

Resting-state functional connectivity of the default mode network subsystems as a potential biomarker for delusions in patients with first-episode drug-naïve schizophrenia

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ABSTRACT

Objectives: Previous studies have indicated a close association between delusions and the default mode network (DMN). This study aimed to explore the relationship between delusions and resting-state functional connectivity (rsFC) of subsystem-specific DMN in patients with first-episode drug-naïve schizophrenia (FESCZ).

Methods: This study recruited 79 FESCZ patients. The severity of delusions was assessed using the PANSS P1 item, with a score of ≥ 4 defining the clear presence of delusions. Seed-to-seed rsFC matrices were calculated between 11 DMN seed regions, which belong to three subsystems: the core, the dorsomedial prefrontal cortex (dMPFC), and the medial temporal lobe (MTL).

Results: Compared with patients without clear delusions, patients with clear delusions exhibited hyper-connectivity between the core and the MTL subsystems. The severity of delusions was positively correlated with the core-MTL rsFC strength. Post-hoc analyses revealed that specific rsFC edges (rsFC between posterior cingulate cortex and retrosplenial cortex, as well as between posterior cingulate cortex and posterior inferior parietal lobule) were significantly correlated with the severity of delusions.

Conclusions: The DMN core-MTL rsFC strength is associated with delusions in FESCZ patients, which may serve as a potential biomarker for the severity of delusions and offer novel neurobiological insights for delusions treatment.

1. Introduction

As a severe and multifactorial psychiatric disorder, schizophrenia (SCZ) affects approximately 1 % of the global population during their lifetimes, based on epidemiological data (Owen et al., 2016; Saha et al., 2005). The disorder is characterized by a constellation of symptoms, including delusions, hallucinations, avolition, and anhedonia (Faden and Citrome, 2023), imposing substantial burdens on both individuals and society. Among the core symptoms, delusions are defined as fixed false beliefs resistant to contradictory evidence (Mohn et al., 2024). For example, persecutory delusions involve patients firmly believing that

others intend to harm them (Coltheart et al., 2011). A longitudinal study reveals that 57 % of patients with SCZ experience delusions during the course of their illness (Harrow and Jobe, 2010). Additionally, delusions usually cause severe impairment in social functioning among patients with SCZ (Baker et al., 2019). Investigating the neural mechanisms underlying delusions can deepen our understanding of this symptom and facilitate its clinical treatment.

The Default Mode Network (DMN) corresponds to the resting state of the brain and remains active when the brain is not engaged in tasks requiring focused attention (Raichle et al., 2001). It plays a crucial role in self-referential processing, episodic memory, and social cognition

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(Andrews-Hanna et al., 2010). Given that the brain regions comprising the DMN exhibit widespread abnormalities in patients with SCZ, and the cognitive processes they subserve are intimately associated with the disorder, the DMN has emerged as one of the critical focuses in investigation for understanding the pathophysiology of SCZ patients (Hu et al., 2017). Resting-state functional connectivity (rsFC) is a technique for mapping the interactions of intrinsic brain networks during rest (Biswal et al., 1995). Altered connectivity in the DMN is one of the most frequently replicated neural signatures differentiating SCZ patients from healthy controls (Hu et al., 2017). This distributed network was initially conceptualized as a unified system (Fox et al., 2005), composed of three functionally specialized subsystems: the core subsystem, the dorsomedial prefrontal cortex (dMPFC) subsystem, and the medial temporal lobe (MTL) subsystem (Andrews-Hanna et al., 2010). Both the dMPFC and MTL subsystems demonstrate close interactions with the core subsystem (Andrews-Hanna et al., 2010). Emerging evidence implicates that subsystem-specific rsFC abnormalities are associated with the psychopathology of SCZ, particularly reduced core-MTL connectivity (Cao et al., 2025; Fan et al., 2022).

