Received: 17 August 2023 | Revised: 12 January 2024 | Accepted: 12 January 2024

DOI: 10.1111/epi.17897

Epilepsia®

RESEARCH ARTICLE

EEG microstates show different features in focal epilepsy and psychogenic nonepileptic seizures

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Abstract

Objective: Electroencephalography (EEG) microstate analysis seeks to cluster the scalp's electric field into semistable topographical EEG activity maps at different time points. Our study aimed to investigate the features of EEG microstates in subjects with focal epilepsy and psychogenic nonepileptic seizures (PNES).

Methods: We included 62 adult subjects with focal epilepsy or PNES who received video-EEG monitoring at the epilepsy monitoring unit. The subjects (mean age = 42.8 ± 21.2 years) were distributed equally between epilepsy and PNES groups. We extracted microstates from a 4.4 ± 1.0-min, 21-channel resting-state EEG. We excluded subjects with interictal epileptiform discharges during resting-state EEGs. After preprocessing, we derived five main EEG microstates—MS1 to MS5—for the full frequency band (1–30 Hz) and frequency subbands (delta, 1–4 Hz; theta, 4–8 Hz; alpha, 8–12 Hz; beta, 12–30 Hz), using the MATLAB-based EEGLAB toolkit. Statistical features of microstates (duration, occurrence, contribution, global field power [GFP]) were compared between the groups, using logistic regression corrected for age and sex.

Results: We detected no differences in microstate parameters in the full frequency band. We found a longer duration (delta: $B = -7.680$, $p = .046$; theta: $B = -16.200$, $p = .043$) and a higher contribution (delta: $B = -7.414$, $p = .035$; theta: $B = -7.509$, $p = .031$) of MS4 in lower frequency bands in the epilepsy group. The PNES group showed a higher occurrence of MS5 in the delta subband ($B = 3.283$, $p = .032$). In the theta subband, a higher GFP of MS1 was associated with the PNES group ($B = 5.674$, $p = .025$), whereas a higher GFP of MS2 was associated with the epilepsy group ($B = -6.579$, $p = .026$).

Significance: Microstate features show differences between patients with focal epilepsy and PNES. EEG microstates could be a promising parameter, helping to understand changes in brain dynamics in subjects with epilepsy, and should be explored as a potential biomarker.

KEYWORDS

biomarkers, differential diagnosis, PNES, resting-state EEG

1 | INTRODUCTION

Electroencephalography (EEG) is a widely used diagnostic tool in neurology. Although EEG bears the capacity to reflect the global neurophysiological activity of the cortex, visual EEG interpretation mainly focuses on circumscribed local and regional changes. EEG microstate analysis provides a technique to visualize the global topographic brain activity on a subsecond timescale.

Microstate analysis was developed by Lehmann et al. in 1987[1] to display the global brain activity, recorded in multichannel EEG, as a series of quasistable microstates. Each microstate has a unique topography over the entire channel array. Data from all EEG electrodes and every recording time point are used to build a global brain activity map with the most active and the least active parts, using the global field power (GFP) calculations. Microstates can be studied by resting-state and event-related approaches. The majority (>70%) of the resting-state EEG data can be represented by only four topographies, canonically labeled as microstates A, B, C, and D.[2,3] Microstates do not gradually change from one into another; instead, they transit instantaneously after maintaining a dominant state for 80–120 ms.[4] Features to characterize microstates include average duration, occurrence, contribution, GFP, and transition probabilities. Functionally, microstates have primarily been interpreted as different topographical activity maps arising from the coordinated activity of distinct neuronal assemblies in the brain.[5] Efforts to link resting-state EEG microstates with resting-state networks in functional magnetic resonance imaging (fMRI) have not yet been conclusive and are a subject of ongoing research.[6,7]

EEG microstate analysis has been probed in multiple neurological and psychiatric disorders, such as Alzheimer disease,[8] primary progressive aphasia,[9] Lewy body disease,[10] and schizophrenia.[2] In the latter, microstate changes might even characterize possible endophenotypes. Despite the growing interest in other neuropsychiatric disorders, only sparse data are available on EEG microstates in people with epilepsy.

