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Shared and distinct electroencephalogram microstate abnormalities across schizophrenia, bipolar disorder, and depression

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Original Article

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Abstract

Background. Microstates of an electroencephalogram (EEG) are canonical voltage topographies that remain quasi-stable for 90 ms, serving as the foundational elements of brain dynamics. Different changes in EEG microstates can be observed in psychiatric disorders like schizophrenia (SCZ), major depressive disorder (MDD), and bipolar disorder (BD). However, the similarities and disparatenesses in whole-brain dynamics on a subsecond timescale among individuals diagnosed with SCZ, BD, and MDD are unclear.

Methods. This study included 1112 participants (380 individuals diagnosed with SCZ, 330 with BD, 212 with MDD, and 190 demographically matched healthy controls [HCs]). We assembled resting-state EEG data and completed a microstate analysis of all participants using a cross-sectional design.

Results. Our research indicates that SCZ, BD, and MDD exhibit distinct patterns of transition among the four EEG microstate states (A, B, C, and D). The analysis of transition probabilities showed a higher frequency of switching from microstates A to B and from B to A in each patient group compared to the HC group, and less frequent transitions from microstates A to C and from C to A in the SCZ and MDD groups compared to the HC group. And the probability of the microstate switching from C to D and D to C in the SCZ group significantly increased compared to those in the patient and HC groups.

Conclusions. Our findings provide crucial insights into the abnormalities involved in distributing neural assets and enabling proper transitions between different microstates in patients with major psychiatric disorders.

Introduction

Schizophrenia (SCZ), major depressive disorder (MDD), and bipolar disorder (BD) are serious psychiatric disorders that can lead to severe public health issues, including mental disability, suicide, and social burden (Huang et al., 2019; Vigod & Kurdyak, 2019). A recent epidemiological survey in China showed that both SCZ and BD have a lifetime prevalence of approximately 0.6%, and MDD has a lifetime prevalence of approximately 3.4% (Huang et al., 2019). While SCZ, BD, and MDD are considered separate diagnostic entities, their shared neurobiological and neuropsychological features, as well as overlapping clinical symptoms, suggest that they might exist along a continuum of psychiatric disorders (Uher & Zwicker, 2017). In clinical practice, the same patient may present with varying diagnoses, and there is the potential for inter-disease transformation within the same patient across different disease stages. Evidence reveals that these disorders share common environmental and genetic risk factors (Consortium, 2013), and neurobiological modifications (Gong et al., 2019; Sha et al., 2018; Yang et al., 2019; Yang et al., 2022). Studies have found that functional brain networks of patients with SCZ, BD and MDD share certain connectivity features (Xia et al., 2019) and have a commonality in their hyper-integrated modular structures (Ma et al., 2020). Delving into the trans-diagnostic research on SCZ, BD, and MDD could provide insight into the underlying neurobiology of these three disorders (Wei et al., 2018; Xia et al., 2019). Yet, the degree to which the underlying pathophysiology of these three disorders remains uncertain.

Resting-state electroencephalography (EEG) is a noninvasive technique that records the rapid change in the neural networks of the brain with remarkable temporal resolution

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(Lavoie, Polari, Goldstone, Nelson, & McGorry, 2019). EEG microstates during resting-state constitute the global field power of spatial topographies, depicting quasi-stable, comprehensive neuronal activity of 60–120 ms prior to transitioning to the subsequent topography, which also remains quasi-stable (Khanna, Pascual-Leone, Michel, & Farzan, 2015). Previous studies on microstates in other diseases have found that the temporal dynamics of microstates can advance our understanding of brain dysfunction and provide quantifiable characteristics, which can serve as auxiliary references for early disease diagnosis (Chu et al., 2020; Schumacher et al., 2019; Yoshimura et al., 2019). The unusual temporal dynamics of canonical EEG microstates are considered promising biomarker candidates for psychiatric disorders and are regarded as fundamental building blocks of brain dynamics (Khanna et al., 2015).

