Ji et al. BMC Neurology (2025) 25:182
https://doi.org/10.1186/s12883-025-04156-x

BMC Neurology

RESEARCH Open Access

Abnormalities of regional brain activity in patients with asymptomatic internal carotid artery occlusion: a resting-state fMRI study

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Abstract

Background Asymptomatic internal carotid artery occlusion (aICAO) disrupts cerebral blood flow and can impair brain function. While previous research has primarily focused on abnormal functional connectivity between brain networks or regions in aICAO patients, less is known about specific regional brain activity alterations. This study investigated changes in local brain activity and their associations with cognitive function in patients with aICAO.

Methods A total of 26 unilateral patients with aICAO without MRI lesions and 25 matched healthy controls (HCs) underwent resting-state functional magnetic resonance imaging and neuropsychological assessment. Local brain activity in patients with aICAO was investigated using percentage amplitude of fluctuation (PerAF) and degree centrality (DC). The association between the abnormal regional brain activity in patients with aICAO and cognitive function was also explored.

Results Compared with HCs, patients with aICAO showed decreased PerAF in the ipsilateral (occlusion side, right) superior temporal gyrus (temporal pole), ipsilateral inferior frontal gyrus (triangular part). In addition, decreased DC was detected in the ipsilateral cuneus of patients with aICAO, while increased DC was observed in the contralateral (opposite to occlusion side, left) precuneus and contralateral inferior frontal gyrus (triangular part) among patients with aICAO. Furthermore, the DC value of contralateral precuneus in aICAO group was negatively correlated with Montreal Cognitive Assessment (MoCA) (r = -0.612, p = 0.002), Forward Digit Span Test (FDST) (r = -0.677, p = 0.001), and Backward Digit Span Test (BDST) (r = -0.531, p = 0.011) scores.

Conclusions Our findings revealed abnormal local spontaneous brain activity within brain regions associated with cognitive functions in patients with unilateral aICAO. Notably, some of these abnormalities correlated with their cognitive impairments. This study contributes to the understanding of potential neural mechanisms underlying cognitive dysfunction in unilateral aICAO patients.

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Keywords Asymptomatic internal carotid artery occlusion, Resting-state functional magnetic resonance imaging, Percentage amplitude of fluctuation, Degree centrality, Cognitive impairment

Introduction

Asymptomatic internal carotid artery occlusion (aICAO) is characterized by internal carotid atherosclerotic occlusion in the ipsilateral carotid perfusion region in individuals without a recent history of ischemic stroke or transient ischemic attack (TIA). Previous studies have demonstrated that about 67% of patients with aICAO have cognitive impairment [1, 2], suggesting that aICAO may not be asymptomatic. A study demonstrated that hemodynamic change and silent infarction may cause cognitive decline in patients with aICAO [3, 4]. However, the underlying neural mechanism remains unclear.

Resting-state functional magnetic resonance imaging (rs-fMRI) is widely used to assess brain activities by detecting the blood-oxygen level dependent (BOLD) signals in patients with various neurological disorders, such as Alzheimer's disease [5] and cerebral vascular diseases [6, 7]. Previous studies using fMRI mainly focused on functional connectivity (FC) of brain networks in asymptomatic carotid artery stenosis/occlusive diseases and showed decreased FC in the affected side [8, 9]. Notably, FC mainly focuses on the synchronization between brain regions, ignoring the abnormalities in local brain activity. A previous study using single-voxel level rs-fMRI metric, such as amplitude of low-frequency fluctuation (ALFF), found patients with asymptomatic carotid artery stenosis exhibited abnormal spontaneous neural activity in frontal lobe [10]. As a novel single-voxel level rs-fMRI metric, percentage amplitude of fluctuation (PerAF) reflects the percentage change in signal by measuring the percentage of BOLD fluctuation relative to the mean BOLD signal intensity at each time point and averaging across the entire time series, thus directly reflecting the fluctuation in the resting-state BOLD signal [11]. Compared with other single-voxel level rs-fMRI metrics, such as ALFF and fractional ALFF (fALFF), the PerAF value is less affected by the signal intensity error. It is also more accurate and suitable for subsequent statistical analysis [12–14]. At whole-brain level, the degree centrality (DC) mainly characterizes the importance of each node in the whole brain by measuring the number of direct connections between a certain node and other voxels [15]. It has been used to investigate abnormal spontaneous neural activity in ischemic stroke [16, 17] and carotid atherosclerotic disease [18, 19]. In conclusion, by combining PerAF and DC, we can achieve a more comprehensive understanding of local brain activity in aICAO. This approach offers the unique ability to analyze both single-voxel and whole-brain functional features, providing a richer picture of brain function in patients with asymptomatic internal carotid artery occlusion.

