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REGULAR ARTICLE

Neural underpinnings of default mode network on empathy revealed by intracranial stereoelectroencephalography

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Background: Empathy is the ability to understand and share the feelings of others. It is fundamental to emotional intelligence and social iterations. Neuroimaging studies have demonstrated that empathy activates brain regions associated with the social cognition network.

Aim: To explore the neural underpinnings of empathy revealed by stereoelectroencephalography utilizing recurrence quantification analysis (RQA).

Methods: This retrospective cohort included 38 epilepsy patients with stereoelectroencephalography implantation. RQA metrics were applied to parameterize the network organization of default mode network (DMN) brain regions. The relationships between DMN, seizure burden activity, and empathy, as measured using the Interpersonal Reactivity Index, were examined using partial least-square regression and mediation analysis.

Results: RQA metrics with DMN ($R^2 = 0.75$, $P_{Bonferroni} < 0.001$) and its subsystems (medial temporal subsystem: $R^2 = 0.53$, $P_{Bonferroni} < 0.001$; core subsystem: $R^2 = 0.70$, $P_{Bonferroni} < 0.001$; dorsal medial subsystem: $R^2 = 0.48$, $P_{Bonferroni} < 0.001$) were positively correlated with empathy scores. Of 13 RQA metrics, the mean diagonal line length, entropy of the diagonal line lengths, trapping time, maximal vertical line length, and recurrence time of second type were found to be statistically higher in patient cohorts with reportedly high empathy. Furthermore, DMN characteristics (*b* path: $F = 3.69$, $P = 0.04$), rather than seizure burdens (direct effect: $t = 0.33$, $P = 0.74$, $c' = -0.007$), mediated empathy status.

Conclusion: The present study used various RQA metrics to parameterize the network organization of DMN and determine the neural underpinning of DMN for empathy modulation.

Keywords: *default mode network, empathy, neural underpinning, partial least-square regression, recurrence quantification analysis.*

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Empathy is a multifaceted human function that consists of our ability to identify and understand another person's perspective.[1] This cognitive human ability involves two distinct phases: a cognitive component, which conceptualizes empathy as a cognitive process in which an individual conceptualizes a situation from another's perspective, and an emotional component, which is often considered as the shared emotional experience with the observed other.[2] Taken together, empathy is a motivated phenomenon, rather than an automatic response, that facilitates one's ability to comprehend human emotions and adjust social behavior.[3,4] Neuroscience insights can provide a precise understanding of the origins and consequences of these motives, laying a foundation for psychological interventions aimed at building empathy.[5]

Earlier researches using functional magnetic resonance imaging (fMRI), identified several brain regions, such as the posterior inferior frontal gyrus and posterior parietal cortex, involved in the processing of cognitive and emotional empathy.[6–8] Subsequent research on the subject had identified core differences in the corresponding neural activity associated with cognitive and emotional empathy, with significant overlap between the neural regions controlling them.[3] One study by Kim *et al*. discovered reduced neural activity in the medial prefrontal lobe in people with lower empathy.[9] These previously identified brain regions are associated with the default mode network (DMN), one of the most studied brain networks. The DMN is associated with enhanced activity when an individual is not engaged by an external environmental stimulus[10–12] and is thought to be involved in internally focused and self-referential mental activity[13,14] and human behaviors required for empathy expression.[6] Several models of regional DMN function in specific types of cognition had been illustrated by different research studies in recent years. For example, the core DMN subsystem has been considered to mediate the retrieval of autobiographical information, while the dorsal medial subsystem has been proposed to ensure long-term knowledge to assist humans in comprehending the world around us.[15]

Intracranial electroencephalography (iEEG), which is technically based on directly implanted electrodes for neurosurgical purposes, records neuronal electric activity via high-level spatiotemporal resolution.[16] A previous study reported that more than 80% of iEEG systems were implanted in nonepileptic neuronal tissue, which could offer a valuable approach for validating and investigating the potential neural basis of blood oxygenation level-dependent functional connectivity.[17] Recurrence is an important concept in brain dynamical neuronal systems[18] and recurrence quantification analysis (RQA) has recently emerged to analyze nonlinear data.[19] RQA is primarily used to characterize periodic processes in a variety of physical and biological settings, such as electrophysiological neuronal activity in the brain.[20]