Jiang et al.[11] reported that subjects with genetic generalized epilepsy (GGE) with ongoing seizures display an increased frequency and coverage of microstate A and lower duration and coverage of microstate C compared with healthy controls and seizure-free GGE subjects. Raj et al.[12] reported that the occurrence and coverage of microstate C could discriminate between subjects with temporal lobe epilepsy and healthy controls with a 76.1% accuracy. Another study with patients with absence epilepsy found that microstate transition parameters differed compared to healthy controls. The same authors also reported a "slowdown" in microstate transitions in postseizure versus preseizure EEGs.[13] Currently, to the best of our knowledge, there is only one study investigating the differences in microstates between subjects with psychogenic nonepileptic seizures (PNES), also referred to as functional or dissociative seizures, and epilepsy. Ahmadi et al.[14] analyzed EEG microstates in 10 subjects with epilepsy and PNES. Researchers described that beta subband and coverage were the most critical features for differentiating between the two groups.

The aim of our study was to investigate and compare the statistical parameters of EEG microstates in subjects with focal epilepsy and PNES.

Key points

- The features of EEG microstates in focal epilepsy and PNES were investigated.
- A longer duration and higher contribution of microstate 4 in theta and delta subbands were associated with the epilepsy group.
- A higher occurrence of microstate 5 in the delta subband was associated with the PNES group.
- Microstate analysis could be a promising EEG tool to investigate the overall brain dynamics in subjects with epilepsy and PNES.

2 | MATERIALS AND METHODS

2.1 | Subjects

We included subjects who were admitted to the EEG monitoring unit of RWTH University Clinic Aachen (Germany), a tertiary referral center for epilepsy, in the time from April 2020 to April 2021 and subsequently diagnosed with either focal epilepsy according to the International League against Epilepsy criteria or PNES. All subjects underwent at least 72 h of continuous video-EEG monitoring. The diagnosis was based on the previous medical history, MRI, and other available imaging

findings, a thorough assessment of the seizure semiology, and the findings of video-EEG monitoring. For the purpose of this study, we collected clinical data on the diagnosis, sex, age, and current antiseizure medications.

2.2 | EEG recordings

We recorded 21-channel resting-state EEG as an integral part of our standard procedure on the first day of admission to the EEG monitoring unit using the Micromed EEG system. The electrodes were placed according to the 10–20 system[15]; the reference electrode was set to average. EEGs were recorded in an awake, eyes-closed condition, in a darkened room without any stimuli at a 256-Hz sampling rate. The mean recording time was 4.4 ± 1.0 min.

2.3 | Exclusion criteria

Persons with a combined diagnosis of epilepsy and PNES were excluded from the study. Also, subjects with too pronounced artifacts in the recording to allow the microstate analysis and/or interictal epileptiform discharges in the resting-state EEGs were not included into the study. We also excluded subjects who had seizures in the past 24 h.

2.4 | EEG preprocessing

We performed preprocessing of the raw EEG data using the MATLAB (R2022b)-based EEGLAB toolkit (v2021.1).[16] First, we applied a band-pass filter from .3 Hz to 54 Hz using a Hamming windowed sinc finite impulse response filter, implemented in the EEGLAB *eegfiltnew* function. The reference channel was set to average. Every recording was checked visually, and segments with pronounced artifacts were removed. Independent component analysis was performed, and the multiple artifact rejection algorithm[17] was used to classify and remove artifacts. Additionally, ocular artifacts were removed using the automated artifact removal algorithm.[18] Finally, the data were filtered for the second time (1–30 Hz).

2.5 | Microstate analysis

We performed the microstate calculation using the Microstate plugin[19] in the EEGLAB toolbox. First, microstates were obtained for each subject individually. The measure of GFP was used to denote the electric activity at each time point, considering the data from all of the electrodes. The topographic plots at GFP peaks were then clustered using the modified *k*-means algorithm.[20] The polarity was ignored. Clustering the whole data into the total of five main microstates was chosen, as it was showing the highest global explained variance (GEV) while retaining a relatively small number of microstates. Microstates were calculated in the full frequency band (1–30 Hz), as well as in different subbands (delta, 1–4 Hz; theta, 4–8 Hz; alpha, 8–12 Hz; beta, 12–30 Hz). After identifying microstates on the individual level, the mean microstate maps across the whole cohort were computed, leading to five main microstates: MS1, MS2, MS3, MS4, and MS5. These were then backfitted to every individual, and statistical microstate features for every subject were calculated. The statistical features included GEV, duration (the length of every microstate in seconds), occurrence (the number of times per second the microstate appeared), contribution (the part of data, explained by particular microstate), and mean GFP. For a semiquantitative analysis of topography, we also calculated microstates in PNES and epilepsy groups separately.

