



Intrinsic brain network alterations in non-clinical adults with a history of childhood trauma

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ABSTRACT

Background: Childhood trauma is a major social public-health problem worldwide. Previous literature suggests childhood trauma is associated with the development of psychiatric disorders and maladaptive behaviours later in life, but little is known about the neural basis underlying these associations.

Objective: The aim of the current study was to investigate intrinsic brain network alterations in non-clinical adults with childhood trauma.

Methods: Resting-state functional magnetic resonance imaging (fMRI) data were collected from 65 non-clinical adults with moderate or severe childhood trauma (CT group), according to the international demarcation criteria of the Childhood Trauma Questionnaire (CTQ), and 73 socio-demographically matched non-clinical controls without childhood trauma (no-CT group). Independent component analysis (ICA) was used to extract subnetworks of the default mode network (DMN), salience network (SN), and central executive network (CEN).

Results: ICA revealed that the CT group had increased FC of the left medial prefrontal cortex (mPFC) in the anterior DMN (aDMN), increased functional connectivity (FC) of the left anterior insula in the SN, and decreased FC of the inferior parietal gyrus of the right CEN (rCEN). Compared to the controls, the CT group had decreased inter-network FCs between the SN and posterior DMN (pDMN), as well as between the pDMN and rCEN.

Conclusions: Impaired FC within the three key brain networks, decreased inter-FC between SN and rCEN, and decreased inter-FC between pDMN and rCEN may reflect biomarkers of childhood trauma.

Alteraciones intrínsecas de redes cerebrales en población adulta no clínica con antecedentes de trauma infantil

Antecedentes: El trauma infantil es un importante problema de salud pública social a nivel mundial. La literatura previa sugiere que el trauma infantil está asociado con el desarrollo de trastornos psiquiátricos y conductas desadaptativas posteriores en la vida, pero se sabe poco acerca de las bases neuronales que subyacen a estas asociaciones.

Objetivo: El objetivo del este estudio fue el de investigar las alteraciones intrínsecas de las redes cerebrales en población adulta no clínica con trauma infantil.

Métodos: Se recolectaron los datos de resonancia magnética funcional (fMRI) en estado de reposo de 65 adultos no-clínicos con trauma infantil moderado o severo (grupo de TI) de acuerdo con los criterios de demarcación internacional del Cuestionario de Trauma Infantil (CTQ en sus siglas en inglés) y de 73 controles no clínicos sin antecedente de trauma infantil (grupo sin-TI) emparejados sociodemográficamente. Se utilizó el análisis de componentes independientes (ACI) para extraer subredes de la red neuronal por defecto (RND), la red de asignación de relevancia (RAR en sus siglas en inglés) y la red ejecutiva central (REC en sus siglas en inglés).

Resultados: El ACI mostró que el grupo de TI presentaba un incremento de la conectividad funcional (CF) de la corteza prefrontal medial izquierda (CPFm) en la RND anterior (RNDa), un incremento de la CF de la ínsula anterior izquierda en la RAR y una CF disminuida en la circunvolución parietal inferior de la REC derecha (REcd). En comparación con los controles, el grupo de TI mostraba menores CF entre redes. Esto se observó entre la RAR y la RND posterior (RNDp), así como entre la RNDp y la REcd.

Conclusiones: Una disfunción en la CF entre tres redes cerebrales clave, una disminución de la CF entre la RAR y la REcd y una disminución de la CF entre la RNDp y la REcd podían mostrarse como biomarcadores del trauma infantil.

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关键词

童年创伤; 功能连接; 独立成分分析

HIGHLIGHTS

- In this paper, we found specific FC alterations within and between three key networks in non-clinical adults with childhood trauma, which may mediate the relationship between childhood trauma and psychiatric disorders in later life.

有童年创伤史的非临床成人的内在脑网络改变

背景: 童年创伤是全世界一个主要的社会公共卫生问题。前人文献表明, 童年创伤与以后生活中精神障碍和适应不良行为的发展有关, 但对这些关联背后的神经基础知之甚少。

目的: 本研究旨在考查有童年创伤的非临床成人的内在脑网络改变。

方法: 数据来源为 65 名患有中度或重度童年创伤 (根据儿童创伤问卷 (CTQ) 的国际分界标准) 的非临床成人 (CT 组) 和 73 名在人口统计学上匹配的无童年创伤的非临床对照 (无 CT 组)。独立成分分析 (ICA) 用于提取默认模式网络 (DMN), 突显网络 (SN) 和中央执行网络 (CEN) 的子网络。

结果: ICA 显示 CT 组前 DMN (aDMN) 的左内侧前额叶皮层 (mPFC) 的功能连接 (FC) 增加, SN 左前岛叶的 FC 增加, 下顶叶 CEN 右回 (rCEN) 的 FC 降低。与对照组相比, CT 组 SN 和后 DMN (pDMN) 之间以及 pDMN 和 rCEN 之间的网络间 FC 减少。