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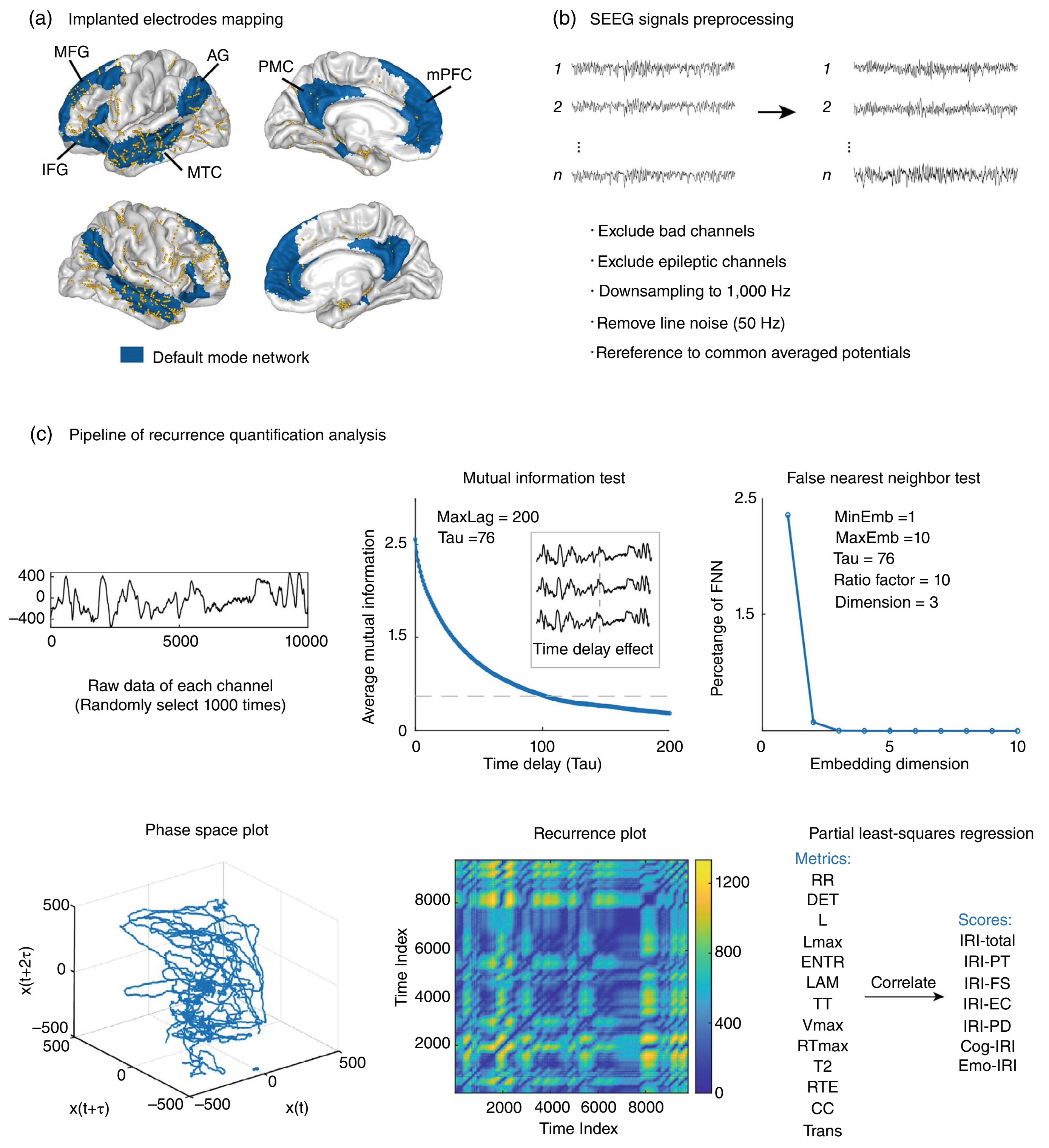

Fig. 1 Processing pipeline for default mode network (DMN) analysis of empathy. (a) Raw stereoelectroencephalography (SEEG) data were recorded from electrodes whose locations are shown as yellow circles. All of the electrodes across the entire cohort were aggregated in MNI coordinates. Blue ranges are the DMN, according to the Yeo atlas. (b) The recordings of each channel were preprocessed for further analysis. (c) The procedure for calculating the correlation between SEEG features and empathy scores. The recurrence quantification analysis (RQA) included the determination of time delay using the mutual information test, embedding dimension, using the false nearest neighbor (FNN) test, and the calculation of 13 measures. The partial least-squares analysis was used to explore the correlation between features and empathy scores. AG, angular gyrus; CC, clustering coefficient; Cog, cognitive; DET, determinism; EC, empathic concern; Emo, emotional; ENTR, entropy of the diagonal line lengths; FS, fantasy; IFG, inferior frontal gyrus; IRI, Interpersonal Reactivity Index; L, mean diagonal line length; LAM, laminarity; Lmax, maximal diagonal line length; MaxLag, the maximum time lag; MinEmb/MaxEmb, minimal/maximal dimension of the delay vectors; MFG, middle frontal gyrus; mPFC, medial prefrontal cortex; MTC, middle temporal cortex; PD, personal distress; PMC, posteromedial cortex; PT, perspective taking; RR, recurrence rate; RTE, recurrence time entropy; RTmax, maximal white vertical line length; T2, recurrence time of second type; Trans, transitivity; TT, trapping time; Vmax, maximal vertical line length.

In the present study, we explored the neural basis that reflects human empathy by leveraging iEEG data with the advantages of high-resolution and temporal regional specificity. Further, we elucidated the neural underpinnings of DMN for human empathy using RQA metrics and demonstrated its interpretability in this cognitive function.

Methods and Materials

Demographic and clinical information

All procedures used in the current study adhered to the ethical standards of the relevant national and institutional committees on human experimentation, as well as the Declaration of Helsinki of 1975, as revised in 2008. All procedures involving human patients were approved by the institutional review board of Beijing Tiantan Hospital (KY 2020–126-01).