Converging evidence from neuroimaging studies has identified the DMN as a critical neural correlate of delusions. Liu et al. (Liu et al., 2024) proposed that DMN dysfunction may promote the formation of abnormal associations between autobiographical memory and trivial stimuli, providing a mechanistic basis for delusional formation. Previous studies have identified associations between DMN rsFC dysfunction and delusions. In previous SCZ studies, reduced DMN rsFC was associated with the severity of positive symptoms, particularly delusions (Bluhm et al., 2007; Garrity et al., 2007; Rotarska-Jagiela et al., 2010). In Alzheimer's disease, reduced DMN rsFC has also been observed in patients with delusions compared to those without (Qian et al., 2019). Mechanistically, DMN rsFC abnormalities may disrupt self-monitoring processes, leading to source monitoring errors manifested as thought insertion and control delusions (Robinson et al., 2016).

The pathophysiological specificity of DMN subsystem-specific connectivity patterns associated with delusional symptoms remains under-explored. To bridge this gap, the present study investigated the relationship between delusions and the rsFC strength within and between DMN subsystems in patients with first-episode drug-naïve SCZ (FESZ). By characterizing these neurofunctional signatures, this study aimed to advance the discovery of biomarkers for delusion identification and provided evidence for personalized neuro-regulatory strategies targeting delusion-related neural circuits. Based on prior evidence, this study proposed two hypotheses: (1) patients with high delusions would show significant differences in the rsFC strength of DMN subsystems compared to patients with low delusions; (2) the rsFC strength of DMN subsystems would be associated with the severity of delusions.

2. Methods

2.1. Participants

A total of 79 FESZ patients were recruited from the First Hospital of Shanxi Medical University. Inclusion criteria required fulfillment of the following conditions: (1) 15–55 years old; (2) ethnic homogeneity (Han Chinese) to control for population stratification effects; (3) the DSM-IV diagnosis of SCZ confirmed by two board-certified psychiatrists using the Structured Clinical Interview for DSM-IV (SCID); (4) at the first onset of SCZ; and (5) no prior exposure to antipsychotic medications. Exclusion criteria were rigorously enforced: (1) pregnancy or lactation; (2) history of alcohol dependence or substance abuse; (3) structural cerebral pathologies or profound systemic disorders; (4) MRI contraindications, including metal implants.

All participants or their legal guardians provided written informed consent forms after fully understanding the study protocol. This study protocol was conducted following the Declaration of Helsinki and was fully approved by the Institutional Review Board of the First Hospital of

Shanxi Medical University (No. 2021-Y17).

2.2. Clinical assessment

Psychiatric symptom profiles were quantified using the Positive and Negative Syndrome Scale (PANSS), the gold-standard tool for assessing the multidimensional symptoms of SCZ (Kay et al., 1987). This 30-item scale covers positive symptoms, negative symptoms, and general psychopathology domains, with higher scores indicating more severe symptoms.

Delusional symptoms were assessed using P1 item of the PANSS, which adopted a 7-point Likert rating: 1 = Absent, 2 = Minimal, 3 = Mild, 4 = Moderate, 5 = Moderate-severe, 6 = Severe, and 7 = Extremely severe. Typically, a score ≥ 4 on individual PANSS items is commonly defined as 'clinically significant' (Kay et al., 1987; Leucht et al., 2005). In this study, the P1 item score was used to measure delusions, with a cut-off value of ≥ 4 indicating the clear presence of delusions (Triola et al., 2024).

2.3. MRI protocol

Images were acquired using a GE Signa HDxT 3 T scanner and a 32-channel head coil. The parameters of resting-state BOLD images were as follows: slice thickness = 4 mm; repetition time = 2000 ms; echo time = 30 ms; flip angle = 90° ; field of view = 240 mm \times 240 mm; matrix = 64 \times 64. Each patient received a 7-minute (210 timepoints) scan. During acquisition, participants were required to remain awake with their eyes closed and lie supine, with a foam pad under their head to minimize head movement.