In this study, we explored localized spontaneous neural activity in patients with aICAO using a combination of PerAF and DC. Subsequently, we investigated the relationship between the altered brain activity and cognitive assessment in aICAO patients. It was hypothesized that patients with aICAO exhibit abnormal neural activity in cognitive-related brain regions, such as the frontal and temporal lobes, which would be related to the clinical cognitive impairments of patients.

Materials and methods

The inclusion and exclusion criteria

A total of 27 patients with aICAO and 25 healthy controls (HCs) were enrolled in the Neurology Department of the First Affiliated Hospital of Zhejiang University from March 2021 to August 2023.

The inclusion criteria for patients with aICAO included: (1) patients whose digital subtraction angiography (DSA) or computed tomography angiography (CTA) met the diagnostic criteria of ICAO; (2) < 50% stenosis of the contralateral carotid artery; (3) patients whose right hand was dominant; (4) patients with no history of stroke, transient ischemic attack (TIA), dementia, or major psychiatric disease; and (5) patients with primary school education or above (≥ 6 years). The exclusion criteria for patients with aICAO were: (1) patients with posterior circulation diseases; (2) patients with non-atherosclerotic carotid artery occlusion, such as arteritis or dissection; (3) patients with other neurodegenerative disease (Alzheimer's disease, Parkinson's disease); (4) patients with any medications that could affect the cognitive function; and (5) patients with any contraindications for MR scan (metal implants). Meanwhile, 25 HCs were recruited in this study according to the following inclusion criteria: (1) healthy participants matching the aICAO group in age, sex, education, handedness, and vascular risk factors; (2) healthy participants without other neurological or psychological diseases; (3) healthy participants who could complete the MRI scan. Due to an abnormality in the raw structural image, one patient with aICAO was excluded from the analysis. This resulted in a final sample of 26 patients with aICAO (19 with right-sided occlusion and 7 with left-sided occlusion) and 25 HCs.

Written informed consent was obtained from all participants. This study followed the principles of the Declaration of Helsinki and was approved by the clinical research ethics committee of the First Affiliated Hospital

of Zhejiang University (Reference number: 2021IIT No. 772).

Cognitive assessments

Cognitive assessments of participants were performed within 7 days before MRI scan. The Montreal Cognitive Assessment (MoCA) (Beijing Version) was utilized to assess global cognition [20]. The Symbol Digit Test (SDT) (Chinese version; Wechsler, 1999) [21] was used to assess visual search, perception, and graphomotor speed, while the Digit Span Test (DST), including forward Digit Span Test (FDST) and backward Digit Span Test (BDST) (Chinese version; Wechsler, 1999) [21] was used to evaluate working memory. Visuospatial ability and executive functions were evaluated using the Trail Making Test (TMT), including TMT-A and TMT-B [22].

MRI data acquisition

MRI data were acquired using two 3.0-Tesla scanners (SIGNA Architect and DISCOVERY MR750, GE, USA) with a 19-channel head coil (GEM HNU, GE Healthcare, USA), where participants were positioned supine using foam padding and a restraining strap, instructed to remain awake with eyes closed and avoid structured thinking; structural T1-weighted imaging on the SIGNA Architect employed repetition time (TR)/echo time (TE) = 7.7/3.1 ms, 1.0 mm^3 isotropic voxels, 256 × 256 mm^2 FOV, 1.0 mm slice thickness, 176 sagittal slices (4 min 39 s), while rs-fMRI used TR/TE = 2000/30 ms, 3.4 × 3.4 × 3.6 mm^3 voxels, 220 × 220 mm^2 FOV, 3.6 mm slice thickness, 36 axial slices (6 patients, 4 HCs; 6 min 40 s), and the DISCOVERY MR750 system included T1 (TR/TE = 8.2/3.2 ms, 1.0 mm^3 voxels, 256 × 256 mm^2 FOV, 1.0 mm slice thickness, 180 sagittal slices; 4 min 52 s) and rs-fMRI (TR/TE = 2000/30 ms, 3.4 × 3.4 × 3.2 mm^3 voxels, 220 × 220 mm^2 FOV, 3.2 mm slice thickness, 45 axial slices; 21 patients, 21 HCs; 6 min 40 s).