A cohort of neurosurgical patients with clinically intractable epilepsy was consecutively selected at the Epilepsy Center of Beijing Tiantan Hospital between July 2019 and May 2021. All of the patients in the current study collectively underwent thorough multidisciplinary clinical evaluation as well as stereoelectroencephalography (SEEG) implantation. The implantation was based on available noninvasive clinical data, which provided sufficient hypotheses regarding the location of the epileptogenicity brain region. Figure 1 depicts the detailed technical information on SEEG implantation, neuronal signal preprocessing, and analyses.

SEEG signal data recording and preprocessing

All patients were stereotactically implanted with multi-lead EEG depth electrodes (HKHS Medical Technology). Clinical depth iEEG was recorded using a clinical long-term monitoring system (Nihon-Kohden Neurofax EEG-1200, 128 or 256 channels) with a sampling rate of 2000 Hz and a bandpass filter of 0.08 to 600 Hz. Each depth electrode had a diameter of 0.8 mm, eight to 16 contacts, and a 3.5-mm (center to center) intercontact spacing. The clinical decision on electrode placement was mainly based on presurgical noninvasive clinical information, which provided the hypotheses and evidence regarding the potential location of the epileptogenic neuronal zone. Prior to surgery, the depth electrodes were surgically positioned using a Sino-Robot system (Sinovation Medical Technology Co., Ltd.) and a predefined anatomical path. A postoperative computerized tomography scan was performed to confirm the absence of intracranial bleeding and the anatomic accuracy of the electrode positioning in the target region. To reduce any distortion during the recording procedures, SEEG signals from the regions were referenced to the most electrographically silent channel outside of the seizure focus of interest (a white matter channel), which acted as a control region. Intracranial resting-state SEEG recordings were obtained at the patient′s bedside. Before each resting-state recording, patients were instructed to close their eyes, feel comfortable and relaxed, and try not to think of anything. Using this approach, we obtained an average of 10 minutes of uninterrupted spontaneous neuronal activity from each patient.[21]

Each resting SEEG session was independently preprocessed using a publicly available MATLAB pipeline (The MathWorks, Inc.) that was developed in-house.[22,23] The in-house pipeline utilizes electrophysiological signal processing functions in SPM12[24] and Fieldtrip fields.[25] Following that, the recorder signals were first down-sampled to a frequency of 1000 Hz. Next, universal notch filtering was performed to eliminate any underlying noise (zero-phase, third order, Butterworth filter with band-stop between 47 and 53, 97 and 103, and 147 and 153 Hz). Subsequently, we used common averaging re-referencing methods. The electrodes that met one of the following criteria were excluded to ensure the robustness of our method: (i) exhibited pathological activity during clinical monitoring (as determined by a neurologist); (ii) were manually labeled as clear outliers on power spectra plots of all channels; (iii) had a variance greater or lesser than five times the median across all channels; or (iv) had more than three times the median number of spikes across all channels, with spikes defined as 100-μV changes between successive samples.[26] Only the contacts located within the DMN, as defined by Yeo atlas,[27] were selected for further statistical analysis. The DMN was further divided into three subsystems as follows: medial temporal subsystem (MTL), core subsystem (Core), and dorsal medial subsystem (dMPFC) based on 17 functional networks previously described by Yeo[27] (Fig. 1a,b).

Recurrence quantification analysis

The corresponding SEEG segments of each channel were extracted for subsequent RQA analysis. Figure 1c illustrates in detail the corresponding RQA stages. To begin, we calculated the minimal parameter τ and the lag-delayed surrogate time series using a mutual information test with a maximum time lag of 200. The embedding dimensions (m) were then determined by applying the false nearest neighbor test. By performing this task, we were able to construct phase portraits of increasing dimension. Subsequently, the smallest value of m that significantly reduced the number of false nearest neighbors was carefully selected. Specifically, the phase-space of the SEEG time series was plotted using the previously derived parameters τ and m. The phase portraits produced using the above sequence of processes were then used to construct a recurrence graphical plot by iteratively applying the threshold function, also known as ε, to each corresponding point in the phase. A recurrence in our system is universally defined as a situation in which a point in our system reoccurs at a specific coordinate space that was previously occupied by another point.[28] Finally, we calculated the following network measures: recurrence rate, determinism, mean diagonal line length, maximal diagonal line length, entropy of the diagonal line lengths (ENTR), laminarity, trapping time (TT), maximal vertical line length (Vmax), maximal white vertical line length, recurrence time of second type (T2), recurrence time entropy, clustering coefficient, and transitivity. Notably, we randomly selected a 10-second SEEG segment and performed 1000 times to obtain the average network characteristics of each channel.

