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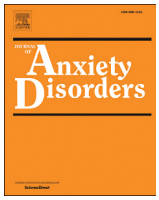

Altered resting-state amygdala-cerebellar functional connectivity is associated with intolerance of uncertainty in patients with obsessive-compulsive disorder: A longitudinal study

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ABSTRACT

Objectives: Intolerance of uncertainty (IU) plays an important role in the pathology of obsessive-compulsive disorder (OCD). The amygdala and anterior insula (AI) appear to be important neural correlates of IU. However, the relationship between altered resting-state functional connectivity (rsFC) and IU in OCD patients has not been reported.

Methods: This study recruited 39 patients with OCD and 45 healthy controls (HC). IU was measured using the Intolerance of Uncertainty Scale (IUS). The seed-to-voxel method was used to construct rsFC maps. Between-group differences in rsFC and their correlations with IU were analyzed. Following an eight-week psychological intervention, OCD patients underwent a second assessment. The association between rsFC changes and IU changes was investigated.

Results: OCD patients exhibited significantly higher IUS scores. Significant alterations in rsFC were observed between the left amygdala and the left cerebellum posterior lobe (CPL), as well as between the left AI and the left cuneus in OCD patients. In the OCD group, only the left amygdala - left CPL rsFC significantly correlated with IUS scores. No significant correlations were found between rsFC and IUS scores in the HC group. Longitudinal analysis revealed that changes in the left amygdala - left CPL rsFC were significantly associated with changes in IUS scores.

Conclusions: This study establishes amygdala-cerebellar rsFC as a specific neural signature of IU in patients with OCD, patterns absent in healthy controls. Moreover, the amygdala-cerebellar rsFC displayed longitudinal coupling with IU changes. These findings provide novel insights into the neural mechanisms of OCD pathology.

1. Introduction

Obsessive-compulsive disorder (OCD) is a prevalent psychiatric disorder with a lifetime prevalence rate of 2~3 % and is classified by the World Health Organization among the top 10 most disabling psychiatric conditions (Kugler et al., 2013). This disorder is characterized by distressing obsessive thoughts and compulsive behaviors, frequently co-occurring with avoidance behaviors (Hirschtritt et al., 2017). Obsessive thoughts induce worry and anxiety, while compulsive behaviors are attempts or efforts to eliminate this psychological distress (Knowles & Olatunji, 2023). Patients with OCD typically experience a chronic and recurring course, resulting in progressive deterioration of both quality of life and social functioning (Bora, 2022; Subramaniam et al., 2013).

Patients with OCD show clinically elevated levels of intolerance of uncertainty (IU) (Tolin et al., 2003). IU is a dispositional incapacity to tolerate perceptions of uncertainty, which can be further categorized into two subtypes: prospective IU and inhibitory IU (Carleton, 2016). Prospective IU involves anxiety about reducing uncertainty or increasing certainty in the future (e.g., 'I should be able to organize everything ahead of time'), whereas inhibitory IU refers to anxiety about inhibiting actions or experiences caused by uncertainty (e.g., 'The smallest doubt prevents me from acting') (Bottesi et al., 2019; Carleton, Norton, et al., 2007). IU, also known as fear of uncertainty, has been considered to be the basic component underlying anxiety-related fears (Carleton, Sharpe, et al., 2007). For example, fear of illness typically

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encompasses the fear of uncertainty caused by the illness: if I get sick, how will I live in the future? Fear is an evolutionarily adaptive emotion that protects individuals away from danger (Carleton, Norton, et al., 2007). However, this adaptive mechanism becomes a double-edged sword when excessive IU creates significant challenges for individuals. Specifically, individuals with excessive IU are more likely to interpret uncertainty as threatening and show heightened stress responses when perceiving such threats (Buhr & Dugas, 2009; Carleton, Norton, et al., 2007).

