childhood Epilepsy With Centrotemporal Spikes: A Magnetoencephalography Study. Front Hum Neurosci. 2021;15:720596. DOI: 10.3389/fnhum.2021.720596, PMID: 34566605
19 Douw L, de Groot M, van Dellen E, Heimans JJ, Ronner HE, Stam CJ, et al. 'Functional connectivity' is a sensitive predictor of epilepsy diagnosis after the first seizure. PLoS One. 2010;5:e10839. DOI: 10.1371/journal.pone.0010839, PMID: 20520774
20 Routley B, Shaw A, Muthukumaraswamy SD, Singh KD, Hamandi K. Juvenile myoclonic epilepsy shows increased posterior theta, and reduced sensorimotor beta resting connectivity. Epilepsy Res. 2020;163:106324. DOI: 10.1016/j.eplepsyres.2020.106324, PMID: 32335503
21 Besseling RMH, Overvliet GM, Jansen JFA, van der Kruijs SJM, Vles JSH, Ebus SCM, et al. Aberrant functional connectivity between motor and language networks in rolandic epilepsy. Epilepsy Res. 2013;107:253-62. DOI: 10.1016/j.eplepsyres.2013.10.008, PMID: 24210960
22 Xiao F, An D, Lei D, Li L, Chen S, Wu X, et al. Real-time effects of centrotemporal spikes on cognition in rolandic epilepsy. Neurology. 2016;86:544-51. DOI: 10.1212/WNL.0000000000002358, PMID: 26747882
23 Hirosawa T, An K, Soma D, Shiota Y, Sano M, Kameya M, et al. Epileptiform discharges relate to altered functional brain networks in autism spectrum disorders. Brain Commun. 2021;3:fcab184. DOI: 10.1093/braincomms/fcab184, PMID: 34541529