Empathy scores

All participants completed the Chinese version of the Interpersonal Reactivity Index (IRI-C), a self-reported metric of empathy. This

Table 1. Demographics and clinical information

Variables	Participants
No.	38
Age, mean ± SD (years)	27.1 ± 6.6 (18.0–42.0)
Women, n (%)	22 (57.9)
Illness duration, mean ± SD (years)	12.9 ± 7.6 (0.3–40.0)
Lesion side, left, n (%)	17 (44.7)
Shafts, mean ± SD	9.6 ± 1.6 (7.0–13.0)
Contacts, mean ± SD	125.8 ± 24.7 (88.0–180.0)
Seizure frequency, mean ± SD (times per month)	49.7 ± 94.6 (0.3–540.0)
Total IRI, mean ± SD	46.2 ± 11.4 (23.0–74.0)
IRI-PT	9.2 ± 3.5 (2.0–17.0)
IRI-FS	10.8 ± 4.6 (0.0–20.0)
IRI-EC	14.8 ± 4.0 (7.0–24.0)
IRI-PD	11.6 ± 6.9 (1.0–22.0)
Cognitive-IRI	20.0 ± 6.7 (6.0–33.0)
Emotional-IRI	26.4 ± 7.6 (14.0–43.0)

Continuous data were presented as mean ± standard deviation (SD) (range) and categorical data were presented as frequency (percentage). EC, empathic concern; FS, fantasy; IRI, Interpersonal Reactivity Index; PD, personal distress; PT, perspective taking.

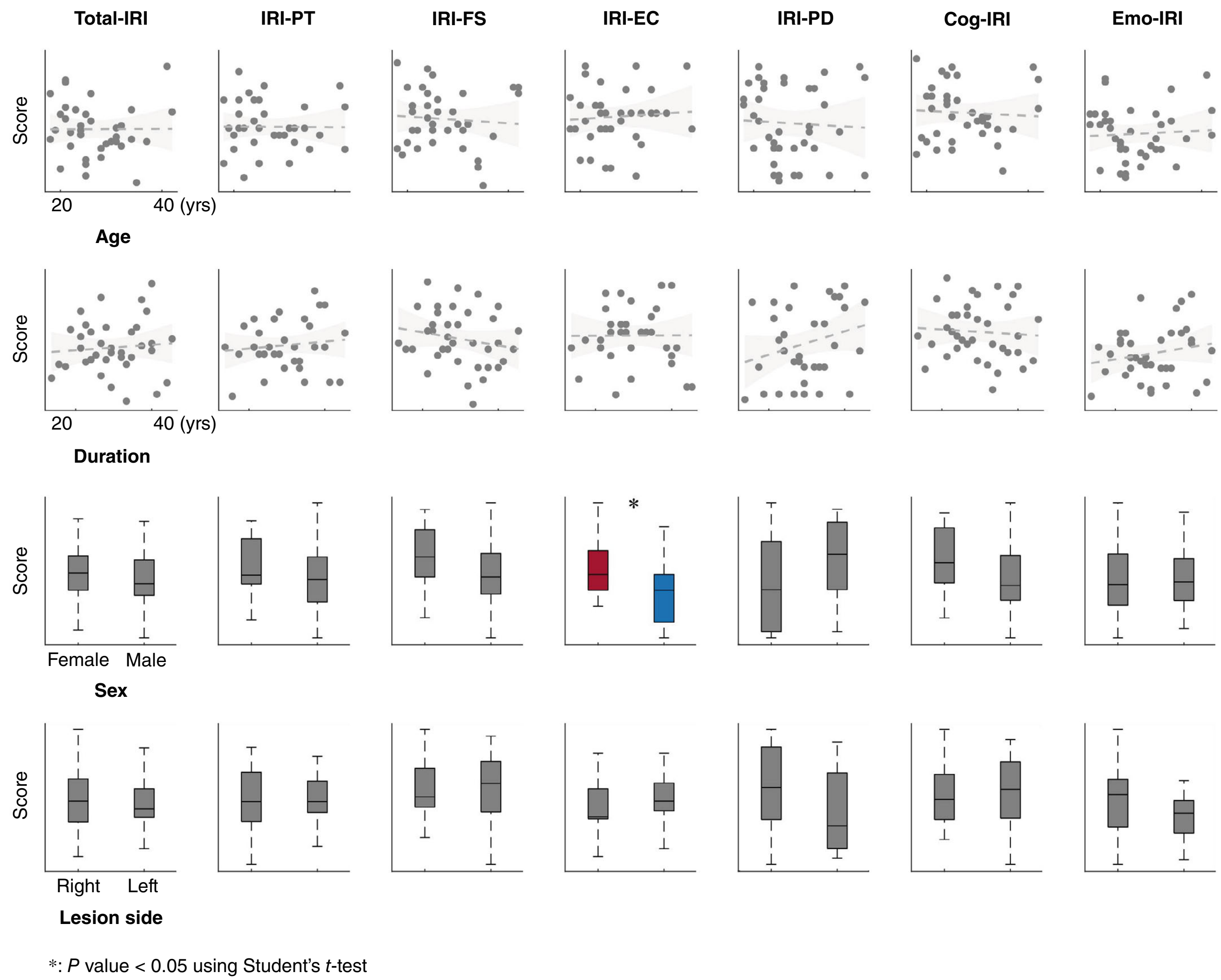

Fig. 2 Correlation between clinical variables and empathy scores. Male patients scored significantly lower on the Interpersonal Reactivity Index (IRI) empathic concern (EC) score than female patients. Colored subplots indicated the significant results. Neither age nor disease duration correlates with IRI scores. Cog, cognitive; Emo, emotional; FS, fantasy; PD, personal distress; PT, perspective taking. *Significant difference.