Higher IU is strongly associated with excessive anxiety and worry (Buhr & Dugas, 2006; Dugas et al., 2012; Ladouceur et al., 2000). Patients with anxiety-related disorders exhibit widespread deficits in IU, including OCD, generalized anxiety disorder, and posttraumatic stress disorder (Fetzner et al., 2013; Kusec et al., 2016; McEvoy et al., 2019; Tolin et al., 2003). Boelen and Reijntjes (2009) demonstrated a positive association between IU and OCD symptoms. In both nonclinical and clinical samples, IU was significantly associated with all four common subdimensions of OCD symptoms (Fourtounas & Thomas, 2016; Pinciotti et al., 2021). Pozza et al. (2019) found that IU can predict the severity of OCD symptoms one year later. Furthermore, IU could be used as a predictor for treatment outcome in OCD patients, with higher IU levels being associated with poorer reduction of OCD symptoms (Kyrios et al., 2015; Wilhelm et al., 2015).

The neural mechanisms underlying IU are still not well understood, but emerging evidence from neuroimaging studies suggests the anterior insula (AI) and amygdala appear to be important neural correlates (Tanovic et al., 2018). The AI is crucial for constructing interoceptive awareness and integrating internal and external interoceptive information (Bud Craig, 2011; Bud Craig & D, A., 2009). The amygdala is mainly involved in emotion, motivation, memory, and processing of input stimuli (Janak & Tye, 2015; LeDoux, 2007). In situations of uncertainty, individuals must evaluate the level of threat and manage aroused emotions based on a variety of information, which implicates the functioning of the AI and the amygdala. Notably, previous literature has supported the associations between IU and neural activity in the AI and the amygdala during uncertainty tasks in both clinical and nonclinical populations. Simmons et al. (2008) found a positive association between IU and insula activity during affective ambiguity in a nonclinical population. Similarly, Gorka et al. (2016) observed increased AI activation during an uncertain reward task, which was positively associated with IU in a nonclinical population. Oathes et al. (2015) found that IU was positively associated with AI activity in patients with generalized anxiety disorder. Associations between amygdala activity and IU have also been reported. For example, Krain et al. (2008) found that IU was positively associated with amygdala activity during decision-making in adolescents with social anxiety disorder. Schienle et al. (2010) found that IU positively correlated with amygdala activity when experiencing uncertainty.

Functional connectivity (FC) between brain regions is another important perspective for understanding neural mechanisms. Both AI-related FC and amygdala-related FC during uncertainty tasks have been found to exhibit associations with self-reported IU. Specifically, a previous study demonstrated that during a computerized gambling task, self-reported IU showed significant associations with FC between the right AI and the dorsal anterior cingulate cortex (dACC), as well as between the amygdala and the prefrontal cortex (Assaf et al., 2018). Radoman and Gorka (2023) found significant correlations between self-reported IU and the right AI-dACC FC, as well as the right AI - dorsolateral prefrontal cortex (dlPFC) FC during unpredictable reward decision-making. Moreover, the resting-state FC (rsFC) also exhibits associations with self-reported IU. A previous study revealed that rsFC between the left AI and the right media or inferior frontal gyrus (M/IFG), as well as between the right AI and the right M/IFG correlated with self-reported inhibitory IU, while rsFC between the left AI and the dACC correlated with self-reported prospective IU (DeSerisy et al., 2020).

Converging evidence from neuroimaging studies demonstrates that patients with OCD exhibit widespread rsFC alterations in both the AI and amygdala (Liu et al., 2022). For example, heightened rsFC between the right amygdala and right postcentral gyrus during resting state has been reported in patients with OCD (Pico-Perez et al., 2019). Heightened rsFC between AI and major brain regions of the default mode network also has been reported in patients with OCD (Xia et al., 2020). Building upon these findings and the close relationship between IU and OCD symptoms, we posited that IU-related rsFC patterns may be pathologically altered in patients with OCD, potentially constituting a neural mechanism underlying OCD pathology.

However, little is known about the specific FC associated with abnormal IU in OCD patients. No studies have explored the relationship between IU and FC in OCD patients. Therefore, this study aimed to explore the rsFC abnormalities and their relationship with IU in patients with OCD, using the AI and amygdala as seeds. Three hypotheses were formulated in this study: (1) IU would be higher in OCD patients than in HC, and IU would be positively associated with the severity of OCD symptoms; (2) rsFC of seeds would be altered in patients with OCD; and (3) these altered rsFC would be significantly associated with IU.

