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Emotional abuse mediated by negative automatic thoughts impacts functional connectivity during adolescence

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ABSTRACT

Background: Emotional abuse during childhood and adolescence is thought to be associated with the brain; however, the neural mechanism underlying the cognitive process remains unknown. Therefore, we aimed to investigate the mediating effect of negative automatic thoughts on the relationship between emotional abuse and resting-state functional connectivity (rsFC) during adolescence.
Method: Our community sample included 54 adolescents aged 13–17 years in the statistical analysis. Resting-state functional and structural magnetic resonance imaging (MRI) was performed, while emotional abuse and negative automatic thoughts were assessed using self-reported scales. A mediation analysis was used to assess the contributions of early traumatic events and negative automatic thoughts to resting functional connectivity.
Result: Higher negative automatic thoughts were associated with lower connectivity in the context of greater emotional abuse (i.e., suppression effect). Thus, the relationships between emotional abuse and connectivity in the precuneus (pCun)-medial prefrontal cortex, parahippocampal cortex-extrastriate cortex, and temporal cortex-temporal pole were decreased by negative automatic thoughts. In contrast, functional connections in the pCun-pCun, pCun-precuneus/posterior cingulate cortex, and nucleus accumbens-somatomotor areas were strongly mediated when emotionally abused adolescents reported a high tendency for negative automatic thoughts.
Conclusion: Negative automatic thoughts strengthened the relationship between emotional abuse and rsFC. These findings highlight the underlying cognitive processing of the traumatic event-neural system, supporting the use of cognitive therapy for post-traumatic symptoms.

1. Introduction

Early life adversity induces structural and functional changes in the brain, increasing vulnerability to various mental illnesses (Cassiers et al., 2018; Dannlowski et al., 2012; McLaughlin et al., 2012). Since adolescence is in a developmental process, mental health is sensitive to environmental factors (Fuhrmann et al., 2015) and is dependent on a history of stressful events, including childhood abuse (American Academy of et al., 2008; Harkness et al., 2006). These traumatic events activate a maladaptive stress response, which modify the underlying neurological mechanisms of brain development (Glaser, 2000; Raymond et al., 2018; Teicher et al., 2003; Tottenham, 2020). In particular, emotional abuse has been suggested to be a strongly influential factor in depression (Gibb et al., 2003), referring to not being provided with an adequate environment or being emotionally supported by parents or guardians (Norman et al., 2012). Emotional abuse is not only associated with the highest rates of revictimization and post-traumatic stress symptom severity, but it often precedes different types of traumatic events (Gama et al., 2021; O'Mahen et al., 2015). Traumatic events are accompanied by poor mental health, particularly after high intensity emotional abuse (Edwards et al., 2003). Furthermore, emotional abuse has long-lasting effects on neurodevelopmental processes (Ibrahim et al., 2021) including changes in brain networks (Ohashi et al., 2017).

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Abbreviations

Amyg	Amygdala
Aud	Auditory network
BG	Basal ganglia
CATS	Children's Automatic Thoughts Scale
Cont	Control network
CSF	Cerebrospinal fluid
Default	Default network
DorsAttn	Dorsal attention network
ETISR-SF	Early trauma inventory self report-short form
ExStr	Extrastriate cortex
FWHM	Full width at half-maximum
Hipp	Hippocampus
L	Left hemisphere
Language	Language network
MNI	Montreal Neurological Institute
MPRAGE	Magnetization-prepared rapid acquisition gradient echo
MRI	Magnetic resonance imaging
NAc	Nucleus accumbens
pCun	Precuneus
pCunPCC	Precuneus and posterior cingulate cortex
PFC	Prefrontal cortex
PHC	Parahippocampal cortex
R	Right hemisphere
rsFC	Resting-state functional connectivity
SalVenAttn	Salience ventral attention network
SD	Standard deviation
SoM	Somatomotor area
SomMot	Somatomotor network
Temp	Temporal cortex
TempPole	Temporal pole
Tha	Thalamus
Visual	Visual network

Several factors may link emotional abuse with neuropsychological vulnerability. Cognitive mediators, including maladaptive schemes, connect emotional abuse and post-traumatic symptoms (i.e., depression) frequently exhibited in trauma victims (Li et al., 2020). Additionally, negative automatic thought is a critical cognitive mediator (Kwon and Oei, 1992; Park et al., 2018), which indicates an internal dialog occurring reflexively on specific themes (Beck, 1979). Negative automatic thoughts dominantly mediate the association between stressful life events and emotional/behavioral problems compared to other maladaptive cognitions (Flouri and Panourgia, 2014). Furthermore, emotional abuse is an active form of maltreatment relative to neglect, which is crucially related to negative self-associations (van Harmelen et al., 2010). Thus, we conceptualized that negative automatic processes would be led by emotional abuse which affects numerous dysfunctional mental outcomes.

Recent neuroimaging studies have investigated the brain network changes affected by automatic thoughts (Cun et al., 2014) and maltreatment during development (Cisler, 2017; Whittle et al., 2013). Automatic thoughts are associated with disrupted resting-state functional connectivity (rsFC) in the brain's default networks covering the precuneus and posterior/anterior cingulate cortex (Peng et al., 2021). Teicher et al. (2016) discussed maltreatment-induced changes in functional connectivity in brain regions, including the precuneus (pCun), prefrontal cortex (PFC), temporal pole (TempPole), amygdala, and network attributes; decreased connectivity of the pCun with the amygdala and ACC in individuals with emotional maltreatment experiences have been reported (van der Werff et al., 2013). Therefore, the adolescent brain undergoes changes in the default network, associated with automatic thought (Calvete et al., 2013; Şoflău and David, 2016).

Fronto-limbic circuits (Teicher and Samson, 2013) and functional coupling between the amygdala and mPFC play critical roles in emotional processing and regulation related to childhood abuse (Uy et al., 2023). Nevertheless, how negative automatic thoughts contribute to spontaneous functional neural systems in adolescents reporting emotional abuse is yet to be elucidated. We, therefore, aimed to examine the associations between emotional abuse, negative automatic thoughts, and rsFC. To test the relationships between emotional abuse and neural correlates, we hypothesized that the cognitive mediator of negative automatic thought can be an underpinning within the variables. Mediation models were used to investigate not only different mediating effect of negative automatic thought (i.e., suppression and mediation) but functional architecture of the brain using whole-brain resting-state functional MRI (rs-fMRI).