metric was originally developed by Davis[29] and successfully translated into Chinese by Zhan (1986). This metric takes into account possible relationships between age, sex-role, and human orientation with empathy (Master's Thesis National Chengchi University, Taipei). The IRI-C is a 22-item questionnaire that provides an excellent multidimensional measurement method of empathy for adults. The IRI-C structure assumes that human empathy consists of four related but conceptually distinct components. Specifically, the IRI-C is composed of four subscales: (i) the perspective taking (PT) scale (five items) assesses the ability to conceive the cognitive point-of-view of others; (ii) the fantasy (FT) scale (six items) assesses empathic responses towards fictional human characters; (iii) the empathic concern (EC) scale (six items) assesses feelings of sympathetic responses oriented by other individuals; and (iv) the personal distress (PD) scale (five items) assesses self-oriented feelings of anxiety and related feelings. The PT and the FT scales are cognitive scales components of the index, while the EC and PD scales are the emotional scales components.[30] Each item in the index can be rated on a five-point Likert scale, ranging from 0 (corresponding to 'does not describe me well') to 4 (corresponding to 'describes me very well').

Statistical analysis

After confirming the normality of data distribution (Lilliefors test) and the homogeneity of variances (Levene test), continuous variables were extensively compared for two independent samples using the Student *t*-test or Kolmogorov-Smirnov *Z* test. The outliers in data were identified and excluded using the *isoutlier* function of Matlab 2021a (MathWorks Inc.) software. The distribution of categorical variables was compared using the χ^2 test. The Pearson *R* or Spearman *Rho* correlation coefficient was applied to perform correlation analyses. The causal relationship between RQA metrics of DMN and empathy score was determined using the partial least-square (PLS) regression model, normalized with Bonferroni multiple comparison corrections. Using mode 4 of PROCESS, a statistical mediation analysis was performed to determine the potential association between the variables of seizure burdens, network characteristics, and empathy status.[31] The statistical significance of the indirect pathways was determined using 5000 bootstrap samples. All statistical analyses were performed using SPSS software version 26.0 (IBM). Two-tailed tests with a $P < 0.05$ threshold were regarded as indicating a statistically significant difference.