2.6 | Statistical analysis

We carried out the statistical analyses using SPSS software (v29.0). The normality of variables was assessed using Kolmogorov–Smirnov test. To investigate the differences in demographic data between the two groups, *t*-test and Mann–Whitney *U*-test were used for continuous variables and Pearson χ^2 for nominal variables. To test the differences between the two groups in terms of microstate parameters, logistic regression method was used. The outcome was diagnosis (PNES or epilepsy), and the covariates were age and sex as well as various microstate features. We performed the correction for multiple testing by placing all the MS parameters from the same group (e.g., duration of MS1 to MS5) into the same logistic regression model. When building the predictive models for the receiver operating characteristic (ROC) curves, the following equation, based on logistic regression models, was used:

$$\text{Model} = \frac{e^{(b_0+b_1x_1+b_2x_2+\ldots+b_nx_n)}}{1+e^{(b_0+b_1x_1+b_2x_2+\ldots+b_nx_n)}}$$

where b_0 is a constant from the regression model, b_1 to b_n are the *B* values of the logistic regression model for specific covariates, and x_1 to x_n are the exact values of the covariates. Significance level was set at <.05.

2.7 | Ethics

The study was approved by the ethical review board of the Faculty of Medicine at RWTH Aachen (EK-Ethics Committee) and the Center for Translational & Clinical Research Aachen (CTC-A; EK 479/21 and CTC-A_21_433). Informed consent for the study was waived by the ethical review board of the Faculty of Medicine at RWTH Aachen (EK 479/21) due to the retrospective nature of the study. The study complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki).

3 | RESULTS

3.1 | Patient characteristics

From the 62 patients included in the study, 31 were in the PNES group and 31 in the epilepsy group. There were more women than men in the PNES group compared to the epilepsy group (18:13 vs. 8:23 respectively; $\chi^2 = 6.624$, $p = .01$). Mean age of the subjects was 43.2 ± 19.5 years, and mean age at the first manifestation was 40.0 ± 20.6 years, both without significant differences between the two groups. There were 17 subjects in the epilepsy group and six subjects in the PNES group receiving antiseizure medication (ASM) at the time of EEG recording. The localization of the epileptogenic focus in the epilepsy group was either temporal (12 subjects), frontal (two subjects), or still unclear at the time of the examination (17 subjects). Additional patient characteristics are shown in Table 1.

3.2 | Microstates in the full frequency band

First, we calculated the five microstates from the full frequency band in the whole cohort. The GEV of five microstates was in line with other studies at 77.3%.[21] The topographies of each microstate are shown in Figure 1. MS1 and MS2 showed a left–right and right–left lateralization, MS3 an anterior–posterior distribution, and MS4 and MS5 corresponded to frontocentral and frontoparietal extreme locations.

We found no significant differences in microstate parameters between the PNES and epilepsy groups in the full frequency band. For the full data, see Table S1.

Additionally, microstate topographies were analyzed separately in PNES and epilepsy groups, and a correlation analysis was performed. The activity maps of each microstate showed a strong correlation between both groups, indicating no significant differences in the topographies of microstates between subjects with epilepsy and PNES (see Figure 2).

TABLE 1 Patient characteristics.

Characteristic	Epilepsy	PNES	*p*
n	31	31	
Age, years, mean ± SD	46.0 ± 20.8 (min. 17, max. 81)	40.5 ± 18.2 (min. 17, max. 75)	.331
Sex, male/female	18/13	8/23	**.010**
First manifestation, years, mean ± SD	42.8 ± 21.2 (min. 17, max. 77)	37.2 ± 20.0 (min. 8, max. 75)	.288
Type of epilepsy, *n*			
Temporal lobe epilepsy	12		
Frontal lobe epilepsy	2		
Unknown focus	17		
Antiseizure medication, *n*			
Levetiracetam	11	0	
Lamotrigine	3	2	
Valproate	1	0	
Carbamazepine	0	1	
Brivaracetam	0	1	
Topiramate	1	0	
Oxcarbazepine	1	0	
Levetiracetam and lacosamide	0	1	
Levetiracetam and lamotrigine	0	1	
No antiseizure medication	14	25	

Abbreviations: max., maximum; min., minimum; PNES, psychogenic nonepileptic seizures, statistically significant *p* values in bold.