结论: 三个关键脑网络内的 FC 受损, SN 和 rCEN 之间的脑区间 FC 减少以及 pDMN 和 rCEN 之间的脑区间 FC 减少可能反映了童年创伤的生物标志物。

1. Introduction

Childhood trauma is a common public health problem with a high prevalence in Western countries and in China (Hillis, Mercy, Amobi, & Kress, 2016). It has been known that childhood trauma is a major risk factor for multiple psychiatric illnesses, including post-traumatic stress disorder (PTSD), schizophrenia, borderline personality disorder, bipolar disorder, and major depressive disorder (MDD). Individuals with a history of childhood trauma, even without psychiatric diagnoses, demonstrate neurobiological abnormalities that appear to be sequelae of childhood trauma exposure (Lu et al., 2016; Philip et al., 2013). However, little is known about neural alterations in adults who experienced childhood trauma.

Functional magnetic resonance imaging (fMRI) studies, which demonstrate activation in specific brain areas in real time, have demonstrated that the brain is organized into spatially segregated functional networks, each of which is associated with particular cognitive functions (Fox & Greicius, 2010). The three most important intrinsic networks of human brain activation that have been demonstrated are the central executive network (CEN), salience network (SN), and default mode network (DMN). The CEN, which has major nodes in the dorso-lateral prefrontal cortex (dlPFC) and posterior parietal cortex, is active during the performance of behavioural tasks (Koechlin & Summerfield, 2007; Sridharan, Levitin, & Menon, 2008). Activation of the SN, which includes dorsal anterior cingulate cortex (ACC) and insular cortex, appears to be related to information filtering, detection, and integration (Menon & Uddin, 2010). The DMN, which has major nodes in medial prefrontal cortex (mPFC) and posterior cingulate cortex (PCC), has been described as a task-negative network because it is active during periods of inactivity (Buckner, Andrews-Hanna, & Schacter, 2008; Ralchle & Snyder, 2007). Indeed, the CEN, SN, and DMN do not function independently, as has been emphasized in the recently proposed triple-network model of cooperation among these networks (Menon, 2011). The SN appears to initiate a network switch from CEN engagement to DMN

disengagement, that is, the SN plays an important role in initiating transient control signals that engage the CEN to mediate cognitive control processes while disengaging the DMN when a salient external stimulus is detected (Menon, 2011).

Childhood trauma has been reported to be associated with changes in the CEN, SN, and DMN. Bluhm et al. (2009) obtained evidence suggesting that childhood abuse may be associated with decreased functional connectivity (FC) of the PCC in the DMN, particularly in individuals who have developed PTSD. Meanwhile, Birn, Patriat, Phillips, Germain, & Heringa (2014) results suggest altered FC between amygdala and hippocampus might lead to adult PTSD. Trend-level increases in amygdala-mPFC connectivity have been observed in no-clinical adults with a history of childhood trauma (Philip et al., 2013), and severity of early life stress has been found to correlate inversely with global connectivity of the left dlPFC (Cisler et al., 2013). Childhood trauma was also found to be associated with altered intrinsic connectivity of the SN in trauma-exposed youth (Marusak, Etkin, & Thomason, 2015), as well as with diminished amygdala-precuneus FC (van der Werff et al., 2013). Teicher, Anderson, Ohashi, & Polcari (2014) proposed that maltreatment may be associated with an enhanced importance of nodal regions (i.e. eigenvector centrality) involved in internal emotional perception within brain networks. Interestingly, whereas MDD patients with a history of childhood trauma have been reported to have widespread reduction of FC strength in the bilateral ventral mPFC and ventral ACC (Wang et al., 2014), non-clinical adults with early life trauma showed decreased regional homogeneity in the right parietal lobule (Lu et al., 2016).

Investigations of connectivity within single networks, as most prior studies have done, may not reveal potential large-scale network alterations that may be associated with early life trauma (Cisler, 2017). Indeed, the CEN, SN, and DMN do not function independently. Although the sample sizes of experimental groups in studies examining these questions

have been relatively small, several studies have been able to detect altered interactions between key nodes of the triple-network model. For example, Philip et al. (2013) found decreased connectivity between the inferior parietal lobule and mPFC in subjects with exposure to early life stress. Graham, Pfeifer, Fisher, Carpenter, & Fair (2015) found altered PCC-mPFC connectivity in infants with high interparental conflict since birth. There has yet to be a systematic study designed to examine the connectivity within these three networks and the coordination among them.

Taken together, these findings indicate that there may be specific FC alterations within and between the three networks in adults with childhood trauma. The primary aim of the present study was to investigate the connectivity within and between the CEN, SN, and DMN systematically, based on the triple-network model in non-clinical adults with a history childhood trauma. Employing fMRI with independent component analysis (ICA), we compared FC within each network (intra-FC) and among the three networks (inter-FC) between a childhood trauma (CT) group and a socio-demographically matched control (no-CT) group.

