Research Paper

Abnormalities in large-scale brain network dynamics in late-life depression with suicidal ideation: an EEG microstate analysis

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Background: Patients with late-life depression (LLD) with suicidal ideation (SI) often have more explicit suicide plans, and suicide attempts among older adults are more highly lethal than in other age groups. Increasing evidence suggests that people with SI in depression exhibit abnormal brain network connectivity; however, the relationship between suicidal ideation in LLD and brain network dynamics is still unclear. **Methods:** We recruited patients with LLD and SI (LLD-SI), patients with LLD without SI (LLD-NSI), and age-matched healthy older adults. We collected 64-channel resting state electroencephalography (EEG) recordings of all participants and used microstate analysis to explore large-scale brain network dynamics. **Results:** We included 33 patients with LLD-SI, 29 patients with LLD-NSI, and 31 controls. We observed abnormal microstate parameters in the LLD-SI group, characterized by higher duration ($p = 0.04$), occurrence ($p = 0.009$), and contribution ($p = 0.001$) of microstate C (reflecting activity of the salience network), compared with the LLD-NSI group, as well as higher occurrence ($p = 0.03$) and contribution ($p = 0.009$) of microstate C compared with the control group. Furthermore, transition probabilities from microstate class A to D ($r = –0.466$, $p = 0.04$) and class D to A ($r = –0.506$, $p = 0.02$) (involving coupling and sequential activation of auditory and executive control network) were negatively correlated with completion time of Stroop Colour and Word Test Part C (a neuropsychological test of executive function) in the LLD-SI group. **Limitations:** The sample size was relatively small, the cross-sectional nature of this study prohibited exploring the causal relationship between abnormal microstate dynamics and suicidal ideation, and we did not include medication-naive patients with first-episode LLD. **Conclusion:** The study reveals altered microstate dynamics among patients with LLD-SI, compared with patients with LLD-NSI and controls. Our findings suggest that microstate dynamics could serve as potential neurobiomarkers for identifying SI in LLD.

Introduction

Suicide is a serious public health problem. Globally, more than 700 000 people die by suicide each year.[1] Older adults are at a higher risk of suicide than other age groups,[2] and suicide rates among older adults are steadily increasing.[3] Late-life depression (LLD) is an important risk factor for suicide, and a significant proportion of older adults who die from suicide have previously experienced depression.[2] Suicidal behaviour among older adults is different from that observed earlier in the lifespan. Compared with younger people, suicidal ideation (SI) in LLD often involves a more definite suicide plan, and suicide attempts among older adults are more highly lethal.[4] Suicidal ideation is the first stage of the suicide continuum, has a high risk of progression to suicide attempt, and is a predictor of complex suicidal behaviour.[5] However, older adults are less likely to openly acknowledge SI,[6] which hampers early identification. Therefore, the search for more objective biomarkers to detect SI, in addition to clinical assessment, will be conducive to early identification and effective avoidance of suicide attempts and death. Moreover, biomarkers may reveal the pathological mechanisms of suicide and facilitate the development of effective interventions.[7]

Previous studies have demonstrated triple-network dysfunctions in LLD.[8,9] These networks include the executive

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control network (ECN), responsible for exerting goal-directed behaviours and regulating emotions;[8] the default mode network (DMN), involved in ruminative, negative self-referential processes;[10] and the salience network (SN), which serves as a hub in mediating dynamics interaction between the ECN and DMN to generate appropriate behavioural responses to salient stimuli.[11] Several studies have also documented that abnormal connectivity within or between these large-scale brain networks may contribute to suicidal ideation.[12–15] However, this evidence mostly comes from functional magnetic resonance imaging (fMRI) studies, which lacks the temporal resolution needed to track the dynamics of brain activities.

Resting-state electroencephalography (EEG) has a high temporal resolution, which can provide complementary information about neural dynamics, and EEG microstate analysis is a powerful approach for capturing the dynamically changing large-scale brain networks in subsecond scales.[16] At resting state, the spontaneous activity of the brain can be characterized as a series of quasi-stable scalp potential topographies that switch between each other in an organized manner.[17] Using this approach, 4 microstate classes — A, B, C, and D — have been widely identified; these correspond to the auditory network, the visual network, the SN, and the ECN, respectively.[16,18–20] A previous study has also suggested that microstate C is associated with the self-referential subnetwork of the DMN.[21] In recent years, microstate analysis has become increasingly popular in the research of psychiatric disorders. In a previous study, Lao and colleagues[22] used EEG microstate analysis to investigate the difference in brain resting-state network dynamics between episodic and remitted LLD. We sought to expand on this research by investigating the dynamics of large-scale brain networks in LLD with SI (LLD-SI) using EEG microstate analysis. We hypothesized that, given their correlation with the ECN, DMN, and SN, we would observe altered patterns involving microstates C and D among patients with LLD-SI, compared with those with LLD without SI (LLD-NSI) and controls.