2. Methods

2.1. Participants

The final study population comprised 39 outpatients with OCD recruited through two recruitment channels: referrals from clinical psychiatrists and social media platforms. From an initial cohort of 40 patients, one individual was excluded due to excessive head motion. Inclusion criteria comprised: 1) age 16–55 years; 2) Han Chinese ethnicity; 3) DSM-5 confirmed diagnosis by certified psychiatrists using the Structured Clinical Interview for DSM-5 (SCID). Exclusion criteria comprised: 1) pregnancy or lactation status; 2) neurostructural abnormalities; 3) substance abuse; 4) high suicide risk; 5) MRI contraindications (e.g., metal implants).

The comparison cohort consisted of 45 demographically matched (age, gender, and years of education) healthy controls (HC) recruited from local communities. Selection required: 1) no diagnosis of any psychiatric disorders; 2) no family history of psychiatric disorders; 3) no psychotropic medication exposure; 4) no substance abuse; 5) no MRI contraindications (e.g., metal implants). All participants provided written informed consent under ethical oversight (Approval No. H22099) from the Institutional Review Board of the Institute of Psychology, Chinese Academy of Sciences.

This study shares partial datasets, MRI protocols, and image preprocessing pipelines with our prior work (Guo et al., 2025). However, significant distinctions exist between the two studies in design, objectives, and analytical frameworks, which ensure the uniqueness of this study. First, Guo et al. (2025) employed a cross-sectional design utilizing baseline data exclusively, whereas this study adopted a longitudinal approach incorporating both baseline and post-treatment datasets to evaluate dynamic neural changes following intervention. Second, Guo et al. (2025) investigated altered subsystem-specific rsFC within the default mode network in OCD, whereas this study specifically targeted the altered rsFC signature of IU in OCD.

2.2. Clinical assessment

This study is an integral component of a clinical trial, which has been registered at https://www.clinicaltrials.gov (NCT05552014). OCD patients underwent the first assessment at baseline and received the second assessment (post-treatment assessment) after an eight-week group psychological intervention based on Natural Psychotherapy, a novel psychotherapy originating from Morita therapy (Zhang et al., 2000). This intervention was structured as weekly sessions (8 total). HCs received a single assessment. The assessments include clinical scales and functional MRI scans.

The Yale-Brown Obsessive-Compulsive Scale (YBOCS), a psychometrically validated tool for assessing OCD symptoms, was implemented to quantify symptom severity (Goodman et al., 1989). Symptom domains were separately scored through its obsession subscale (YBOCS-O) and compulsion subscale (YBOCS-C), with higher scores indicating greater severity. OCD patients were personally interviewed by psychological assessors using the YBOCS. The psychological assessors were professionally trained with excellent inter-rater consistency (Cronbach's $\alpha = 0.865$).

The 12-item Intolerance of Uncertainty Scale (IUS) was used to measure IU. The Chinese version of the 12-item IUS has robust reliability and validity (Zhang et al., 2017). A higher IUS score indicates greater IU. The IUS was initially conceptualized as comprising two factors: prospective (items 1–7), and inhibitory (items 8–12) (Carleton, Norton, et al., 2007; Khawaja & Yu, 2010), but contemporary psychometric evidence supports that a bifactor model structure is more suitable for this scale, which suggests it is appropriate to use the total score of IUS when assessing IU (Hale et al., 2016; Shihata et al., 2018).

2.3. MRI protocol

A GE Discovery MR750 3 T scanner was used to acquire the resting-state functional MRI images with the following parameters: repetition time = 2000 ms; flip angle = 90°; echo time = 30 ms; field of view = 224 mm; voxel size = 3.5 mm; 64 × 64 acquisition matrix. Each participant experienced 240 consecutive scans lasting 8 min. During scanning, participants were instructed to relax, close their eyes, and remain awake.

2.4. Image preprocessing

Neuroimaging preprocessing was executed in DPABI V8.0_231111 using standardized pipelines. The preprocessing steps included: 1) Spatial normalization of T1-weighted images to the Montreal Neurological Institute template standard space (MNI152); 2) Removal of the initial 10 timepoints (230 timepoints retained) of the functional image to stabilize signal acquisition; 3) Slice-timing correction; 4) Head motion correction; 5) Spatial realignment; 6) Covariate regression; 7) Two-stage normalization: functional image normalized to T1 space followed by normalization to MNI152 space; and 8) Bandpass filtering (0.01–0.1 Hz). Quality control eliminated one OCD patient due to excessive head motion based on the thresholds of average FD-Jenkinson (> 0.2 mm).