2. Materials and methods

2.1. Participants

Participants were recruited from a survey that we carried out to investigate the psychometric properties of the Chinese version Childhood Trauma Questionnaire (CTQ); they had been recruited originally from local communities and colleges through posters and advertisements. All subjects were interviewed independently by two psychiatrists using the Structured Clinical Interview for DSM-IV-TR Axis I Non-patient Edition.

All participants were right-handed. Study inclusion criteria were (1) a history of trauma exposure as a child, defined as a CTQ subscale classification score of 'moderate' or 'severe' (CT group), or absence of such experience, confirmed with the same instrument (no-CT group); (2) absence of any current or lifetime history of psychiatric disorders, assessed by Structured Clinical Interview for DSM-IV-TR Axis I Non-patient Edition (Philip et al., 2013); The two groups were matched on the basis of age, gender, and education level. Exclusion criteria were (1) any prior DSM-IV-TR Axis I disorder; (2) history of psychotropic medication use or psychotherapy; (3) history of alcohol/substance abuse; and (4) diagnosed neurological disorder, structural brain abnormality, or contraindication for MRI.

Ultimately, 72 (37 females) participants who had a history childhood trauma and 81 (39 females) controls were recruited for the study. This study was conducted with the approval of the Ethics committee

of the Second Xiangya Hospital of Central South University, and participants were compensated for their time. All subjects were aware of the study's purpose and provided written informed consent.

2.2. Trauma and assessments

Childhood trauma severity was assessed with the Chinese version CTQ, a 28-item self-report measure which has been shown repeatedly with good reliability and validity among Chinese (He, Zhong, Gao, Xiong, & Yao, 2019). The CTQ assesses exposure to five aspects of childhood trauma: emotional neglect, physical neglect, emotional abuse, physical abuse, and sexual abuse (Bernstein et al., 2003). It is a good tool for childhood trauma assessment and has been widely used in Chinese studies (He et al., 2019; Lu et al., 2016). Participants who obtained scores higher than any the following subscale thresholds for moderate-severe trauma were assigned to the CT group: emotional neglect ≥ 15 ; physical neglect ≥ 10 ; emotional abuse ≥ 13 ; physical abuse ≥ 10 ; and sexual abuse ≥ 8 (Bernstein, Stein, & Handelsman, 1998).

Depressiveness level was determined with the Beck Depression Inventory-II (BDI) (Beck, Steer, & Brown, 1996). Anxiety symptoms were assessed with the State Trait Anxiety Inventory (SAI/TAI) (Spielberger, 1983).

2.3. Data acquisition and preprocessing

All imaging data were acquired on a 3.0-T Siemens Magnetom Skyra scanner at the Second Xiangya Hospital of Central South University. All participants were asked to lie in a supine position with their eyes closed, to remain still, and to think of nothing in particular while not falling asleep. Their heads were fixed snugly with foam pads and straps to minimize head movement. Blood-oxygen-level-dependent data were obtained with the following parameters: 2000-ms repetition time, 30-ms echo time, 80° flip angle, 4 × 4 × 4-mm voxel size, 256-mm field of view, 4-mm slice thickness, 1-mm slice gap, 32 axial slices.

We processed imaging data in DPARSF (Data Processing Assistant for Resting-State fMRI software, version 2.3; Yan & Zang (2010), <http://www.restfmri.net>). Processing included removing the first 10 volumes from each subject's series, aligning slice timing, and applying head motion correction. Data from 15 participants (8 controls) who displayed excessive head motion (translation > 1.5 mm or rotation > 1.5°) were excluded from further analyses. The images were spatially normalized to a standard Montreal Neurological Institute (MNI) template, resampled to a voxel size of 3 × 3 × 3 mm, and smoothed spatially with a Gaussian Kernel (6 × 6 × 6 mm full-width at half maximum). We calculated the mean framewise

Table 1. Demographic and clinical characteristics of all subjects.

Characteristic	CT group (N = 65)	no-CT group (N = 73)	χ^2/t	<i>p</i>	Cohen's <i>d</i>
Age, years	20.69 ± 2.27	20.70 ± 1.82	-0.018	0.986	-
Education, years	14.58 ± 1.59	14.51 ± 1.33	0.312	0.755	-
Gender, male/female	35/30	34/39	0.73	0.394	-
CTQ scores					
Emotional abuse	7.55 ± 2.67	6.04 ± 1.21	4.35	<0.001***	0.72
Physical abuse	6.03 ± 1.59	5.23 ± 0.65	3.92	<0.001***	0.65
Sexual abuse	5.94 ± 1.40	5.14 ± 0.45	4.62	<0.001***	0.76
Emotional neglect	12.92 ± 4.43	8.48 ± 2.56	7.30	<0.001***	1.23
Physical neglect	9.91 ± 2.65	6.47 ± 1.53	9.46	<0.001***	1.63
Total scale	42.35 ± 6.66	31.36 ± 3.86	12.03	<0.001***	2.01
BDI score	5.05 ± 4.05	4.55 ± 4.65	0.666	0.506	-
SAI score	37.98 ± 8.51	36.40 ± 6.94	1.21	0.230	-
TAI score	41.94 ± 7.96	40.73 ± 5.56	1.04	0.300	-
FD	0.11 ± 0.05	0.13 ± 0.06	1.49	0.139	-

Mean values are reported with standard deviations; BDI, Beck Depression Inventory; CT, childhood trauma; CTQ, childhood trauma questionnaire; SAI, State Anxiety Inventory; TAI, Trait Anxiety Inventory; FD, framewise displacement.

displacement (FD) for the two groups, and there was no difference in the mean FD between groups (Table 1).