Methods

Participants

We recruited all participants from the Affiliated Brain Hospital of Guangzhou Medical University and Guangzhou community screening centres. All participants received free clinical examinations, and the results for hospitalized patients were provided to their bedside physicians to assist in their diagnosis and treatment.

For the LLD groups, we included patients aged 60–85 years who met the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) criteria for single or current major depressive disorder with current major depressive episodes, diagnosed by at least 2 proficient psychiatrists. The severity of depressive symptoms was assessed using the Hamilton Rating Scale for Depression (HAMD), with a cut-off value of 17 used to classify patients with current major depressive episodes. Patients were required to be right-handed and have normal or corrected-to-normal visual and auditory senses. We included controls if they demonstrated normal cognition and had no history of depressive episodes. We excluded patients with LLD and controls with any other DSM-IV Axis I disorders (e.g., severe or unstable mental conditions), a lifetime history of neurologic disorders (e.g., stroke, delirium, Parkinson disease, brain tumours), other conditions that could cause depression (e.g., hypothyroidism, drug use), a current history of alcohol use to alcohol dependence, or a history of head injury with loss of consciousness exceeding 30 minutes.

We subsequently divided patients with LLD into LLD-SI and LLD-NSI groups based on whether they had current SI as assessed by item 3 of the 17-item HAMD.[23] The threshold for SI was a score of 2 or higher on item 3 ("wishes to be dead or has any thoughts of possible death to self") of the HAMD.[24] Current SI was defined as having had suicidal thoughts in the past week.

Demographic and clinical assessments

We collected demographic information for all participants, including age, sex, education, medical history, and current medication. Before the EEG recording, all participants underwent a comprehensive assessment by 2 trained psychiatrists.

Neuropsychological assessments

We used the Mini-Mental State Examination (MMSE) to assess global cognitive function. We determined cut-off scores for categorizing normal cognition among controls using MMSE scores adjusted according to Chinese norms for participants' education levels (17 for those without formal education, 20 for those who receive elementary education, and 24 for those with middle school or higher education).[25] Subsequently, a neuropsychologist administered a series of neuropsychological tests to evaluate 5 distinct cognitive domains. Memory capabilities were assessed by the Auditory Verbal Learning Test, which measures the ability to learn and recall a list of words over multiple trials. Information processing speed was evaluated using the Symbol Digit Modalities Test, in which participants were required to match symbols with corresponding numbers as quickly as possible. Scores on this test are determined by the number of symbols recorded accurately within 90 seconds. The evaluation of executive function was conducted using the Stroop Colour and Word Test Part C (Stroop C), in which participants named the colour of the ink in which words were printed, regardless of the meaning of the words. Language skills were evaluated through the Boston Naming Test, where participants were required to identify pictures of several objects based on verbal descriptions. The assessment of visuospatial skills was conducted using the Rey–Osterrieth Complex Figure Test. This test comprises the tasks of copying, memorizing, and reproducing a complex geometric figure.

Electroencephalography data acquisition and processing

All participants were prohibited from consuming alcohol, sleep medication, caffeine, and nicotine within 24 hours before the examination. We collected all EEG data in the morning to control circadian rhythm effects. To ensure optimal electrode placement and EEG data collection, we instructed participants to wash their hair upon arrival at the laboratory. The recording environment was a sound-attenuated, shielded room maintained at constant light and temperature levels. A 5-minute resting-state EEG was recorded under eyes-closed conditions using the Electrical Geodesics 64-channel system at a sampling rate of 1000 Hz, using the midline central (Cz) electrode as the online reference. All electrode impedance remained below 50 kΩ throughout the EEG recording.

We conducted offline preprocessing of the EEG data using the EEGLAB version 14.1.1 toolbox in MATLAB R2016b. The data were filtered with a bandpass of 0.1–70 Hz and a notch of 48–52 Hz. We performed segmentation into 2-second epochs and interpolated noisy electrodes using spherical spline interpolation. We removed artifacts such as eye movements, blinks, or muscle activity using independent component analysis in EEGLAB. Finally, we excluded data with excessive artifact contamination (exceeding ± 100 mV) before averaging.

Microstate analysis

We performed EEG microstate analysis using the Microstate 0.3 plug-in in EEGLAB (http://sccn.ucsd.edu/wiki/EEGLAB_Extensions_and_plug-ins). Initially, EEG data were re-referenced to an average reference, filtered with a bandpass of 1–40 Hz.[26] We computed the global field power for each time point, representing the variance of potential across all electrodes at a certain instance. We conducted the EEG microstate analysis by calculating peaks of the global field power, as these topographies have the highest signal-to-noise ratio and stability. Next, all maps marked as peaks of global field power were extracted and submitted to a k-means clustering algorithm.[16] The number of desired microstates was set to k value of 4 for better comparability with well-established studies.[27] During microstate clustering, polarity can be ignored.[17] We calculated mean values of the EEG microstate group for each group by sorting individual EEG microstates first and then finding the common topology for all participants. We then fitted individual EEG sets using group mean topographies. Finally, we extracted characteristics of EEG microstates from each participant, including duration (the mean duration of each given microstate class present in milliseconds), occurrence (the mean number of times a microstate class occurs per second), contribution (the percentage of total occupied time for a given microstate class), and transition probability (the probability of mutual transition between microstate class).