2. Materials and methods

2.1. Participants

A community sample was collected from 56 middle adolescents, between 13 and 17 years of age, using flyers in schools and libraries in Seoul, South Korea. We included patients with no history of neurological disorders; and no psychiatric or developmental disorders, language abnormalities, learning difficulties, or uncorrected sensory impairments. The children and their parents provided written informed consent before the study. We analyzed the data of 54 participants, excluding two with missing data and exceeding the criteria of 3 standard deviation (SD). This study was approved by the Institutional Review Board of Seoul National University Hospital, South Korea (IRB number: C-1412-081-633) and conformed to the guidelines of the Declaration of Helsinki. Table 1 summarizes detailed demographic information and descriptive statistics of the measurements.

2.2. Measures

2.2.1. Emotional abuse

Early traumatic events were assessed using the Early Trauma Inventory Self Report-Short Form (ETISR-SF), which consists of four domains: general trauma, emotional abuse, physical punishment, and sexual events occurring before the age of 18 (Bremner et al., 2007). Among the domains, emotional abuse (e.g., most of the time treated in a

Table 1
Demographic and clinical characteristics.

Characteristics		Mean	SD
Age		14.7222	1.3656
Sex, No. (%)		54	
Male		32 (59.3)	–
Female		22 (40.7)	–
ETISR-SF			
	General trauma (0–6)	1.2222	1.7339
	Physical abuse (0–5)	2.1852	1.8022
	Emotional abuse (0–4)	0.963	1.1969
	Sexual abuse (0–3)	0.1667	0.5408
	Total (0–17)	4.537	3.725
CATS			
	Phyiscal threat (0–28)	5.6296	5.9883
	Social threat (0–15)	3.7222	3.6981
	Personality failure (0–27)	8.3333	8.463
	Hostility (0–26)	7.5741	6.8311
	Total (0–76)	25.2593	20.0435

cold or uncaring way) was used to examine the effects of emotionally abused experiences in children from early childhood to adolescence. The ETISR-SF measures 27 dichotomous items (yes = 1, no = 0) and has been validated with Korean adolescent samples with higher internal reliability (Cronbach's = 0.87) (Jeon et al., 2012).

2.2.2. Negative automatic thought

Negative automatic thoughts were measured using the Children's Automatic Thoughts Scale (CATS), which assesses four cognitive subscales: physical threat (e.g., I'm going to have an accident), social threat (e.g., I'm worried that I'm going to get teased), personal threat (e.g., I've made such a mess of my life) and hostility (e.g., If someone hurts me, I have the right to hurt them back) (Cronbach's = 0.83, 0.92, 0.90 and 0.75, respectively) (Moon et al., 2002; Park et al., 2016). The subscales consist of 10 items scored on a 5-point Likert scale (0 = not at all, 4 = all the time). The total scale of CATS is calculated by summing the subscales with high internal reliability (Cronbach's = 0.94). Unlike other scales that measure automatic thoughts, the CATS is designed to assess automatic thoughts that are specific to children (Schniering and Rapee, 2002).

2.3. MRI data acquisition

A 3.0-T scanner (MAGNETOM Tim Trio; Siemens Medical Solutions, Erlangen, Germany) was used to acquire images of the adolescents at Seoul National University, Republic of Korea. The rs-fMRI imaging parameters were as follows: repetition time (TR) = 3000 ms, echo time (TE) = 40 ms, flip angle (FA) = 90°, matrix size = 128 × 128, voxel size = 1.88 × 1.87 × 4.8 mm^3, field of view (FOV) = 241 × 240 mm^2, and number of volumes = 190. Anatomical T1-weighted images were obtained using a magnetization-prepared rapid acquisition gradient echo (MPRAGE) pulse sequence with the following parameters: TR = 1900 ms, TE = 3.13 ms, FA = 9°, voxel size = 0.898 × 0.898 × 0.9 mm^3, and FOV = 230 × 201 mm^2. During the scan, participants are instructed to keep their eyes closed and remain in a relaxed state. A foam pad was used to reduce head motion artifacts, and the participants were not allowed to fall asleep or focus on specific thoughts.

2.4. Resting-state-fMRI preprocessing

The rs-fMRI images were preprocessed by canonical procedures using SPM12 (https://www.fil.ion.ucl.ac.uk/spm/) (Friston et al., 1994). First, we excluded the three initial scans to allow the magnetization to reach the equilibrium of the MRI time series. Second, slice-time correction was implemented to adjust the acquisition times for all slices. Third, rigid-body registration to model head positions was conducted and, fourth, co-registration was performed to register functional data to the segmented individual T1-weighted data. Fifth, each image was sequentially aligned to the standard stereotactic Montreal Neurological Institute (MNI) space. Finally, the normalized fMRI images were spatially smoothed using an isotropic three-dimensional Gaussian kernel with a 6 mm full width at half-maximum (FWHM).

Average BOLD signals were extracted for each predefined region and preprocessed using conventional procedures (Power et al., 2012; Weissenbacher et al., 2009). First, we regressed out a linear detrend, the effects of six rigid movements, their derivatives, and five principal components of white matter and cerebrospinal fluid (CSF) masks. Spike detection and despiking were conducted with four times the median absolute deviation. Lastly, band-pass filtering (0.01–0.1 Hz) was processed to estimate low frequency fluctuation of resting-state fMRI signals. All procedures were performed using the MATLAB-based custom software.

2.5. rsFC analysis

The rsFC between the BOLD signals of the two distinct regions was calculated using Pearson's correlation and transformed using Fisher's r-to-z test. The whole-brain rsFC was calculated based on mediation models to investigate the impact of negative automatic thoughts. The entire brain was subdivided into 236 distinct areas, with each region defined using the Kong 2022 atlas for 200 cortical areas (Kong et al., 2021; Schaefer et al., 2018) and the Brainnetome atlas for 36 subcortical areas (Fan et al., 2016) (Fig. S1). Previous neuroimaging studies have suggested that adult template on developing brain did not affect the significant differences (Kang et al., 2003; Richards et al., 2016). The brain features have gradual developmental trajectories during preadolescence in the size, total surface area, and gradients of macroscale cortical organizations (Bethlehem et al., 2022; Dekaban and Sadowsky, 1978; Dong et al., 2021). Moreover, the standard adult brain template extends the results beyond specific age groups (Ross et al., 2019; Weiss and Booth, 2017).

