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RESEARCH LETTER

EEG correlates of seizure without awareness and depression in patients with epilepsy: A secondary analysis of a 2022 study on EEG correlates of quality of life

Epilepsy is a neurological disorder characterized by the unpredictable occurrence of seizures. Despite treatment with antiseizure medicine (ASM), some patients still experience uncontrolled seizures. We previously reported that seizures without awareness and depression affect the quality of life (QOL) of patients with epilepsy.[1] Then, in 2022, we investigated electroencephalography (EEG) correlates of QOL in patients with seizure without awareness and depression.[2] The present study is a secondary analysis based on that 2022 report.[2]

Study 1

We investigated the EEG regions associated with seizure without awareness (focal impaired awareness seizure, focal to bilateral tonic–clonic seizure, and generalized tonic–clonic seizure), depression, and depression with the interval from seizure without awareness to EEG examination (depression with EEG interval). The sample entropy[2] of the EEG data (SampEn EEG) was calculated and the effects were examined by four machine learning methods (Tables S1–S11). We then identified the bilateral CP and FzCz EEG regions for seizure without awareness and depression, and the FzCz EEG region for depression with EEG interval (Tables 1 and S12; Data S1).

Study 2

Nine new patients with epilepsy were added along with the patients from our 2022 report[1] (Table S13). We then investigated whether the EEG regions confirmed in Study 1 were effective using similar methods to Study 1 in all 72 patients. When calculating SampEn (N, m, r), the parameter $m = 2$ is typically used as the length of the template.[3] In Study 2, $m = 2$–12 was also investigated (Tables S14–S25). As a result, we identified that the SampEn EEG of the non-smoothing filter, high-cut filter (30 Hz), and time constant (0.3 s) were effective for seizure without awareness in the bilateral CP and FzCz, as well as that of Savitzky–Golay filter, high-cut filter (15 Hz), and time constant (0.1 s) for depression in patients with epilepsy. To our knowledge, this study was the first to report that the brain region of the bilateral CP and FzCz was associated with not only seizure without awareness, but also depression, and that EEG findings showed significantly different characteristics from each other (Tables S26–S28). The detailed methods and results are shown in Data S1.

An ^{18}F-FDG-PET study of patients with temporal lobe epilepsy with seizure-impaired awareness showed hypermetabolism in the cortical and subcortical network, and although our scalp EEG study cannot directly be compared with that ^{18}F-FDG-PET study,[4] our findings indicate that the EEG regions of the bilateral CP and FzCz are associated with thalamocortical function. As there are reportedly changes other than interictal epileptiform discharges in EEG signals embodying seizure propensity,[5] the EEG in the present study in the interictal state without any epileptic or paroxysmal discharges demonstrated the propensity of seizure without awareness in the bilateral CP and FzCz. Furthermore, we previously found that the SampEn EEG in the frontal and frontal–temporal EEG regions changed before and after psychosis in patients with epilepsy.[6] We can therefore hypothesize that these clustered EEG regions, in association with seizure without awareness, depression, psychosis, and QOL, mutually change and function as state markers. The changes in these state markers may reflect therapeutic status more accurately. However, the sample sizes in our present and previous studies were relatively small, and thus, the results cannot be generalized. Further studies are needed to elucidate the differences between brain functions and these EEG regions in line with the complex networks in patients with epilepsy.[7]

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TABLE 1 EEG regions associated with SEALS and the presence or absence of seizure without awareness within 1 year, depression, and depression with EEG interval.