2.5. rsFC

The seed-to-voxel method was applied to detect brain regions associated with the regions of interest (ROIs). Four ROIs were included in this study: the left AI, the right AI, the left amygdala, and the right amygdala. Masks for the bilateral AI were obtained from a previous insula parcellation study (Kelly et al., 2012). Spherical masks for the bilateral amygdala were obtained from the Anatomical Automatic Labeling (AAL3) atlas (Rolls et al., 2020), centered on peak coordinates with a radius of 4 mm. Fisher's z-transformations were performed to normalize the correlation coefficients to generate standardized rsFC maps.

2.6. Statistical analysis

Two-sample t-tests and x^2 tests were employed to detect between-group differences in demographic variables, with Cohen's d as effect size. One-way analysis of covariance was used to detect between-group differences in IUS scores, with age, gender, and years of education as covariates, and partial η^2 as effect size.

For functional images, ANCOVAs were used to detect between-group differences in rsFC maps, with head motion, age, gender, and years of education as covariates. Gaussian random field (GRF) correction (cluster threshold $p < 0.05$, voxel threshold $p < 0.01$) was applied to adjust for multiple comparisons in rsFC. The peak MNI coordinate for each cluster exhibiting significant between-group differences was selected as the central point for a spherical mask, with a radius of 4 mm, from which rsFC values were extracted. Subsequently, ANCOVAs were applied to detect between-group differences in these extracted rsFC values, with head motion, age, gender, and years of education as covariates, and partial η^2 as effect size. Partial correlation analyses were performed to detect correlations between altered rsFC and clinical variables in patients with OCD, using head motion, gender, age, and years of education as covariates. Bonferroni correction was applied to adjust for multiple statistical comparisons in partial correlation analyses.

In the data of the second assessment, paired-sample t-tests were employed to detect within-group differences in IUS scores and altered rsFC among OCD patients after an eight-week psychological intervention. A partial correlation analysis was performed to detect the correlation between changes in altered rsFC and changes in IUS scores among patients with OCD. Statistical analyses were conducted using DPABI (V8.0_231111) and SPSS (V25.0). Statistical significance was defined as P-values less than 0.05 (two-tailed).

3. Results

3.1. Demographic and clinical characteristics

Table 1 demonstrates that the HC and OCD groups did not exhibit significant differences in terms of gender, age, and years of education (all $p > 0.05$). The OCD group exhibited significantly higher IUS scores ($F = 7.707$, $p = 0.007$, partial $\eta^2 = 0.117$) than the HC group.

3.2. Between-group differences in rsFC

As shown in Fig. 1, the rsFC was significantly altered in the OCD group compared to the HC group between the left amygdala and left cerebellum posterior lobe (CPL) (34 voxels, peak MINI coordinate: −36, −63, −21) ($F = 31.840$, $p < 0.001$, partial $\eta^2 = 0.290$), and between the left AI and the left cuneus (39 voxels, peak MINI coordinate: −18, −84, 21) ($F = 22.119$, $p < 0.001$, partial $\eta^2 = 0.221$). No significant differences were found between the two groups in the rsFC maps with the right amygdala or the right AI as seeds.

Table 1
Demographic and clinical characteristics.

	HC (n=45)	OCD (n = 39)	$t/F/x^2$	p-value	Cohen's d/ $\eta 2$
Gender (M/F)	26/19	23/17	0.012	0.912	
Age	28.32 ± 9.586	30.7 ± 9.083	−1.168	0.246	−0.275
Years of education	15.33 ± 3.912	15.5 ± 2.766	−0.238	0.813	−0.055
Onset age		19.53 ± 7.474			
Illness duration		11.28 ± 8.078			
YBOCS		20.21 ± 6.182			
YBOCS-O		10.56 ± 3.152			
YBOCS-C		9.64 ± 20.21			
IUS	28.93 ± 9.012	35.15 ± 12.156	7.707	**0.007**	0.117

Note: IUS = Intolerance of Uncertainty Scale; YBOCS = Yale-Brown Obsessive-Compulsive Scale; YBOCS-O = obsession subscale of YBOCS; YBOCS-C = compulsion subscale of YBOCS. Bold font indicates statistical significance.