2.4. ICA and selection of networks-of-interest

For each of the 138 participants, we conducted a spatial ICA employing the Infomix algorithm in GIFT (Group ICA 4.0 fMRI toolbox, <http://www.icatb.sourceforge.net>). Principal component analysis was conducted to decompose preprocessed data into 75 independent components (ICs). We chose this number of ICs based on previous studies (Chen et al., 2016; Dong et al., 2019; Fan et al., 2017; Manoliu et al., 2014a, 2014b) suggesting that high-model-order ICA models can refine components corresponding to known anatomical and functional segments, thereby providing highly detailed and robust decomposition of subnetworks. Resampling of 20 ICAs was conducted with the ICASSO tool in GIFT to ensure stability of the decomposition. These processes produced a set of average group components, which were then back-constructed into a single subject space with the GICA3 algorithm. After these steps, for each component, we produced a spatial z-map, its corresponding time course for each subject, an average z-map, and an average time course.

In terms of selecting ICs related to networks of interest, we first visually inspected the obtained components for the presence of artefacts. Subsequently, we performed multiple spatial regression analyses of our 75-IC average z-map on templates that were previously developed T-maps based on 603 healthy subjects (Allen et al., 2011) and that have been applied in studies of various disorders (Dong et al., 2019; Fan et al., 2017; Manoliu et al., 2014a, 2014b). Separated ICs with the strongest correlation coefficients with respect to the templates were selected as networks of interest for our triple-network model, we obtained the following five networks of

interest: anterior DMN (aDMN); posterior DMN (pDMN); left CEN (lCEN); right CEN (rCEN); and SN.

2.5. Outcome measures

The five ICs related to the aforementioned triple-network model were extracted from all of the subjects' data. For each subject, each component's z-map and its corresponding time course represented measure of intra-intrinsic FC. Before measuring inter-FC, further linear detrending, de-spiking, and temporal filtering were conducted for all networks of interest time courses (Fan et al., 2017; Manoliu et al., 2014b). We calculated Pearson's correlation coefficients of the time courses for each network pair among the SN, CEN, and DMN subnetworks, and then transformed the coefficients into z-scores with Fisher's z-transformation. These transformed z-scores were considered indexes of the inter-FC of each network pair.

2.6. Statistical analysis

Two-sample t-tests (continuous data) and chi-squared tests (categorical data) were conducted to detect demographic and psychometric differences between the two groups. To test the networks of interest, IC z-maps were gathered for each group and subjected to separate one-sample t-tests. Two-sample t-tests were applied to analyse group differences in intra-FC within the network mask created by combining the results of the aforementioned one-sample t-tests for each group. Age, gender, education level, BDI score, SAI score, and TAI score were included as covariates of no interest in the comparisons. All imaging results were subjected to false discovery rate (FDR) correction (initial voxel threshold of $p < .001$; significance at $p < .05$).

To analyse group differences in inter-FC, z-scores of each network pair were subjected to a multivariate

analysis of variance (MANOVA). The significance criterion was $p < .05$ with FDR correction for multiple comparisons. We extracted FC values of altered clusters within networks of interest and also extracted z values for correlations between each pair of networks with a group difference. Multiple stepwise regression analyses were conducted for the CT group to evaluate potential correlations of CTQ scores with intra-FC or inter-FC.

Statistical analysis of z -maps was performed with REST software (Resting-State fMRI Data Analysis Toolkit, version 1.8; Song et al., 2011; <http://www.restfmri.net>). Demographic, clinical, and extracted z -score data analyses were conducted in SPSS (Statistical Package for Social Sciences, version 22.0).

3. Results

3.1. Demographic and clinical characteristics

The participants' demographic and clinical characteristics are summarized in Table 1. The CT and no-CT groups did not significantly differ in terms of age, gender, educational level, BDI score, SAI score, and TAI score ($p > .05$). The CT group scored significantly higher than the no-CT group on the CTQ and its subscales ($p < .05$).

3.2. Identification of network of interests

The respective spatial pattern of networks of interest for the two groups revealed by combined one-sample t -tests are shown in Figure 1 (FDR-corrected, $p < .05$). The aDMN was comprised mainly of the ACC and mPFC. The pDMN included primarily the PCC and precuneus. The lCEN included mainly the left inferior parietal lobule, left superior parietal gyrus, and left dlPFC, while the rCEN was comprised mainly of the right inferior parietal lobule, right angular gyrus, and right dlPFC. The SN included primarily the insular cortex and cingulate cortex.