2.4. Image preprocessing

DPABI V8.0 was used to conduct data preprocessing. Preprocessing included the following steps: (1) exclusion of the initial 10 functional timepoints to stabilize signal acquisition, retaining 200 timepoints; (2) slice timing correction for temporal alignment; (3) head motion correction using 6-parameter rigid-body transformation; (4) functional image realignment; (5) regression of Friston 24 motion parameters and signals from the whole brain, white matter and cerebrospinal fluid to control for noise; (6) two-stage spatial normalization of functional images (firstly transformed to individual T1 space, and then to MNI152 space); (7) bandpass filtering (0.01–0.1 Hz). Framewise displacement (FD) was calculated as an indicator to measure the magnitude of head motion, and patients with a mean FD > 0.2 mm were excluded (Lu and Yan, 2023). The mean FD in patients without clear delusions was 0.073 ($SD = 0.042$, $min = 0.026$, $max = 0.187$), and that in patients with clear delusions was 0.073 ($SD = 0.036$, $min = 0.029$, $max = 0.177$). There was no significant difference between the two groups in mean FD ($t = -0.007$, $p = 0.994$). No patients were excluded due to large head motion.

2.5. rsFC strength

Functional connectivity was calculated using 11 predefined spherical seed regions (6 mm radius), which were selected based on the DMN framework from prior research (Andrews-Hanna et al., 2010), and designated as regions of interest (ROIs) (Fig. 1). These regions were divided into three subsystems: the core subsystem (including the anterior medial prefrontal cortex [aMPFC], and posterior cingulate cortex [PCC]), the dMPFC subsystem (including the dorsomedial prefrontal cortex [dMPFC], temporal parietal junction [TPJ], lateral temporal cortex [LTC], temporal pole [TempP]), and the MTL subsystem (including the ventral medial prefrontal cortex [vMPFC], posterior inferior parietal lobule [pIPL], retrosplenial cortex [Rsp], parahippocampal cortex [PHC], and hippocampal formation [HF+]). The MNI coordinates of these ROIs are provided in **Supplementary Table 1**.