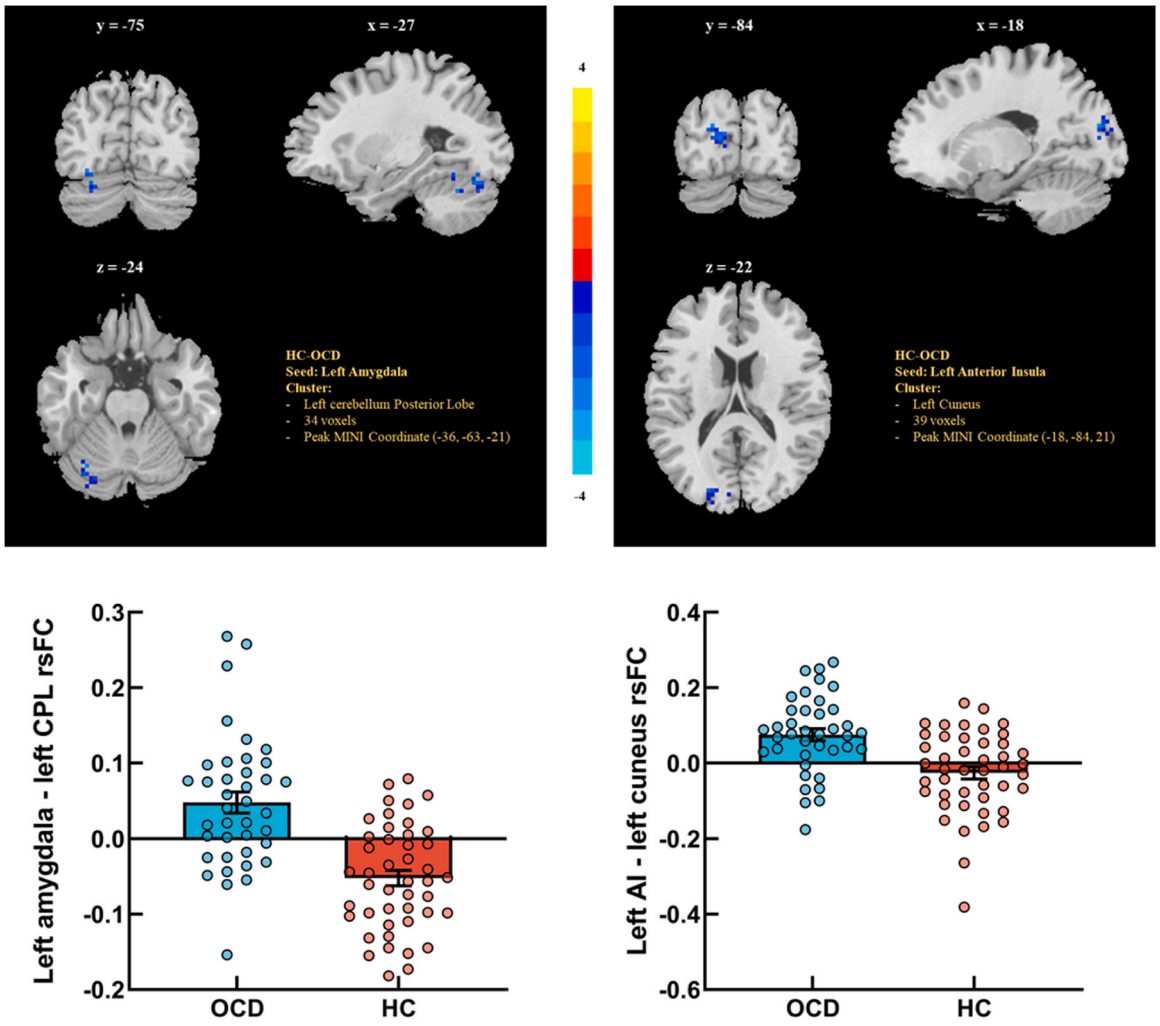

Fig. 1. group comparisons in resting-state functional connectivity maps. note: AI = anterior insula; CPL = cerebellum posterior lobe.

