ORIGINAL RESEARCH

Differential Alterations in Topology Property of Resting State Networks Associated With Mental Health and Childhood Trauma

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ABSTRACT

Context • Childhood trauma can lead to greater vulnerability to psychopathology and can affect person's mental health throughout his or her life cycle. Research on the associations between childhood trauma and developmental outcomes is critical to creating effective interventions.

Objective • The study intended to identify brain networks that are susceptible to childhood trauma by comparing differences in the networks of individuals with and without trauma, to investigate how changes in networks can mediate the effects childhood adversity on mental health.

Design • The research team performed a prospective cross-sectional survey.

Setting • The study took place at the Second Hospital of Hebei Medical University in Shijiazhuang, China.

Participants • Participants were 80 individuals aged 18-30 years, with and without childhood trauma.

Outcome Measures • Participants underwent resting-state functional magnetic resonance imaging (rs-fMRI). The research team: (1) assessed participants' depressive symptoms using the Beck Depression Inventory (BDI); anxiety levels using the State-Trait Anxiety Inventory (STAI); personality traits using the Three-Dimensional Personality Questionnaire (TPQ), and childhood traumatic experiences using the Childhood Trauma Questionnaire (CTQ); (2) analyzed the data using independent component analysis (ICA) and graph theory based on resting-state functional networks to assess the functional connectivity (FC) and global efficiency of participants' brains; (3) performed a correlation analysis between changes in the topological properties of participants' brains and neglect and abuse, (4) explored the mediating effects between childhood trauma and mental health, and (5) explored gender as a moderator of the relationship between neglect and changes in the global efficiency of within-network connectivity.

Results • Childhood trauma was associated with altered global efficiency of the salience network (SAN) and the default mode network (DMN). Compared with the healthy control group, the childhood trauma group's global efficiency of the SAN for the left ($P = .022$) and right ($P = .013$) bilateral anterior insula were significantly higher and the global efficiency of the DMN for the right lateral precuneus was significantly lower ($P = .022$). Compared with males, neglect was significantly more likely to affect the global efficiency of the SAN for females ($R2 = 0.473$, $t = -2.33$, $F_{(3,76)} = 24.66$, $B = -0.005$, and $P = .022$). The childhood trauma group's mean score for novelty seeking on the TPQ was significantly higher than that of the healthy control group ($P = .029$), showing that the global efficiency of the SAN and DMN had a significant role as a mediator between neglect and novelty seeking.

Conclusions • These findings indicate that childhood trauma can alter resting-state functional networks in healthy youth. This abnormality in brain circuitry is especially relevant to the DMN and SAN networks. (*Altern Ther Health Med.* 2023;29(8):426-434).

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Childhood trauma can have profound effects on mental, social, and emotional outcomes in adulthood, leading to greater vulnerability to psychopathology, including depression,[1] anxiety,[2] posttraumatic stress disorder (PTSD), and suicidal ideation.[3] Takizawa et al found that childhood trauma can explain about 30% of mental disorders.[3]

Pechtel and Pizzagalli found that childhood trauma can affect mental health throughout a person's life cycle,[4] but the complex relationship between the timing of childhood trauma and neurobiology remains to be studied.

Currently, the study of childhood trauma and neural development involves two types of approaches: (1) the cumulative risk model and (2) the Dimensional Model of Adversity and Psychopathology (DMAP) that McLaughlin and Sheridan proposed.[5]

Risk Models

The cumulative risk model, the more-common research method in the past decade, counts the number of different forms of adversity; creates a risk score without regard to the type, chronicity, or severity of the experience; and uses that score as a predictor of outcomes.[6] It focuses on the number of childhood-trauma experiences rather than the type or severity of those experiences.[7] However, it has significant limitations in determining the mechanism of the association between childhood trauma and developmental outcomes.

The DMAP model conceptualizes two main dimensions of childhood trauma: threat and deprivation. The dimension of threat encompasses physical, sexual, and emotional abuse; exposure to domestic violence; and exposure to other forms of violence. The dimension of deprivation includes institutional rearing, physical and emotional neglect, and extreme material deprivation.

The DMAP not only retains many of the benefits of the cumulative-risk method but also provides developmental mechanisms that can identify specific trauma and determine whether these mechanisms are related to the severity of exposure. In addition, the mechanisms that DMAP identifies are crucial for developing effective interventions to prevent the negative effects of childhood trauma on neural development. Clinicians can use this method as a screening tool to identify children most in need of an intervention.

McLaughlin et al's recent systematic review of the literature has supported some hypotheses about the DMAP model.[7] They found that threat, as the DMAP defines it, can affect children's neural circuits that are involved in significant processing, aversive learning, and emotion regulation. Compared to children not exposed to trauma, the study found that the children exposed to trauma had lower volumes in the amygdala, medial prefrontal cortex (mPFC), and hippocampus; a higher activation of the amygdala; a lower volume in the frontoparietal circuits; and an altered function in the frontoparietal regions.

Independent Component Analysis (ICA)

Researchers have used structural and functional magnetic resonance imaging (fMRI) to investigate the role of childhood trauma in the development of psychiatric disorders,[8] including bipolar disorder[9,10] and depression,[11] and to detect changes in brain morphology and functional connectivity (FC).