Consistent with the established protocols, only left-hemisphere

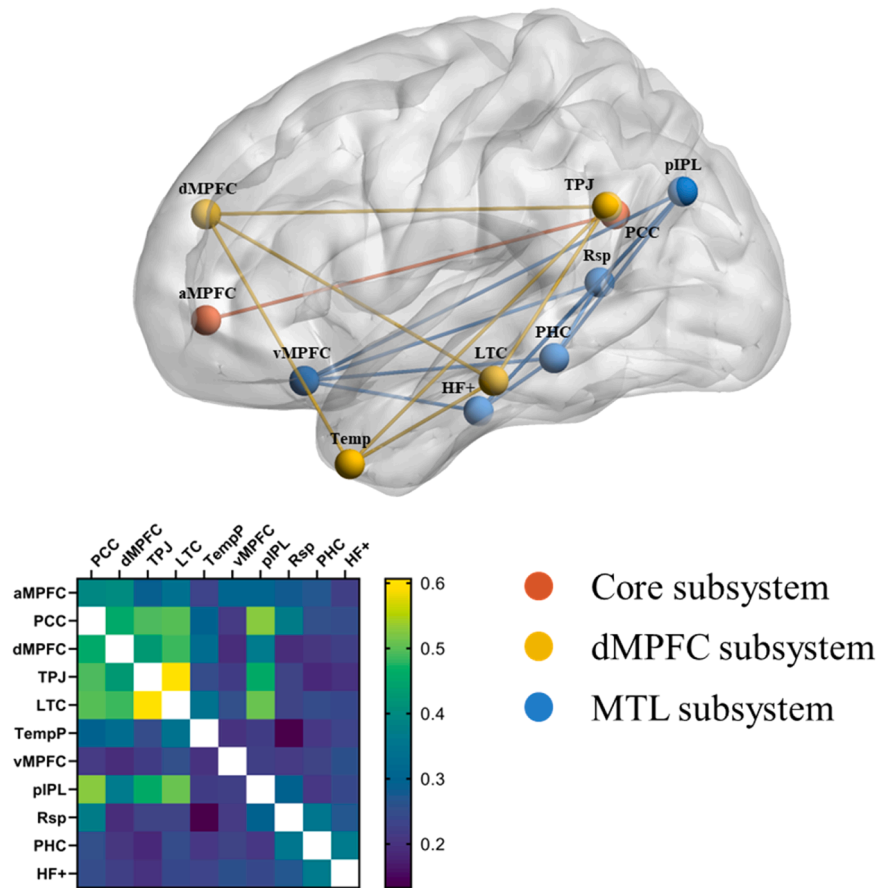


Fig. 1. ROIs of the default mode network and resting-state functional connectivity matrix. aMPFC = anterior medial prefrontal cortex; dMPFC = dorsomedial prefrontal cortex; HF+ = hippocampal formation; LTC = lateral temporal cortex; MTL = medial temporal lobe; PCC = posterior cingulate cortex; PHC = parahippocampal cortex; pIPL = posterior inferior parietal lobule; Rsp = retrosplenial cortex; TempP = temporal pole; TPJ = temporal parietal junction; vMPFC = ventral medial prefrontal cortex.

regions were analyzed to mitigate hemispheric lateralization effects (Fan et al., 2022; Guo et al., 2025). Seed-to-seed connectivity matrices were generated for each participant, and correlation coefficients were converted to z-scores via Fisher's z-transformation. Notably, only positive correlations were included for analyses to minimize false positives. Subsystem connectivity strength was quantified as follows: within-subsystem strength = average z-transformed connectivity across all region pairs within the same subsystem; between-subsystem = average z-transformed connectivity across cross-subsystem region pairs.

2.6. Statistical analysis

Intergroup comparisons of demographic and clinical characteristics were analyzed utilizing analysis of variance (ANOVA) for continuous variables and χ^2 tests for categorical variables. To assess differences between the non-clear delusional group and the clear delusional group in the rsFC strength of subsystems, one-way ANCOVA models were implemented, adjusting for covariates including head motion, gender, age, and years of education. Partial correlation analyses (covariates: age, gender, years of education, head motion) were performed to explore the association between rsFC strength and delusions, with Bonferroni correction applied for multiple comparisons. All statistical calculations were performed using SPSS v25.0, with a two-tailed alpha level of 0.05 as the empirically established threshold for statistical significance.

3. Results

3.1. Comparisons between patients with and without clear delusions

The demographic and clinical characteristics of SCZ patients stratified by the presence or absence of clear delusions are shown in Table 1. No significant intergroup differences were observed in terms of gender, years of education, illness duration, and PANSS negative subscale score (all $p > 0.05$). Significant differences were observed between the two groups in terms of age, severity of delusions, PANSS total score, PANSS positive subscale score, and PANSS general psychopathology subscale score (all $p < 0.05$). Additionally, the group with clear delusions exhibited significantly higher rsFC strength between the core and MTL subsystems, compared to the group without clear delusions ($F = 7.477$, $p = 0.008$), while there were no significant differences in other subsystems (all $p > 0.05$). Complete statistical details are presented in Table 1.

3.2. Correlations between delusions and DMN rsFC strength

The severity of delusions was positively correlated with the rsFC strength between the core and MTL subsystems ($r = 0.370$, $p = 0.001$, Bonferroni corrected $p = 0.006$, Fig. 2a) and between the dMPFC and MTL subsystems ($r = 0.270$, $p = 0.019$, Bonferroni corrected $p = 0.114$), while other subsystems rsFC strength did not show significant correlations (all $p > 0.05$). The correlation matrix is shown in Table 2. Moreover, the positive subscale score of PANSS also showed a significant positive correlation with rsFC strength between the core-MTL

Table 1

Comparisons between patients with and without clear delusions.