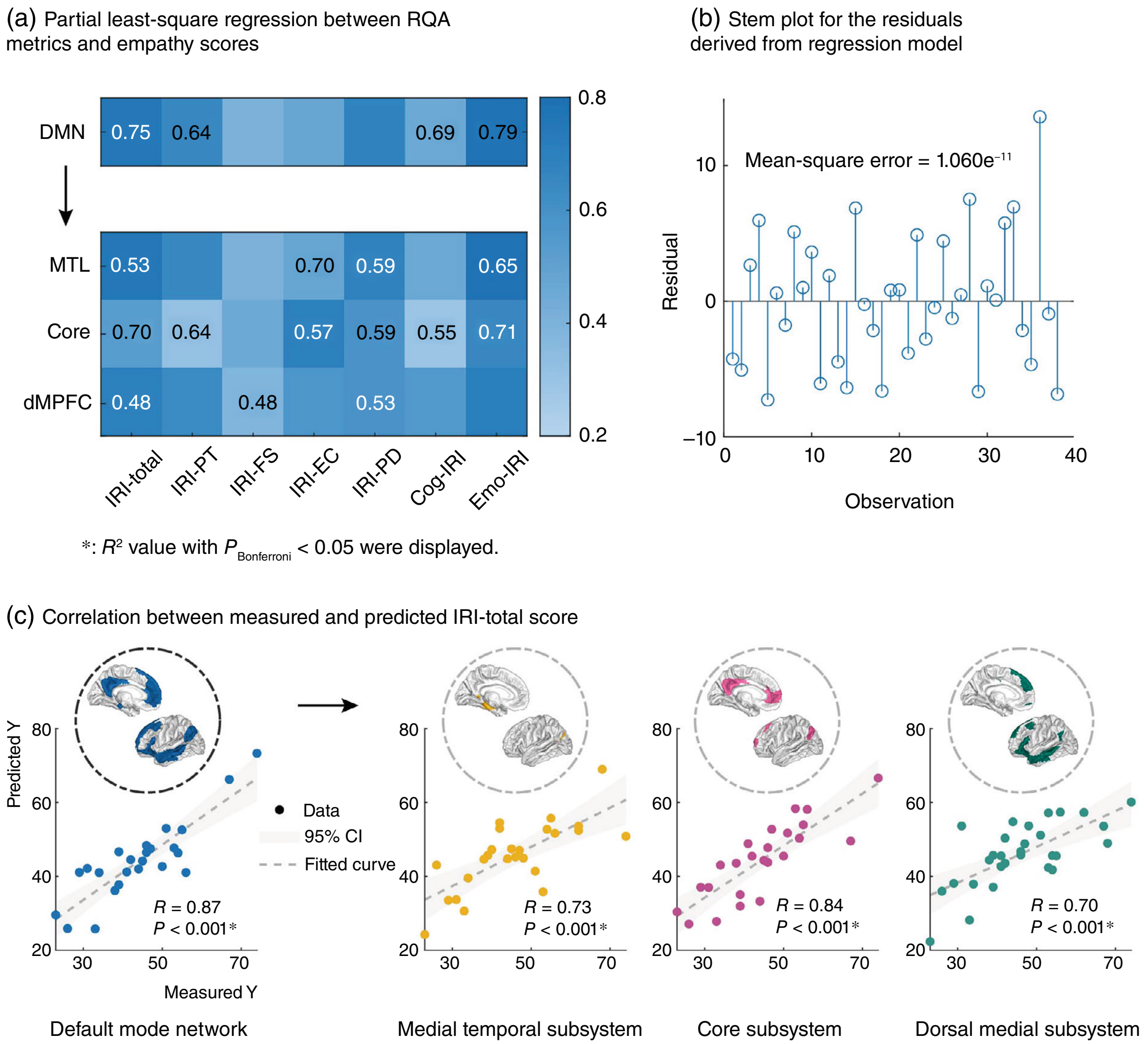

Fig. 3 Regression correlation between recurrence quantification analysis (RQA) metrics and empathy score. (a) Partial least-square regression shows the relationship between RQA metrics and empathy scores in the default mode network (DMN) and its subsystems. Only the R^2 values with $P_{Bonferroni} < 0.05$ are displayed. (b) The stem plot displays the residuals for each of the predicted observations. The estimated mean-squared errors = 1.060e^{-11}. (c) Correlation between actual and predicted Interpersonal Reactivity Index (IRI)-total score in DMN and its subsystems. Cog, cognitive; Core, core subsystem; dMPFC, dorsal medial subsystem; EC, empathic concern; Emo, emotional; FS, fantasy; MTL, medial temporal subsystem; PD, personal distress; PT, perspective taking.

Results

Participant characteristics

Intracranial recordings were obtained from a total of 38 (22 women [57.9%] and 16 men [42.1%]) participants, with a mean age of 27.1 years(standard deviation [SD] = 6.6 years) and a mean illness duration of 12.9 years (SD = 7.6 years). On average, each patient had 9.6 (SD = 1.6) shafts with a total of 125.8 (SD = 24.7) electrode contacts (left hemisphere: 127.5 ± 27.3, right hemisphere: 124.4 ± 1.7 contacts). Table 1 outlines patient-specific clinical information and IRI scores.

Correlation between clinical variables with empathy scores

After removing the outliers, there was no significant correlation between age, disease duration and IRI scores. Additionally, we compared the IRI level between different sex and lesion side groups. The male patients in the study had a lower IRI-EC score than female patients ($t = -2.35$, $P = 0.02$). There was no significant correlation between age and IRI scores, as well as between different lesion side groups (Fig. 2). Table S1 displays the detailed statistical results.

Correlation between RQA metrics and empathy scores

Multivariable PLS regression revealed a statistically significant correlation between the canonical brain systems network as measured by RQA metrics and empathy scores (13 components explained 78.62% of the original variance) (Fig. S1a). As shown in Fig. S1b, the DMN had the most robust correlation with IRI-total ($R^2 = 0.75$, $P_{Bonferroni} < 0.001$). Subsequently, we investigated the relationship between DMN subsystems and empathy. Specifically, DMN was significantly positively correlated with IRI-total, IRI-PT ($R^2 = 0.64$), IRI-PD ($R^2 = 0.69$), and Emo-IRI ($R^2 = 0.79$); MTL was correlated with IRI-total ($R^2 = 0.53$, $P_{Bonferroni} < 0.001$), IRI-EC ($R^2 = 0.70$), IRI-PD ($R^2 = 0.59$), and Emo-IRI ($R^2 = 0.65$); Core was correlated with IRI-total ($R^2 = 0.70$, $P_{Bonferroni} < 0.001$), IRI-PT ($R^2 = 0.64$), IRI-EC ($R^2 = 0.57$), IRI-PD ($R^2 = 0.59$), Cog-IRI ($R^2 = 0.55$),