Four archetypal microstate classes (designated as A, B, C and D) explain 65–84% of EEG microstates as previous work (de Bock et al., 2020; Michel & Koenig, 2018). These four microstates have proven highly reliable and reproducible within and across individuals (da Cruz et al., 2020; Khanna, Pascual-Leone, & Farzan, 2014). It has been found that EEG microstates are closely related to resting-state functional brain networks, which may have resulted from evolutionarily co-activated patterns representing environmentally relevant information (Britz, Van De Ville, & Michel, 2010; Michel & Koenig, 2018). Microstate classes A, B, C, and D are related to the auditory network, the visual network, the saliency and default mode networks, and the control and attention networks, respectively (Baradits, Bitter, & Czobor, 2020; Vellante et al., 2020).

Microstate classes are marked by several temporal parameters: mean duration, time coverage, occurrence, and transition probability (da Cruz et al., 2020; Khanna et al., 2015; Murphy et al., 2020; Vellante et al., 2020). Mean duration represents the average period of time during which a microstate remains stable upon its occurrence, reflecting the stability of the underlying neuronal assemblies. The time coverage of a microstate is calculated by measuring its dominance in comparison to other neural generators throughout the total recording period. Occurrence represents the average frequency per second at which the microstate is the most prominent during the recording, which might mirror the neural generators' propensity to be activated. Transition probability is the probability of transition between the four classes of microstates, usually understood as the encoded sequential activations of neural assemblies responsible for generating the microstates (Khanna et al., 2015). Studies have shown that microstate parameters representing large-scale brain networks may reveal disruptions between brain networks, thereby explaining the dysfunctional behaviors in patients (Khanna et al., 2015).

Due to discrepancies in data collection and processing, the amount of microstate categories, and the manner in which microstate analysis is performed, it is difficult to make direct comparisons across studies (Khanna et al., 2015). As shown in Table 1, which summarizes EEG microstate parameter (duration, occurrence, and coverage) findings across prior studies of SCZ, BD, and MDD, most EEG microstate studies in major psychiatric disorders showed inconsistent results (Andreou et al., 2014; Baradits et al., 2020; Chen, Ku, Wang, Kang, & Hsu, 2023; da Cruz et al., 2020; He et al., 2021; Kim, Duc, Choi, & Lee, 2021; Lei et al., 2022; Nishida et al., 2013; Sun et al., 2021; Sun, Zhao, & Tan, 2022; Vellante et al., 2020; Wang, Hujjaree, & Wang, 2021).

The transition probabilities from microstates A, C, and D to microstate B was significantly decreased in patients with SCZ, while the transitions from microstates C and D to microstate A and the transition from microstates A and C to microstate D were both significantly increased (Baradits et al., 2020). Patients with BD exhibited considerably greater transitions between A and B compared to healthy controls (HC) (Wang et al., 2021). Patients with first-episode MDD had a lower probability of transition between A and D, C and D compared with a HC group. Conversely, they had a higher probability of transition from A to B and B to A, A to C, and C to B compared with the HC group (He et al., 2021). Additional research is required to elucidate the diagnostic boundaries of EEG microstates in major psychiatric disorders.

Therefore, the objective of this study was to investigate (1) microstate dynamic abnormalities among individuals diagnosed with SCZ, BD, or MDD and (2) whether there were shared and/or distinct EEG microstate abnormalities across SCZ, BD, and MDD. Our hypothesis was that microstate abnormalities, both in information processing and transitions across the brain networks, existed in patients with SCZ, BD, and MDD with common or unique patterns. From the above aspects, we explore whether EEG microstates might be promising candidate endophenotypes for distinguishing these major psychiatric disorders.

Methods and materials

Participants

We recruited 922 subjects (aged 18–65 years), including 380 hospitalized patients with SCZ, 330 with BD, and 212 with MDD between February 2017 and October 2020 from the Mental Health Center of West China Hospital, Sichuan University. A total of 190 age- and sex-matched HCs were acquired through advertisements in the local community. All patients met the diagnostic criteria of the International Classification of Diseases 10th Revision (ICD-10) for SCZ, BD, or MDD. The diagnoses were made based on the discharge diagnosis by professional psychiatrists. The patients were excluded if (1) they had serious physical disease, brain organic disease, or nervous system disease, and (2) they received electroconvulsive therapy within six months.

As part of the evaluation, professional psychiatrists excluded HCs with prior histories of any psychiatric disorder. The HCs were excluded if (1) they had taken antipsychotics, antidepressants, and mood stabilizers, and (2) mental illness was present in a first/second/third-degree relative.

The Ethics Committee on Biomedical Research of West China Hospital of Sichuan University granted approval for this study (Approval No. 758), and all participants provided informed consent.