3.3. Group differences in intra-FC

Significant intra-FC differences between the CT and no-CT groups are reported in Table 2 and shown in Figure 2. Briefly, compared to the no-CT group, the CT subjects exhibited significantly greater FC in the left mPFC of the aDMN as well as greater FC in the left anterior insular cortex of the SN (FDR corrected, $p < .05$; Figure 2(a) and (b)). Relative to the no-CT group, the CT group had decreased FC in the right inferior parietal gyrus of the rCEN (FDR-corrected, $p < .05$; Figure 2(c)). Effect sizes (Cohen's d values) for altered clusters ranged from 0.55 to 1.05 (Table 2). No other significant group differences in intra-FC were detected.

3.4. Group differences in inter-FC

A MANOVA revealed that the CT group had significantly decreased inter-FC between the SN and pDMN, as well as between the pDMN and rCEN (FDR-corrected, $p < .05$; Table 3, Figure 3). These alterations reflect impaired FC among intrinsic networks. No other significant group differences in inter-FC were detected.

3.5. Brain-behaviour analyses

Correlational analysis results are reported in Table 4. Notably, altered intra-FC in the aDMN of CT subjects correlated significantly with CTQ total scores ($r = 0.328$, $p < .01$) and emotional neglect subscale scores ($r = 0.259$, $p < .05$). Additionally, altered pDMN-rCEN inter-FC in CT subjects correlated significantly with physical abuse subscale scores ($r = -0.261$, $p < .05$).

4. Discussion

The current systematic investigation of FC within and between the CEN, SN, and DMN based on the triple-network model showed that, compared to controls, people with childhood trauma in the CT group had increased intra-FC in the left mPFC of the aDMN and left anterior insular cortex of the SN, decreased intra-FC in the right inferior parietal lobule of the rCEN, decreased inter-FC between the SN and pDMN, and decreased inter-FC between the pDMN and the rCEN. The most outstanding results were the decreased SN-pDMN and pDMN-rCEN inter-FCs in the CT group. The findings of triple-network model in our study provide experiment evidence to the point that individuals with a history of childhood trauma, even without psychiatric diagnoses, demonstrate neurobiological abnormalities.

These atypical FCs may represent potential imaging biomarkers of childhood trauma. According to the triple network model, the SN, CEN, and DMN do not function independently, with the SN initiating a network switch from CEN engagement to disengagement of the DMN (Menon, 2011). The SN plays an important role in saliency detection. The CEN is crucial for the active maintenance and manipulation of information in working memory as well as for judgment and decision-making during goal-directed behaviour. And the DMN has been suggested to be involved in self-examination, self-consciousness, and biographical memory (Koechlin & Summerfield, 2007; Petrides, 2005). Many psychiatric disorders are characterized by deficits in the cooperation of these networks. The presently observed SN-pDMN inter-FC alterations in the CT group might reflect atypical SN involvement in compromised DMN-CEN switching