	Non-clear delusions (n=19)	Clear delusion (n=60)	F/x ²	P-value
Gender (M/F)	5/14	25/35	1.444	0.230
Age (years old)	29.95 ± 10.086	24.93 ± 7.824	5.133	0.026
Years of education (years)	11.32 ± 3.367	11.80 ± 3.349	0.301	0.585
Duration of illness (years)	2.5 ± 1.777	2.21 ± 1.929	0.332	0.566
Delusions	1.74 ± 0.806	5.57 ± 0.927	261.108	< 0.001
PANSS	118.95 ± 14.539	143.95 ± 20.085	25.162	< 0.001
Positive symptoms	15.32 ± 4.217	28.85 ± 5.480	87.302	< 0.001
Negative symptoms	35.00 ± 5.963	34.45 ± 6.371	0.111	0.740
General psychopathology symptoms	57.32 ± 8.551	67.45 ± 10.346	14.954	< 0.001
DMN subsystem rsFC strength				
core	0.36 ± 0.206	0.40 ± 0.226	0.334	0.565
dMPFC	0.40 ± 0.138	0.43 ± 0.139	0.247	0.620
MTL	0.23 ± 0.068	0.26 ± 0.088	1.152	0.287
core-dMPFC	0.34 ± 0.118	0.39 ± 0.13	1.073	0.304
core-MTL	0.25 ± 0.063	0.30 ± 0.081	7.477	0.008
dMPFC-MTL	0.23 ± 0.052	0.26 ± 0.071	3.020	0.086

Note: DMN = default mode network; dMPFC = dorsomedial prefrontal cortex; MTL = medial temporal lobe; PANSS = Positive and Negative Syndrome Scale; rsFC = resting-state functional connectivity. Bold font indicates statistical significance.

subsystems ($r = 0.330$, $p = 0.004$, Bonferroni corrected $p = 0.024$, Fig. 2b) and between the dMPFC-MTL subsystems ($r = 0.254$, $p = 0.028$, Bonferroni corrected $p = 0.168$).

We additionally investigated correlations between core-MTL rsFC strength and other items of the PANSS positive subscale (e.g., grandiosity, suspiciousness, hostility). Results revealed that the correlations of grandiosity, suspiciousness, and hostility showed significance, but no associations survived multiple comparison correction (all Bonferroni corrected $p > 0.05$). Please see **Supplementary Table 2** for details. Given these suggestive (though non-significant after correction) relationships, we performed competitive regression analyses to examine the unique contribution of delusions. After controlling for other positive symptoms, delusions remained a significant independent factor of core-MTL rsFC strength, accounting for an additional 6.1 % of variance ($\Delta R^2 = 0.061$, $F(\Delta R^2) = 5.457$, $p(\Delta R^2) = 0.022$). Please refer to **Supplementary. Competitive Regression Analyses** for the details.

3.3. Edge-specific correlations between core-MTL rsFC strength and delusions

All rsFC edges between the core and MTL subsystems were extracted, totaling 10 edges: aMPFC-vMPFC, aMPFC-pIPL, aMPFC-Rsp, aMPFC-PHC, aMPFC-HF+, PCC-vMPFC, PCC-pIPL, PCC-Rsp, PCC-PHC and PCC-HF+. Correlation analysis results showed that three edges were significantly correlated with delusions, but only PCC-pIPL ($r = 0.369$, $p = 0.001$, Bonferroni corrected $p = 0.011$, Fig. 2c) and PCC-Rsp ($r = 0.320$, $p = 0.005$, Bonferroni corrected $p = 0.046$, Fig. 2d) remained statistically significant after multiple comparisons correction. Comparisons between patients with and without clear delusions were also conducted regarding the PCC-Rsp and PCC-pIPL rsFC edges. The rsFC of PCC-Rsp showed a significant difference between the two groups ($F = 13.450$, $p < 0.001$, Bonferroni corrected $p < 0.001$), while the group difference in PCC-pIPL rsFC showed marginal significance ($F = 3.483$, $p = 0.066$, Bonferroni corrected $p = 0.132$).