EEG data recording and preprocessing

Resting-state EEG data were collected from all participants by experienced technicians using a dynamic electroencephalograph (NATION8128W) of Shanghai Nuocheng device. EEG signals were recorded on the grounds of the 10–20 international system, with F3, F4, Fp1, Fp2, P3, P4, C3, C4, T3, T4, F7, F8, O1, O2, T5, and T6 as the selected locations on the scalp. While recording, the participants were given instructions to stay awake in a tranquil room. EEG data were collected over a span of 7 min and we chose 3-min eye-closed data for analysis. The data were sampled at a frequency of 128 Hz. We selected averaged references for all recordings, and the electrode impedance was maintained below ten kΩ.

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Table 1. Summary results of EEG microstates analyses in major psychiatric disorders

Study	Population	Microstate A	Microstate B	Microstate C	Microstate D
Baradits M (Baradits et al., 2020) et al., 2020	75 HCs and 70 SCZ	Occurrence↑; Coverage↑	Duration↓; Occurrence↓; Coverage↓	/	Occurrence↑; Coverage↑
Nishida K (Nishida et al., 2013) et al., 2013	19 HCs, 20 SCZ, 18 FTD, and 19 AD	SCZ: Duration↓; Occurrence↑	SCZ: Duration↓	SCZ: Occurrence↑	SCZ: Duration↓
Wang F (Wang et al., 2021) et al., 2021	35 HCs, 20 SCZ, and 26 BD	SCZ: Occurrence↓; BD: /	SCZ: Occurrence↓; BD: Occurrence↑; Coverage↑	SCZ: Duration↑; Coverage↑; BD: /	SCZ: Occurrence↓; BD: /
da Cruz JR (da Cruz et al., 2020) et al., 2020	75 HCs, 101 SCZ, and 43 Siblings	SCZ: /	SCZ: Duration↓	SCZ: Duration↑; Occurrence↑; Coverage↑	SCZ: Duration↓; Occurrence↓; Coverage↓
Sun Q (Sun et al., 2021) et al., 2021	39 HCs and 46 SCZ	/	Occurrence↓; Coverage↓	Duration↑; Coverage↑	/
Sun Q (Sun et al., 2022) et al., 2022	23 HCs and 23 FES	/	/	Duration↑; Occurrence↑; Coverage↑	Coverage↓; Occurrence↓
Kim K (Kim et al., 2021) et al., 2021	14 HCs and 14 SCZ	/	Duration↑; Occurrence↑; Coverage↑	Duration↑; Coverage↑	Duration↓; Occurrence↓; Coverage↓
Chen P-H (Chen et al., 2023) et al., 2022	16 HCs, 40 SCZ, and 19 BD	/	/	/	/
Andreou C (Andreou et al., 2014) et al., 2014	22 HCs, 18 SCZ, and 18 HR	/	/	/	/
Vellante F (Vellante et al., 2020) et al., 2020	19 HCs and 19 BD	/	Duration↑; Occurrence↑; Coverage↓	/	/
Lei L (Lei et al., 2022) et al., 2022	45 HCs and 101 FED	Occurrence↑	Occurrence↑	/	Duration↓
He Y (He et al., 2021) et al., 2021	35 HCs and 35 adolescents with FED	/	Occurrence↑; Coverage↑	/	Occurrence↓; Coverage↓

Note: HC, healthy control; SCZ, schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; FTD, frontotemporal dementia; AD, Alzheimer's disease; FED, first-episode untreated depression; FES, first-episode schizophrenia; HR, high-risk individuals; '/' represents no significant differences between groups.

Preprocessing of EEG data was conducted using MATLAB (version 2013b) and the EEGLAB toolbox (Delorme et al., 2011). We meticulously reviewed all EEG data from patients and HCs, and disqualified any EEG data of poor quality (e.g. bad channels) at the outset. The raw EEG data was filtered using a bandpass filter (0.1–40 Hz) and a notch filter (50 Hz) to avoid powerline interference. To remove artifacts, an independent component analysis (ICA) was conducted with the Infomax ICA algorithm (Bell & Sejnowski, 1995; Lee, Girolami, & Sejnowski, 1999), and we removed the ocular artifacts from all sixteen components. After referencing the data to the average reference, we divided it into epochs of 2 s and then applied a bandpass filter with a range of 2–20 Hz.