2.6. Mediation analysis

Mediation analyses were conducted using the M3 Mediation Toolbox of CANlab (https://github.com/canlab/MediationToolbox). In this study, we examined the association between early emotional abuse as a predictor variable and rsFC as an outcome variable through negative automatic thoughts as a mediator using mediation models.

In detail, mediation analysis considered two regression models as follows:

a. $M = \beta_0 + aX + \epsilon_M$

b. $Y = \beta_1 + c'X + bM + \epsilon_Y$

Where X, Y, and M each represents predictor, outcome, and mediator variable. The values of β_0 and β_1 indicate intercept and ϵ_M and ϵ_Y are measurement errors. The regression coefficient, path *a*, is the association between the predictor and mediator; path *b* is the association between the mediator and outcome; and path *c* refers to the total effect of the predictor on the outcome, with no consideration of the mediator. Path *c* indicates the direct effect between the predictor and outcome, separating the contribution of the mediator. Path *ab* represents the indirect effect between the predictor and outcome through the mediator, which is estimated as $a \times b$. Each mediation model was tested with 10,000 bootstrapping by sampling with replacement of the potential score from the population. A false discovery rate (FDR) < 0.05 was applied to consider testing multiple connections.

The mediation results can be interpreted as mediation or suppression (MacKinnon et al., 2000). The difference between total effect (path *c*) and direct effect (path c') determines whether the mediator functions in mediation or suppression according to mediator. If the total effect is positive and indirect effect (path *ab*) is negative, then the direct effect will be more positive than the total effect in suppression. That is, suppression indicates that the magnitude of total effect is less positive when the mediator variable is intervened. If direct effect is reduced by the mediator in mediation, especially, the mediation effect can be referred to as a complete mediation effect when direct effect is not significant.

3. Results

The association between emotional abuse and rsFC was examined using negative automatic thoughts in adolescents. Higher emotional abuse was associated with higher negative automatic thought (β = 12.45, $P < 0.001$), which determined the effect of the mediator on rsFC. We found that regions of the bilateral pCun predominantly exhibited significant rsFCs.

3.1. Negative automatic thought suppresses emotional abuse-rsFC

Negative automatic thoughts mediated the positive association between emotional abuse and rsFC. Most negative indirect effects were observed in FC cored at the left pCun of control network C (pCun.Cont C) which connected with several subregions within the mPFC; link with left mPFC (β = −0.85, FDR = 0.018), right mPFC2 (β = −0.98, FDR = 0.018), and right mPFC3 (β = −0.82, FDR = 0.029). Connections showing the same pattern were observed in each pair between the left extrastriate cortex (ExStr) and bilateral parahippocampal cortex (PHC) (right, β = −0.82, FDR = 0.039; left, β = −0.77, FDR = 0.029), and between the right temporal cortex (Temp) and left temporal pole (TempPole) (β = −0.97, FDR = 0.011) (Table 2; Fig. 1).

Furthermore, we performed supplementary analyses using subscales of the CATS that reported partially overlapped pairs with total score of CATS. The connections of pCun-mPFC (β = −0.56, FDR = 0.032; β = −0.77, FDR = 0.001 in Supplementary Table S1; β = −0.53, FDR = 0.022; β = −0.48, FDR = 0.043; β = −0.47, FDR = 0.008 in Supplementary Table S2; β = −0.48, FDR = 0.034; β = −0.61, FDR = 0.017 in Supplementary Table S3) were obtained the same for physical threat, social threat, personal failure and hostility. The hostility was shown in significant connection of ExStr-PHC (β = −0.52, FDR = 0.015; β = −0.52, FDR = 0.01) and Temp-TempPole (β = −0.59, FDR = 0.001) (Supplementary S4). Corresponding results of the CATS were depicted in Supplementary Fig. S2.

3.2. Negative automatic thought mediates emotional abuse-rsFC

The positive association between emotional abuse and rsFC between the right pCun.Cont C and left pCun of default network C (pCun.default C) (β = −0.57, FDR = 0.018) and between the right pCun.Cont C and left precuneus/posterior cingulate cortex (pCunPCC) (β = 1.04, FDR = 0.008) was completely mediated by negative automatic thought. Otherwise, the negative association between emotional abuse and the right nucleus accumbens (NAc) and right somatomotor area (SoM) was mediated through negative automatic thought (β = −0.57, FDR = 0.018) (Table 2; Fig. 2).

The physical threat was shown significant connection of pCun-pCunPCC (β = 0.79, FDR = 0.015) (Supplementary Table S1). The connection between NAc and SoM (β = −0.33, FDR = 0.013) was obtained at the mediation model using personal failure (Supplementary Table S3).

4. Discussion

We investigated the reorganization of brain functional networks induced by mechanisms of the relationship with negative automatic thoughts in adolescents who experienced traumatic emotional events. Our findings showed that the frequency of negative automatic thought suppressed the relationship between emotional abuse and connections of pCun-mPFC, PHC-ExStr, and Temp-TempPole, while it mediated the relationship with pCun-pCun, pCun-pCunPCC, and NAc-SoM functional connectivities. This extends the concept of emotional abuse to the effect of functional connectivity patterns that depend on negative automatic thoughts.

The positive relationship between emotional abuse and patterns of the pCun-mPFC, PHC-ExStr, and Temp-TempPole rsFC was suppressed by negative automatic thought, such that higher negative automatic thought was associated with lower rsFC. Thus, more negative automatic thoughts were associated with lower connectivity in the context of greater emotional abuse. Decreasing pCun-mPFC rsFC would not be a normal brain network pattern depending on negative automatic thoughts, since individuals with post-traumatic-stress disorder show a decline in rsFC between the pCun and dorsal lateral PFC (Olson et al., 2019). The pCun and the mPFC contribute to self-referential processing, autobiographical memory, and mental imagery (Cavanna and Trimble, 2006; Freton et al., 2014; Gusnard et al., 2001; Northoff et al., 2006). This internal mentation makes the tendency of trauma sufferers to be hypervigilant to the negative aspects of ambiguous events (Phillips et al., 2010; Steinberg et al., 2003). Negative automatic thoughts play a critical role in these processes.