3.3. Relationship between altered rsFC and clinical scales

At the first assessment, all correlations between the IUS, YBOCS, and YBOCS subscales were significant in the OCD group (all Bonferroni corrected $p < 0.05$). The rsFC between the left amygdala and left CPL significantly correlated with IUS scores ($r = -0.419$, $p = 0.021$). In contrast, the rsFC between the left AI and left cuneus was not significantly correlated with the IUS scores ($r = -0.315$, $p = 0.090$). In addition, neither altered rsFC correlated with the scores of YBOCS or any YBOCS subscales (all Bonferroni corrected $p > 0.05$). In the HC group, neither altered rsFC significantly correlated with the IUS scores ($r = 0.209$, $p = 0.316$). Please see Table 2 for details.

At the second assessment, the rsFC between the left amygdala and left CPL also showed significant correlation with IUS scores in the OCD group ($r = -0.447$, $p = 0.025$), while the rsFC between the left AI and left cuneus showed no significant correlation with IUS scores ($r = -0.004$, $p = 0.987$). These findings were consistent with the findings at the first assessment. Please see Table 2 for details.

3.4. Relationship between the changes of altered rsFC and IU in OCD patients

Following an eight-week psychological intervention, no significant changes were observed in either the rsFC between the left amygdala and

Table 2
Correlations between altered rsFC and clinical scales.

	All $r(p)$	HC $r(p)$		First assessment of OCD $r(p)$		Second assessment of OCD $r(p)$	
	IUS	**Left amygdala - left CPL**	**Left AI - left cuneus**	**Left amygdala - left CPL**	**Left AI - left cuneus**	**Left amygdala - left CPL**	**Left AI - left cuneus**
IUS		0.209(0.316)	−0.185(0.376)	**−0.419(0.021)**	−0.315(0.090)	**−0.447(0.025)**	−0.004(0.987)
YBOCS	**0.671 (<0.001)**			−0.007(0.969)	−0.247(0.187)	−0.288(0.117)	−0.132(0.478)
YBOCS-O	**0.681 (<0.001)**			−0.009(0.962)	−0.405(0.026)	−0.243(0.189)	−0.223(0.227)
YBOCS-C	**0.527 (<0.001)**			−0.004(0.984)	−0.051(0.790)	−0.225(0.225)	−0.001(0.994)

Note: AI = anterior insula; CPL = cerebellum posterior lobe; IUS = Intolerance of Uncertainty Scale; YBOCS = Yale-Brown Obsessive-Compulsive Scale; YBOCS-O = obsession subscale of YBOCS; YBOCS-C = compulsion subscale of YBOCS. Bold font indicates statistical significance after Bonferroni correction.

left CPL ($t = 1.097$, $p = 0.280$, Cohen's $d = 0.248$) or IUS scores ($t = 0.557$, $p = 0.581$, Cohen's $d = 0.126$) in patients with OCD. But changes in rsFC between the left amygdala and left CPL significantly correlated with changes in IUS scores ($r = -0.348$, $p = 0.030$). Please see Fig. 2 for details.

4. Discussion

In this study, we found that (1) IU was significantly higher in OCD patients than in HCs, and IUS scores positively correlated with YBOCS scores; (2) OCD patients showed altered rsFC between the left amygdala and the left CPL, as well as between the left AI and the left cuneus; (3) Only the altered rsFC between the left amygdala and the left CPL showed a significant negative correlation with the IU; (4) Longitudinal changes in rsFC between the left amygdala and left CPL significantly correlated with changes in IU. These findings collectively highlight the close relationship between the left amygdala - left CPL rsFC and IU.

Our first hypothesis was confirmed in this study that IU was higher in OCD patients and that IU positively correlated with the severity of OCD symptoms, which is consistent with the findings of previous studies (Holaway et al., 2006; Pinciotti et al., 2021; Tolin et al., 2003). These findings further validate the strong relationship between IU and OCD symptoms. IU is recognized as a core factor in the pathology of OCD and plays an important role in the development and maintenance of OCD (Carleton, 2012; Knowles & Olatunji, 2023). According to the IU model, if a situation involving uncertainty exceeds the threshold of IU, negative emotions will be triggered and then the individuals' preventive system is activated to engage in safety behaviors, rumination, compulsions, and avoidance to eliminate uncertainty (Einstein, 2014). Thus, excessive IU may lead to excessive worry and repetitive behaviors. For example, when faced with the same dirty stimulus, OCD patients may experience an emotional meltdown and wash their hands multiple times, whereas HCs may tolerate the uncertainty of being dirty. Furthermore, previous studies have revealed that OCD symptoms can be improved through manipulating uncertainty beliefs in laboratory settings (Faleer et al., 2017; Geok et al., 2022). Thus, as summarized in a previous review (Knowles & Olatunji, 2023), IU may be a cognitive vulnerability in OCD patients.