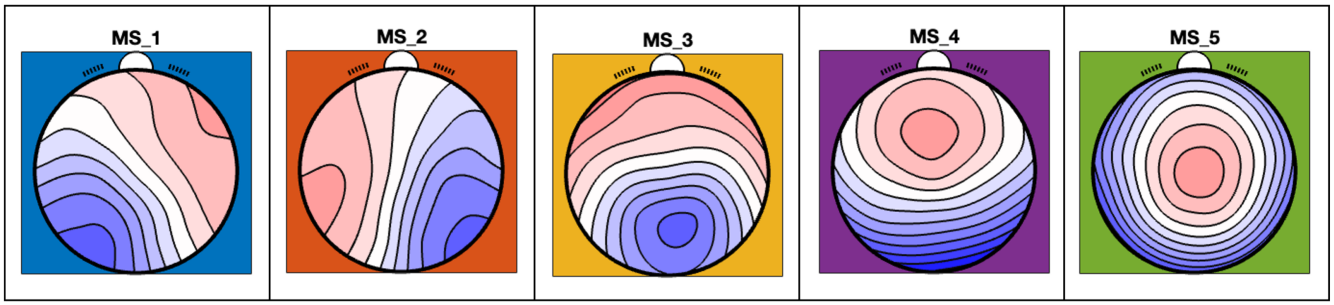
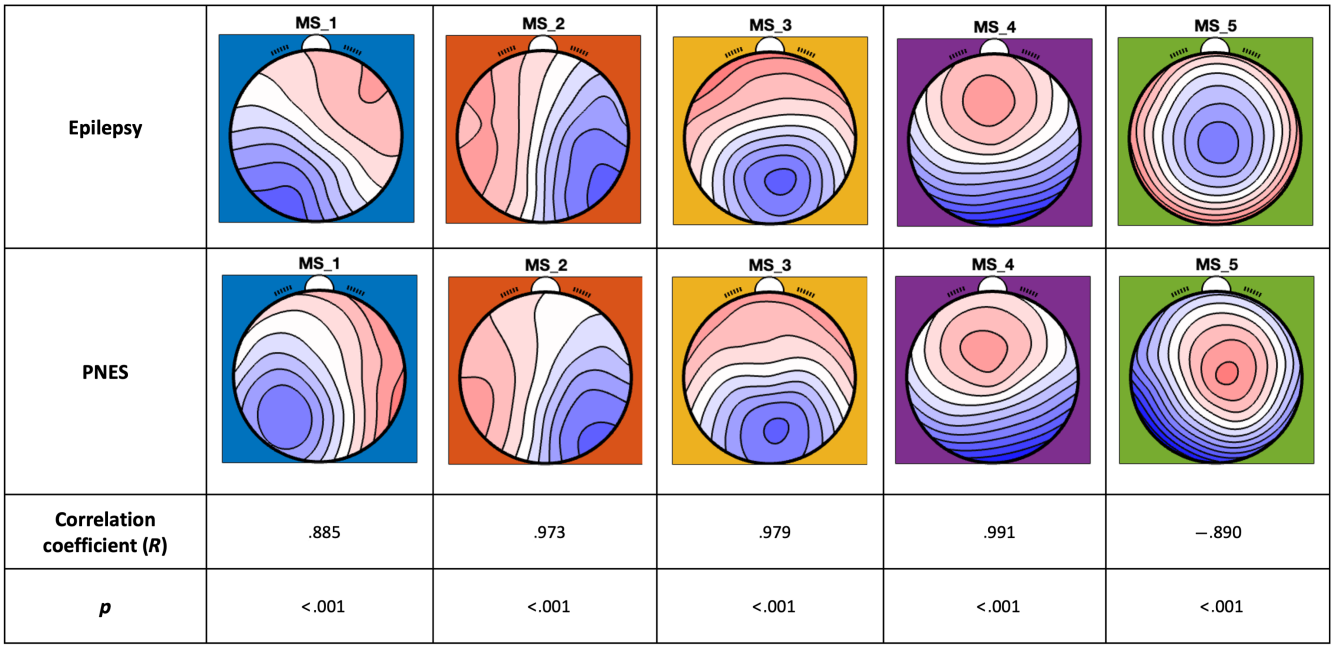


FIGURE 1 Topographies of microstates in the full frequency band.