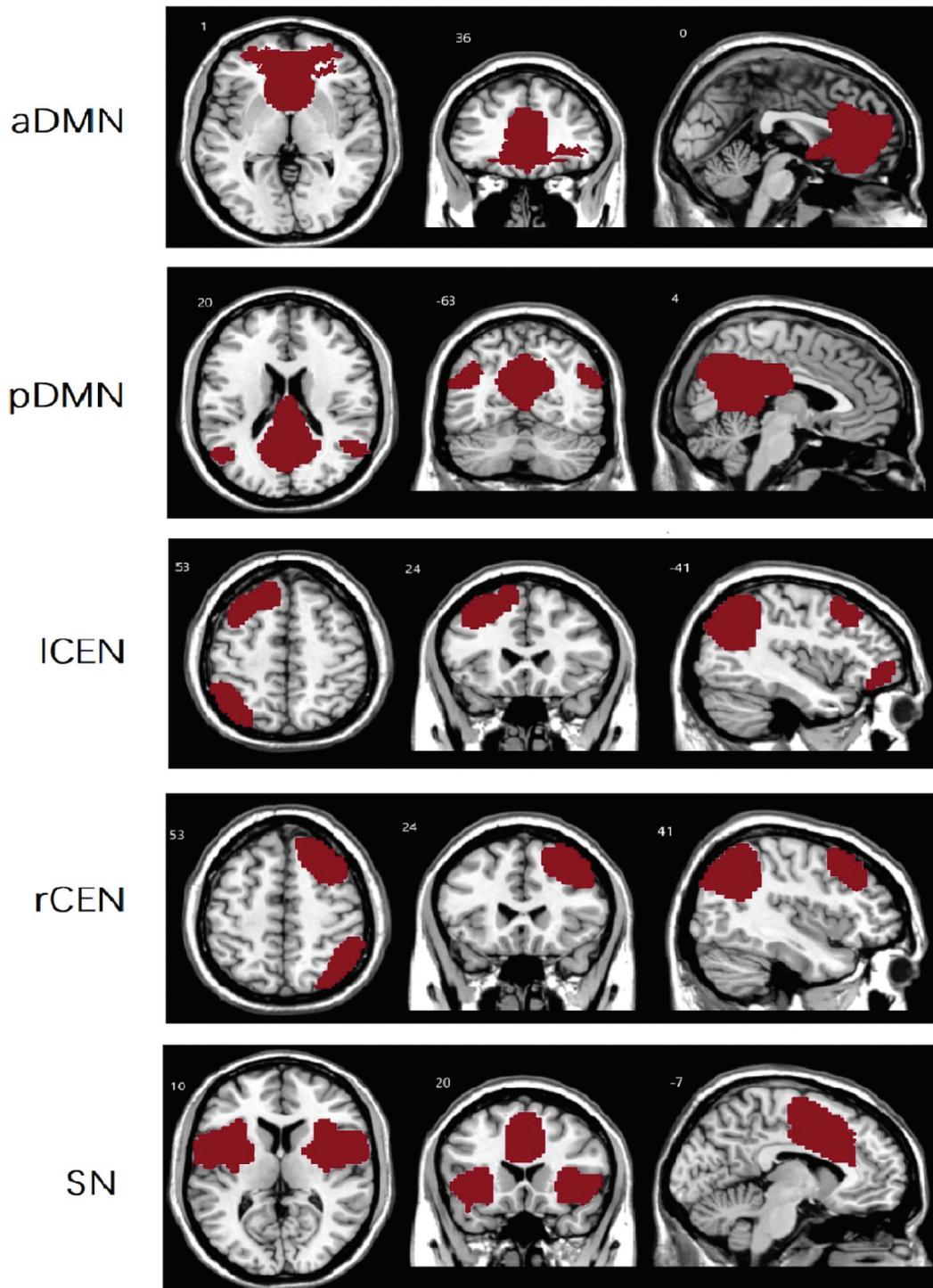


Figure 1. Spatial patterns of SN, CEN, and DMN components. The patterns for each network were combined with one-sample t-test results for each group's reconstructed spatial maps (FDR-corrected, $p < .05$). aDMN, anterior default mode network; pDMN, posterior default mode network; ICEN, left central executive network; rCEN, right central executive network; SN, salience network.

in subjects with childhood trauma. Impaired SN-pDMN might suppress internal self-referential cognition, resulting in inefficiently performing the cognitive tasks, which may further lead to the cognitive deficits. The presently observed decreased inter-FC between the SN and pDMN may underlie risk mechanisms for cognitive deficits of psychiatric disorders.

To the best of our knowledge, this report provides the first evidence of reduced inter-FC between the pDMN and rCEN in individuals who have

experienced childhood trauma. The DMN and CEN may exhibit a competitive relationship, with each exhibiting distinct patterns of information processing, and this relationship may reflect a basic function of the brain. Chen et al. (2013) found that the CEN can induce negative CEN-DMN FC that is suggestive of inhibition of DMN activity consistent with DMN regulation. A prior high-model-order ICA study demonstrated that both networks consist of functional subnetworks (Allen et al., 2011). High temporal

resolution resting-state fMRI experiments showed that distinct subnetworks within the DMN have characteristic connectivity patterns among themselves as well as relative to the characteristic patterns in other networks (ref). Thus, the presently observed alterations in inter-FC between the pDMN and rCEN may reflect an atypical suppression between these networks in subjects with a history of childhood trauma.

It is noteworthy that we observed hypoactivity of the anterior insula, a key node of the SN that plays an important role in detecting and processing negative emotions (Menon & Uddin, 2010). In trauma-exposed youth, Marusak et al. (2015) found altered intrinsic connectivity of the SN that could be related to decreased reward sensitivity. Increased FC of the

insular cortex could thus disrupt saliency detection, leading to atypical detection and attention processing, including a negative bias.

Meanwhile, the inferior parietal lobule, a key node of CEN, plays an important role in the focusing of attention. The current finding of decreased intra-FC in the right inferior parietal lobule of the rCEN is consistent with Lu et al.'s (2016) prior finding indicating that subjects with early life trauma have decreased regional homogeneity in the right parietal lobule. Given these findings, it would be of great interest to examine the hypothesis that hypoactivity of the inferior parietal lobule may impair one's ability to concentrate in the context of goal directed behaviour, particularly in a study in which brains are examined with fMRI during the performance of attention tasks.

The mPFC, a critical component of the DMN, has been suggested to be involved in self-examination, self-consciousness, and biographical memory (Johnson et al., 2006, 2002; Northoff, 2007). Given that MDD patients have been shown to have augmented FC of the mPFC (Zhu et al., 2012), the presently observed increased intra-FC in the left mPFC of our CT group subjects may reflect a neural basis by which childhood trauma becomes a risk factor for MDD. Moreover, enhanced introverted thinking due to

Table 2. Group differences in intra-FC.