3.4. Sensitivity analyses and Exploratory analyses

To evaluate the robustness of the primary findings, sensitivity analyses were performed by incorporating both positive and negative rsFC edges (rather than positive-only edges) in calculating DMN subsystem connectivity strength. Replicating our main results, the core-MTL rsFC strength remained significantly different between groups with and without delusions ($F = 0.436$, $p = 0.040$) and correlated with delusion severity ($r = 0.343$, $p = 0.003$, Bonferroni corrected $p = 0.015$). Please see **Supplementary. Sensitivity Analyses** for details.

Moreover, to address potential spatial specificity concerns, exploratory analyses extended the framework to include whole-brain DMN regions (rather than only left-hemisphere DMN regions). While the group difference in core-MTL connectivity showed marginal significance ($F = 2.230$, $p = 0.060$), the correlation with delusion severity remained significant ($r = 0.283$, $p = 0.014$, Bonferroni corrected $p = 0.084$), though attenuated after multiple comparison correction. Please see **Supplementary. Exploratory Analyses** for details.

4. Discussion

This study provides novel neurobiological evidence revealing subsystem-specific DMN connectivity patterns associated with delusions in patients with FESCZ. Three key findings are as follows: (1) compared with patients without clear delusions, patients with clear delusions displayed significantly enhanced rsFC strength between the core-MTL subsystems; (2) the rsFC strength in the core-MTL subsystems was positively correlated with the severity of delusions and PANSS positive subscale score; (3) two specific rsFC edges (PCC-Rsp and PCC-pIPL) exhibited significant correlations with delusions.

The differential connectivity patterns observed in the core-MTL subsystems hold particular clinical significance, since these subsystems play established roles in self-referential processing and memory integration. According to a previous study, reduced rsFC strength between the core-MTL subsystem is a stable deficit in patients with SCZ (Fan et al., 2022). Our findings further indicated that patients with clear delusions exhibited higher rsFC strength in the core-MTL subsystem compared to those without clear delusions. The core subsystem plays a foundational role in self-referential processing, while the MTL subsystem is involved in memory retrieval, information integration, and prospective scenario construction (Andrews-Hanna et al., 2014, 2010; Jenkins and Mitchell, 2011). A previous study has observed enhanced core-MTL connectivity during rumination, a repetitive self-referential processing (Chen et al., 2020). Therefore, increased rsFC strength between the core-MTL subsystems may indicate heightened self-referential processing involving memory retrieval, which may lead to delusions. We hypothesize that increased rsFC strength between the core-MTL subsystems may represent the neural substrate of abnormal integration of self-referential memory and information, potentially facilitating the formation and maintenance of delusions in FESCZ patients.

The results of the post-hoc analyses further support our hypothesis. Specifically, the post-hoc analysis revealed significant differences in PCC-Rsp and PCC-pIPL between the two groups. Both rsFC edges contained the PCC, a key component of the midline cortical structures, and is closely associated with self-referential processing (Andrews-Hanna et al., 2010). Damage to midline cortical structures may lead to delusions by misinterpreting the emotional significance of social events. SCZ patients exhibit stronger midline cortical activation when faced with neutral emotional contexts (Holt et al., 2011). The PCC is involved in self-referential processing, episodic memory, and navigation (Andrews-Hanna et al., 2014; Rolls et al., 2023). Patients with persecutory delusions exhibit increased PCC activation during self-referential tasks (Blackwood et al., 2004). Relatives of SCZ patients also exhibited abnormal PCC response amplitudes during social reflection processing, which is associated with delusional thinking (Brent et al., 2014). Additionally, a study found that the decreased degree centrality of the dorsal