Correlation coefficient (*R*)	.885	.973	.979	.991	−.890
p	<.001	<.001	<.001	<.001	<.001

FIGURE 2 Comparison of microstate topographies between epilepsy and psychogenic nonepileptic seizures (PNES) groups.

3.3 | Microstates in delta subband

The analysis of microstates in the delta frequency subband revealed some additional insights. A longer duration (B [SE] = −7.680 [3.845], p = .046, model χ^2 = 14.02, p = .048) and a higher contribution (B [SE] = −7.414 [3.511], p = .035, model χ^2 = 14.819, p = .022) of MS4 were associated with the epilepsy group compared to the PNES group. On the other hand, a higher occurrence of MS5 was associated with being in the PNES group (B [SE] = 3.283 [1.529], p = .032, model χ^2 = 17.194, p = .016). For full data, see Table 2.

3.4 | Microstates in theta subband

In the theta frequency subband, a similar trend for MS4 emerged. A longer duration (B [SE] = −16.200 [7.987], p = .043, model χ^2 = 16.732, p = .019) and a higher contribution of MS4 (B [SE] = −7.509 [3.474], p = .031, model χ^2 = 15.523, p = .017) were associated with the epilepsy group compared to the PNES group.

Additionally, differences in the GFP between the two groups were observed. A higher GFP of MS1 was associated with being in the PNES group (B [SE] = 5.674 [2.537], p = .025, model χ^2 = 19.931, p = .006), whereas a higher GFP of MS2 was associated with being in the epilepsy group (B [SE] = −6.579 [2.958], p = .026, model χ^2 = 19.931, p = .006). For full data, see Table 3.

3.5 | Microstates in alpha and beta subbands

There were no significant differences in the statistical parameters of microstates between PNES and epilepsy groups in higher frequency alpha and beta subbands. For full data, see Tables S2 and S3.

TABLE 2 Data from logistic regression analysis in delta subband.

	Mean	SD	*B*	SE	*p*	OR	95% CI for OR	
Duration, s								
Sex			1.541	.605	.011	4.669	1.426	15.286
Age			−.02	.017	.232	.98	.949	1.013
Duration MS1	.256	.057	1.335	5.541	.81	3.799	0	197 697.951
Duration MS2	.249	.049	4.476	6.338	.48	87.856	0	21 799 807.08
Duration MS3	.279	.058	−3.045	5.284	.564	.048	0	1497.749
Duration MS4	.299	.106	−7.68	3.845	**.046**	0	0	.866
Duration MS5	.265	.095	1.406	3.402	.679	4.08	.005	3210.33
Constant			1.23	3.687	.739	3.42		
Occurrence, x/s								
Sex			1.817	.676	.007	6.151	1.634	23.162
Age			−.017	.017	.319	.983	.951	1.016
Occurrence MS1	.697	.258	2.247	1.361	.099	9.459	.657	136.148
Occurrence MS2	.633	.236	.754	1.503	.616	2.126	.112	40.488
Occurrence MS3	.728	.245	−.71	1.283	.58	.491	.04	6.074
Occurrence MS4	.777	.273	−.387	1.2	.747	.679	.065	7.135
Occurrence MS5	.692	.247	3.283	1.529	**.032**	26.653	1.331	533.795
Constant			−3.881	3.158	.219	.021		
Contribution, %								
Sex			1.66	.63	.008	5.259	1.531	18.06
Age			−.02	.016	.213	.98	.949	1.012
Contribution MS1	.186	.099	−1.666	3.905	.67	.189	0	398.29
Contribution MS2	.164	.084	−2.002	4.263	.639	.135	0	574.769
Contribution MS3	.213	.105	−6.232	3.878	.108	.002	0	3.935
Contribution MS4	.245	.139	−7.414	3.511	**.035**	.001	0	.587
Constant			3.699	2.637	.161	40.412		
GFP, μV								
Sex			1.558	.652	.017	4.747	1.322	17.049
Age			−.032	.02	.112	.968	.93	1.008
GFP MS1	1.613	.705	1.223	2.339	.601	3.397	.035	332.531
GFP MS2	1.585	.759	−.491	2.133	.818	.612	.009	40.077
GFP MS3	1.780	.843	−1.242	1.993	.533	.289	.006	14.362
GFP MS4	1.799	.930	−2.468	1.422	.083	.085	.005	1.375
GFP MS5	1.646	.747	2.783	1.967	.157	16.17	.342	764.114
Constant			1.331	1.593	.403	3.787		