Statistical analysis

We used SPSS 26.0 for statistical analyses. The significance level was set at 0.05, and all statistical tests were 2-tailed.

For demographic characteristics and clinical and neuropsychological scores, we evaluated group differences using 1-way analysis of variance to compare continuous variables and the χ^2 test to compare categorical variables.

We conducted a repeated-measures analysis of covariance (ANCOVA) to assess differences in microstate dynamics across groups, with microstate classes (A–D) as a within-subject factor; group (LLD-SI, LLD-NSI, control) as a between-subject factor; and age, sex, and antipsychotic use as controlling factors. We performed a post hoc univariate ANCOVA if the interaction effect between microstate class and group was significant. We also applied repeated-measures ANCOVA for each transition probability, with transition probabilities between each microstate class (A–D) as a within-subject factor and group as a between-subject factor, using the same covariates mentioned above. We used the Bonferroni correction for multiple comparisons.

We used Pearson correlation analysis to explore the relationship between significantly different microstate parameters, HAMD scores, and neuropsychological tests, corrected with the false discovery rate.

Ethics approval

The study was approved by the Ethics Committees of the Affiliated Brain Hospital of Guangzhou Medical University (no. 2014, 078).

Results

Demographic and clinical characteristics

A total of 93 people participated in our study, including 62 patients with LLD (33 patients with LLD-SI, 29 patients with LLD-NSI) and 31 controls. Table 1 shows the demographic and clinical characteristics. No significant group differences were found in age, sex, years of education, and smoking status. Moreover, we did not observe any difference in medications used between the LLD-SI and LLD-NSI groups. For clinical measures, both LLD groups exhibited worse HAMD scores than the control group, but there was no significant difference in HAMD scores between the LLD-SI and LLD-NSI groups. Both the LLD-SI and LLD-NSI groups exhibited worse cognitive performance than the control group. However, no significant differences in any assessment were found between the LLD-NS and LLD-S groups.

Microstate analysis

Figure 1 shows the topographical maps of the 4 microstate classes for patients with LLD and for controls.

Repeated-measures ANCOVA showed significant microstate class by group interactions for mean duration ($F = 2.868$, $p = 0.01$, $\eta^2 = 0.091$), occurrence ($F = 2.763$, $p = 0.01$, $\eta^2 = 0.086$), and contribution ($F = 3.063$, $p = 0.007$, $\eta^2 = 0.096$).

Post hoc tests revealed that the LLD-SI group exhibited significantly higher duration ($p = 0.04$), occurrence ($p = 0.009$) and contribution ($p = 0.001$) values in microstate class C,

Table 1: Demographic and clinical characteristics of participants

Characteristic	No. (%) of participants*			F or χ^2†	p value	Post hoc test
	Patients with LLD-SI n = 33	Patients with LLD-NSI n = 29	Controls n = 31			
Demographic						
Age, yr, mean ± SD	67.36 ± 4.50	68.03 ± 6.06	69.84 ± 4.47	2.045	0.1	
Sex, male/female				1.125	0.6	
Male	9 (27.3)	9 (31.0)	6 (19.4)			
Female	24 (72.7)	20 (69.0)	25 (80.6)			
Years of education, mean ± SD	9.27 ± 2.54	9.14 ± 2.55	10.29 ± 3.05	10.165	1.6	
Smoking history, yes/no				0.304	0.8	
Yes	3 (9.1)	3 (10.3)	2 (6.4)			
No	30 (90.9)	26 (89.6)	29 (93.5)			
Assessments						
HAMD-17, mean ± SD	22.97 (3.11)	21.62 (2.37)	2.83 (2.42)	552.806	< 0.001	LLD-SI and LLD-NSI > Control
MMSE, mean ± SD	19.91 (3.96)	20.38 (3.99)	26.26 (1.46)	34.690	< 0.001	LLD-SI and LLD-NSI < Control
AVLT short-term delayed recall, mean ± SD	2.45 (1.84)	2.86 (2.15)	6.71 (2.31)	38.891	< 0.001	LLD-SI and LLD-NSI < Control
SDMT, s, mean ± SD	17.94 (10.48)	19.66 (9.24)	35.32 (6.91)	35.087	< 0.001	LLD-SI and LLD-NSI < Control
Stroop C, s, mean ± SD	112.67 (35.12)	114.34 (22.92)	79.51 (14.69)	17.696	< 0.001	LLD-SI and LLD-NSI > Control
BNT, mean ± SD	16.52 (4.34)	18.28 (3.84)	23.65 (1.68)	35.481	< 0.001	LLD-SI and LLD-NSI < Control
ROCF, mean ± SD	18.33 (5.47)	19.19 (9.97)	27.47 (4.48)	16.439	< 0.001	LLD-SI and LLD-NSI < Control
Medications						
Unmedicated	15 (45.4)	18 (62.1)		1.711	0.2	
SSRI	7 (21.2)	6 (20.7)		0.003	1.0	
SNRI	7 (21.2)	4 (13.8)		0.582	0.4	
NASSA	8 (24.2)	3 (10.3)		2.043	0.2	
Antipsychotic	11 (33.3)	4 (13.8)		3.213	0.07	
Buspirone or tandospirone	2 (6.1)	1 (3.4)		0.000	1.000	
BZD	13 (39.4)	10 (34.5)		0.160	0.7	