We found that emotional abuse affects negative automatic thoughts and, in turn, that the variable conveys the effect on PHC-ExStr and Temp-TempPole rsFC. The parahippocampal region is involved in autobiographical memory and extends to the recollection of traumatic events (Sakamoto et al., 2005). The PHC-ExStr structural connection also shows the anatomical basis for memory processing and integration of surroundings (Powell et al., 2004). Temp and TempPole are related to social and emotional processing, such as interpreting mental state and integrating perceptual input from external stimuli with emotional responses, respectively (Andrews-Hanna et al., 2014; Olson et al., 2007). Thus, we suggest that the suppressive effect of negative automatic thoughts on rsFCs is responsible for the ability to organize traumatic memory and social and emotional processing among individuals who

Table 2
Negative automatic thought suppressed and mediated the relationship between emotional abuse and resting-state functional connectivity.

		Suppression effect						Mediation effect		
Path	Region	pCun.Cont C.L			ExStr.L		Temp.R	pCun.Cont C.R	pCun.Cont C.R	NAc.R
	Region	mPFC.L	mPFC2.R	mPFC3.R	PHC.L	PHC.R	TempPole.L	pCun.Default C.L	pCunPCC.L	SoM.R
a (X→M)	B (SE)	12.43 (1.69)	12.42 (1.65)	12.43 (1.69)	12.43 (1.66)	12.44 (1.66)	12.43 (1.66)	12.41 (1.67)	12.46 (1.67)	12.46 (1.68)
	Z	3.56	3.58	3.55	3.57	3.59	3.56	3.59	3.51	3.54
	FDR	0.0023	0.0023	0.0023	0.0023	0.0023	0.0023	0.0023	0.0023	0.0023
b (M→Y)	B (SE)	−0.07 (0.02)	−0.08 (0.02)	−0.07 (0.02)	−0.07 (0.03)	−0.06 (0.02)	−0.08 (0.02)	0.08 (0.03)	0.07 (0.03)	−0.05 (0.02)
	Z	−2.79	−2.85	−2.85	−2.59	−2.84	−2.69	3.18	2.58	−2.83
	FDR	0.016	0.0187	0.0257	0.0411	0.0329	0.0186	0.0072	0.0494	0.0158
c' (X→Y)	B (SE)	1.98 (0.43)	1.96 (0.39)	1.84 (0.37)	1.5 (0.4)	1.62 (0.44)	1.69 (0.39)	−0.14 (0.48)	0.19 (0.49)	0.15 (0.24)
	Z	3.53	3.58	3.61	3.84	3.11	3.65	−0.20	0.39	0.64
	FDR	0.0023	0.0035	0.0023	0.0023	0.0081	0.0023	0.9418	0.8981	0.8018
c (X→Y)	B (SE)	1.14 (0.27)	0.99 (0.26)	1.02 (0.26)	0.68 (0.24)	0.84 (0.24)	0.72 (0.25)	0.89 (0.29)	1.09 (0.31)	−0.42 (0.16)
	Z	3.84	3.66	3.96	2.83	3.49	2.61	2.74	2.89	−2.82
	FDR	0.0023	0.0023	0.0023	0.0294	0.0023	0.0487	0.0231	0.0113	0.0316
ab (X→M→Y)	B (SE)	−0.85 (0.33)	−0.97 (0.29)	−0.82 (0.28)	−0.82 (0.34)	−0.77 (0.35)	−0.96 (0.36)	1.03 (0.42)	0.9 (0.41)	−0.57 (0.23)
	Z	−2.76	−2.87	−2.79	−2.59	−2.89	−2.86	3.15	2.58	−2.77
	FDR	0.018	0.0179	0.0288	0.0387	0.0291	0.0108	0.0083	0.0489	0.0184

B, Path coefficients; Z, z-statistics; SE, standard error.

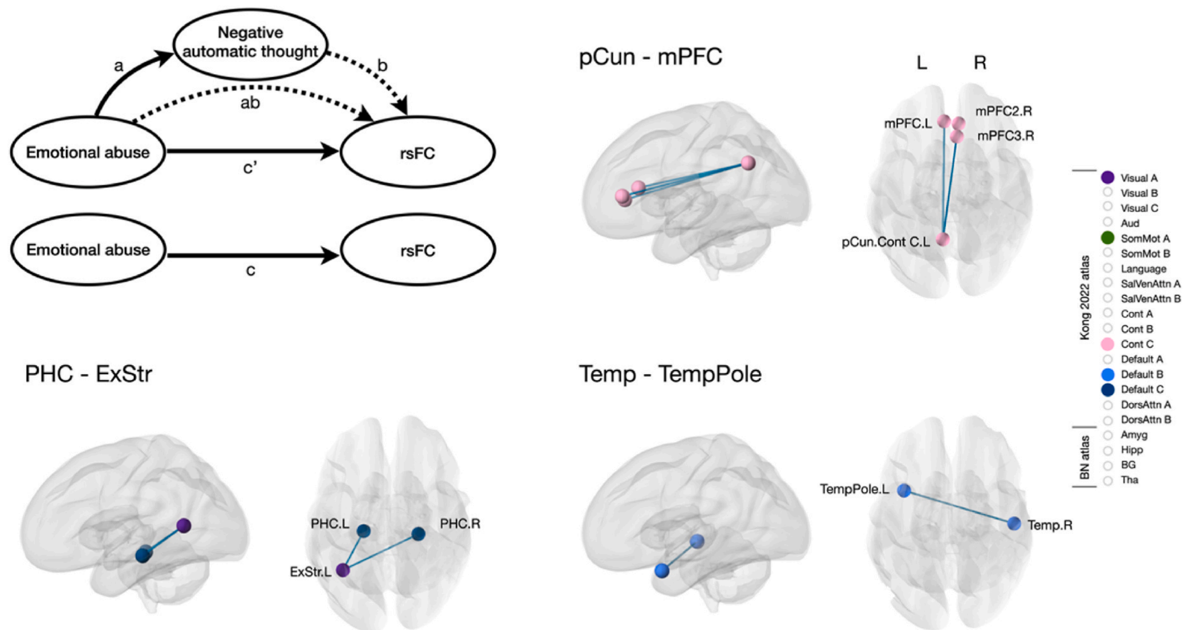

Fig. 1. The suppressed mediation models with the relationship between emotional abuse and functional connectivity through negative automatic thought. The pCun-mPFC, PHC-ExStr, and Temp-TempPole rsFC have suppression effects within the mediation models. The solid and dotted line indicate positive and negative path coefficients respectively. Brain maps representing multiple pairs of functional connectivity with positive (red) and negative (blue) path *ab* except for the mediation model on the top left. The color chart represents each network for atlases including significant areas.

are emotionally abused.