Abbreviations: CI, confidence interval; GFP, global field power; OR, odds ratio; x/s, times per second.

Statistically significant *p* values in bold.

3.6 | Predictive models

Furthermore, we built explorative predictive models to differentiate between epilepsy and PNES groups. For delta subband, we included the duration and contribution of MS4, occurrence of MS5, and sex into the model, as they all showed significant differences between epilepsy and PNES groups in logistic regression analyses. In the theta subband, duration and contribution of MS4, GFP of MS1 and MS2, and sex were included into the predictive model due to their statistical significance in logistic regression. Both models showed good predictive performance, with area under the curve (AUC) of .753 and .780 in delta and theta subbands, respectively (see Figure 3).

TABLE 3 Data from logistic regression analysis in theta subband.

	Mean	SD	*B*	SE	*p*	OR	95% CI for OR	
Duration, s								
Sex			1.717	.632	.007	5.569	1.614	19.217
Age			−.021	.017	.228	.979	.946	1.013
Duration MS1	.129	.025	16.623	16.327	.309	16 562 666.5	0	1.30722E+21
Duration MS2	.125	.026	.186	12.889	.988	1.205	0	1.12636E+11
Duration MS3	.146	.068	−2.421	5.47	.658	.089	0	4024.522
Duration MS4	.151	.063	−16.2	7.987	**.043**	0	0	.579
Duration MS5	.134	.047	3.084	6.65	.643	21.846	0	9 987 929.295
Constant			.077	3.768	.984	1.08		
Occurrence, x/s								
Sex			1.653	.627	.008	5.22	1.528	17.837
Age			−.014	.016	.373	.986	.956	1.017
Occurrence MS1	1.379	.503	.855	.637	.18	2.35	.674	8.196
Occurrence MS2	1.306	.371	.656	.864	.448	1.927	.354	10.487
Occurrence MS3	1.399	.421	−.365	.749	.626	.694	.16	3.015
Occurrence MS4	1.490	.518	−1.087	.647	.093	.337	.095	1.199
Occurrence MS5	1.387	.441	.929	.717	.196	2.531	.62	10.327
Constant			−1.562	2.653	.556	.21		
Contribution, %								
Sex			1.67	.623	.007	5.312	1.567	18.008
Age			−.018	.016	.268	.982	.952	1.014
Contribution MS1	.187	.090	2.417	4.029	.549	11.217	.004	30 159.915
Contribution MS2	.169	.071	−2.176	4.933	.659	.113	0	1794.685
Contribution MS3	.214	.131	−3.079	3.336	.356	.046	0	31.811
Contribution MS4	.235	.134	−7.509	3.474	**.031**	.001	0	.496
Constant			2.108	2.328	.365	8.231		
GFP, µV								
Sex			1.593	.692	.021	4.916	1.265	19.102
Age			−.025	.018	.171	.975	.941	1.011
GFP MS1	1.587	.761	5.674	2.537	**.025**	291.299	2.019	42 025.021
GFP MS2	1.525	.735	−6.579	2.958	**.026**	.001	0	.457
GFP MS3	1.629	.768	−1.5	2.271	.509	.223	.003	19.123
GFP MS4	1.770	.995	−3.195	1.82	.079	.041	.001	1.452
GFP MS5	1.621	.794	5.243	3.051	.086	189.232	.478	74 852.635
Constant			.734	1.402	.6	2.084		

Abbreviations: CI, confidence interval; GFP, global field power; OR, odds ratio; x/s, times per second, statistically significant *p* values in bold.