AVLT = Auditory Verbal Learning Test, BNT = Boston Naming Test, BZD = benzodiazepine, HAMD = Hamilton Rating Scale for Depression, LLD-NSI = late-life depression without suicidal ideation, LLD-SI = late-life depression with suicidal ideation, MMSE = Mini-Mental State Examination, NASSA = noradrenergic and specific serotonergic antidepressant, ROCF = Rey–Osterrieth Complex Figure, SD = standard deviation, SDMT = Symbol Digit Modalities Test, SNRI = serotonin–norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor, Stroop = Stroop Colour and Word Test.
*Unless indicated otherwise.
†Continuous variables compared with analysis of variance; categorical variables compared with χ^2 test.

compared with the LLD-NSI group. In addition, the LLD-SI group showed significantly higher occurrence (p = 0.027) and contribution (p = 0.009) values in microstate class C than controls. Details are provided in Figure 2.

Repeated-measures ANCOVA also showed significant transition probability by group interactions (F = 2.045, p = 0.006, η^2 = 0.224). Compared with the control group, the LLD-SI group exhibited significantly higher transition probabilities from class C to D (p = 0.03) and from class D to C (p = 0.047), while transition probabilities A to D (p = 0.008) and D to A (p = 0.01) were significantly lower. In addition, the LLD-NSI group had significantly higher transition probabilities from class B to D than both the LLD-SI group (p = 0.02) and the control group (p = 0.03). The transition probabilities from class D to B were also significantly higher in the LLD-NSI group than in both the LLD-SI group (p = 0.03) and the control group (p = 0.03). Details are provided in Figure 3 and Appendix 1, Table S1, available at www.jpn.ca/lookup/doi/10.1503/jpn.240115/tab-related-content.

The relationship between EEG microstate parameters and neuropsychological characteristics in LLD-SI

Pearson correlation analysis revealed that the completion time of Stroop C was negatively correlated with transition probabilities from microstate class A to D (r = –0.466, p = 0.04) and from microstate class D to A (r = –0.506, p = 0.02) in the LLD-SI group (Figure 4). There were no other significant correlations between EEG microstate parameters and cognitive or depression scores in the LLD-SI group (corrected $p > 0.05$), nor were there significant associations between EEG microstate parameters and cognitive or depression scores in the LLD-NSI or control groups (corrected $p > 0.05$).