The positive relationship between emotional abuse and rsFC, including pCun-pCun and pCun-pCunPCC, was completely mediated by negative automatic thoughts such that more negative automatic thoughts were positively associated with rsFC when reporting more emotional abuse. The pCun-pCun represents the connection between pCun of default network and pCun of control network. The pCun of the default mode network is located at anterior portion of pCun which is responsible for contributing to self-referential thinking and episodic memory (Cavanna and Trimble, 2006). The pCun of control network is dorsal subregions of precuneus which may not related to the default network (Buckner et al., 2008). Furthermore, the medial surface of parietal cortex is proposed as para-cingulate network part which is likely to function self-referential processes (Dadario and Sughrue, 2023). These studies are consistent with our results of precuneus partitioning into different network. However, additional research is needed to clarify networks of the precuneus differentiated into subregions.

While the pCun appears to be the critical brain region for trauma sufferers, increasing its central importance (i.e., centrality) (Teicher et al., 2014), the pCunPCC has been known to play a central role in interconnecting with other regions throughout the default network (Fransson and Marrelec, 2008). Therefore, the increased functional coupling within the posteromedial cortical brain regions could be explained by strengthening the impact of negative automatic thoughts.

In contrast to other rsFCs, the NAc-SoM rsFC is negatively associated with emotional abuse and is completely mediated by negative automatic thoughts, indicating that higher emotional abuse is associated with lower NAc-SoM rsFC when negative automatic thoughts are included. By analyzing the mediating effect of negative automatic thoughts, the direction of the relationship changed from positive to negative. A negative relationship is found between adverse childhood experiences and rsFC, including that in the NAc (Park et al., 2021). However, to the best of our knowledge, it is unknown whether cognitive mediators affect the direction of this relationship. In addition, the NAc and SoM are important brain regions related to symptoms in trauma victims. While NAc hypoactivation is related to atypical reward functioning in individuals with early adversities in childhood and/or adolescence (Goff et al., 2013), the SoM structure and functional changes shown among those who are emotionally abused may be linked to abnormal sensorimotor function and emotional regulation of traumatic events (Li et al., 2022). Through mediation analysis, we suggest that cognitive factors play a critical role in the neural mechanism of evaluating and recognizing emotional abuse.

Our study had several limitations. First, a modest number of community samples were used to test the mediation analysis. Second, self-reported scores were used to measure emotional abuse and negative automatic thoughts. As with most self-reported questionnaires, the answers to items may reflect subjective judgments with individual differences. Furthermore, our measurements of traumatic events and negative automatic thoughts did not cover the duration or exact time points of the experience. However, the strength and frequency of the trauma and negative automatic thoughts reflect hardship and distress. Third, our observations were based on the general population, making it difficult to generalize our findings to clinical cohorts. However, our examination provides promising evidence to account for the external environment affecting the neural system through cognitive processing. Finally, we cross-sectionally identified rsFCs affected by negative automatic thoughts in individuals with emotionally traumatic events. Additionally, a mediation analysis was performed on the hypothesized associations with emotional abuse, negative automatic thoughts, and rsFCs. Further studies need to be conducted using a longitudinal design to clarify more robust causation among the variables.

5. Conclusion

We examined how the association between emotional abuse and rsFC is mediated or suppressed by negative automatic thoughts. We identified the suppression and mediation effect of negative automatic thoughts in some rsFCs. These results highlight the importance of cognitive mediators by showing that negative automatic thoughts accelerate or reverse the strength and direction of association. To the best of our knowledge, this is the first study to investigate the mediating effect of cognitive mediators on the association between emotional abuse and rsFC. Some rsFCs have not been reported in previous studies on traumatic events. Thus, we speculate that the rsFCs were discovered by assuming the