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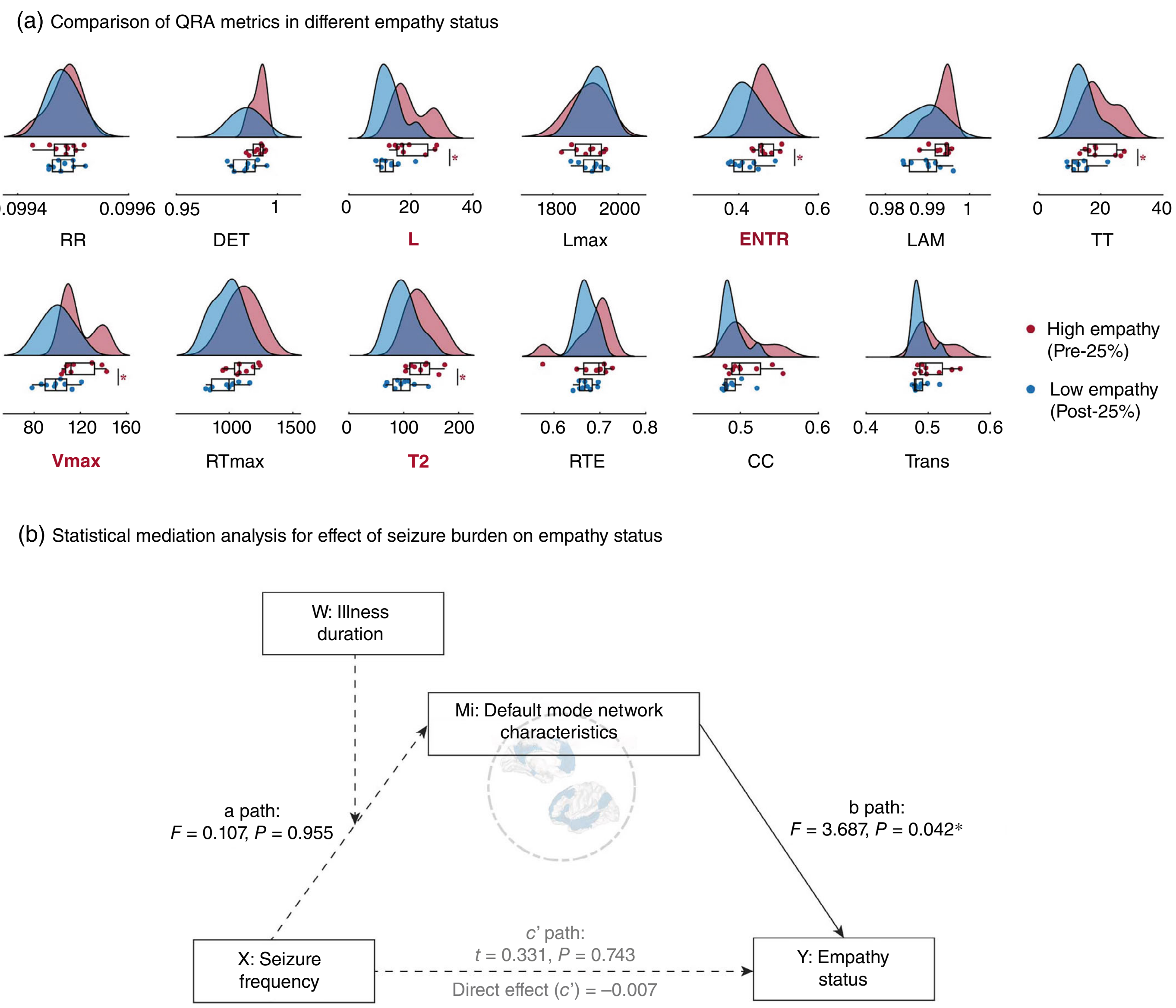

Fig. 4 The effect of recurrence quantification analysis (RQA) metrics on empathy status. (a) A comparison of RQA metrics for those with high (pre-25%) and low (post-25%) empathy status (b) Statistical mediation analysis illustrates that seizure burden is not a significant predictor of empathy status, while the default mode network (DMN) characteristics mediate the modulation of empathy. The mediation effect of DMN subsystems is displayed in Fig. S2. CC, clustering coefficient; DET, determinism; ENTR, entropy of the diagonal line lengths; L, mean diagonal line length; LAM, laminarity; Lmax, maximal diagonal line length; RR, recurrence rate; RTE, recurrence time entropy; RTmax, maximal white vertical line length; T2, recurrence time of second type; Trans, transitivity; TT, trapping time; Vmax, maximal vertical line length.*Significant difference with Bonferroni correction.

and Emo-IRI ($R^2 = 0.71$); dMPFC was correlated with IRI-total ($R^2 = 0.48$, $P_{\text{Bonferroni}} < 0.001$), IRI-FS ($R^2 = 0.48$), and IRI-PD ($R^2 = 0.53$) (Fig. 3a). The mean-square error of residuals derived from the regression model was as low as 1.060e^{-11} (Fig. 3b). The regression model performed well, since the fitted responses were significantly correlated with the actual response across networks (DMN: $R = 0.87$, $P_{\text{Bonferroni}} < 0.001$; MTL: $R = 0.73$, $P_{\text{Bonferroni}} < 0.001$; Core: $R = 0.84$, $P_{\text{Bonferroni}} < 0.001$; dMPFC: $R = 0.70$, $P_{\text{Bonferroni}} < 0.001$) (Fig. 3c).

Effect of RQA metrics on empathy status

Next, we determined which specific RQA metrics acted as the primary effector of the network and demonstrated whether seizure burden may influence an individual's empathy. The patients were divided into high- and low-empathy groups (pre-25% and post-25% of IRI-total score) and compared their average RQA metrics. Compared with the low-empathy cohort, the high-empathy cohort exhibited significantly higher average values in five metrics: mean diagonal line length, ENTR, TT, Vmax, and T2 ($Z = 0.67$, $P = 0.02$) (Fig. 4a).

The brain network characteristics and seizure burden affecting empathy status was determined using the significant metrics of the brain networks along with their corresponding weights. Our findings showed that empathy representation was not a byproduct of increased seizure burden, and no mediation was detected (direct effect: $t = 0.33$, $P = 0.74$, $c' = -0.007$). However, we found that the empathy status was fully mediated by the DMN characteristics (b path: $F = 3.69$, $P = 0.04$) (Fig. 4b). Moreover, we performed the replication analysis in the DMN subsystems and found that the subsystems did not significantly mediate empathy status (MTL: $F = 0.01$, $P = 0.98$; Core: $F = 2.42$, $P = 0.11$; dMPFC: $F = 0.20$, $P = 0.82$) (Fig. S2).