Microstate analysis

Microstate analysis was conducted in MATLAB (version 2013b) utilizing functions from the EEGLAB plugin (version 0.3) for microstates. To assess the degree of coordination between the neurons in the neural generators, the global field power (GFP) was determined by computing the standard deviation between all electrode potentials. To conduct further analysis, only the EEG topographies at the GFP peaks were selected since they were stable and had a high signal-to-noise ratio.

The GFP-reduced data was extracted and processed through the *k*-means clustering algorithm to determine the most dominant topography classes that best explained the variance of the EEG topographies. Initially, we carried out clustering analysis at the individual level, then proceeded to analyze each group of participants. To make an equal contribution of microstates per subject, each subject underwent *k*-means clustering utilizing the four most dominant microstates. The temporal dynamics of the microstates for each subject were calculated using four microstate parameters per class: mean duration, time coverage, occurrence, and transition probability. We utilized the MNE-Python plugin (Gramfort et al., 2013) along with custom code written in python 3.0 to obtain the four canonical topographic configurations for each group.

Statistical analysis

To assess the disparities in duration, time coverage, occurrence, and transition probabilities among the groups, we employed a repeated-measures analysis of variance (rm-ANOVA) in SPSS

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(Version 22.0). A two-way rm-ANOVA was performed for each microstate parameter (mean duration, occurrence, and time coverage), with a between-subject factor (microstates A, B, C, or D) and a within-subject factor (Group: SCZ, BD, MDD, or HC). To determine the overall significance, we conducted a univariate ANOVA and then used post-hoc tests with Bonferroni correction to identify which microstate classes were significantly different. The transition probability was analyzed using the aforementioned statistical tests. When needed, adjustments were made to the degrees of freedom using the Greenhouse-Geisser correction. Chi-squared (χ^2) tests were conducted to analyze qualitative data, and significance level was set at $p < 0.05$ in all tests, with a two-tailed test. Multiple analyses utilized the Bonferroni correction.

Results

Demographic data

An analysis of 1112 participants was conducted, of which 380 were patients diagnosed with SCZ, 330 with BD, 212 with MDD, and 190 were age- and sex-matched HCs (Table 2). The age and sex of the SCZ, BD, MDD and HC groups showed no significant difference between them ($F = 1.846$, $p = 0.137$; $\chi^2 = 7.448$, $p = 0.059$).

Microstate parameters: mean duration, occurrence, and time coverage

The four microstate classes explained 81.01, 79.59, 79.75, and 79.93% of the global variance in the SCZ, BD, MDD, and HC groups, respectively (Fig. 1). For the four groups, a two-way rm-ANOVA showed a non-significant group × microstate class interaction for mean duration ($F_{(7,\ 2657)} = 1.796$, $p = 0.08$, $\eta^2 = 0.005$), time coverage ($F_{(6,\ 2332)} = 1.703$, $p = 0.112$, $\eta^2 = 0.005$), and occurrence ($F_{(6,\ 2171)} = 1.832$, $p = 0.091$, $\eta^2 = 0.005$) (Table 2). For the purpose of examing group differences within specific microstate classes, we conducted separate one-way ANOVAs. The analyses yielded that there were significant differences among the groups in the occurrence of microstate A ($F_{(3,\ 1108)} = 4.083$, $p = 0.007$, $\eta^2 = 0.011$), occurrence of microstate B ($F_{(3,\ 1108)} = 5.791$, $p = 0.001$, $\eta^2 = 0.015$), duration of microstate C ($F_{(3,\ 1108)} = 3.119$, $p = 0.025$, $\eta^2 = 0.008$), and duration of microstate D ($F_{(3,\ 1108)} = 9.322$, $p < 0.001$, $\eta^2 = 0.025$). There were no significant results for time coverage. Group comparisons with post-hoc pairwise analysis (Table 2) revealed that the mean duration of microstate C in MDD patients was significantly reduced than that of HCs. The occurrence of microstate A in patients with BD increased significantly relative to that in HCs. Microstate B occurrence in patients with MDD showed significantly statistical differences from HCs and patients with SCZ or BD. And the mean duration of microstate D in both BD and MDD patients was significantly decreased compared to that of HCs. Meanwhile, the mean duration of SCZ patients was significantly higher than that of MDD patients.