Several studies have evaluated childhood trauma's effects for healthy adults, compared to adults without trauma, finding differences in the volumes of the amygdala, anterior cingulate cortex, and hippocampus[12]; in the amygdala's FC[13]; in the connectivity of white matter[14]; in regional homogeneity[15]; and in the networks of the prefrontal cortex, the insula,[16] and the motor cortex.

However, most previous studies, based on defined seed and anatomical regions, have analyzed changes in FC and volume. Mckeown et al first proposed the application of independent component analysis (ICA) to fMRI data in 1998.[17] ICA can deconstruct the mixed signals of some of the independent signals that fMRI provides, and the independent signals truly represent the brain's activities in the mixed signals.

The advantages of using ICA-based methods for FC analysis lie in the fact that it doesn't require explicit prior knowledge of brain activity, and the selection of different seed regions isn't biased. The independent components that ICA identifies from a rs-fMRI are the resting state network (RSN).[18-20] The common networks are the default mode network (DMN), sensorimotor network (SMN), salience network (SAN), dorsal attention network (DAN), and visual network.

RSN could help researchers to understand the operative mechanism of the brain and of the pathogenesis of mental disorders. Philip et al found a dysfunction of the DMN and Cisler et al of the SAN in association with childhood trauma.[21,22]

Graph Theory

Graph analysis focuses on the interactions within the networks obtained using ICA. Graph theory is another method to describe the characteristics of brain networks by defining a series of indicators, such as the clustering coefficient and path length.[23] Graph theory regards the brain as a whole-network framework with a set of nodes or vertices, representing brain regions, and links or edges, representing anatomical, functional, or effective connections. Researchers can find abnormal connections between different brain regions by calculating the topology index, so as to further explore the pathophysiological mechanism of diseases.

Rubinov and Sporns and de Haan et al found that computation of the clustering coefficient for nodes of the graph can allow measurement of the tendency of network elements to form local clusters.[24,25] Rubinov and Sporns indicated that integration refers to the capacity of network-exchange information to become interconnected, and the characteristic path-length coefficient defines it.[24]

Although researchers have used graph theory to study the effects of childhood trauma on brain networks, most studies have focused on specific anatomical regions or specific networks,[26] such as the amygdala or insula,[22] rather than on brain networks as a whole.

The Brain's Networks

DMN. The precuneus cortex is an important component of the DMN, located in the brain's medial hemisphere, and its cognitive functions involve episodic memory encoding and retrieval, visuospatial imagery, and self-related information processing[27] as well as metacognition[28] and consciousness. Van der Werff et al also found a reduced FC in the precuneus of normal adults who had emotional maltreatment in childhood.[29]

SAN. Zhou et al found a negative correlation between DMN and SAN for externally oriented tasks.[30] Therefore, the mediating effects of the two networks may be opposite.

Researchers consider SAN to be the hub of emotional-information integration, which evaluates surrounding information to find the relevant stimulus. The SAN is an intrinsic connectivity network involved in detecting, integrating, and filtering relevant interoceptive, autonomic, and emotional information.[31]

The anterior insula is the SAN's core hub, and studies have found more and more evidence that abnormal activation of the insula can contribute to negative biases in attention and thought that are inherent in many psychiatric disorders. For example, Rakesh et al found that the SAN plays a crucial role in integrating sensory information from multiple patterns to support cognitive awareness and recognize salient information.[32] Marusak et al found disrupted, insula-based, neural-circuit organization in trauma-exposed youth.[33]

Abuse and neglect may affect SAN connectivity through different underlying mechanisms. In 2014, McLaughlin et al found that abuse can affect the superior thalamic connection by activating hormonal and metabolic changes in the hypothalamic axis and downstream.[34] Neglect may alter SAN connectivity and topological properties due to deviations from anticipated cognitive, social, and other forms of stimulation, as McLaughlin et al reported in 2017.[35]

Childhood trauma can have a negative influence on growth and personality formation.[35] Neglect can increase an individual's high levels of aggression, decrease self-esteem, and increase insensitivity to rewards, which can lead to an increase in novelty-seeking and emotional problems.[36] The mechanism of action may be overactivation of the SAN.

DAN. Researchers have rarely reported studies on the relationship between DAN and childhood trauma. Crum et al's study evaluated the use of oxytocin to help ameliorate attentional neurocircuitry dysfunction for individuals with PTSD and with maltreatment histories and found that PTSD and sexual abuse were associated with a reduction in the ventral and dorsal, neural attention networks.[37] Severe childhood trauma can lead to attention-deficit hyperactivity disorder,[38] which may be due to changes in the topological properties of the DAN.

Gender and Brain Structure

Some recent studies have observed gender effects on FC that are related to maltreatment in childhood.[32,39-40] Bath found that gender, as a biological variable, is critical for understanding the broad range of physiological, neurobiological, and behavioral consequences of early life adversity.[41] Several studies have reported that childhood trauma can cause male-specific changes in brain structure,[42-46] but few studies have occurred on changes in the topological properties of the internal FC network.

Rakesh et al found that higher neglect scores were associated with increased within-DMN integration in males and reported that maltreatment-related changes in the marginal circuitry are specific to males.[32]

Kirsi Kettunen et al found that gender differences in brain development in the timing of neural development may lead to differences in sensitivity between males and females.[47] Furthermore, Susan Baidawi et al found that males and females experience different levels of abuse and neglect in childhood trauma.[48]

Developmental epigenetic programming may be associated with different sensitivities to exogenous stimuli in males and females. For example, Bath found that a surge in testosterone in males before birth can lead to changes in the epigenetic programming of the genes involved in brain development that alter the sensitivity to signals from stressful environments.[41]

Current Study

The current study intended to identify brain networks that are susceptible to childhood trauma by comparing differences in the networks of individuals with and without trauma, to investigate how changes in networks can mediate the effects childhood adversity on mental health.