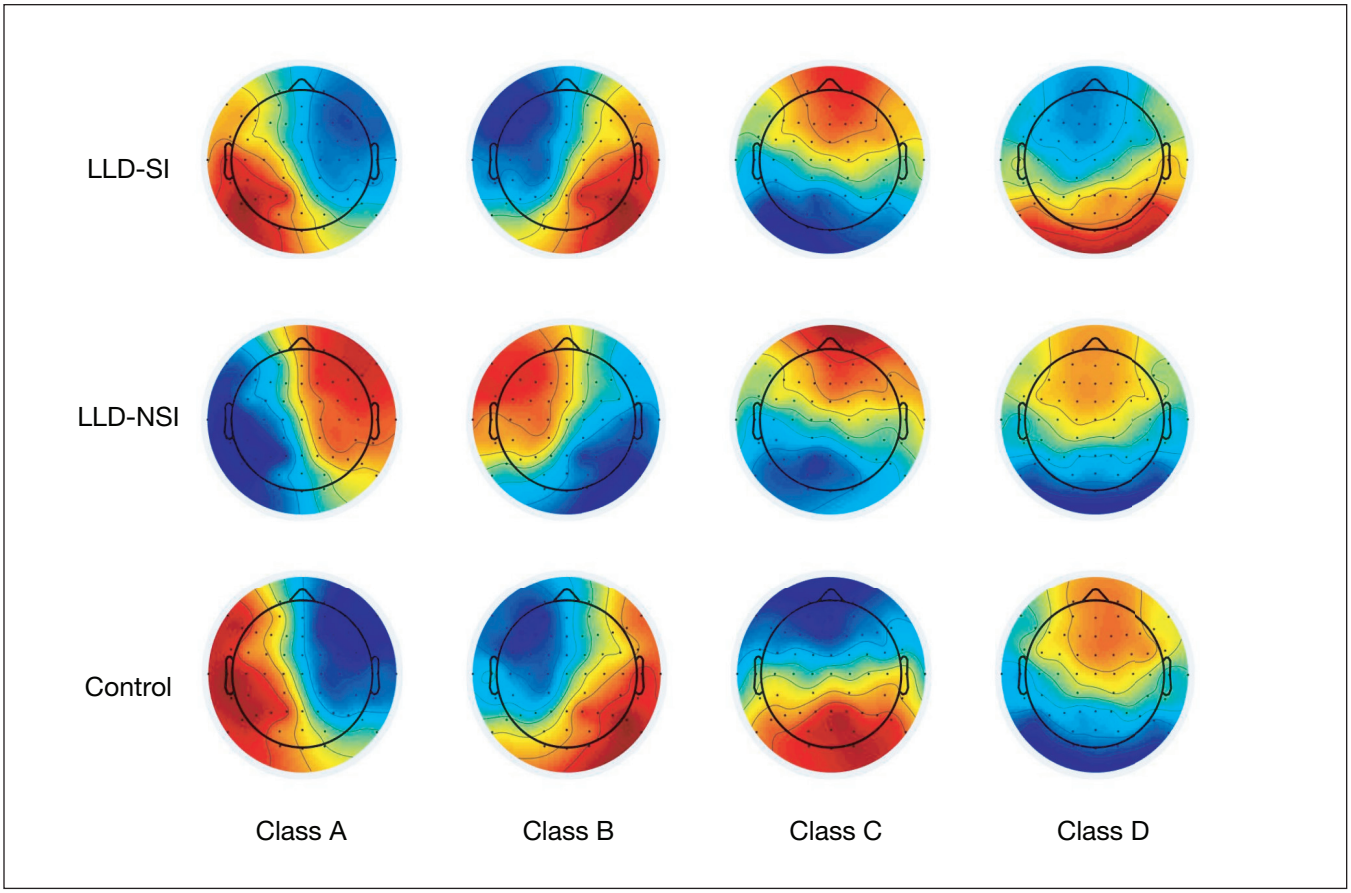

Figure 1: The topographical maps of the 4 microstate classes (A–D) among patients with late-life depression with suicidal ideation (LLD-SI), patients with late-life depression without suicidal ideation (LLD-NSI), and controls. Red and blue indicate positive and negative values, respectively. In the current microstate analysis, the polarity of the maps was not considered during the clustering procedure.

Discussion

We used resting-state EEG microstate analysis to explore the alternations in large-scale brain network dynamics in LLD-SI, which revealed abnormal dynamic activity of global brain resting-state networks, particularly involving microstate C in LLD-SI. This included a significantly higher duration than in the LLD-NSI group and significantly higher occurrence and contribution than in the LLD-NSI and control groups.

In previous studies, researchers have found that patients with depression exhibit higher microstate C parameters than healthy controls.[28,29] Interestingly, in the present study, patients with LLD-SI showed abnormalities in microstate C parameters compared with those with LLD-NSI even when depression severity was similar. Microstate C reflects the neural activity in the SN and activation of the anterior cingulate cortex and insula.[16] The heightened temporal dynamics of microstate C have been linked to SN dysfunctions,[20,30] and brain regions within the SN are associated with suicidality.[31] Previous studies have suggested that the insula may serve as a neurostructure for the development of suicide in LLD.[32] Moreover, task-based imaging has shown that patients with depression who had attempted suicide exhibited reduced connectivity between the dorsal anterior cingulate cortex and the insula during emotion-processing tasks.[33] Patients with depression with reduced coherence in the SN are more likely to engage in suicidal ideation.[34] Furthermore, the increased contribution of microstate C could reflect higher occipital α power,[35] which has been found in patients with SI or a history of suicide attempts.[36] Our findings indicate that the underlying abnormalities involved in the SN, reflected by increased microstate class C parameters, could potentially serve as neurobiomarkers for SI in LLD.

However, in another study, He and colleagues[37] used microstate analysis to investigate abnormal brain network dynamics among adolescents with major depressive disorder (MDD) and SI. They found that significantly lower occurrence and contribution of microstate B among patients with SI than those without SI,[37] which contrasts with the increased parameters in microstate class C found in our current research. Several reasons may contribute to this difference. As mentioned in a previous meta-analysis, LLD and MDD in younger age groups have differences in the visual network since LLD uniquely affects this brain network.[38]