Microstate parameters: transition probabilities

We found significant group × transition probability interactions for transition probabilities ($F_{(7,\ 2641)} = 2.730$, $p = 0.008$, $\eta^2 = 0.007$) (Fig. 2, Table 3). These interactions suggest that group differences depend on transition probabilities. Group comparisons with post-hoc pairwise analysis (Table 3) revealed statistically significant differences in the probability to transition from microstate A to B and B to A between each group of patients and

Table 2. Demographic variables and means for mean duration, time coverage and occurrence

	SCZ ($n = 380$)	BD ($n = 330$)	MDD ($n = 212$)	HC ($n = 190$)	F/χ^2	p Value	Post hoc
Age, years	26.37 (7.53)	26.43 (8.17)	26.78 (7.94)	25.14 (5.34)	1.85	0.137	
Sex (M:F)	183:197	126:204	96:116	86:104	7.45	0.059	
Duration (ms)							
A	66.39 (10.10)	66.59 (9.38)	64.80 (9.49)	67.06 (11.51)	2.03	0.108	
B	64.32 (13.22)	62.62 (13.19)	64.10 (14.57)	63.83 (12.74)	1.05	0.371	
C	61.93 (13.65)	61.24 (14.41)	59.33 (12.87)	63.47 (14.97)	3.12	0.025	MDD < HC
D	59.09 (8.87)	57.67 (8.99)	56.17 (8.78)	60.81 (11.98)	9.32	<0.001	BD, MDD < HC; SCZ > MDD
Coverage (%)							
A	26.67 (7.61)	27.87 (7.68)	27.02 (8.15)	26.59 (8.07)	1.71	0.164	
B	25.18 (7.69)	24.51 (7.59)	26.25 (8.12)	24.51 (8.30)	2.50	0.058	
C	24.08 (7.16)	24.18 (7.07)	23.93 (7.09)	25.14 (8.33)	1.14	0.331	
D	24.06 (7.25)	23.45 (6.94)	22.80 (6.76)	23.76 (9.35)	1.36	0.255	
Occurrence/s							
A	4.06 (0.91)	4.23 (0.94)	4.20 (1.04)	3.98 (0.85)	4.08	0.007	BD > HC
B	3.93 (0.70)	3.93 (0.69)	4.13 (0.66)	3.85 (0.87)	5.79	0.001	MDD > SCZ, BD, HC
C	3.92 (0.65)	4.00 (0.63)	4.07 (0.66)	3.98 (0.71)	2.47	0.060	
D	4.11 (0.99)	4.11 (1.01)	4.10 (0.98)	3.89 (1.12)	2.30	0.076	

Note: SCZ, schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; HC, healthy control. Values are mean (s.d.), significance level is set at 0.05; Only statistically significant differences between groups are presented for post hoc comparisons (Bonferroni corrected).