Network: region	BA	Peak MNI coordinates			Voxels	Peak <i>t</i> values	Cohen's <i>d</i>
		x	y	z			
aDMN: left mPFC	32	-6	54	-3	57	7.15	1.05
rCEN: right IPL	40	60	-36	42	17	-4.79	0.55
SN: left anterior insular	47	-24	6	-18	26	4.63	0.91

BA, Brodmann's area; FC, functional connectivity; MNI, Montreal Neurological Institute; aDMN, anterior default mode network; mPFC, medial prefrontal cortex; rCEN, right central executive network; IPL, inferior parietal lobule; SN, salience network.

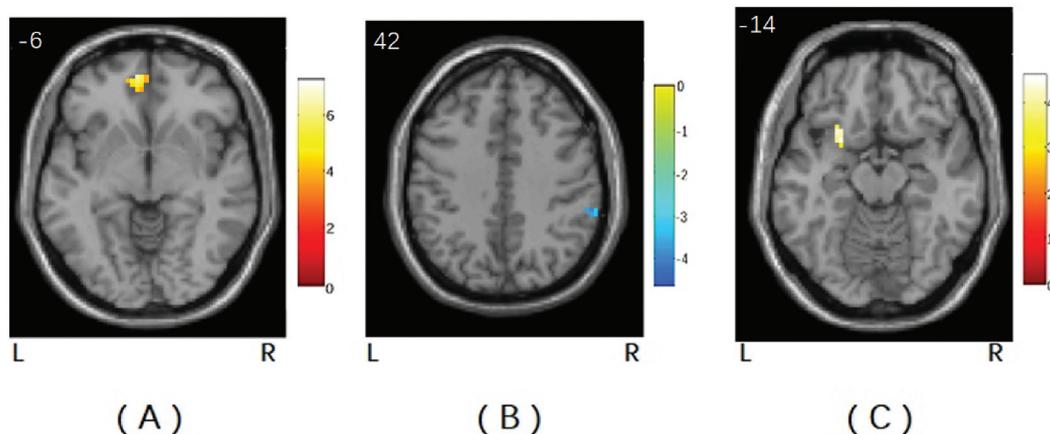


Figure 2. Visualization of intra-FC differences observed in the CT group relative to the no-CT (reference) group. (a) Increased FC of the left mPFC within the aDMN. (b) Reduced FC of the right inferior parietal gyrus within the rCEN. (c) Increased FC of the left anterior insula within the SN. The significance criterion was FDR corrected $p < .05$.

Table 3. Group differences in inter-FC.

Network pair	CT group (<i>N</i> = 65)	no-CT group (<i>N</i> = 73)	<i>t</i>	<i>p</i> uncorrected	Cohen's <i>d</i>
SN-aDMN	0.07 ± 0.25	0.12 ± 0.23	-2.692	0.012	-
SN-pDMN	-0.12 ± 0.22	0.01 ± 0.24	-3.188	0.002*	0.56
SN-ICEN	0.15 ± 0.26	0.19 ± 0.25	-1.022	0.308	-
SN-rCEN	0.21 ± 0.25	0.22 ± 0.23	-0.208	0.836	-
aDMN-pDMN	0.43 ± 0.20	0.42 ± 0.20	0.178	0.859	-
aDMN-ICEN	0.31 ± 0.24	0.40 ± 0.23	-2.003	0.047	-
aDMN-rCEN	0.30 ± 0.23	0.34 ± 0.20	-1.839	0.068	-
pDMN-ICEN	0.43 ± 0.22	0.49 ± 0.22	-1.514	0.132	-
pDMN-rCEN	0.42 ± 0.19	0.58 ± 0.20	-4.780	< 0.001*	0.82
ICEN-rCEN	0.85 ± 0.28	0.86 ± 0.22	-0.303	0.762	-

aDMN, anterior default mode network; CT, childhood trauma; pDMN, posterior default mode network; ICEN, left central executive network; rCEN, right central executive network; SN, salience network. *Significant at $p < 0.05$ after FDR correction.