METHODS

Participants

The research team performed a prospective cross-sectional survey, which took place at the Second Hospital of Hebei Medical University in Shijiazhuang, China. Potential participants were college students from The Hebei Medical University. We recruited the subjects in the following ways, such as sending recruitment information via wechat and posting recruitment information on the publicity board of The Hebei Medical University.

The study included potential participants if: (1) they were aged 18-30 years; (2) if female, they didn't take oral contraceptives; (3) had a junior-high-school education or above; (4) were Han Chinese; and (5) were right-handed.

The study excluded potential participants if: (1) they had a history of mental illness, (2) they had any first-degree relatives with mental disorders, (3) they had a history of alcohol or drug dependence, (4) they had cerebral organic and serious physical diseases, (5) they had had seizures previously or had a family history of epilepsy; (6) they were receiving hormone therapy; (7) they had current infections, traumas, or associated immune or other medical diseases; or (8) they had any contraindications for participation.

The research team provided a complete description of the study to participants, after which they signed a written informed consent. The Ethics Committee of the hospital approved the study's protocols (approval number 2016277). The research team conducted the study in accordance with the Declaration of Helsinki.

Procedures

Three dimensional (3D)-T1 structural MRI. The research team performed a scan to obtain a sagittal, high-resolution, structural image in a T1-fast field echo (FFE) sequence. The scan baseline was parallel to the anterior and posterior joint lines and: (1) the repetition time (TR) = 7.8 ms, (2) the time to echo (TE) = 3.8 ms, (3) the turn angle = 8°, (4) the matrix =252×227, (5) the voxel size = 1 × 1 × 1 mm, (6) the field of view (FOV) = 250

× 250 × 180 mm, (7) the layer thickness = 1 mm, (8) the layer spacing = 0 mm, (9) the scanning layer number = 180, and (10) the number of excitations (NEX) = 1. Two experienced imaging diagnosticians diagnosed these conventional MRI images, excluding participants with obvious lesions and multiple foci of abnormal signals.

Measures of depression, anxiety, and personality traits. The research team measured: (1) depressive symptoms using the Beck Depression Inventory (BDI)[49]; (2) anxiety levels using the State-Trait Anxiety Inventory (STAI)[50]; and (3) personality traits using the Three-Dimensional Personality Questionnaire (TPQ).[51] Participants completed the BDI, STAI, and TPQ before the fMRI scanning, with participants not taking any medication within the imaging hours.

Measures of abuse and neglect. The research team assessed participants' childhood traumatic experiences using the Childhood Trauma Questionnaire (CTQ) before the fMRI scanning.[52]

Groups. The research team divided participants into a childhood trauma group and a healthy control group based on their total CTQ scores.

rs-fMRI. Before performing the scanning, the research team asked participants to remain awake, close their eyes, be relaxed, avoid any body activity, and try not to do any systematic thinking.

The team used the echo-planar imaging (EPI)-gradient echo sequences (GRE) sequence: (1) the TR = 2000 ms, (2) the TE = 30 ms, (3) the fractional anisotropy (FA) = 90°, (4) the layer thickness = 4 mm, (5) the interval = 0 mm, (6) the scanning layer number = 33, (7) the FOV = 24 cm × 24 cm, (8) the matrix = 64 × 64, (9) the time points = 180, (10) the scanning time = 360 s, and (11) the number of images = 5940.

Data preprocessing. The same two experienced imaging diagnosticians as mentioned above: (1) converted the Digital Imaging and Communications in Medicine (DICOM)-format images to Neuroimaging Informatics Technology Initiative (NIFTI) format; (2) used the CONN18.b software [53] (Gabrieli Lab. McGovern Institute for Brain Research, https://web.conn-toolbox.org/) to preprocess the resting state functional images; and (3) generated a reference volume and its skull-stripped version using a custom methodology of the CONN-default pipeline for analyses in the Montreal Neurological Institute and Hospital (MNI)-space.

The diagnosticians then: (1) co-registered the fMRI reference to the T1WI reference, (2) used slice-time correction to perform head-movement correction with removal of non-steady-state volumes, and (3) used isotropic gaussian kernels to perform spatial smoothing. The diagnosticians registered the functional images and resampled them to the MNI standard space using a gaussian kernel at 8 mm for the full width half maximum (FWHM). Finally, the diagnosticians band-pass-filtered the blood-oxygen-level-dependent (BOLD) time series at 0.008–0.09 Hz.

ICA. The research team use the CONN18.b software based on the stable group ICA algorithm—G1 Fast ICA + group independent component analysis 3 (gICA 3) back-projection—for the ICA. The team performed the gICA on two groups of preprocessed resting-state data.