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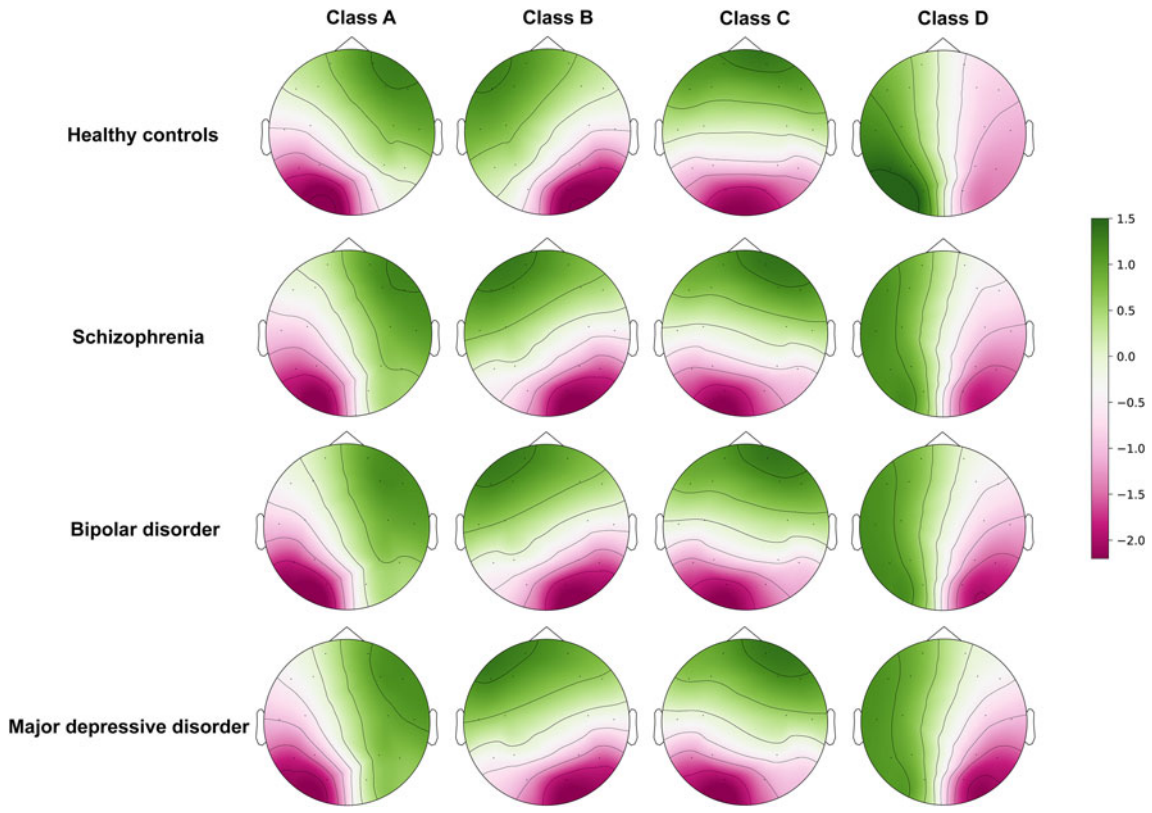


Figure 1. Spatial configuration of the four microstate classes. Each row displays four canonical topographic configurations (A–D) for each group. Green represents high activation of the brain area: the darker the color, the more activation. Purple represents low activation of the brain area: the lighter the color, the less activation.

HCs. The probability of the microstates to transition from A to C and C to A in the SCZ and MDD groups decreased significantly compared with that in HCs. The probability of the microstates to transition from C to D and D to C in the SCZ group increased significantly compared with that in the HC, BD, and MDD groups. The probability of transition from D to C increased significantly in the BD group compared with that in the HC group.

Discussion

In this study, we found that SCZ, BD, and MDD exhibit distinct patterns of transition among the four EEG microstate states (A, B, C, and D). Among the three major psychiatric disorders, the transition probabilities of microstates A to B and B to A may have shared underlying disruptions. Conversely, the probabilities of microstates C to D and D to C may be specific to SCZ compared to HCs and patients with BD or MDD. And there was also a significant increase in microstate B occurrence among patients with MDD, as compared to HC and patients with SCZ, or BD. Our results imply that resting-state EEG microstates could be used as biological markers for major psychiatric disorders.

We also found that the occurrence of microstate A in patients with BD increased significantly compared to that in HCs. Previous research has revealed that euthymic patients with BD show elevated microstate A occurrence and coverage (Damborská et al., 2019). An earlier study combining fMRI and EEG showed that microstate A was associated with the auditory network (Britz et al., 2010), and may be generated by the source of left-lateralized activity in the insula, temporal lobe, occipital gyri, and medial prefrontal cortex (Bréchet et al., 2019; Custo et al., 2017). These results

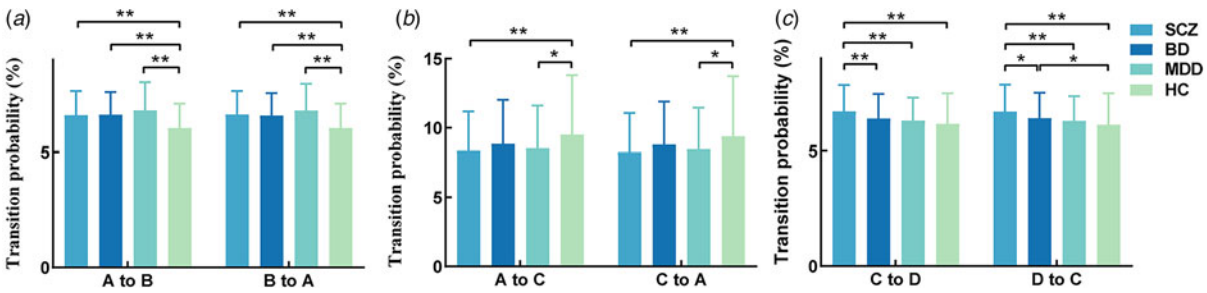


Figure 2. Microstate transition probabilities. (a) Transition probability from microstate A to B and B to A, (b) Transition probability from microstate A to C and C to A, (c) Transition probability from microstate C to D and D to C. We found significant results of transition probability for each group. See Table 3 for detailed information on statistics. SCZ, schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; HC, healthy control. $^{*}p < 0.05$, $^{**}p < 0.01$.