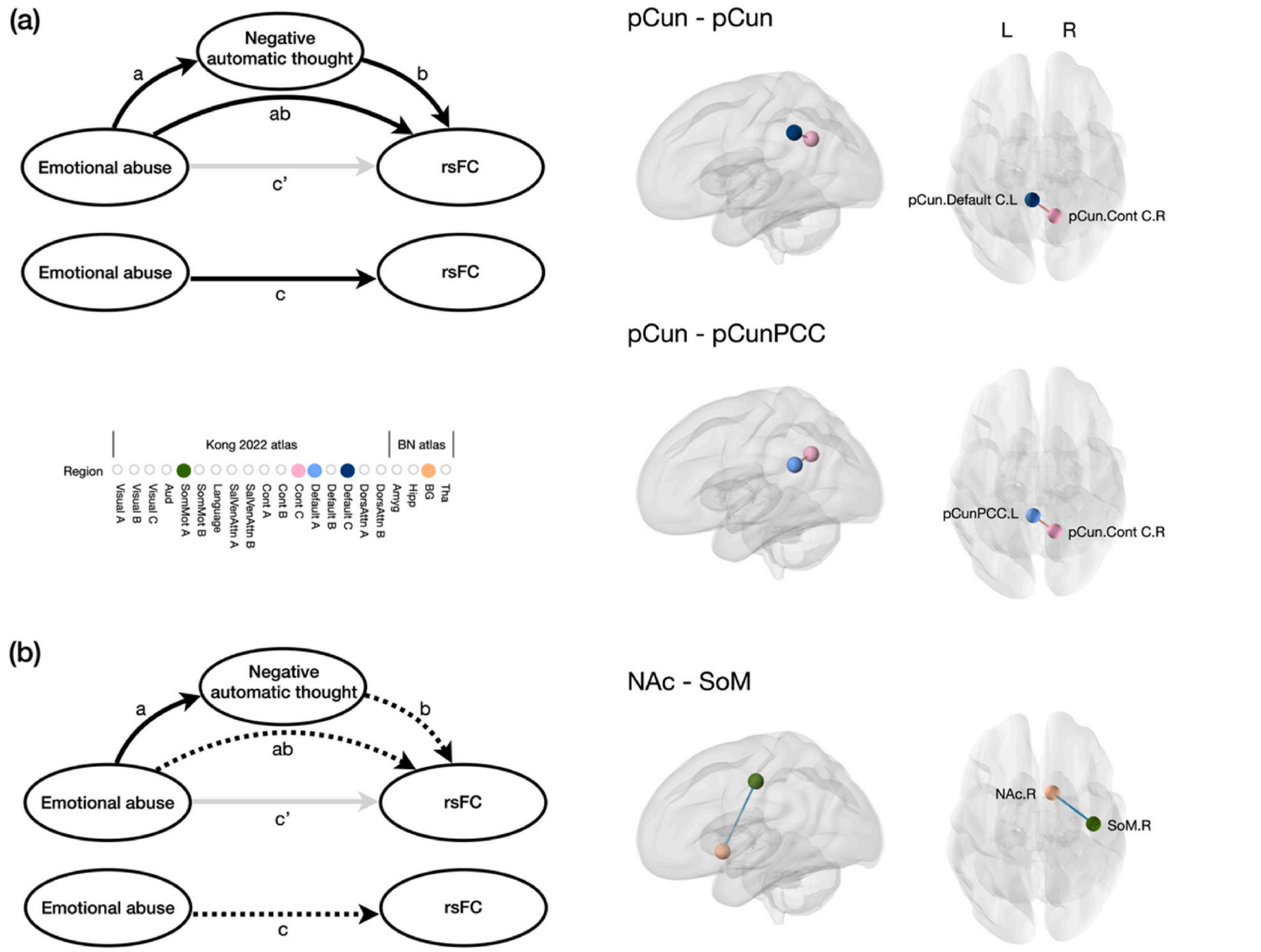

Fig. 2. Complete mediation models. (a) The positive relationship between emotional abuse and functional connectivity were mediated by negative automatic thought. The pCun-pCun and pCun-pCunPCC rsFC have mediation effects within the mediation models. The gray solid line represents the non-significant path coefficient. (b) The negative relationship between emotional abuse and functional connectivity were mediated by negative automatic thought. The NAc and SoM rsFC was completely mediated by negative automatic thought. Both mediation models have a non-significant path *c*' at the level of FDR ≤0.05. The concept of brain map and color chart is the same as Fig. 1.

underlying cognitive processing of the traumatic event-neural system. This investigation of cognitive mediators would be helpful in broadening our understanding of the causality of brain states and symptoms in post-traumatic adolescents.

CRediT authorship contribution statement

Dageon Yeo: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Conceptualization. **Seulgi Lee:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Haemi Choi:** Investigation. **Min-Hyeon Park:** Writing – review & editing, Supervision, Resources, Funding acquisition. **Bumhee Park:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References

American Academy of, Pediatrics, Stirling Jr., J., Amaya-Jackson, L., Committee on Child Ause and Neglect, Section on Adoption and Foster Care, American Academy of Child and Adolescent Psychiatry, Amaya-Jackson, L., National Center for Child Traumatic Stress, 2008. Understanding the behavioral and emotional consequences of child abuse. Pediatrics 122, 667–673.

Andrews-Hanna, J.R., Saxe, R., Yarkoni, T., 2014. Contributions of episodic retrieval and mentalizing to autobiographical thought: evidence from functional neuroimaging, resting-state connectivity, and fMRI meta-analyses. Neuroimage 91, 324–335.

Beck, A.T., 1979. Cognitive Therapy and the Emotional Disorders. Penguin.

Bethlehem, R.A., Seidlitz, J., White, S.R., Vogel, J.W., Anderson, K.M., Adamson, C., Adler, S., Alexopoulos, G.S., Anagnostou, E., Areces-Gonzalez, A., 2022. Brain charts for the human lifespan. Nature 604, 525–533.

Bremner, J.D., Bolus, R., Mayer, E.A., 2007. Psychometric properties of the early trauma inventory-self report. J. Nerv. Ment. Dis. 195, 211–218.

Buckner, R.L., Andrews-Hanna, J.R., Schacter, D.L., 2008. The brain's default network: anatomy, function, and relevance to disease. Ann. N. Y. Acad. Sci. 1124, 1–38.