First, the team performed dimensionality reduction on participants' fMRI data through principal component analysis (PCA). Two-to-three-step PCA allows achievement of multiple nesting and generally guarantees a 99% data difference to determine independent components. Then according to the maximum algorithm—the infomax algorithm, the team deconstructed the data after dimensionality reduction using ICA. Finally, the team reconstructed the spatial brain map of each participant's brain-network components and the map's corresponding time courses, using the group-ICA back-construction method to obtain individual components. The team then converted that data into two values to obtain the time courses of relevant network components and the synchronization-degree index of the voxel BOLD signals. The team used that result for the final statistical analysis at the group level.

Graph theoretical analysis. The research team performed graph-theory analysis to compare the networks' topological properties. The team included evaluated the total, DMN, SMN, SAN, DAN, and frontoparietal (FPN) networks. The team global evaluated the efficiency, local efficiency, average path length, clustering coefficient, and degree using two sample *t* tests, a threshold of $P < .05$, and a false discovery rate (FDR), corrected with age, gender, educational level, BDI score, STAI score, and TPQ score as covariates.

Outcome Measures. Participants underwent rs-fMRI. The research team: (1) assessed participants' depressive symptoms using the Beck Depression Inventory (BDI); anxiety levels using the State-Trait Anxiety Inventory (STAI); personality traits using the Three-Dimensional Personality Questionnaire (TPQ), and childhood traumatic experiences using the Childhood Trauma Questionnaire (CTQ); (2) analyzed the data using independent component analysis (ICA) and graph theory based on resting-state functional networks to assess the functional connectivity (FC) and global efficiency of participants' brains; (3) performed a correlation analysis between changes in the topological properties of participants' brains and neglect and abuse, (4) explored the mediating effects between childhood trauma and mental health, and (5) explored gender as a moderator of the relationship between neglect and changes in the global efficiency of within-network connectivity.

Outcome Measures

BDI.[49] was created by Aaron T. Beck. BDI is world-wide among the most used self-rating scales for measuring depression. It contains 21 items, each representing different manifestations of depression. A higher score indicates more severe depressive symptoms in an individual, with an overall score of 0-13 indicating moderate depression, 14-19 indicating mild depression, 20-28 indicating moderate depression, and 29-63 indicating severe depression.

STAI.[50] was created by Spielberger and his colleagues. State anxiety (A-State:) is defined as a transitory emotional state or condition characterized by subjective feelings of

tension and apprehension, and by activation of the autonomic nervous system. Trait anxiety (A-Trait) refers to relatively stable individual differences in anxiety proneness. STAI consists of two 20-item self-report scales. The STAI-Y1 measures state anxiety and the STAI-Y2 measures trait anxiety.

TPQ.[54] was created by Cloninger CR. It consists of three independent dimensions, novelty seeking (NS), which is related to dopaminergic neurotransmitter, harm avoidance (HA), associated with serotonergic neurotransmitters, reward-dependence (RD) is associated with norepinephrine neurotransmitters. All three dimensions have corresponding genetic basis. TPQ) was developed and divided into three dimensions and twelve factors. There are 100 yes/no questions. It will take about 15-20 minutes to answer all the questions.

CTQ.[52] This scale has acceptable psychometric properties, with the Cronbach α = 0.90.[55] The questionnaire consists of five subscales: (1) physical abuse, (2) emotional abuse, (3) sexual abuse, (4) physical neglect, and (5) emotional neglect. The current study used the CTQ-Short Form (CTQ-SF) that consists of 28 items. Cutoff scores were ≥13 for emotional abuse, ≥10 for physical abuse, ≥8 for sexual abuse, ≥15 for emotional neglect, and ≥10 for physical neglect. Scores at or above these thresholds indicate the presence of childhood trauma.

To determine the different effects of abuse and neglect on the brain's functional connectivity, the team calculated a total score for abuse using the sum of the scores for physical, emotional, and sexual abuse and a total score for neglect using the sum of the scores emotional and physical neglect.

Global efficiency. Global efficiency is a scalar measure of the information-flow exchange in the brain's functional networks, which measures the global transmission capacity of the networks. The current study focused on analyzing the effects of childhood trauma on the global efficiency of participants' brain networks.

Gender as a moderator. Bath reported that gender can moderate the relationship between childhood trauma and changes in the brain's FC.[41]

Global efficiency and mental health. The mediated effect analysis explored the role of a difference in global efficiency as a mediator between TPQ-NS and trait anxiety, and neglect and abuse.

Statistical Analyses

The research team used: (1) an unpaired *t* test to compare the unpaired data that conformed to normal distribution and homogeneity of variance, (2) the Wilcoxon rank-sum test for other continuous variables, (3) the Chi-square (χ^2) test for categorical variables. The team expressed continuous variables as means ± standard deviations (SDs), expressed parametric continuous variables as numbers (N) and percentages (%), and expressed nonparametric continuous variables as medians and interquartile ranges.

The team analyzed the correlations between the topological properties of RSN and abuse and of RSN and neglect using ordinary least squares regression, with age, gender, years of education, STAI anxiety scores, BDI depression scores, and TPQ scores as covariates for multiple comparisons to avoid any confounding effects. To determine whether findings were specific to abuse or neglect, the team covaried abuse in neglect models and vice versa.

The team assessed mediation models with abuse or neglect scores as the predictors, the topological properties of RSN differences as the mediators, and psychological traits—STAI anxiety and TPQ—as the outcome variables. The team included gender, age, years of education, and BDI score as covariates. The team then ran the moderated mediation models to assess the role of gender as a moderator and included age, years of education, STAI anxiety scores, BDI depression scores, and TPQ scores as covariates. The team conducted the mediation analyses using the model 4 PROCESS macro from the SPSS 27.0 software (IBM, Chicago, IL, USA), using 5000 bootstrap samples to estimate 95% confidence.