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Table 3. Means for transition probabilities

	SCZ	BD	MDD	HC	*F Value*	*p* Value	Post hoc
Transition probabilities (%)							
A to B	6.59 (1.05)	6.61 (0.98)	6.80 (1.22)	6.03 (1.06)	19.22	<0.001	HC < SCZ, BD, MDD
A to C	8.34 (2.84)	8.85 (3.17)	8.52 (3.09)	9.51 (4.30)	5.86	0.001	HC > SCZ, MDD
A to D	9.22 (3.50)	9.34 (3.35)	8.88 (3.17)	8.76 (3.48)	1.60	0.188	
B to A	6.62 (1.02)	6.57 (0.98)	6.79 (1.16)	6.03(1.06)	20.19	<0.001	HC < SCZ, BD, MDD
B to C	8.71 (4.16)	8.64 (3.79)	9.12 (4.31)	9.03 (4.48)	0.84	0.475	
B to D	8.42 (2.62)	8.20 (2.65)	8.41 (2.99)	8.48 (3.20)	0.57	0.633	
C to A	8.24 (2.83)	8.79 (3.11)	8.46 (3.00)	9.38 (4.35)	5.65	0.001	HC > SCZ, MDD
C to B	8.81 (4.20)	8.70 (3.89)	9.16 (4.24)	9.08 (4.52)	0.71	0.548	
C to D	6.70 (1.15)	6.39 (1.07)	6.30 (1.00)	6.16 (1.33)	11.54	<0.001	SCZ > HC, BD, MDD
D to A	9.30 (3.48)	9.45 (3.33)	8.97 (3.18)	8.89 (3.47)	1.56	0.197	
D to B	8.36 (2.62)	8.09 (2.59)	8.37 (2.96)	8.40 (3.11)	0.81	0.489	
D to C	6.69 (1.17)	6.41 (1.10)	6.29 (1.07)	6.12 (1.37)	11.84	<0.001	SCZ > HC, BD, MDD; BD > HC

Note: SCZ, schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; HC, healthy control. Values are mean (s.d.), significance level is set at 0.05; Only statistically significant differences between groups are presented for post hoc comparisons (Bonferroni corrected).

indicate that an increase of occurrence in microstate A may represent a potential state marker in patients with BD.

A significantly higher occurrence of microstate B was observed in patients with MDD compared to HCs and patients with SCZ or BD. Previous studies have found that microstate B occurrence increases in adolescents with MDD (He et al., 2021) and first-episode untreated MDD (Lei et al., 2022). Microstate B consists of bilateral occipital areas in the left lingual and middle occipital gyri, bilateral cuneus, and bilateral inferior occipital gyri, which may represent the visual network (Britz et al., 2010; Murphy et al., 2020). Other studies have shown that patients with MDD have attentional biases for dysphoric information and take longer to disengage from depression-related stimuli, implying abnormalities in the visual network (Kellough, Beevers, Ellis, & Wells, 2008; Sanchez, Vazquez, Marker, LeMoult, & Joormann, 2013). Microstate B is also linked to negative BOLD activation in the bilateral occipital cortex (Britz et al., 2010) and its increased presence is associated with severe anxiety (Damborská et al., 2019).

Our study found that microstate C duration decreased significantly in patients with MDD compared to HCs, and there was no significant difference in the duration of microstate C between the SCZ and BD groups and the HC group. This is in line with previous studies (Chen et al., 2023; de Bock et al., 2020; Vellante et al., 2020; Wang et al., 2021), although some studies have shown that microstate C duration in a SCZ group was significantly higher compared to that in the HC group (Sun et al., 2021, 2022). Microstate C has been correlated with positive BOLD activation in the bilateral inferior frontal gyri, the right anterior insula, and the posterior part of the anterior cingulate cortex, which are regarded as the salience network (Britz et al., 2010). However, recent research suggests that microstate C mirrors default mode activity (Michel & Koenig, 2018). Thus, the function of microstate C is still a matter of debate.