Data preprocessing

Rs-fMRI data were preprocessed using RESTplus V1.24 (http://restfmri.net/forum/restplus) [23] based on Statistical Parametric Mapping 12 (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) and MATLAB 2017b (https://uk.mathworks.com/products/matlab). To avoid the impact of different slices, data from different centers were preprocessed separately, with the preprocessing parameters being consistent across all rs-fMRI data. The initial pre-processing step included flipping the T1 and fMRI images of patients with left-sided carotid occlusion along the midsagittal plane, standardizing the affected hemisphere to the right-hand side across all participants. Specifically, the first 10 time points were discarded for the stabilization of magnetic field and the adaptation of participants. Slice timing of the remaining volumes was corrected by matching the center slice to remove the influence of timing difference. Head motion was corrected by taking the first image as the reference layer. Spatial transformation of six parameters was achieved using rigid body transformation [24] to ensure that the time series at the same location belong to the same voxel. A 2-step normalization was conducted by first co-registering the high-resolution T1 structural images to the mean rs-fMRI images to obtain the co-registered T1 images. The obtained images were then normalized to the Montreal Neurological Institute (MNI) standard space, with each voxel resampled to 3 × 3 × 3 mm^3. The resampled images were smoothed using a 6-mm full-width half-maximum (FWHM) Gaussian kernel to reduce the registration error between subjects and improve signal-to-noise ratio [25]. For DC, smoothing was conducted after the metric calculation. Detrending was then conducted to reduce the noise. In addition, the Friston-24 head motion parameters were regressed [25] to decrease the movement effects. Signals in the frequency band ranging from 0.01 to 0.08 Hz were extracted using a bandpass filter.

Global signal regression (GSR) and white matter (WM) signal regression were intentionally omitted from our resting-state fMRI preprocessing step, as emerging evidence highlights the neurobiological significance of BOLD signals in WM [26, 27]. For instance, Ji et al. [28] identified a white matter dysfunction pattern associated with specific neurotransmitter profiles in patients with psychiatric disorders—a finding that would have been obscured by WM signal regression. Thus, regressing out white matter signals may bias results by masking potentially meaningful neurobiological information. Additionally, the controversial application of GSR may introduce spurious negative functional connectivity and reduce the interpretability of global neurovascular coupling dynamics [29].

PerAF and DC values

PerAF and DC values were calculated using RESTplus v1.24. PerAF was performed by calculating the percent of BOLD fluctuations relative to the average BOLD signal strength for each time point and averaging over the entire time series [11]. For each voxel, the PerAF value was calculated using the following equations:

$$PerAF = \frac{1}{n}\sum_{i=1}^{n}\left|\frac{X_i-\mu}{\mu}\right| \times 100\%$$

$$\mu = \frac{1}{n}\sum_{i=1}^{n} X_i$$

in which X_i, n and μ represent the signal strength at the i_{th} time point, total number of time points in the time series, and mean of the time series, respectively [11]. The PerAF value of each voxel was divided by the global mean PerAF of each subject to obtain mPerAF.

The preprocessing data without smoothing were used to calculate the binary DC value. First, the Pearson correlations of the time series between each voxel and other voxels in the whole brain were calculated [17]. The Pearson correlation coefficient (r) was regarded as the FC between voxels if it was greater than 0.25 [30]. The number of FC between a given voxel and all the other voxels was calculated as global binary DC [31]. The global binary DC of each voxel was divided by the average value of the whole brain in each participant to increase normality [32]. Finally, the standardized binary DC maps were smoothed spatially using a 6-mm FWHM Gaussian kernel.

Statistical analysis

IBM SPSS Statistics 26 (https://www.ibm.com/spss) was used to compare the demographic and clinical data of the two groups. Specifically, Mann-Whitney U test were implemented to examine the differences in age, education and cognitive scale between the two groups, while chi-square test was used to compare gender differences and the vascular risk factors between the two groups. Two-tailed test with a significant level $p < 0.05$ was applied in all comparisons.

Two sample t-test was conducted using RESTplus V1.24 to compare the PerAF and binary DC values between the two groups, with the center as a covariate. For rs-fMRI analysis, subjects were grouped according to their scanning center. One group consisted of 10 subjects (6 patients and 4 healthy controls) who underwent scans with 36 slices at center (1) The other group included 41 subjects (20 patients and 21 healthy controls) scanned with 45 slices at center (2) Gaussian random field (GRF) correction with the voxel level $p < 0.001$ and cluster level $p < 0.05$ was applied in both analyses.

The PerAF and DC values of the abnormal brain regions in patients with aICAO were extracted using RESTplus V1.24 based on the results of the comparative analyses. Partial correlation analysis was performed to assess the relationship between the PerAF/binary DC value and the cognition assessments (including those tested by MoCA, SDT, TMT, and DST) in patients with aICAO, with the center (slices), age and education as covariates. P-value less than 0.05 was regarded as a significant difference.