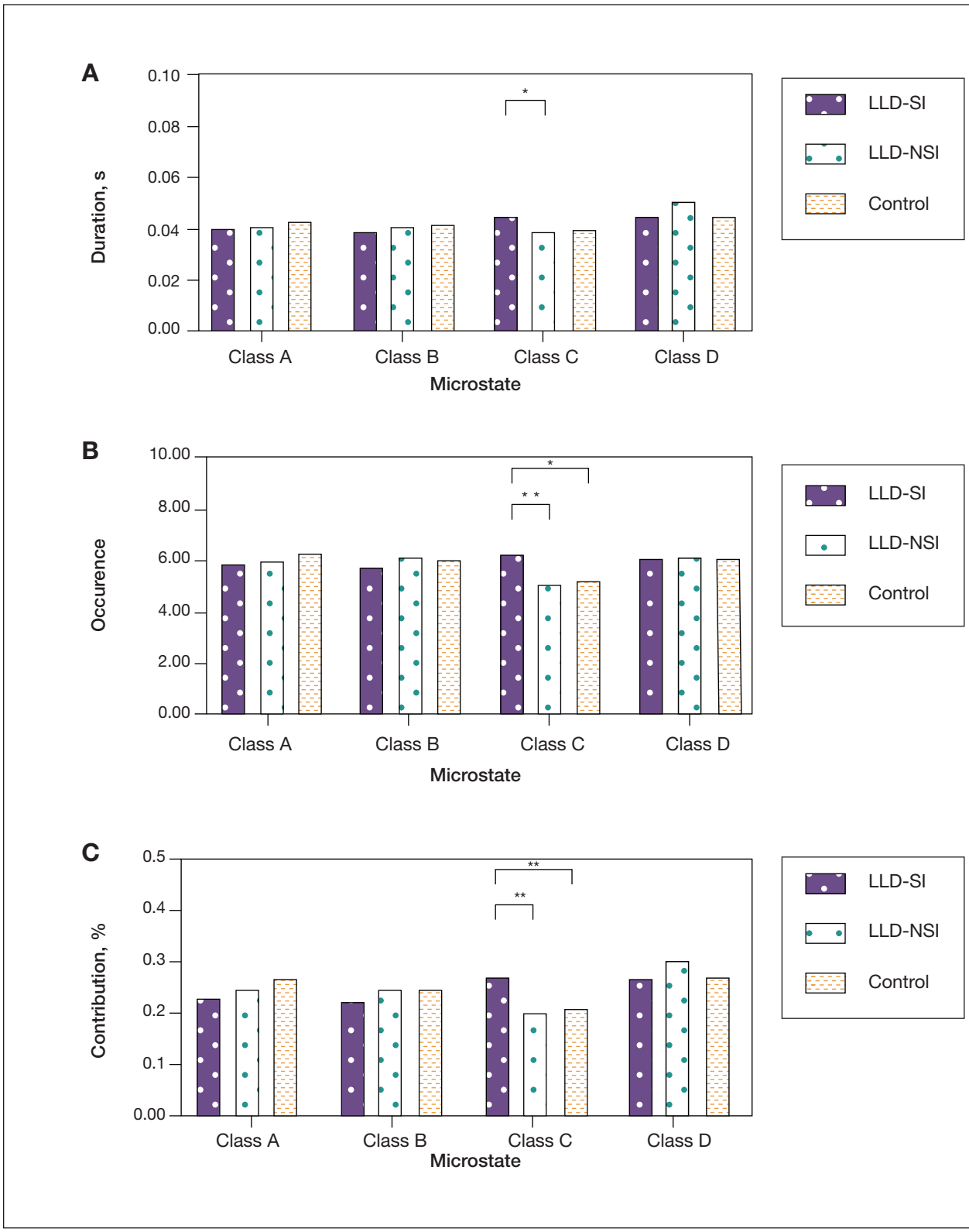

Figure 2: Microstate parameters of (A) duration, (B) occurrence, and (C) contribution among patients with late-life depression with suicidal ideation (LLD-SI), patients with late-life depression without suicidal ideation (LLD-NSI), and controls. The LLD-SI group exhibited significantly higher duration ($p = 0.04$), occurrence ($p = 0.009$), and contribution ($p = 0.001$) values in microstate class C than the LLD-NSI group, and significantly higher occurrence ($p = 0.027$) and contribution ($p = 0.009$) values in microstate class C than controls. *$p < 0.05$, **$p < 0.01$.