Our rsFC findings revealed amygdala–cerebellar connectivity as a neural correlate of IU specifically in OCD. The cerebellar plays a crucial role in motor control and learning (Freeman, 2015; Hull & Regehr, 2022; Kim et al., 2024). A previous study indicated that the amygdala regulates sensory input to the cerebellar (Farley et al., 2016). According to the neural two-process learning theory, the amygdala mediates memory for high emotional arousal stimuli, which then enhances the cerebella's second memory for behavioral patterns (Mintz & Wang-Ninio, 2001). This model has been validated in rats (Farley et al., 2016; Freeman et al., 2021). Based on our clinical experiences, this model may reflect reinforcement learning mechanisms in OCD pathology. For example, if patients are initially distressed by the thought that they may lose their confidential USB flash drive, they might only check their pockets once to eliminate the uncertainty. However, as symptoms progress, they may check it more and more often and generalize these checking behaviors to other situations, reflecting an increase in IU and reinforcement learning of checking behaviors. Therefore, we speculated that the altered rsFC between the left amygdala and the left CPL may be related to the reinforcement process of IU in patients with OCD. Notably, this rsFC showed no significant correlation with IU in HCs. Thus, the relationship between left amygdala - left CPL rsFC and IU may be a special feature of OCD. This finding highlights the potential application of amygdala-targeted neuromodulation as a precision medicine strategy for OCD. Given the established role of IU in the development and maintenance of OCD symptoms (Carleton, 2012; Knowles & Olatunji, 2023), amygdala-targeted interventions may achieve better outcomes in OCD patients with elevated IU.

Notably, both the IU-related FC during the task and IU-related FC during the resting state have been identified by previous studies (Assaf et al., 2018; DeSerisy et al., 2020; Radoman & Gorka, 2023). Our study also provides evidence for the existence of IU-related FC during resting state in OCD patients. Previous studies found that there was substantial spatial overlap between task-based and resting-state FC networks, which indicates that the brain network exhibits similar connection patterns during the resting state as those during the task (Cole et al., 2014; Smith et al., 2009). A study further demonstrates that rsFC can effectively predict individual differences in brain activity across diverse task conditions (Tavor et al., 2016). These insights may provide a neurobiological framework for understanding why rsFC is implicated in IU even without the evocation of the task. Therefore, we hypothesize that the resting-state IU-related FC identified in this study may reflect latent connectivity features that manifest similarly during task engagement, which warrants systematic validation by future studies.

Interestingly, in this study, only the rsFC in the left amygdala was abnormal in OCD patients. This lateralized abnormality is supported by previous structural findings demonstrating only the left amygdala showed increased size in OCD patients (Szeszko et al., 2004). Previous studies have consistently indicated that the amygdala exhibits hemispheric asymmetries in function and structure (Ocklenburg et al., 2022). The right amygdala is larger than the left amygdala (Pedraza et al., 2004). According to the valence lateralization hypothesis, bilateral amygdalae demonstrate divergent functional specializations in emotional processing (Palomero-Gallagher & Amunts, 2022). Moreover, in this study, altered rsFC between the left AI and the left cuneus was