Table 1 Demographics and cognitive test scores of aICAOs and HCs

	aICAOs ($n = 26$)	HCs ($n = 25$)	p-value
Gender (M/F)	18/8	18/7	0.828
Age (years) [a]	61.5 [57.0;68.0]	58 [55.0;60.0]	0.08
Education (years) [a]	6.0 [6.0;9.0]	9.0 [6.0;9.0]	0.170
Hypertension	20	15	0.193
Diabetes Mellitus	7	3	0.180
Smoking	10	6	0.266
Drinking	7	4	0.343
Occlusion side (R/L)	19/7	NA	NA
MoCA [a]	26.0 [23.0;26.0]	28.0 [27.0;28.0]	**< 0.001**
SDT [a]	17.5 [12.0;25.0]	30.0 [28.0;32.0]	**< 0.001**
TMT-A [a]	93.5 [85.0;120.0]	48.0 [42.0;50.0]	**< 0.001**
TMT-B [a]	135.5 [85.0;120.0]	88.0 [80.0;90.0]	**< 0.001**
FDST [a]	7.0 [7.0;7.0]	8.0 [8.0;8.0]	**< 0.001**
BDST [a]	5.0 [5.0;5.0]	7.0 [6.0;7.0]	**< 0.001**

Boldface type indicates statistical significance. [a]: Mann-Whitney U test, data are expressed as mean with IQR in square brackets. **Abbreviations**: aICAO, asymptomatic internal carotid artery occlusion; HC, healthy control; M, male; F, female; R, right; L, left; MoCA, Montreal Cognitive Assessment; SDT, Symbol Digit Test; TMT, Trail Making Test; FDST, forward Digit Span Test; BDST, backward Digit Span Test

Results

Demographic and clinical characteristics

The educational years, gender ratio, age, and vascular risk factors were not significantly different between the two groups (Table 1). Compared with HCs, patients with aICAO had significantly poorer performances on global cognition, working memory, and visuospatial and executive function (Table 1).

PerAF between the two groups

Compared with HCs, patients with aICAO demonstrated significantly decreased PerAF in the ipsilateral (occlusion side, right) superior temporal gyrus (temporal pole), ipsilateral inferior frontal gyrus (triangular part). (voxel $p < 0.001$, cluster $p < 0.05$, GRF correction) (Table 2; Fig. 1).

Binary DC between the two groups

Patients with aICAO exhibited significantly lower binary DC in the ipsilateral cuneus compared to HCs. In

Table 2 Altered brain regions detected by PerAF in aICAOs group compared with HCs group

Brain regions	Number of voxels	Peak MNI coordinates			T (peak intensity)
		X	Y	Z	
Temporal_Sup_R (Ipsi)	40	39	15	-24	-4.7348
Frontal_Inf_R (Ipsi)	74	54	42	6	-5.063

Abbreviations: PerAF, percentage amplitude of fluctuation; aICAO, asymptomatic internal carotid artery occlusion; HC, healthy control; MNI, montreal neurological institute; Temporal_Sup_R, right superior temporal gyrus; Frontal_Inf_R, right inferior frontal gyrus. Ipsi, ipsilateral (occlusion side).