No. of EEG region[a]	EEG regions associated with SEALS	Seizure without awareness (odds ratio [95% CI])	Depression (odds ratio [95% CI])	Depression with EEG interval[b] (odds ratio [95% CI])
1	T5O1-C3P3-P3O1-FzCz-C4P4-P4O2-T6O2	2[c]/96[d] (0.021 [0.003, 0.073])	11/96 (0.115 [0.059, 0.196])	19/96 (0.198 [0.124, 0.292])
2	FzCz	0/96 (0.000 [0.000, 0.038])	0/96 (0.000 [0.000, 0.038])	13/96 (0.135 [0.074, 0.220])
3	C3P3-FzCz-CzPz-P4O2-T6O2	3/96 (0.031 [0.006, 0.089])	2/96 (0.021 [0.003, 0.073])	22/96 (0.229 [0.150, 0.326])
4	T3T5-T5O1-C3P3-P3O1-C4P4-P4O2-T4T6-T6O2	0/96 (0.000 [0.000, 0.038])	0/96 (0.000 [0.000, 0.038])	1/96 (0.010 [0.000, 0.057])
5	T5O1-C3P3-P3O1-FzCz-C4P4-P4O2-T4T6-T6O2	0/96 (0.000 [0.000, 0.038])	4/96 (0.042 [0.011, 0.103])	19/96 (0.198 [0.124, 0.292])
6	FzCz-P4O2-T6O2	0/96 (0.000 [0.000, 0.038])	0/96 (0.000 [0.000, 0.038])	17/96 (0.177 [0.107, 0.268])
7	C3P3-FzCz-C4P4-P4O2-T6O2	17/96 (0.177 [0.107, 0.268]	0/96 (0.000 [0.000, 0.038])	19/96 (0.198 [0.124, 0.292])
8	FzCz-P4O2	0/96 (0.000 [0.000, 0.038])	0/96 (0.000 [0.000, 0.038])	23/96 (0.240 [0.158, 0.337])
9	C3P3-FzCz-C4P4	24/96 (0.250 [0.167, 0.349])	9/96 (0.094 [0.044, 0.171])	26/96 (0.271 [0.185, 0.371])
10	C3P3-FzCz-CzPz-C4P4	15/96 (0.156 [0.090, 0.245]	2/96 (0.021 [0.003, 0.073])	21/96 (0.219 [0.141, 0.315])
11	CzPz	0/96 (0.000 [0.000, 0.038])	0/96 (0.000 [0.000, 0.038])	0/96 (0.000 [0.000, 0.038])

Note: EEG regions 7, 9, and 10 were equally effective for seizure without awareness. The most effective EEG region with the fewest number of electrodes for seizure without awareness was C3P3-FzCz-C4P4. EEG regions 1, 3, 5, 9, and 10 were equally effective for depression. The most effective EEG region with the fewest number of electrodes for depression was C3P3-FzCz-C4P4. EEG regions 1–3, 5–9, and 10 were equally effective for depression with EEG interval. The most effective EEG region with the fewest number of electrodes for depression with EEG interval was Fz-Cz. We considered that the fewest electrodes necessary is sufficient for detecting fundamental physiological function (Data S1).

Abbreviations: CI, confidence interval; EEG, electroencephalography; SEALS, Side Effects and Life Satisfaction Inventory.

[a]Nos. 1–8, see Azuma and Akechi (2022).[2] As a simplified composition of effective EEG region No. 7 and other noneffective EEG regions for seizure without awareness, the new EEG regions Nos. 9–11 were created for further investigation (Data S1).

[b]Depression with EEG interval indicates that the interval from seizure to EEG was added as a predictor for discriminating depression.

[c]Number of EEG datasets that satisfy the conditions of both accuracy and AUC more than 0.7 using a machine learning method (Linear SVM, Tree, Linear discriminant, Logistic regression).

[d]EEG datasets, N15-1, N15-3, N30-1, N30-3, N60-1, N60-3, N12-1, N12-3, S15-1, S15-3, S30-1, S30-3, S60-1, S60-3, S12-1, S12-3, W15-1, W15-3, W30-1, W30-3, W60-1, W60-3 W12-1, W12-3. N, no smoothing filters; S, Savitzky-Golay (SG) filter; W, wavelet denoising (WD) filter; 15, 30, 60, 120; low-pass filter (Hz), respectively, 1, 3; 0.1 and 0.3 time constant(s), respectively. Thus, 3 filters (non-filter, SG filter, and WD filter) × 4 machine learning methods × 8 high-pass and low-pass filter combinations.

AUTHOR CONTRIBUTION

Hideki Azuma designed the study, wrote the protocol, and managed the data acquisition. All authors critically reviewed the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. Tatsuo Akechi is the Vice Editor-in-Chief of *Psychiatry and Clinical Neurosciences Reports* and a co-author of this article. He was excluded from editorial decision-making related to the acceptance and publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the Supporting Information.

ETHICS APPROVAL STATEMENT

This research was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans and was approved by the Ethics Committee of the Nagoya City University Medical School Ethics Committee.

PATIENT CONSENT STATEMENT

Written, informed consent was obtained from all participants.

CLINICAL TRIAL REGISTRATION

N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.