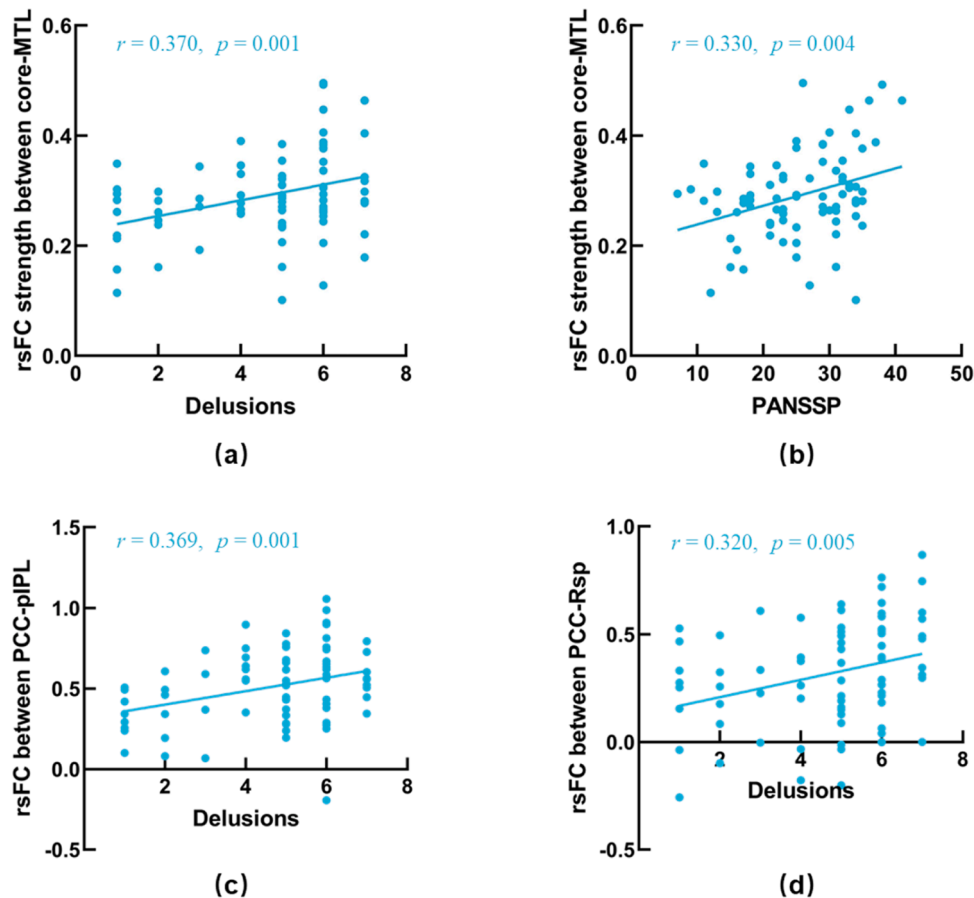


Fig. 2. Correlations between delusions and DMN subsystem rsFC strength. MTL = medial temporal lobe; PANSSP = positive subscale of Positive and Negative Syndrome Scale; PCC = posterior cingulate cortex; pIPL = posterior inferior parietal lobule; Rsp = retrosplenial cortex; TempP = temporal pole; rsFC = resting-state functional connectivity.

Table 2
Correlations between delusions and DMN rsFC strength.

<i>r</i> (<i>p</i>)	Delusions	PANSS	Positive symptoms	Negative symptoms	General psychopathology symptoms
DMN subsystems rsFC strength					
core	0.085(0.470)	0.045(0.704)	0.060(0.611)	−0.114(0.330)	0.067(0.570)
dMPFC	0.062(0.599)	0.120(0.305)	0.061(0.605)	0.047(0.690)	0.127(0.278)
MTL	0.179(0.124)	0.093(0.430)	0.134(0.253)	−0.120(0.304)	0.123(0.294)
core-dMPFC	0.124(0.288)	0.184(0.115)	0.217(0.062)	−0.059(0.616)	0.188(0.106)
core-MTL	0.370(0.001)	0.176(0.131)	0.330(0.004)	−0.109(0.351)	0.124(0.291)
dMPFC-MTL	0.270(0.019)	0.130(0.267)	0.254(0.028)	−0.080(0.497)	0.060(0.608)

Note: DMN = default mode network; dMPFC = dorsomedial prefrontal cortex; MTL = medial temporal lobe; PANSS = Positive and Negative Syndrome Scale; rsFC = resting-state functional connectivity. Bold font indicates statistical significance.