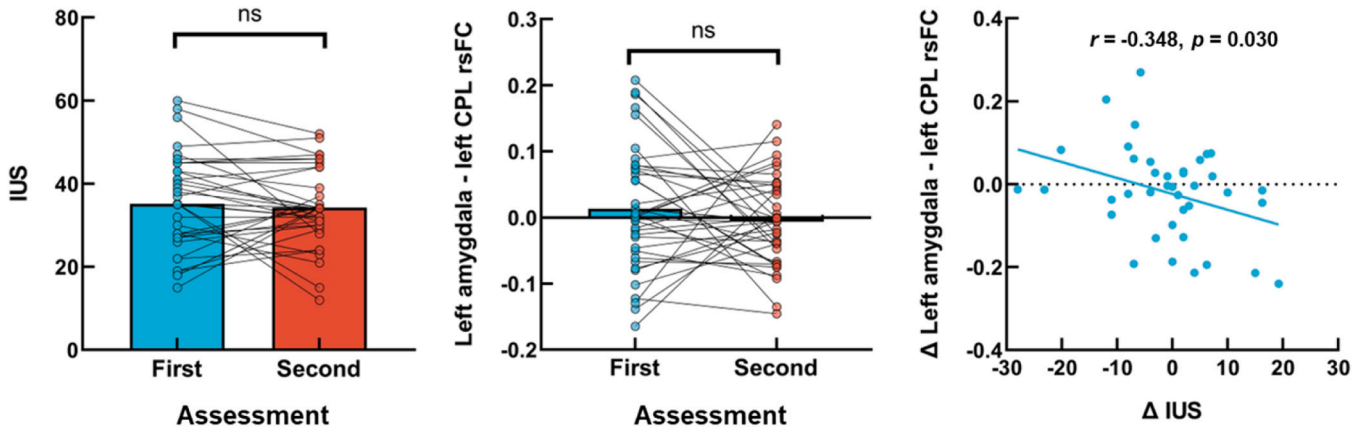

Fig. 2. changes on the left amygdala – cpl resting-state functional connectivity and ius in ocd patients. note: AI = anterior insula; CPL = cerebellum posterior lobe; IUS = intolerance of uncertainty scale; first = first assessment in OCD patients; second = s assessment in OCD patients; ns = no significance; Δ = values in second assessment minus values in the first assessment.

also observed in OCD patients, but it did not show a significant correlation with IU. The cuneus is part of the occipital cortex. A previous study also found altered rsFC between the insula and occipital cortex in OCD patients (Geffen et al., 2021). However, no specific impact of this altered rsFC on OCD symptoms was found. Future studies are necessary to further elucidate the impact of this altered rsFC on OCD.

There are several limitations in this study. First, the self-reported measurement of IU may induce potential bias, as subjective reports may not fully capture implicit cognitive processes. Future studies could benefit from incorporating task-based behavioral paradigms to obtain objective IU metrics with stronger neurobiological correspondence. Second, both the AI and amygdala can be further divided into additional subregions (Kelly et al., 2012; Sah et al., 2003). Differences between these subregions may potentially impact the accuracy of the results. Third, the results may potentially be influenced by the heterogeneity among OCD patients. Notably, IU demonstrates differential associations with OCD symptoms during treatment between the autogenous and reactive subgroups (Belloch et al., 2010). Fourth, this study didn't conduct a priori power analysis to determine the sample size. Due to massive multiple comparisons, general power analysis approaches are not suitable for MRI studies (Joyce & Hayasaka, 2012). Some specialized software programs have been developed for power analysis in the task-based brain activation study (Joyce & Hayasaka, 2012; Mumford & Nichols, 2008). However, to our best knowledge, no tools were developed for the power analysis in the rsFC study, which is a methodological gap requiring urgent resolution in the future. As an interim measure, we performed post-hoc power estimation using a general tool for power analysis to provide some reference information about the power of this study (please see Supplementary. Post-hoc power analysis), acknowledging that these conventional statistical estimates may inadequately capture the analytical complexity of rsFC data. Future studies are necessary to identify these limitations.

5. Conclusions

This study establishes amygdala-cerebellar rsFC as a specific neural signature of IU in patients with OCD, patterns absent in healthy controls. Moreover, the amygdala-cerebellar rsFC displayed longitudinal coupling with IU changes. These findings provide novel insights into the neural mechanisms of OCD pathology.

Financial support

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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

Huixia Zhou: Methodology. **Dongmei Wang:** Writing – review & editing, Project administration. **Xiangyang Zhang:** Writing – review & editing, Project administration, Funding acquisition. **Qihui Guo:** Writing – original draft, Methodology, Formal analysis, Conceptualization. **Rongrong Zhu:** Data curation, Conceptualization.

Declaration of Competing Interest

The authors report no competing interests.

Acknowledgments

We are thankful to all patients who participated in the study.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.janxdis.2025.103048.

Data availability

Data will be made available on request.

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