Discussion

Highlight

We investigated the neural underpinning of empathy using SEEG. The present study applied RQA to explicitly parameterize the network organization of DMN and its subsystems, whereas PLS regression was used to characterize the neural underpinning of the DMN for individual empathy modulation. Thus, we found that the RQA metrics of DMN and its subsystems had a positive correlation with empathy. Further analysis identified specific RQA features between different empathy statuses. The empathy status was significantly mediated by the DMN characteristics, rather than the seizure burden. Based on our findings, we suggest that the DMN plays a crucial role in the modulation of empathy.

DMN network and empathy

In the present study, we identified DMN as the most important determinant of empathy score among the seven Yeo brain networks. We further confirmed that the subsystems MTL, Core, and dMPFC were statistically associated with empathy indicating that DMN modulates empathy. Using independent component analysis, two fMRI studies demonstrated a robust positive correlation between empathy and functional connectivity of the medial prefrontal cortex and anterior cingulate cortex.[9,32] These findings were partially consistent with our dorsal medial subsystem findings. Nevertheless, we used PLS regression and calculated the residuals to validate the DMN and its subsystems were associated with the representation of empathy.

Representations of RQA metrics

We attempted to interpret the indication of RQA metrics on empathy in patients. There were statistically significant differences between RQA metrics of mean diagonal line length, ENTR, TT, Vmax, T2, and empathy status. The mean diagonal line length quantifies the duration of periodic processes using the simple mean of the distribution of diagonal line lengths; the ENTR is a measure (Shannon Entropy) derived from Information Theory that quantifies the predictability and variability in the distribution of diagonal line lengths; the TT is the average length of the vertical lines; the Vmax is the maximum vertical line length; the T2 is the average time taken for a point in the embedding space to be 'revisited' excluding times of one unit.[28] In summary, these measures were used to quantify the prevalence, duration, and complexity of periodic processes in DMN SEEG signals, demonstrating that DMN interaction mechanisms affect empathy. Furthermore, our findings indicate that all RQA metrics are significantly increased in the high-empathy group when compared with the low-empathy group, indicating that the brain network of high-empathy individuals had stronger internal functional connectivity and information communication. The novel analytical approach (RQA) used to characterize and relate periodicity in the DMN to empathy may provide a sensitive complement to existing correlation-based measures of functional connectivity.

Mediation effect of DMN on empathy status

In the present study, clinical variables, disease severity, and seizure burden had no significant effect on individual empathy. The baseline data for age duration (except the IRI-EC score), sex, and lesion side were nonsignificant. Previous research has found that men have less affective empathy compared with women.[33] Finally, mediation analysis demonstrated that the seizure burden has no statistical effect on empathy status in the DMN and its subsystems.

Limitations

Regardless of how far our research has progressed, it is not without limitations. First, even though the intracranial electrodes of the enrolled patients covered all the analyzed brain regions, the interaction effects need to be evaluated and confirmed in larger cohorts. Future research could further investigate the application of these methods to complementary conditions, particularly task performance. Second, the complete utilization of interictal SEEG data should be explored. The average SEEG monitoring time of our center is approximately 10 days, which generates a significant amount of interictal electrophysiological data. Because of the objective limitation of computing power, we were compelled in the current study to strictly extract 10 minutes of SEEG without any artifacts, epileptogenic activities, and pre-ictal alterations, and to perform the permutation test with 1000 random selections on the clips to ensure the high statistical power of the data. Consequently, the majority of our data had to be ignored during the initial enrollment because of technical challenges. To circumvent this challenge, improved algorithm approaches should be developed and tested.

Conclusion

The present study used RQA metrics to parameterize the network organization of DMN and identify the robust neural underpinning of DMN for empathy modulation. Determining the empathy-related neural responses and executive brain regions may promote spontaneous prosocial behavior.

Acknowledgments

Not applicable.

Author contributions

J.M. and C.Z. contributed to data analysis, interpretation of data, and drafting the manuscript, and approved the manuscript for publication. K.Z. contributed to the conception of the study and data acquisition, and approved the manuscript for publication. J.Z. contributed to the conception of the study. W.H., X.W., and B.Z. contributed to data collection and data analysis.

Consent for Publication

Not applicable.

Disclosure statement

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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Data Availability Statement

The data that support the findings of this study are available upon reasonable request from the corresponding author.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 Statistical analyses between clinical variables and empathy scores

Fig. S1 Correlation between recurrence quantification analysis (RQA) metrics and empathy scores using partial least-square (PLS) regression. (a) Variance is explained by PLS regression components. (b) The plot of the matrix indicates the R^2 value. Only the correlation results with $P_{\text{Bonferroni}} < 0.01$ are displayed. Cog, cognitive; DAN, dorsal attention network; DMN, default mode network; EC, empathic concern; Emo, emotional; FPN, frontoparietal network; FS, fantasy; IRI, Interpersonal Reactivity Index; LIM, limbic network; PD, personal distress; PT, perspective taking; SMN, somatomotor network; VAN, ventral attention network; VIS, visual network.

Fig. S2 Statistical mediation analysis for exploring the effect of seizure burden on empathy status. There are no significant predictive values of seizure burden and subsystems characteristics on empathy status.