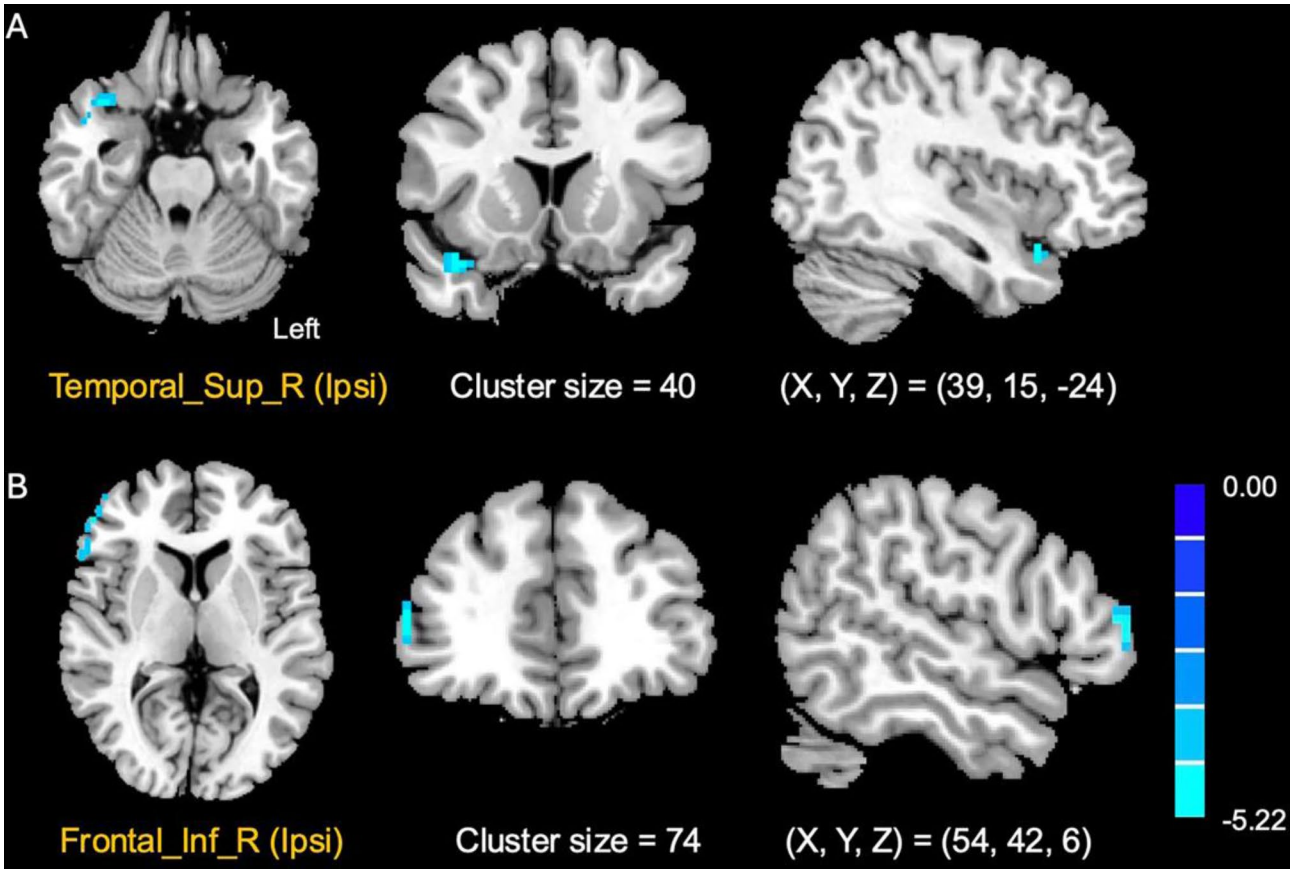

Fig. 1 2 clusters revealed by PerAF in aICAO patients compared to HCs, including Temporal_Sup_R (Ipsi) and Frontal_Inf_R (Ipsi). Areas with decreased PerAF relative to HCs are displayed in blue. Color bars represent T values. The result was corrected using the GRF correction with the voxel level $p < 0.001$ and cluster level $p < 0.05$. PerAF, percentage amplitude of fluctuation; aICAO, asymptomatic internal carotid artery occlusion; HCs, healthy controls; Temporal_Sup_R, right superior temporal gyrus; Frontal_Inf_R, right inferior frontal gyrus. Ipsi, ipsilateral (occlusion side). Gaussian random field, GRF

Table 3 Altered brain regions detected by binary DC in aICAOs group compared with HCs group

Brain regions	Number of voxels	Peak MNI coordinates			T (peak intensity)
		X	Y	Z	
Precuneus_L (Contra)	59	-18	-45	3	5.4892
Frontal_Inf_L (Contra)	99	-54	27	21	5.8183
Cuneus_R (Ipsi)	54	9	-81	42	-4.8228

Abbreviations: DC, degree centrality; aICAO, asymptomatic internal carotid artery occlusion; HC, healthy control; MNI, montreal neurological institute; Frontal_Inf_L, left inferior frontal gyrus; Precuneus_L, left precuneus; Cuneus_R, right cuneus. Ipsi, ipsilateral; Contra, contralateral (opposite to occlusion side).

addition, binary DC in the contralateral precuneus and contralateral inferior frontal gyrus (triangular part) (voxel $p < 0.001$, cluster $p < 0.05$, GRF correction) was increased among the patients with aICAO (Table 3; Fig. 2).

Relationship between abnormal brain regions and cognitive assessments in patients with aICAO

This study identified significant correlations between abnormal regional brain activity in patients with aICAO and their performance on cognitive assessment scales. The binary DC value of contralateral precuneus was significantly negatively correlated with MoCA (r = -0.612, $p = 0.002$), FDST (r = -0.677, $p = 0.001$), and BDST (r = -0.531, $p = 0.011$) scores in the aICAO group (Fig. 3).