Calvete, E., Orue, I., Hankin, B.L., 2013. Early maladaptive schemas and social anxiety in adolescents: the mediating role of anxious automatic thoughts. J. Anxiety Disord. 27, 278–288.
Cassiers, L.L.M., Sabbe, B.G.C., Schmaal, L., Veltman, D.J., Penninx, B., Van Den Eede, F., 2018. Structural and functional brain abnormalities associated with exposure to different childhood trauma subtypes: a systematic review of neuroimaging findings. Front. Psychiatr. 9, 329.
Cavanna, A.E., Trimble, M.R., 2006. The precuneus: a review of its functional anatomy and behavioural correlates. Brain 129, 564–583.
Cisler, J.M., 2017. Childhood trauma and functional connectivity between amygdala and medial prefrontal cortex: a dynamic functional connectivity and large-scale network perspective. Front. Syst. Neurosci. 11, 29.
Cun, L., Wang, Y., Zhang, S., Wei, D., Qiu, J., 2014. The contribution of regional gray/white matter volume in preclinical depression assessed by the Automatic Thoughts Questionnaire: a voxel-based morphometry study. Neuroreport 25, 1030–1037.
Dadario, N.B., Sughrue, M.E., 2023. The functional role of the precuneus. Brain 146, 3598–3607.
Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd, D., Domschke, K., Hohoff, C., Ohrmann, P., Bauer, J., Lindner, C., Postert, C., Konrad, C., Arolt, V., Heindel, W., Suslow, T., Kugel, H., 2012. Limbic scars: long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. Biol. Psychiatr. 71, 286–293.
Dekaban, A.S., Sadowsky, D., 1978. Changes in brain weights during the span of human life: relation of brain weights to body heights and body weights. Ann. Neurol.: Official Journal of the American Neurological Association and the Child Neurology Society 4, 345–356.
Dong, H.-M., Margulies, D.S., Zuo, X.-N., Holmes, A.J., 2021. Shifting gradients of macroscale cortical organization mark the transition from childhood to adolescence. Proc. Natl. Acad. Sci. USA 118, e2024448118.
Edwards, V.J., Holden, G.W., Felitti, V.J., Anda, R.F., 2003. Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: results from the adverse childhood experiences study. Am. J. Psychiatr. 160, 1453–1460.
Fan, L., Li, H., Zhuo, J., Zhang, Y., Wang, J., Chen, L., Yang, Z., Chu, C., Xie, S., Laird, A. R., Fox, P.T., Eickhoff, S.B., Yu, C., Jiang, T., 2016. The human brainnetome atlas: a new brain atlas based on connectional architecture. Cerebr. Cortex 26, 3508–3526.
Flouri, E., Panourgia, C., 2014. Negative automatic thoughts and emotional and behavioural problems in adolescence. Child Adolesc. Ment. Health 19, 46–51.
Fransson, P., Marrelec, G., 2008. The precuneus/posterior cingulate cortex plays a pivotal role in the default mode network: evidence from a partial correlation network analysis. Neuroimage 42, 1178–1184.
Freton, M., Lemogne, C., Bergouignan, L., Delaveau, P., Lehericy, S., Fossati, P., 2014. The eye of the self: precuneus volume and visual perspective during autobiographical memory retrieval. Brain Struct. Funct. 219, 959–968.
Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.P., Frith, C.D., Frackowiak, R.S., 1994. Statistical parametric maps in functional imaging: a general linear approach. Hum. Brain Mapp. 2, 189–210.
Fuhrmann, D., Knoll, L.J., Blakemore, S.J., 2015. Adolescence as a sensitive period of brain development. Trends Cognit. Sci. 19, 558–566.
Gama, C.M.F., Portugal, L.C.L., Goncalves, R.M., de Souza Junior, S., Vilete, L.M.P., Mendlowicz, M.V., Figueira, I., Volchan, E., David, I.A., de Oliveira, L., Pereira, M. G., 2021. The invisible scars of emotional abuse: a common and highly harmful form of childhood maltreatment. BMC Psychiatr. 21, 156.
Gibb, B.E., Butler, A.C., Beck, J.S., 2003. Childhood abuse, depression, and anxiety in adult psychiatric outpatients. Depress. Anxiety 17, 226–228.
Glaser, D., 2000. Child abuse and neglect and the brain-A review. JCPP (J. Child Psychol. Psychiatry) 41, 97–116.
Goff, B., Gee, D.G., Telzer, E.H., Humphreys, K.L., Gabard-Durnam, L., Flannery, J., Tottenham, N., 2013. Reduced nucleus accumbens reactivity and adolescent depression following early-life stress. Neuroscience 249, 129–138.
Gusnard, D.A., Akbudak, E., Shulman, G.L., Raichle, M.E., 2001. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. Proc. Natl. Acad. Sci. USA 98, 4259–4264.
Harkness, K.L., Bruce, A.E., Lumley, M.N., 2006. The role of childhood abuse and neglect in the sensitization to stressful life events in adolescent depression. J. Abnorm. Psychol. 115, 730–741.
Ibrahim, P., Almeida, D., Nagy, C., Turecki, G., 2021. Molecular impacts of childhood abuse on the human brain. Neurobiol Stress 15, 100343.
Jeon, J.R., Lee, E.H., Lee, S.W., Jeong, E.G., Kim, J.H., Lee, D., Jeon, H.J., 2012. The early trauma inventory self report-short form: psychometric properties of the Korean version. Psychiatry Investig 9, 229–235.
Kang, H.C., Burgund, E.D., Lugar, H.M., Petersen, S.E., Schlaggar, B.L., 2003. Comparison of functional activation foci in children and adults using a common stereotactic space. Neuroimage 19, 16–28.
Kong, R., Yang, Q., Gordon, E., Xue, A., Yan, X., Orban, C., Zuo, X.N., Spreng, N., Ge, T., Holmes, A., Eickhoff, S., Yeo, B.T.T., 2021. Individual-specific areal-level parcellations improve functional connectivity prediction of behavior. Cerebr. Cortex 31, 4477–4500.
Kwon, S.-M., Oei, T.P., 1992. Differential causal roles of dysfunctional attitudes and automatic thoughts in depression. Cognit. Ther. Res. 16, 309–328.
Li, E.T., Luyten, P., Midgley, N., 2020. Psychological mediators of the association between childhood emotional abuse and depression: a systematic review. Front. Psychiatr. 11, 559213.
Li, J., Zhang, G., Wang, J., Liu, D., Wan, C., Fang, J., Wu, D., Zhou, Y., Tian, T., Zhu, W., 2022. Experience-dependent associations between distinct subtypes of childhood trauma and brain function and architecture. Quant. Imag. Med. Surg. 12, 1172–1185.
MacKinnon, D.P., Krull, J.L., Lockwood, C.M., 2000. Equivalence of the mediation, confounding and suppression effect. Prev. Sci. 1, 173–181.
McLaughlin, K.A., Green, J.G., Gruber, M.J., Sampson, N.A., Zaslavsky, A.M., Kessler, R. C., 2012. Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. Arch. Gen. Psychiatr. 69, 1151–1160.
Moon, K.J., Oh, K.J., Moon, H.S., 2002. Validation sutdy of Korean Children's automatic thoughts scale. Kor. J. Clin. Psychol. 21, 955–963.
Norman, R.E., Byambaa, M., De, R., Butchart, A., Scott, J., Vos, T., 2012. The long-term health consequences of child physical abuse, emotional abuse, and neglect: a systematic review and meta-analysis. PLoS Med. 9, e1001349.
Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., Panksepp, J., 2006. Self-referential processing in our brain–a meta-analysis of imaging studies on the self. Neuroimage 31, 440–457.
O'Mahen, H.A., Karl, A., Moberly, N., Fedock, G., 2015. The association between childhood maltreatment and emotion regulation: two different mechanisms contributing to depression? J. Affect. Disord. 174, 287–295.
Ohashi, K., Anderson, C.M., Bolger, E.A., Khan, A., McGreenery, C.E., Teicher, M.H., 2017. Childhood maltreatment is associated with alteration in global network fiber-tract architecture independent of history of depression and anxiety. Neuroimage 150, 50–59.
Olson, E.A., Kaiser, R.H., Pizzagalli, D.A., Rauch, S.L., Rosso, I.M., 2019. Regional prefrontal resting-state functional connectivity in posttraumatic stress disorder. Biol Psychiatry Cogn Neurosci Neuroimaging 4, 390–398.
Olson, I.R., Plotzker, A., Ezzyat, Y., 2007. The Enigmatic temporal pole: a review of findings on social and emotional processing. Brain 130, 1718–1731.
Park, A.T., Tooley, U.A., Leonard, J.A., Boroshok, A.L., McDermott, C.L., Tisdall, M.D., Mackey, A.P., 2021. Early childhood stress is associated with blunted development of ventral tegmental area functional connectivity. Dev Cogn Neurosci 47, 100909.
Park, S., Kim, B.-N., Park, M.-H., 2016. The relationship between parenting attitudes, negative cognition, and the depressive symptoms according to gender in Korean adolescents. Int. J. Ment. Health Syst. 10, 1–8.
Park, S., Lee, Y., Jun, J.Y., 2018. Trauma and depression among north Korean refugees: the mediating effect of negative cognition. Int. J. Environ. Res. Publ. Health 15.
Peng, X., Wu, X., Gong, R., Yang, R., Wang, X., Zhu, W., Lin, P., 2021. Sub-regional anterior cingulate cortex functional connectivity revealed default network subsystem dysfunction in patients with major depressive disorder. Psychol. Med. 51, 1687–1695.
Phillips, W.J., Hine, D.W., Thorsteinsson, E.B., 2010. Implicit cognition and depression: a meta-analysis. Clin. Psychol. Rev. 30, 691–709.
Powell, H.W., Guye, M., Parker, G.J., Symms, M.R., Boulby, P., Koepp, M.J., Barker, G.J., Duncan, J.S., 2004. Noninvasive in vivo demonstration of the connections of the human parahippocampal gyrus. Neuroimage 22, 740–747.
Power, J.D., Barnes, K.A., Snyder, A.Z., Schlaggar, B.L., Petersen, S.E., 2012. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage 59, 2142–2154.
Raymond, C., Marin, M.F., Majeur, D., Lupien, S., 2018. Early child adversity and psychopathology in adulthood: HPA axis and cognitive dysregulations as potential mechanisms. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 85, 152–160.
Richards, J.E., Sanchez, C., Phillips-Meek, M., Xie, W., 2016. A database of age-appropriate average MRI templates. Neuroimage 124, 1254–1259.
Ross, P., de Gelder, B., Crabbe, F., Grosbras, M.-H., 2019. Emotion modulation of the body-selective areas in the developing brain. Developmental Cognitive Neuroscience 38, 100660.
Sakamoto, H., Fukuda, R., Okuaki, T., Rogers, M., Kasai, K., Machida, T., Shirouzu, I., Yamasue, H., Akiyama, T., Kato, N., 2005. Parahippocampal activation evoked by masked traumatic images in posttraumatic stress disorder: a functional MRI study. Neuroimage 26, 813–821.
Schaefer, A., Kong, R., Gordon, E.M., Laumann, T.O., Zuo, X.N., Holmes, A.J., Eickhoff, S. B., Yeo, B.T.T., 2018. Local-Global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. Cerebr. Cortex 28, 3095–3114.
Schniering, C.A., Rapee, R.M., 2002. Development and validation of a measure of children's automatic thoughts: the children's automatic thoughts scale. Behav. Res. Ther. 40, 1091–1109.
Şoflău, R., David, D.O., 2016. A meta-analytical approach of the relationships between the irrationality of beliefs and the functionality of automatic thoughts. Cognit. Ther. Res. 41, 178–192.
Steinberg, J.A., Gibb, B.E., Alloy, L.B., Abramson, L.Y., 2003. Childhood emotional maltreatment, cognitive vulnerability to depression, and self-referent information processing in adulthood: reciprocal relations. J. Cognit. Psychother. 17, 347–358.
Teicher, M.H., Andersen, S.L., Polcari, A., Anderson, C.M., Navalta, C.P., Kim, D.M., 2003. The neurobiological consequences of early stress and childhood maltreatment. Neurosci. Biobehav. Rev. 27, 33–44.
Teicher, M.H., Anderson, C.M., Ohashi, K., Polcari, A., 2014. Childhood maltreatment: altered network centrality of cingulate, precuneus, temporal pole and insula. Biol. Psychiatr. 76, 297–305.
Teicher, M.H., Samson, J.A., 2013. Childhood maltreatment and psychopathology: a case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. Am. J. Psychiatr. 170, 1114–1133.
Teicher, M.H., Samson, J.A., Anderson, C.M., Ohashi, K., 2016. The effects of childhood maltreatment on brain structure, function and connectivity. Nat. Rev. Neurosci. 17, 652–666.
Tottenham, N., 2020. Early adversity and the neotenous human brain. Biol. Psychiatr. 87, 350–358.