RESULTS

Participants

The research team initially included 200 participants. We found that 40 of 200 participants had childhood trauma experience. We randomly selected another 40 participants with normal childhood trauma scores as controls (Table 1). Most participants were college students. Based on participants' total CTQ scores, the team assigned 40 young adults to the childhood trauma group and 40 to the healthy control group. No significant differences existed between the groups in age, gender, or education.

All participants' BDI scores were lower than 10, indicating that none had signs of depression and no significant difference existed between the . Both groups' STAI-Y1 scores for state anxiety and STAI-Y2 scores for trait anxiety were lower than 41. However, the childhood trauma group's scores for trait anxiety, at 40.80 ± 5.83, were significantly higher than those of the healthy control group, at 34.3 ± 7.65 ($P = .0045$). Also, the childhood trauma group's mean score for novelty seeking on the TPQ was significantly higher than that of the healthy control group ($P = .029$).

The childhood trauma group's mean emotional neglect score, at 15.70 ± 2.23 ($P < .0001$); physical neglect score, at 11.05 ± 2.44 ($P < .0001$); total neglect score, at 27.25 ± 3.67 ($P < .0001$); emotional abuse score, at 8.25 ± 2.67 ($P = .003$); sexual abuse score, at 5.80 ± 1.36 ($P = .020$); total abuse score, at 20.65 ± 5.34 ($P < .0001$); and total CTQ score, at 46.9 ± 7.64 ($P < .0001$) were significantly higher than those of the healthy control group, at 6.95 ± 1.99, 5.85 ± 1.35, 13.3 ± 2.66, 6.15 ± 1.27, 5.05 ± 0.22, 16.85 ± 1.42, and 29.15 ± 3.26, respectively.

Of the 40 participants in the childhood trauma group (data not shown), 32 had traumatic experiences of neglect (80%) and 28 of abuse (70%).

Functional Connectivity

Figure 1A shows the matching relationship between 30 independent components (ICs) and the corresponding brain networks. The best matches appear at the bottom of the X-axis and on the right side of the Y-axis.

Table 1. Demographic and Neuropsychological Characteristics

Characteristics	Childhood Trauma Group n = 40 Mean ± SD n (%) Median (Q1- Q3)	Healthy Control Group n = 40 Mean ± SD n (%) Median (Q1-Q3)	*t*/U/χ^2	*P* value
Age	22.05 ± 1.15	21.80 ± 2.26	0.44	.66
Gender			0.053 (χ^2)	.82
Male	16 (40.00)	14 (35.00)		
Female	24 (60.00)	26 (65.00)		
Education, y	15.2 ± 1.67	15.0 ± 0.56	0.51	.62
Beck Depression Inventory	5.50 (2.0-10.50)	3.5 (0-6.00)	138.5 (U)	.095
STAI-Y1	37.10 ± 6.70	35.75 ± 8.53	1.21	.33
STAI-Y2	40.80 ± 5.83	34.3 ± 7.65	3.02	.0045[b]
TPQ				
NS	13.70 ± 3.77	11.15 ± 3.31	2.27	.029[a]
HA	15.95 ± 6.71	14.30 ± 6.25	0.80	.43
RD	19.55 ± 2.52	19.70 ± 2.68	0.18	.86
CTQ				
Emotional neglect	15.70 ± 2.23	6.95 ± 1.99	13.1	<.0001[c]
Physical neglect	11.05 ± 2.44	5.85 ± 1.35	8.35	<.0001[c]
Neglect total	27.25 ± 3.67	13.3 ± 2.66	19.46	<.0001[c]
Emotional abuse	8.25 ± 2.67	6.15 ± 1.27	3.17	.003[b]
Physical abuse	6.10 ± 2.15	5.15 ± 0.37	1.95	.059
Sexual abuse	5.80 ± 1.36	5.05 ± 0.22	2.43	.020[a]
Abuse total	20.65 ± 5.34	16.85 ± 1.42	4.35	<.0001[c]
CTQ total	46.9 ± 7.64	29.15 ± 3.26	9.55	<.0001[c]

[a]$P < .05$, indicating that the childhood trauma group's scores for novelty seeking on the TPQ and for sexual abuse on the CTQ were significantly higher than those of the healthy control group
[b]$P < .01$, indicating that the childhood trauma group's scores for trait anxiety on the STAI and for emotional abuse on the CTQ were significantly higher than those of the healthy control group
[c]$P < .001$, indicating that childhood trauma group's scores for emotional neglect, physical neglect, total neglect, total abuse, and total CTQ on the CTQ were significantly higher than those of the healthy control group

Abbreviations: CTQ, Childhood Trauma Questionnaire; HA, harm avoidance; NS, novelty seeking; RE, reward dependence; STAI-Y1, State-Trait Anxiety Inventory-State Anxiety; STAI-Y2, State-Trait Anxiety Inventory-Trait Anxiety; TPQ, Three-Dimensional Personality Questionnaire.