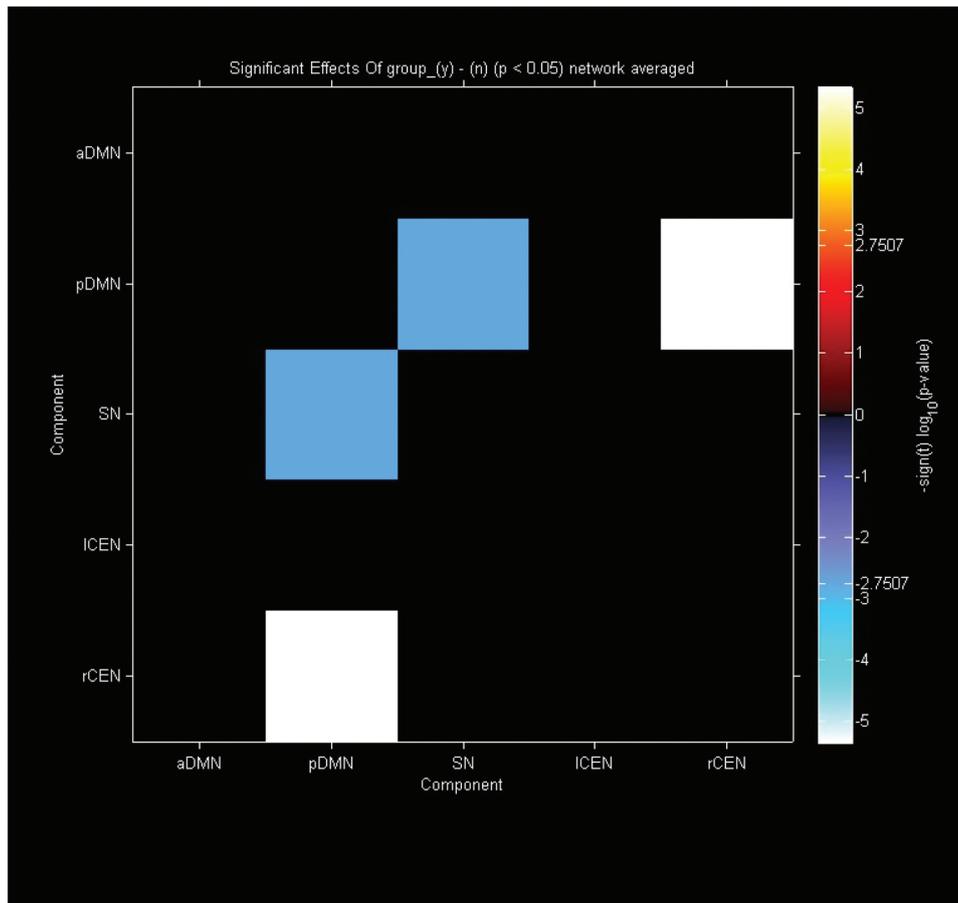


Figure 3. Visualization of inter-FC differences observed in the CT group relative to the HC (reference) group. aDMN, anterior default mode network; pDMN, posterior default mode network; ICEN, left central executive network; rCEN, right central executive network; SN, salience network. The significance criterion was FDR corrected $p < .05$.

Table 4. Correlations between CTQ scores and FC values in the CT group.

CTQ score	aDMN	SN	rCEN	SN- pDMN	pDMN- rCEN
Total	0.328**	0.207	0.089	-0.110	-0.090
Emotional abuse	0.237	-0.068	0.097	-0.169	-0.196
Physical abuse	0.113	0.207	0.242	-0.175	-0.261*
Sexual abuse	-0.231	-0.191	-0.046	-0.111	-0.116
Emotional neglect	0.259*	0.244	0.111	-0.038	0.050
Physical neglect	0.207	0.089	0.198	0.122	0.106

CT, childhood trauma; CTQ, childhood trauma questionnaire; aDMN, anterior default mode network; FC, functional connectivity; pDMN, posterior default mode network; ICEN, left central executive network; rCEN, right central executive network; SN, salience network. * $p < 0.05$; ** $p < 0.01$.

increased mPFC-aDMN connectivity may be related to the generation of depressive cognitive styles, including increased self-attention and deliberate thinking. In people with dissociative subtype of PTSD, which is often associated with more childhood trauma, Nicholson et al. (2020) found more DMN functional connectivity in the left middle dorsal PFC. The presently observed increased intra-FC in the left mPFC may reflect risk mechanisms for PTSD following childhood trauma.

Interestingly, among our CT group subjects, we found that intra-FC in the left mPFC of the aDMN correlated with CTQ total scores. The mPFC has been

shown to exhibit particularly strong activity when subjects answer questions related to their abilities and attitudes (Johnson et al., 2002). Thus, childhood trauma-associated disruption of the performance of tasks involving self-attention may be related to trauma severity. We also found associations between altered FC and CTQ subscale scores for emotional neglect and physical abuse, suggesting that core cognitive networks may be particularly sensitive to these two aspects of childhood trauma. These findings support Wang et al.'s (2014) suggestion that different types of childhood trauma have differentiable impacts.

Several study limitations should be noted. First, there is not yet a clear computational criterion for IC decomposition and there is not yet a consensus regarding the best ICA model to be used in this context. Second, we did not separate subjects by the type or (multiple) types of childhood trauma that they experienced. Third, childhood trauma was assessed mainly with retrospective questionnaires, which can result in information bias. Ideally, childhood trauma should be examined more comprehensively based on multiple forms of assessment, such as face-to-face interviews with subjects and guardians. Finally, our use of a cross-sectional, rather than longitudinal, study design limits our ability to make conclusions

regarding the relationship between childhood trauma and dynamic alterations in FC.

5. Conclusion

Non-clinical adults with a history of childhood trauma were found to exhibit hypoactivity of key nodes of the CEN, SN, and DMN, as well as altered inter-FC between subnetworks of these networks. The presently observed childhood trauma biomarkers may mediate the relationship between childhood trauma and psychiatric disorders in later life.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author, S. Yao. The data are not publicly available due to privacy restrictions, as they contain information that could compromise the privacy of research participants.

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