Uy, J.P., Tan, A.P., Broeckman, B., Gluckman, P.D., Chong, Y.S., Chen, H., Fortier, M.V., Meaney, M.J., Callaghan, B.L., 2023. Effects of maternal childhood trauma on child emotional health: maternal mental health and frontoamygdala pathways. JCPP (J. Child Psychol. Psychiatry) 64, 426–436.
van der Werff, S.J., Pannekoek, J.N., Veer, I.M., van Tol, M.J., Aleman, A., Veltman, D.J., Zitman, F.G., Rombouts, S.A., Elzinga, B.M., van der Wee, N.J., 2013. Resting-state functional connectivity in adults with childhood emotional maltreatment. Psychol. Med. 43, 1825–1836.
van Harmelen, A.L., de Jong, P.J., Glashouwer, K.A., Spinhoven, P., Penninx, B.W., Elzinga, B.M., 2010. Child abuse and negative explicit and automatic self-associations: the cognitive scars of emotional maltreatment. Behav. Res. Ther. 48, 486–494.
Weiss, Y., Booth, J.R., 2017. Neural correlates of the lexicality effect in children. Brain Lang. 175, 64–70.
Weissenbacher, A., Kasess, C., Gerstl, F., Lanzenberger, R., Moser, E., Windischberger, C., 2009. Correlations and anticorrelations in resting-state functional connectivity MRI: a quantitative comparison of preprocessing strategies. Neuroimage 47, 1408–1416.
Whittle, S., Dennison, M., Vijayakumar, N., Simmons, J.G., Yücel, M., Lubman, D.I., Pantelis, C., Allen, N.B., 2013. Childhood maltreatment and psychopathology affect brain development during adolescence. J. Am. Acad. Child Adolesc. Psychiatr. 52, 940–952. e941.