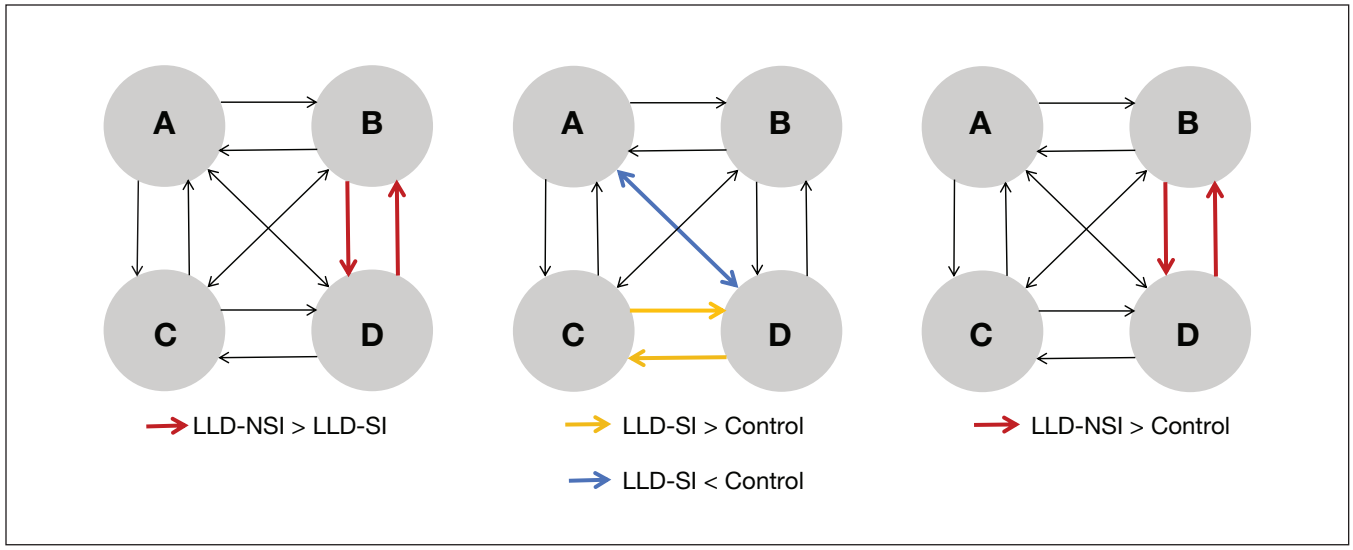

Figure 3: Transition probability analysis. As indicated with red arrows, patients with late-life depression without suicidal ideation (LLD-NSI) had significantly higher transition probabilities between microstate class B to D than those with late-life depression with suicidal ideation (LLD-SI) (p = 0.02) and the control group (p = 0.03). Yellow arrows indicate significantly higher transition probabilities between microstate class C and D in the LLD-SI group, and blue arrows indicate significantly lower transition probabilities between microstate class A and D in the LLD-SI group, compared with the control group.

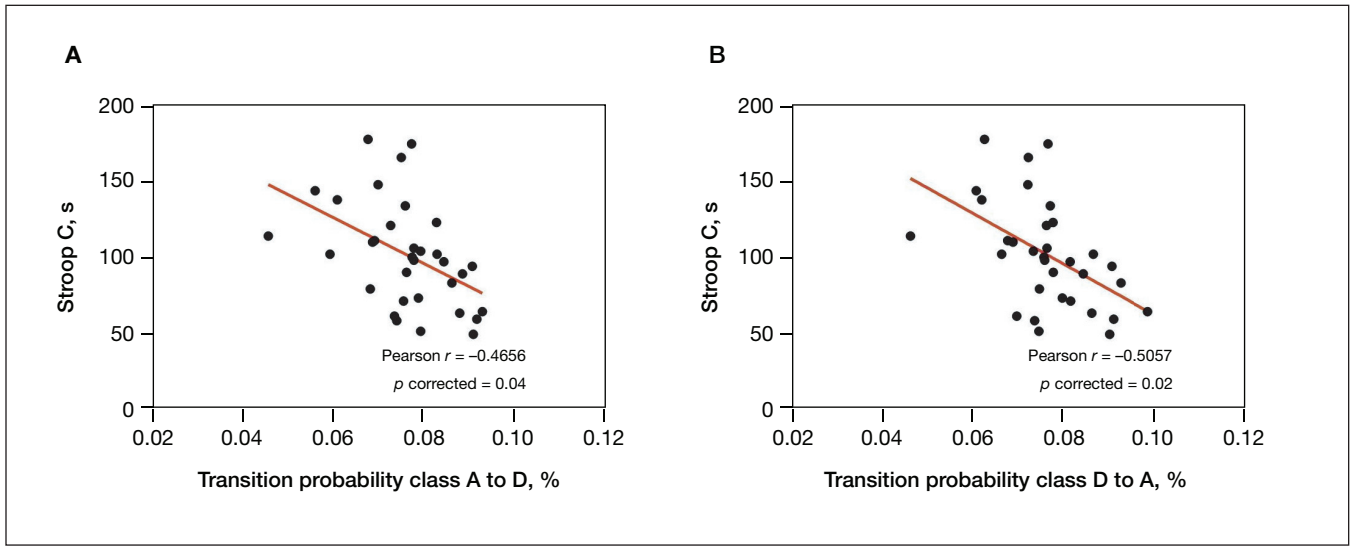

Figure 4: Correlation between completion time on Stroop Colour and Word Test Part C and transition probabilities from (A) microstate class A to class D (r = –0.4656, p = 0.04) and (B) from microstate class D to class A (r = – 0.5057, p = 0.02) among patients with late-life depression with suicidal ideation.

Furthermore, a series of studies have shown that the parameters of microstate C were correlated with aging, cognitive decline, and Alzheimer disease pathology.[39–41] Cognitive decline is a vital risk factor for late-life suicide,[42] and LLD is considered prodromal to dementia.[43] This evidence could explain why we did not observe abnormalities in microstate B, but found increased duration, occurrence, and contribution in microstate class C. The unique alterations in microstate C parameters may serve as a distinctive biomarker for diagnosing SI in LLD.

In the previous study conducted by Lao and colleagues,[22] higher parameters of microstate D were primarily found among patients with episodic LLD compared with those with remitted LLD and controls, and these parameters were positively correlated with depressive severity. However, they did not observe increased parameters of microstate C in the episodic LLD group. In contrast, all patients with LLD in the present study were in depressive episodes, and there was no significant difference in depressive severity between the LLD-SI and LLD-NSI groups. In addition, our

results showed no difference in parameters of microstate C between LLD-NSI and controls. These findings suggested that the observed increase in parameters of microstate C may be more specific to SI rather than a general aspect of depression in LLD.