Figure 1. Independent Components (ICs). Figure 1a shows the graph of the degree of matching for 30 ICs in eight brain networks. The bigger the red square, the better the match. Figure 1b shows a composite map of 18 ICs identified through independent component analysis (ICA) for all participants. The analysis sorted these 18 identified ICs into eight functional networks: (1) default-mode (DMN)—ICs 5 and 22, (2) sensorimotor (SMN)—ICs 24 and 27, (3) visual—ICs 9, 10, and 23, (4) salience (SAN)—IC 13, (5) dorsal attention (DAN)—ICs 16, 25, and 28, (6) frontoparietal (FPN)—ICs 6, 7, and 12, (7) language—ICs 8 and 20, and (8) cerebellar—ICs 1 and 26.

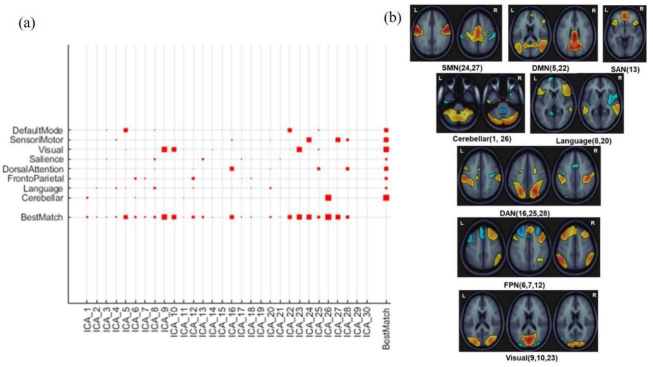


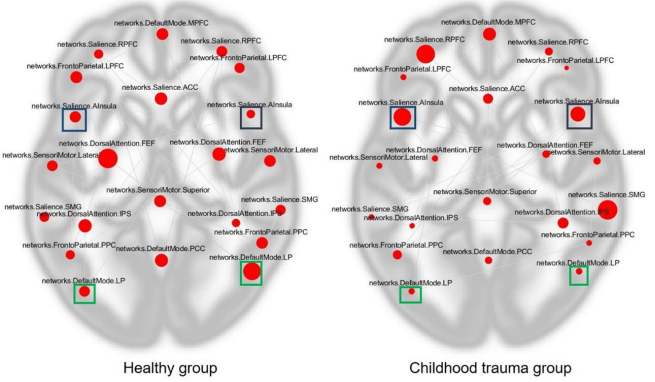
Table 2. Comparison of the Global Efficiency of Brain Networks Between the Childhood Trauma and Healthy Control Groups

Network	MNI Coordinate (x, y, z)	Global Efficiency: Childhood Trauma Group Mean ± SE	Global Efficiency: Healthy Control Group Mean ± SE	*P* value
networks.DefaultMode.MPFC	1; 55; -3	0.41 ± 0.045	0.43 ± 0.022	.61
networks.DefaultMode.LP (L)	-39; -77; 33	0.42 ± 0.040	0.37 ± 0.035	.32
networks.DefaultMode.LP (R)	47; -67; 29	0.34 ± 0.036	0.45 ± 0.033	.022[a]
networks.DefaultMode.PCC	1; -61; 38	0.42 ± 0.042	0.39 ± 0.037	.56
networks.SensoriMotor.Lateral (L)	-55; -12; 29	0.35 ± 0.043	0.38 ± 0.043	.63
networks.SensoriMotor.Lateral (R)	56; -10; 29	0.38 ± 0.043	0.37 ± 0.035	.91
networks.SensoriMotor.Superior	0; -31; 67	0.39 ± 0.043	0.41 ± 0.035	.84
networks.Salience.ACC	0; 22; 35	0.37 ± 0.039	0.40 ± 0.028	.47
networks.Salience.AInsula (L)	-44; 13; 1	0.46 ± 0.018	0.35 ± 0.041	.022[a]
networks.Salience.AInsula (R)	47; 14; 0	0.45 ± 0.021	0.31 ± 0.048	.013[a]
networks.Salience.RPFC (L)	-32; 45; 27	0.44 ± 0.053	0.38 ± 0.016	.27
networks.Salience.RPFC (R)	32; 46; 27	0.40 ± 0.049	0.42 ± 0.036	.83
networks.Salience.SMG (L)	-60; -39; 31	0.38 ± 0.045	0.33 ± 0.047	.52
networks.Salience.SMG (R)	62; -35; 32	0.45 ± 0.047	0.37 ± 0.016	.11
networks.DorsalAttention.FEF (L)	-27; -9; 64	0.47 ± 0.032	0.37 ± 0.041	.053
networks.DorsalAttention.FEF (R)	30; -6; 64	0.39 ± 0.038	0.41 ± 0.038	.67
networks.DorsalAttention.IPS (R)	39; -42; 54	0.35 ± 0.055	0.41 ± 0.026	.33
networks.FrontoParietal.LPFC (L)	-43; 33; 28	0.42 ± 0..046	0.39 ± 0.045	.66
networks.FrontoParietal.PPC (L)	-46; -58; 49	0.33 ± 0.047	0.43 ± 0.032	.097
networks.FrontoParietal.LPFC (R)	41; 38; 30	0.38 ± 0.049	0.33 ± 0.050	.46
networks.FrontoParietal.PPC (R)	52; -52; 45	0.39 ± 0.044	0.38 ± 0.046	.92

*$P < .05$, indicating that the childhood trauma group's global efficiency of the SAN for the left ($P = .022$) and right ($P = .013$) bilateral anterior insula were significantly higher and the global efficiency of the DMN for the right lateral precuneus was significantly lower than those of the healthy control group

Abbreviations: ACC, anterior cingulate cortex; AInsula, anterior insula; FEF, frontal eye fields; IPS, intraparietal sulcus; L, left; LP, lateral precuneus; LPFC, lateral prefrontal cortex; MPFC, medial prefrontal cortex; PCC, posterior cingulate cortex; PPC, posterior parietal cortex; R, right; RPFC, rostral lateral prefrontal cortex; SMG, supramarginal gyrus.