Discussion

In the present study, PerAF and binary DC methods were used to explore the abnormal neural basis and its relationships with the cognitive functions in patients with aICAO. Our findings revealed significant differences in PerAF and binary DC values between patients with aICAO and HCs across various brain regions, including the frontal lobe, temporal lobe, precuneus, cuneus. Meanwhile, alteration of neural activity in contralateral (opposite to occlusion side, left) precuneus were correlated with cognitive assessments. These findings provide new insights into neural mechanism underlying the decline of cognition in patients with aICAO.

Compared with HCs, patients with aICAO manifested significantly decreased PerAF in the ipsilateral (occlusion side, right) superior temporal gyrus. The superior temporal gyrus (STG), a critical hub for social perception and

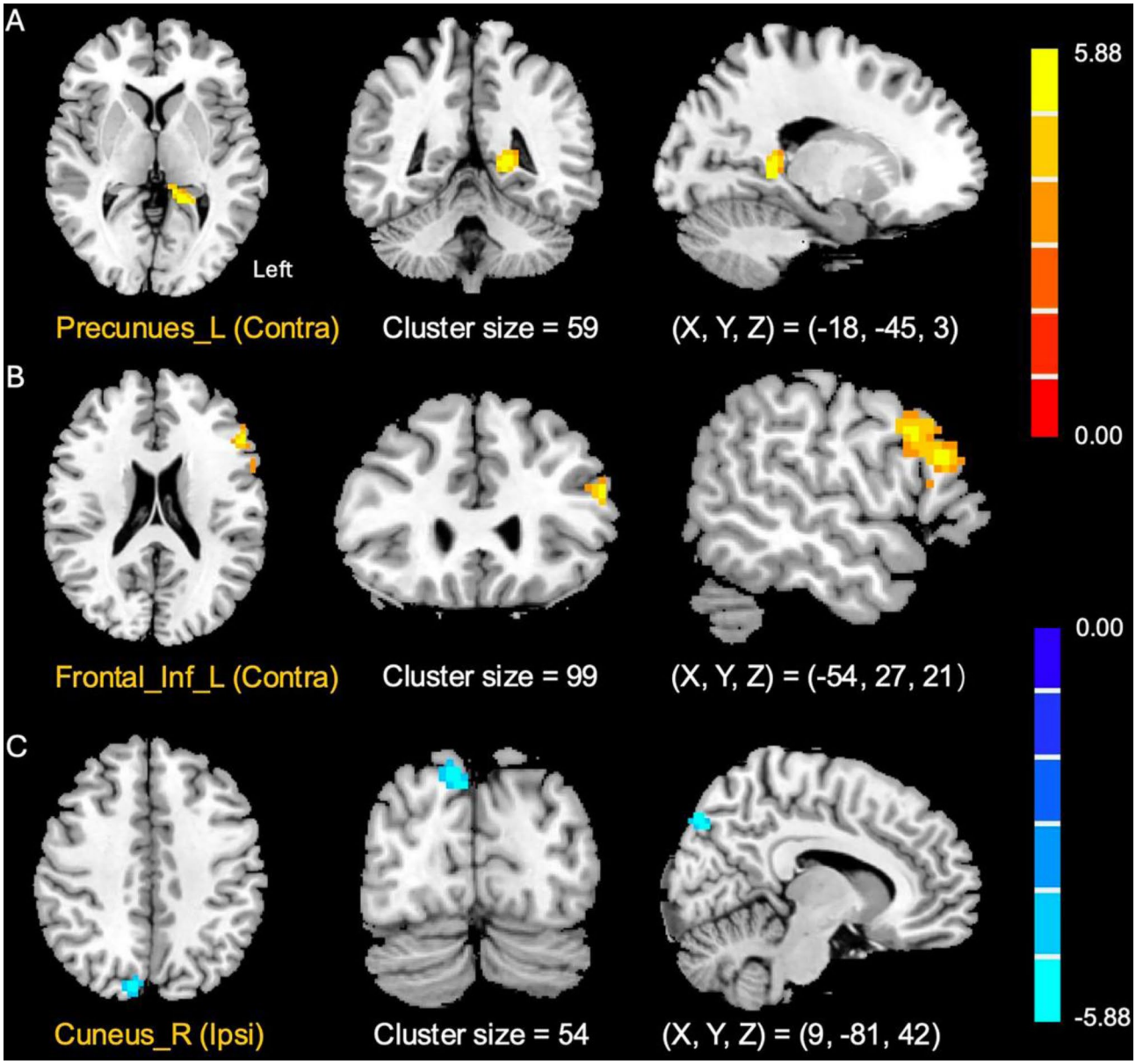

Fig. 2 3 clusters revealed by Binary DC in aICAO patients compared to HCs, including Precuneus_L (Contra), Frontal_Inf_L (Contra), and Cuneus_R (Ipsi). Areas with decreased Binary DC relative to controls are displayed in blue, and areas with increased Binary DC are displayed in red. Color bars represent T values. The result was corrected using the GRF correction with the voxel level $p < 0.001$ and cluster level $p < 0.05$. DC, degree centrality; aICAO, asymptomatic internal carotid artery occlusion; HC, healthy control; Frontal_Inf_L, left inferior frontal gyrus; Precuneus_L, left precuneus; Cuneus_R, right cuneus. Ipsi, ipsilateral (occlusion side); Contra, contralateral (opposite to occlusion side). Gaussian random field, GRF