In our transition probability analysis, we observed specific interaction modes between different large-scale brain networks among patients with LLD-SI, including increased transition probabilities between microstates C and D (C to D and D to C), as well as decreased transition probabilities between A and D (A to D and D to A), compared with controls. Moreover, transition probabilities between microstate B and D (B to D and D to B) were significantly higher among patients with LLD-NSI than among both patients with LLD-SI and controls. These findings indicated that patients with LLD-SI exhibited disrupted sequence of large-scale brain networks.

A particularly notable result is that the heightened transition probability between microstates C and D, which represents enhanced interaction between the SN and ECN in LLD-SI. This result was aligned with a previous MRI study, which found enhanced functional connectivity between the SN and ECN among adolescents with depression who had attempted suicide compared with those who had not made such attempts.[13] In previous studies, an increased transition to microstate C could also represent resting-state network disconnection, notably failure of the SN to initiate normal switching between ECN-based goal-directed and DMN-controlled self-referential processes.[20,44,45] The enhanced interaction between the SN and ECN could be driving abnormal switching between the ECN and DMN, contributing to overall depressive severity and increasing vulnerability to suicide behaviours in depression.[9]

In addition, we observed that the interaction between the ECN and the visual network was significantly higher in the LLD-NSI group than in the LLD-SI and control groups, as reflected by increased transition probabilities between microstates B and D. The enhanced large-scale brain network activity may act as protective factors for the formation of SI in LLD. The ECN plays a critical role in cognitive control. Impairments in this network can cause difficulties in regulating emotions, which may contribute to suicidal behaviours.[46] The dorsolateral prefrontal cortex (DLPFC) is the key hub of the ECN; it can interact with a variety of networks throughout the brain and plays a compensatory role in inhibiting abnormalities that cause depressive symptoms.[44,47] In previous research, Lin and colleagues[48] used seed-based functional connectivity analysis base of fMRI data, which found reduced DLPFC functional connectivity in the LLD-SI group. In a recent functional near-infrared spectroscopy study, researchers found hyperactivation of the DLPFC among patients with depression without SI compared with both the SI group and healthy controls.[49] Overall, the enhanced microstate parameter in our current research may represent a compensatory recruitment of resources for the ECN in LLD.

In our research, both LLD groups exhibited worse executive function (higher completion time of Stroop C) than the control group. Moreover, the transition probabilities between microstates class A and D were both negatively correlated with completion time of Stroop C in LLD-SI. Decreased transition probabilities between microstates A and D in LLD-SI may be related to executive dysfunction. This finding seems to align with a previous study that found abnormal interactions between microstates A and D among older adults at different stages of cognitive impairment.[41] According to the resting-state functional networks corresponding to these microstates, the interaction between the auditory network and ECN may be impaired. The ECN is involved in modulating the operation of other cognitive and emotional systems to enable the individual to support goal-directed behaviours. Moreover, the intrinsic and extrinsic connectivity of the ECN is likely to deteriorate in aging,[50] which contributes to both the cognitive and affective symptoms of LLD. Late-life depression is always accompanied by cognitive impairments,[4] such as executive dysfunction (including impaired cognitive inhibition[51] and cognitive flexibility)[42] and impaired cognitive control.[52] Cognitive impairment may also serve as risk factor for suicidal behaviour in LLD.[53]

Limitations

Our sample size was relatively small. Our study was cross-sectional, meaning that the causal relationship between abnormal microstate dynamics and suicidal ideation remains unclear. Prospective longitudinal studies or advanced neuromodulation protocols are necessary to explore this causal relationship. We did not include medication-naive patients with first-episode LLD; the pharmacologic effect of antidepressants may influence brain network dynamics. However, there were no significant differences in medication use between the LLD-SI and LLD-NSI groups, so the potential confounding effect of medication should be minimal. This study focused solely on SI in LLD. Further exploration should include both people with SI and those who have attempted suicide to investigate the full continuum of suicidal behaviour, from ideation to action, to achieve a comprehensive understanding of this complex phenomenon.

Conclusion

In our research, we revealed distinct patterns in microstate dynamics among patients with LLD-SI, in comparison with patients with LLD-SI and controls, primarily involving microstate C. Furthermore, we observed reduced transition probabilities between microstate class A and D, which may represent executive dysfunction in LLD-SI. The present study sheds light on the neural underpinnings of SI in LLD, suggesting that microstate dynamics might serve as a possible neurobiomarker for identifying SI in LLD.

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Data sharing: The raw and processed data generated in this study are not publicly available because of ethical restrictions and the need to protect participant privacy. However, these data can be made available upon reasonable request to the corresponding author for the purpose of verifying the research findings. Requests will be reviewed to ensure compliance with ethical and legal guidelines.

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