Our results indicated the duration of microstate D decreased significantly in individuals diagnosed with BD and MDD when compared to HCs. In comparison with the BD group, the SCZ group had a significantly longer microstate duration. Previous studies have reported a decrease in the duration of microstate D in patients with MDD (Lei et al., 2022; Murphy et al., 2020). Lei et al. (Lei et al. 2022) identified microstate D to be a possible electrophysiological marker of MDD that can predict treatment responses to selective serotonin reuptake inhibitors. Microstate D is also related to negative BOLD activation in the right-lateralized ventral and dorsal areas of the parietal and frontal cortices, which are considered the attention/cognitive control network (Britz et al., 2010; Michel & Koenig, 2018). Our results imply that BD and MDD may share common neural abnormalities regarding how long each semi-stable state is retained in microstate D of the brain, which correlates with the attention/cognitive control network.

Abnormalities in the EEG microstates in psychiatric disorders imply breakdown of normal resting-state network activities, which may underlie the disease pathogenesis. Transition probabilities among microstates may lead to disruption in the coupling and the sequential activation of the related neural assemblies (Baradits et al., 2020). Our study showed that the transition probabilities between microstates A and B were both higher in the patient groups than in the HC group, whereas the transition probabilities between microstates A and C were both lower in the SCZ and MDD groups than in the HC group. In addition, the transition probabilities between microstates C and D in the SCZ group both increased significantly compared with that in the other patient and HC groups. A previous study found increased transitions probabilities between microstate A and B in patients with BD compared to those with SCZ and HCs and increased transition probabilities between microstate C and D in patients with SCZ in contrast to those with BD. These findings endorse the consistent observation of abnormal EEG microstate transition patterns in our study (Wang et al., 2021). Resting-state EEG has a comparative advantage in terms of high temporal resolution, adaptability, accessibility, and cost-effectiveness compared to other techniques, such as fMRI. This positions it as a compelling biomarker (Biasiucci, Franceschiello, & Murray, 2019). Moving forward, an exploration of the correlation between patient scales and microstate functions is essential for optimizing the utility of EEG microstate biomarkers.

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To sum up, our study compared the microstate transition probabilities in the three major psychiatric disorders and found abnormalities in the transitions. These results suggest that disturbed coupling and sequential activation of the related neural assemblies occurring during casual resting states differs in these major psychiatric disorders.

Limitations

Our study had some limitations. First, the cross-sectional design restricted our capability to assess the effects of illness severity, progression, and medication exposure. In present study, we included patients with bipolar disorder who met the diagnostic criteria of the ICD-10 for BD without categorizing these patients into specific types, such as manic, depressive episodes. In future study, it is necessary to explore differences in EEG microstates among various clinical episodes in patients with BD. Second, the majority of our patients were receiving medication, and such drug use could potentially influence the EEG signals. However, reports from prior studies have demonstrated that the dosage of medication has no effect on the natural frequencies (Canali et al., 2015; Ferrarelli et al., 2012; Minzenberg et al., 2010). And it would be best if there were follow-up opportunities to test in the first-episode population.

Conclusions

In conclusion, our study shows that SCZ, BD, and MDD exhibit distinct patterns of transition between four EEG microstate states. The transition probabilities of microstates A to B and B to A appear to be disrupted in all three types of psychiatric disorders. And the transition probabilities from microstates C to D and D to C in the SCZ group showed a significant increase when compared to the other patient and HC groups. Additionally, there was a significant increase in the microstate B occurrence in patients with MDD when compared with HCs and patients with SCZ or BD. This study offers a reference point for future investigations into the mechanisms of SCZ, BD, and MDD. Moreover, it provides crucial insights into the abnormalities involved in distributing neural assets and enabling proper transitions between different microstates in major psychiatric disorders.

Author contributions. Study concept and design: RX, XJL, WD. Acquisition, analysis, and interpretation of data: RX. Drafting the manuscript: RX. Critical revision: XJL, WD, CQL, MXC, JNC, SGL, WW, YMZ, WJG, HY, YX, TL. All authors accepted the last draft of the manuscript.

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Competing interest. The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be considered as a potential conflict of interest.

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