cognition [33], exhibits functional coupling with core default mode network (DMN) regions during higher-order cognitive processes such as semantic integration and social reasoning [34, 35]. Zhao et al. (2014) found that spontaneous neuronal activity in the superior temporal gyrus was decreased in patients with mild cognitive impairment when compared with HCs [36]. Our result was consistent with the aforementioned study. This finding suggests that the superior temporal gyrus may serve as a potential biomarker for predicting cognitive decline in this patient population.

The PerAF value in the ipsilateral inferior frontal lobe was lower in the aICAO group than in the HCs. As a key component of the brain, the inferior frontal lobe is responsible for higher cognitive functions, especially in memory, language and execution [37–39]. He et al. (2021) revealed that patients with asymptomatic carotid artery stenosis have decreased FC in the inferior frontal gyrus of the affected side [40]. These findings indicate that the decreased regional neuronal activity (PerAF) in the inferior frontal lobe may induce aberrant FC in patients with aICAO. In addition, binary DC in the contralateral

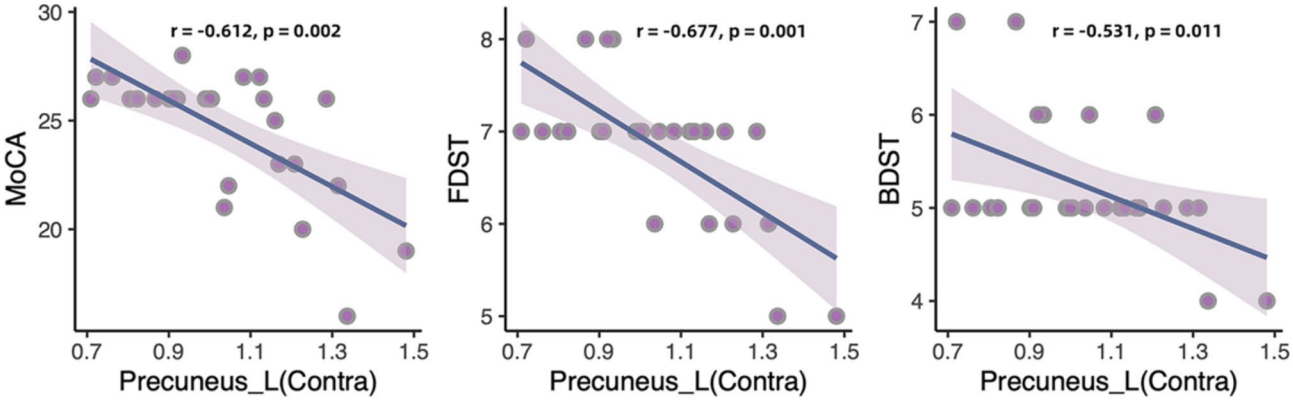

Fig. 3 Significant correlations between Binary DC value of the abnormal brain region and the cognitive assessments ($p < 0.05$). (**A**-**C**) Correlations between the binary DC value of left precuneus and MoCA, FDST, BDST scores. DC, degree centrality; MoCA, montreal cognitive assessment; FDST, forward Digit Span Test; BDST, backward Digit Span Test. Precuneus_L, left precuneus; Contra, contralateral (opposite to occlusion side)

inferior frontal gyrus was increased in patients with aICAO. The increase or decrease of DC suggests the alterations of nodal importance in brain function among patients with neurological disorders [41], and can help understand the changes in brain function related to the disease. Increased binary DC in the contralateral inferior frontal gyrus among patients with aICAO might suggests a maladaptive or compensatory mechanism to maintain normal brain function.

Moreover, patients with aICAO exhibited decreased binary DC in the ipsilateral cuneus, a region within the visual association cortex that also serves as a critical hub in the visual-spatial sketchpad, a well-known working-memory processing system [42, 43]. The decreased binary DC in the ipsilateral cuneus indicates decreased function of this region in the brain of patients with aICAO, which may cause cognitive decline, especially in working memory and visuospatial processing. To the best of our knowledge, this is the first study to report the decreased DC of ipsilateral cuneus in patients with aICAO with cognitive impairment. This novel finding may provide a new perspective for the underlying mechanism of cognitive decline in patients with aICAO.