4 | DISCUSSION

Our study showed distinct differences in EEG microstate parameters in lower frequency subbands between subjects with focal epilepsy and PNES, yet no differences in alpha and beta frequencies. Both in delta and theta subbands, subjects with epilepsy showed a longer duration and higher contribution of MS4. In the delta subband, a higher occurrence of MS5 was associated with PNES. In the theta subband, a higher GFP of MS1 was associated with the PNES group, whereas a higher GFP of MS2 was associated with the epilepsy group. Our explorative models were based on significant microstate parameters and sex and showed a good performance in discriminating between epilepsy and PNES subjects (AUC of .753 and .780 in delta and theta subbands, respectively).

Overall, only several studies show data from functional measurement techniques such as fMRI and MRI diffusion

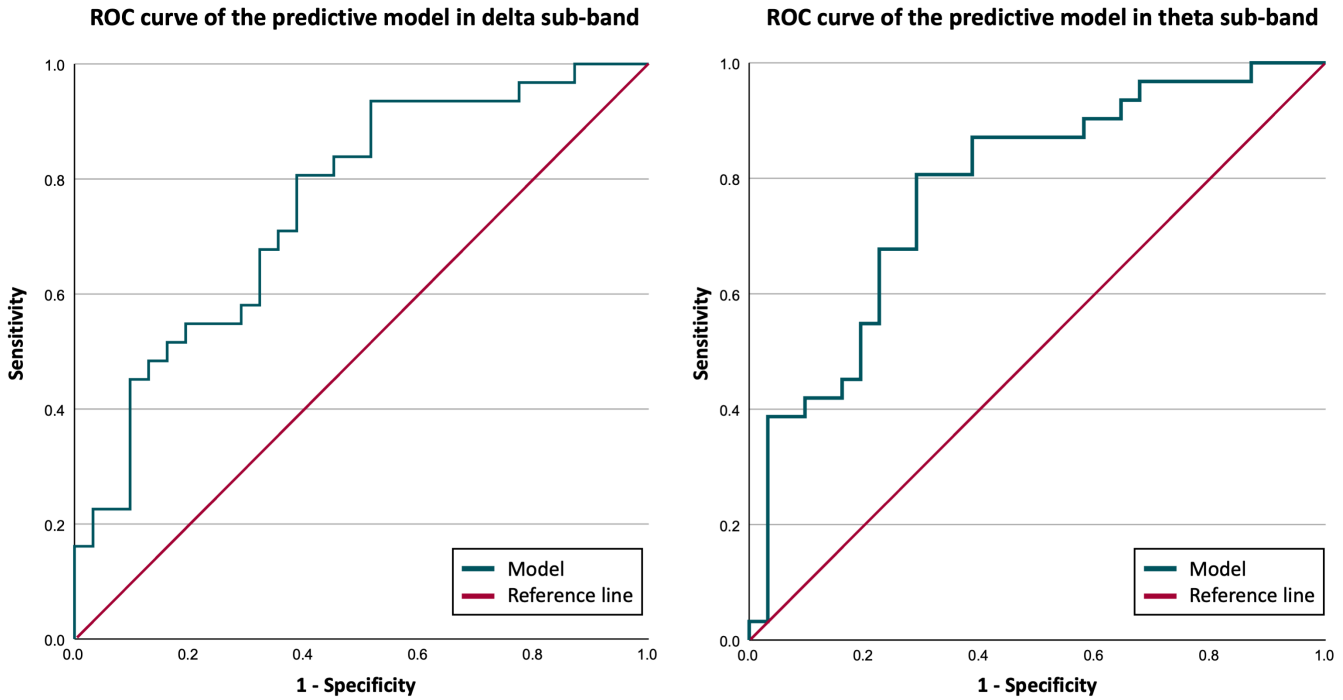


FIGURE 3 Receiver operating characteristic (ROC) curves of the predictive model in delta and theta subbands.

tensor imaging (DTI) in PNES subjects.[22] However, preliminary MRI-DTI data show altered connectivity patterns in persons with PNES,[23] specifically, a disrupted structural frontolimbic connectivity.[23,24] In analogy to our findings, a less dominant MS4, reflecting a frontocentral extreme location, could point to the same underlying pathophysiology. Although it might be too early to discuss the clinical meaning of these electrophysiological characteristics, clear differences in microstate parameters between epilepsy and PNES groups suggest characteristic changes in the overall topographic brain activity in the cases of these pathologies. Further combined EEG microstate and functional imaging studies are required to explore microstates as possible biomarkers for both epilepsy and PNES.