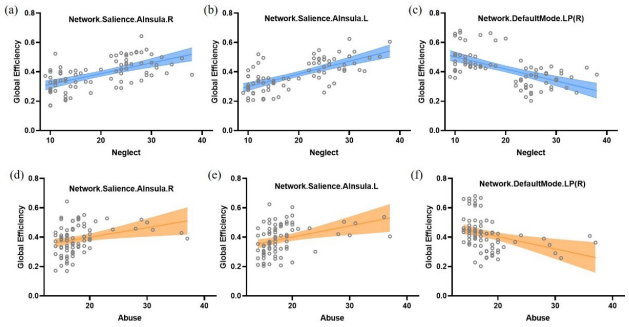
Figure 2. Comparison of Differences in Global Efficiency in Brain Networks Between the Childhood Trauma and Healthy Control Groups. Each red circle represents a changed cluster within a network.



Abbreviations: ACC, anterior cingulate cortex; AInsula, anterior insula; MPFC, medial prefrontal cortex; LP, lateral precuneus; PCC, posterior cingulate cortex; RPFC, rostral lateral prefrontal cortex; SMG, supramarginal gyrus; FEF, frontal eye fields; IPS, intraparietal sulcus; LPFC, lateral prefrontal cortex; L, left; R, right.

Two neuroradiologists visually identified the components, and they assigned (Figure 1B): (1) the ICs 5 and 22 to the DMN; (2) the ICs 24 and 27 to the SMN; (3) the ICs 9, 10, and 23 to the visual network; (4) the IC 13 to the SAN; (5) the ICs 16, 25, and 28 to the DAN; (6) the ICs 6, 7, and 12 to the FPN; (7) the ICs 8 and 20 to the language network; and (8) the ICs 1 and 26 to the cerebellar network.

Figure 3. Scatter Diagram Showing the Relationships Between Neglect and Abuse and the Global Efficiency in the AInsula and LP Networks. Figures 1A and 1B show that neglect was significantly positively correlated with the global efficiency of the SAN for the right and left bilateral anterior insula, respectively. Figures 1D and 1E show that abuse was significantly positively correlated with the global efficiency of the SAN for the right and left bilateral anterior insula, respectively. Figures 1C and 1F show that the DMN for the right lateral precuneus was significantly negatively correlated with neglect and abuse.



Abbreviations: AInsula, anterior insula; LP, lateral precuneus; L, left; R, right.

Global Efficiency

Figure 2 shows the differences between the groups in the brain networks' global efficiency. Compared with the healthy control group (Table 2), the childhood trauma group's global efficiency of the SAN for the left ($P = .022$) and right ($P = .013$) bilateral anterior insula were significantly higher and the global efficiency of the DMN for the right lateral precuneus was significantly lower ($P = .022$).

Abuse and Neglect and Global Efficiency

Figure 3 shows the analysis of the correlation between the global efficiency of networks and participants' psychological scores. Neglect was significantly positively correlated with the global efficiency of the SAN for the right bilateral anterior insula—B = 0.0073, SE = 0.0011, and $P < .0001$ (Figure 3A) and of the SAN for the left bilateral anterior insula—B = 0.0086, SE = 0.0010, and $P < .0001$ (Figure 3B).

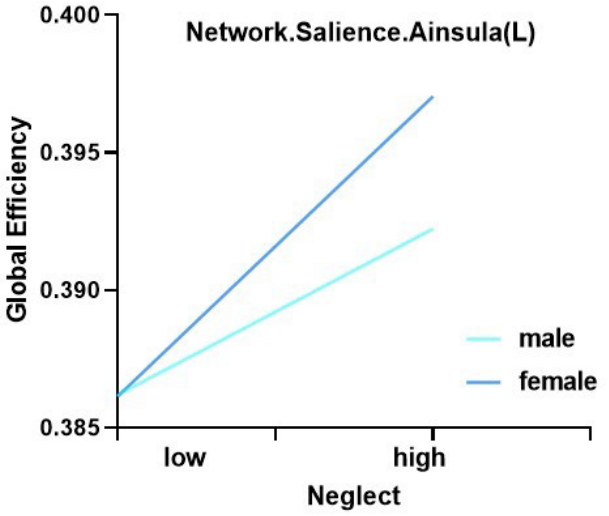
Similarly, abuse was significantly positively correlated with the global efficiency of the SAN for the right bilateral anterior insula—B =v0.0065, SE = 0.0024, and $P = .0071$ (Figure 3D) and of the SAN for the left bilateral anterior insula—B = 0.0077, SE = 0.0023, and $P = .0019$ (Figure 3E).

The DMN related to the right lateral precuneus was significantly negatively correlated with neglect—B = -0.0082, SE = 0.0012, and $P < .0001$ (Figure 3C) and with abuse B = -0.0084, SE = 0.0028, and $P = .0020$ (Figure 3F).