Besides, binary DC of the contralateral precuneus increased in patients with aICAO, indicating increased connectivity in this region. The precuneus, a functional node of the extended DMN, participates in various higher-order cognitive functions such as visuospatial processing and episodic memory [44, 45]. A recent rs-fMRI study showed hyper-connectivity of the precuneus on the left side of cerebral hemisphere in patients with right side internal carotid artery stenosis/occlusion, possibly suggesting a compensation of brain activity to maintain clinical asymptomatic cognitive performance [46]. In this study, the increased binary DC of the precuneus may play a role in mitigating the effects of hypoperfusion on cognition in patients with aICAO, consistent with the aforementioned study. Notably, correlation analysis showed that the DC value of the contralateral precuneus was negatively correlated with MoCA, FDST, and BDST scores. Cognitive assessment showed that multiple cognitive domain impairment occurred in patients with aICAO, indicating that the DC changes in the contralateral precuneus may play a compensatory role in maintaining normal cognition.

Nonetheless, this study has some limitations. First, the study had a relatively small sample size. Therefore, future studies with large samples are needed to identify more reliable and replicable differences between patients with aICAO and HCs since brain activity is complicated and divergent. Second, the type of cognitive impairment may differ according to the occlusion side of carotid artery in patients. Therefore, further studies should include more patients to facilitate a comprehensive analysis of the relationship between brain activity changes associated with carotid occlusion on different sides and the correlation of cognitive impairment. Third, the cross-sectional data may not present a comprehensive neural mechanism in patients with aICAO with cognitive decline, necessitating a longitudinal study for validation. Fourth, data were acquired from two MRI systems with slightly divergent BOLD-sequence parameters, which may introduce confounding effects due to inter-scanner variability; to minimize these effects, the two sets of data are processed separately and scanner model was incorporated as a covariate in the statistical analysis. Fifth, our study focused exclusively on localized resting-state neural activity and did not investigate static or dynamic FC, which precludes direct comparisons with prior FC-based findings in carotid stenosis/occlusion cohorts. Future investigations should incorporate multimodal analyses combining localized activity, static FC, and dynamic FC to delineate how network-level dysregulation interacts with focal hemodynamic impairments to drive cognitive

decline in this population. Finally, the observed associations between alterations in brain activity and cognitive scores are preliminary and have not been subjected to False Discovery Rate (FDR) correction, as this was an exploratory study. Therefore, our findings should be interpreted cautiously, pending further replication.

Conclusion

In this study, we combined PerAF and DC to comprehensively investigate the alterations in local brain activity among patients with aICAO. It was observed that patients with aICAO developed abnormal spontaneous neural activity in the frontal, temporal, and DMN brain regions, some of which play significant roles in cognitive impairment in multiple domains. In summary, this study provides a more comprehensive analysis of the localized neural activity associated with cognitive deficits in aICAO patients, which contributes to the understanding of underlying mechanisms from the perspective of neuroimaging.

Abbreviations

aICAO	Asymptomatic internal carotid artery occlusion
HC	Healthy control
MoCA	Montreal Cognitive Assessment
SDT	Symbol Digit Test
TMT	Trail Making Test
FDST	Forward Digit Span Test
BDST	Backward Digit Span Test
PerAF	Percentage amplitude of fluctuation
DC	Degree centrality
MNI	Montreal neurological institute
Temporal_Sup_R	Right superior temporal gyrus
Frontal_Inf_R	Right inferior frontal gyrus
Frontal_Inf_L	Left inferior frontal gyrus
Precuneus_L	Left precuneus
Cuneus_R	Right cuneus
Ipsi	Ipsilateral
Contra	Contralateral
GRF	Gaussian random field
FDR	False Discovery Rate

Acknowledgements

None.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Renjie Ji, Chunlan Deng, Jianxin Zhang, Hanfeng Chen, Ziqi Xu. The first draft of the manuscript was written by Renjie Ji, Chunlan Deng and Jianxin Zhang and revised by Benyan Luo and Zeqi Hao, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding

None.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the clinical research ethics committee of the First Affiliated Hospital of Zhejiang University (Reference number: 2021IIT No. 772). Written informed consent was obtained from all patients.

Consent for publication

Written informed consent was obtained from the patients to publish the clinical information in this article.

Competing interests

The authors declare no competing interests.

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Received: 6 July 2024 / Accepted: 24 March 2025
Published online: 25 April 2025

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