Other comparable investigations are sparse. The study of Ahmadi et al.,[14] aiming to compare persons with epilepsy and PNES in 10 subjects, primarily analyzed different EEG parameters, including microstates, statistical methods, and their predictive performance to find the best possible algorithm to assign patients to different groups. They found that the beta subband as well as coverage of microstates showed the best predictive performance. However, in this study EEG data were clustered into a different number of microstate maps (three or four, depending on the frequency), rendering a direct comparison with our study results difficult.

Although the results from our investigation cannot be compared with other studies with epilepsy or PNES patients, changes in microstate parameters have been associated with other diseases. Schumacher et al.[10] found that the duration of all microstate classes was increased in Lewy body dementia compared to subjects with Alzheimer disease and healthy controls, suggesting that this parameter represents a disintegration of the dynamic properties of the brain, therefore causing a loss of flexibility and adaptability that are crucial for functioning of a healthy brain. Also, changes in the duration, occurrence and contribution in microstate classes C and D were found in patients with schizophrenia and their siblings.[2] The authors suggested these characteristic dynamics as a candidate endophenotype for schizophrenia.

The syntax and naming of microstates often pose an additional challenge, when comparing results across different studies. We avoided the traditional naming "microstates A–D," not only because in our data clustering into five microstates, instead of the canonical four, was better explaining the variance, but also because adhering to a strict nomenclature in this explorative analysis too early might lead to potentially biased interpretation of results in the follow-up studies. Nevertheless, visually our MS1–MS4 showed similarities with previously the published microstates A–D.[21]

Compared to the other studies in the field,[11,13] our study was based on a larger sample size. It is also one of the first studies to approach the differences in microstates between subjects with epilepsy and PNES,[14] and the first one to do so in a clinical setting.

The clinical nature of our investigation, however, also leads to some limitations. Sex is not equally distributed in the groups, making this an important covariate in the

regression analyses. Although a clear additive value of microstates was found in the ROC analysis—AUC increased significantly after adding microstate parameters—future studies should employ stricter matching criteria.

We also cannot rule out an effect of ASM on microstates. Although some subjects in the PNES cohort were receiving ASM at the time of EEG recording due to nonfinalized diagnostic procedures, the share of subjects with ASM treatment in the epilepsy group was higher. To the best of our knowledge, there are currently no available studies investigating the effect of ASM on microstates. However, a small study showed that piracetam, which is a modulator of neural membrane ion permeability, as well as the ASM levetiracetam, alters the topography of fronto-occipital microstates.[25] Other drugs, such as risperidone, were investigated in another study, which found some microstate parameters to be significantly changed in patients with schizophrenia who responded to treatment compared to patients who did not respond.[26] These first findings should be further investigated and validated in future studies, which should also consider microstates as a potential biomarker for treatment efficacy next to other EEG parameters.

Our study is the first one to report differences of EEG microstates in lower frequency bands between subjects with epilepsy and PNES. Although a validation in independent cohorts is necessary, microstates are a promising EEG parameter to help unravel changes in the overall brain dynamics in epilepsy. Future studies should further investigate microstates as a possible biomarker to discriminate epilepsy and conditions with nonepileptic events.

AUTHOR CONTRIBUTIONS

Stefan Wolking designed and supervised the study. Katharina Timpte and Jan Heckelmann acquired the data. Ravichandran Rajkumar analyzed and interpreted the data. Domantė Kučikienė acquired the data, analyzed and interpreted the data, provided statistical analysis, had full access to all of the data in the study, is responsible for the integrity of the data and the accuracy of the data analysis, and drafted the manuscript. Yvonne Weber and Irene Neuner critically revised the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

ACKNOWLEDGMENTS

The study has not received any funding. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

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

How to cite this article: Kučikienė D, Rajkumar R, Timpte K, Heckelmann J, Neuner I, Weber Y, et al. EEG microstates show different features in focal epilepsy and psychogenic nonepileptic seizures. Epilepsia. 2024;65:974–983. https://doi.org/10.1111/epi.17897