Gender as a Moderator

A simple slope chart shows that neglect was significantly more likely to affect females' global efficiency of the SAN for the left anterior insula (Figure 4) for males (R2 = 0.473, t = -2.33, $F_{(3,76)} = 24.66$, B = -0.005, and $P = .022$).

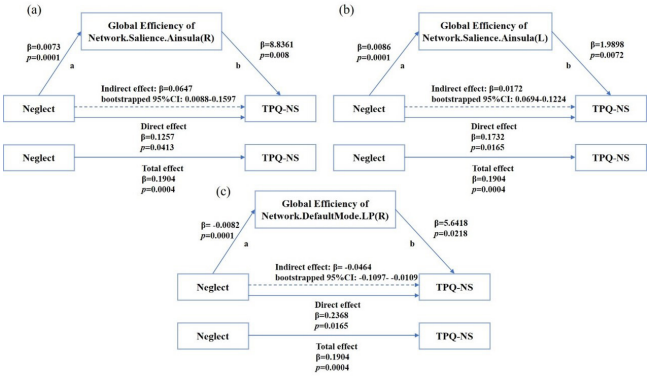
Figure 4. Scatter Diagram Showing the Relationship Between Neglect and Abuse and the Global Efficiency for Males and Females in the left AInsula Network



Note: $P < .05$, indicating that neglect was significantly more likely to affect females' global efficiency of the SAN for the left anterior insula than that of males

Abbreviations: AInsula, anterior insula; LP, lateral precuneus; L, left; R, right.

Figure 5. Mediation Role of the Global Efficiency of the SAN and DMN Between Neglect and High Scores on the TPQ-NS. (Figure 5a shows the SAN, for the right side of the anterior insula; Figure 5b shows the SAN for the left side of the anterior insula; and Figure 5c shows the DMN for the right lateral precuneus.



Abbreviations: DMN, default mode network; SAN, salience network; TPQ-NS, Three-Dimensional Personality Questionnaire-Novelty Seeking.

Global Efficiency and Mental Health

There was a total effect between neglect and TPQ-NS (β = 0.1904). The total effect is the sum of direct effect and indirect effect. We found that three networks had indirect effects on neglect and TPQ-NS. Differences in the global efficiency of the SAN for the right and left of the anterior insula had significant roles as mediators between neglect and the TPQ-NS—right: β = 0.0647, CI 0.0088, 0.1597 (Figure 5A) and left: β = 0.0172, CI 0.0694 to 0.1224 (Figure 5B). Similarly, the same mediated effect occurred in the DMN for

the right lateral precuneus—β = -0.0464, CI -0.1097, -0.0109 (Figure 5C).

DISCUSSION

The current study found that abuse and neglect scores were significantly associated with changes in the network topology properties of the DMN and the SAN, such that higher abuse and neglect scores were associated with a higher global efficiency in the SAN and a lower global efficiency in the DMN for the childhood trauma group than for the healthy control group.

The study also found that higher neglect scores were significantly more likely to affect females' global efficiency of the SAN than for males and that increases in the global efficiency of the SAN mediated the association between neglect and the novelty-seeking score on the TPQ. The results of previous studies[28,41,44-46] and the current study provide evidence that early life adversity has different effects on resting-state functional networks in the brains of males and females. It is important to pay attention to examining gender differences in the future in exploring the association between childhood trauma and neural networks.

The current study also found that the global efficiency of DMN for the right lateral precuneus was significantly lower for adults with traumatic childhoods than for those without such experiences. Traumatic childhoods may cause specific impairments in emotional and cognitive processing, resulting in a decrease in the global efficiency of the precuneus.

In addition, the current study found that the global efficiency of the SAN for the bilateral anterior insula was significantly higher for the childhood trauma group than for the control group and was significantly positively associated with scores for abuse and neglect.

This current study also found that the average path length of the right intraparietal sulcus of the DAN was significantly greater for the childhood trauma group than for the control group.

This current study had some limitations. First, most participants were from schools and communities, and few had experienced severe abuse and neglect, so it was difficult to draw conclusions about the unique consequences of severe childhood abuse and neglect on personality and psychological problems.

Second, the CTQ is a retrospective survey, which may have memory bias. Only prospective studies of participants from childhood to adulthood can overcome this methodological problem when studying the effects of childhood trauma on the resting state networks.

Third, the current study didn't examine changes in the structure and function of specific brain regions such as the amygdala, hippocampus, medial prefrontal cortex, which studies have previously associated with abuse, and of the frontoparietal cortex, which studies have previously associated with deprivation, in relation to childhood trauma, personality formation, and psychological state.

Finally, the was a cross-sectional survey and didn't examine the effects of age and duration of childhood trauma. The mean age of participants was young. The complex relationship between the timing of childhood trauma and neurobiology remains to be studied. Future studies should investigate this in more detail.

CONCLUSIONS

These findings indicate that childhood trauma can alter resting-state functional networks in healthy youth. This abnormality in brain circuitry is especially relevant to the DMN and SAN networks.

AVAILABILITY OF DATA AND MATERIALS

The article includes all data generated.

AUTHORS' DISCLOSURE STATEMENT

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AUTHOR CONTRIBUTIONS

Yankai Wu and Kailiang Fu contributed equally to this work.

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