PCC during working memory tasks was negatively associated with delusion severity in SCZ patients (Wang et al., 2022). These findings suggest that the PCC plays a key role in delusions in patients with FESCZ. Rsp serves as an essential gateway to facilitate information transmission supporting episodic memory (Kaboodvand et al., 2018), and delusions are closely associated with fictional memories in episodic memory (Lee et al., 2007). A lesion network mapping study provided convergent evidence identifying Rsp as a common connector among all lesion brain locations associated with delusions (Darby et al., 2017). Additionally, the IPL plays an essential role in integrating sensory information to support complex cognitive tasks, and its diverse functions highlight its importance in cognition (Catani et al., 2017). Impaired integration of sensory information may contribute to the emergence of positive symptoms in SCZ (Weilnhammer et al., 2020). In patients with Alzheimer’s disease, those with delusions showed significantly reduced

connectivity between the left IPL and other regions of the DMN (Qian et al., 2019). Furthermore, a study suggests that connectivity between the PCC and IPL is involved in the integration of spatial and contextual information (Rolls et al., 2023). Based on these findings, we speculate that alterations in PCC-Rsp and PCC-pIPL connectivity may induce delusions in patients with FESCZ by promoting the integration of distorted memory and distorted sensory information. This study elucidated the relationship between delusions and subsystems of the DMN. A key methodological strength lies in the exclusive recruitment of drug-naïve SCZ patients, eliminating confounding effects of antipsychotic medications on DMN activity. The findings in this study suggest some potential clinical applications. The core-MTL connectivity patterns may serve as a potential biomarker to aid psychiatrists in assessing delusion severity. Additionally, interventions targeting core-MTL pathways may alleviate the severity of delusions in SCZ patients.

PCC-focused neuromodulation may be a promising intervention for normalizing core-MTL hyperconnectivity.

The following limitations should be acknowledged. First, the small sample size (especially in the non-clear delusional subgroup) may constrain statistical power and generalizability. Second, the cross-sectional design of this study precludes causal inferences. Future studies with larger sample sizes and longitudinal designs are needed to address this issue. Third, we operationalized delusions as a single construct, overlooking the phenomenological heterogeneity of delusional subtypes, such as influential delusions, religious delusions, paranoid delusions, negative affective delusions, and somatic delusions (Paolini et al., 2016). Different delusional subtypes may exhibit distinct neurofunctional signatures. Fourth, the P1 item of the PANSS serves as a useful but rough measure for assessing delusions. Further studies should incorporate scales specifically designed for delusion assessment, such as the Dimensions of Delusional Experience Scale (Kendler et al., 1983) and the Peters et al. Delusions Inventory (Wang et al., 2017).

5. Conclusions

In summary, our study demonstrates that SCZ patients with clear delusions exhibit increased rsFC strength between the core and MTL subsystems. Moreover, the rsFC strength is correlated with the severity of delusions. These findings suggest that connectivity between the core-MTL subsystems of DMN may serve as a potential biomarker for delusions in patients with FESCHZ, which holds significant implications for the identification and treatment of delusions.

Ethical statement

The authors declare that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

CRedit authorship contribution statement

Liusu Wang: Writing – review & editing. **Anzhen Wang:** Resources. **Ruomei Fan:** Writing – review & editing. **Rongrong Zhu:** Resources. **Data curation.** **Jianliang Gao:** Resources. **Qihui Guo:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **Dongmei Wang:** Writing – review & editing, Project administration. **Zhang Xiang-Yang:** Writing – review & editing, Project administration, Funding acquisition.

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Declaration of Competing Interest

The authors report no competing interests.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.ajp.2025.104733](https://doi.org/10.1016/j.ajp.2025.104733).

Data availability

The data that support the findings of this study are publicly available.

The corresponding author can be contacted upon reasonable request.

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