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A Functional Magnetic Resonance Imaging Meta-Analysis of Childhood Trauma

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ABSTRACT

BACKGROUND: Traumatic experiences during childhood significantly impact the developing brain and contribute to the development of numerous physical and mental health problems. To date, however, a comprehensive understanding of the functional impairments within the brain associated with childhood trauma histories does not exist. Previous functional magnetic resonance imaging (fMRI) meta-analytical tools required homogeneity of task types and the clinical populations studied, thus preventing the comprehensive pooling of brain-based deficits present in children who have trauma histories. We hypothesized that the use of the novel, data-driven Bayesian author-topic model approach to fMRI meta-analyses would reveal deficits in brain networks that span fMRI task types in children with trauma histories.

METHODS: To our knowledge, this is the first study to use the Bayesian author-topic model approach to fMRI meta-analyses within a clinical population. Using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, we present data-driven results obtained by combining activation patterns across heterogeneous tasks from 1428 initially screened studies and combining data from 14 studies that met study criteria (285 children with trauma histories, 297 healthy control children).

RESULTS: Altered brain activity was revealed within 2 clusters in children with trauma histories compared to control children: the default mode/affective network/posterior insula and the central executive network. Our identified clusters were associated with tasks pertaining to cognitive processing, emotional/social stress, self-referential thought, memory, unexpected stimuli, and avoidance behaviors in youths who have experienced childhood trauma.

CONCLUSIONS: Our results reveal disturbances in children with trauma histories within the modulation of the default mode and central executive networks—but not the salience network—regardless of whether children also presented with posttraumatic stress symptoms.

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In the United Kingdom, it is estimated that 1 in 5 people have experienced trauma, particularly in the form of childhood maltreatment, by the age of 16 years (1). During childhood, the human brain undergoes rapid development, which makes it vulnerable to the external world experienced by a growing child. Childhood trauma produces severe stress on the brain, and this can lead to significant changes such as depleted functioning and lasting structural alterations (2). From a physiological perspective, it has been documented that early traumatic experiences disrupt the overall course of neurodevelopment (3). Given previous research indicating that severe exposure to trauma during childhood has negative implications for the developing brain, there is a clear need to understand the neural underpinnings of these effects (4–6).

Despite growing evidence from task-based functional magnetic resonance imaging (fMRI) studies that have shown the deleterious effects of childhood trauma on specific brain regions (5,7–19), an overarching view of brain activation patterns obtained by combining data from across all previously collected whole-brain task-based fMRI studies associated with childhood trauma does not yet exist. We aimed to close this gap in the literature by conducting the first known meta-analysis to combine results from all previously collected whole-brain task-based fMRI data in youths with previous trauma. This is now possible given our ability to apply the data-driven Bayesian author-topic model meta-analytic method (never used before in a clinical population) to a clinical population (20). Like other activation likelihood estimation–based fMRI approaches, this innovative approach allows for the identification of common brain patterns from numerous studies. It also allows for data-driven comparisons from across clinical groups and comparisons across fMRI task types for the first time. This allows for the identification of both homogeneous and heterogeneous clusters of brain activity, which can assist with diagnostic classifications and identify unknown functional overlaps that naturally occur across brain networks for various tasks. For this study, we applied this approach, which allowed us to combine all previously conducted task-based whole-brain fMRI studies of children who have experienced trauma or maltreatment and who may or may not demonstrate posttraumatic stress disorder or symptoms (21) in comparison to healthy control children (HCs). To perform this

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meta-analysis under the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, the literature search strategy was adapted from PICOS (patient population, intervention, comparison, outcomes, and setting) to fit the requirements for this analysis. However, a previous review of 12 structural MRI and fMRI network studies suggests that impairment in the salience network (SN), central executive network (CEN), and default mode network (DMN) occurs in response to childhood trauma and severe early-life stress. These findings are consistent with adult studies; however, this has not yet been confirmed by neuroimaging meta-analyses in children with trauma histories (22). We are also unsure whether such activation patterns are consistent across children who have experienced trauma or maltreatment and who may or may not have trauma symptoms. However, we hypothesized that when pooling activation patterns from across all fMRI studies of children with trauma histories, we would detect disturbances in the modulation of the DMN, SN and CEN.

METHODS AND MATERIALS

Search Strategy

To identify all relevant studies, the online academic search engines PubMed, Web of Science, and PsychInfo were searched according to the PRISMA guidelines. Records from 1994 until April 2021 were evaluated. The following search parameters were used: 1) (children AND post-traumatic stress) AND fMRI, 2) (adolescents AND post-traumatic stress) AND fMRI, 3) children AND PTSD AND fMRI, 4) (adolescents AND PTSD) AND fMRI, and 5) (adolescents AND childhood abuse) AND fMRI. A total of 1428 records were found by these means, of which 847 were duplicates, which left 581 records. Only studies involving human participants were included.

Inclusion and Exclusion Criteria

The studies were evaluated according to a set of inclusion and exclusion criteria. Original articles were included if they 1) were published in a peer-reviewed journal, 2) had youth participants, and 3) had coordinates from a whole-brain analysis. Diagnostic inclusion criteria included whether the study included participants under the age of 18 who had a history of trauma. We defined having a trauma history using the following criteria: 1) experienced a traumatic event during childhood (and may or may not necessarily report trauma symptoms); 2) experienced maltreatment and developed significant trauma symptoms, under the label of posttraumatic stress symptoms; and 3) met full diagnostic criteria for post-traumatic stress disorder (PTSD).

Regarding exclusion criteria, other brain scanning modalities, such as structural MRI or electroencephalogram, were excluded from analyses. Studies found using the search terms also identified papers involving brain trauma such as traumatic brain injury. These were also excluded because the primary focus of this analysis was childhood traumatic stress. Other exclusion criteria included 1) review papers, 2) case studies, 3) studies that included adult participants, and 4) studies that did not include a control group.

Screening Procedure

After an initial screening of abstracts, 482 of the initially retrieved 581 records were excluded according to the criteria listed above. The 99 remaining records underwent full-text screening for eligibility. During the full-text screen, an additional 67 studies were excluded due to their use of resting-state fMRI (n = 13), only region-of-interest coordinates (n = 14), adult studies (n = 11), structural MRI (n = 12), no control group (n = 16), review (n = 1), and other psychiatric disorders (n = 6), which left 14 studies for inclusion in the meta-analysis. Details of the search procedure are presented in the PRISMA diagram (Figure 1).

Data Extraction

The relevant data were extracted from the included studies and briefly summarized. For this meta-analysis of case-controlled studies, PICOS characteristics were modified for its usage for a study of fMRI by removing typical PICOS intervention characteristics; we also adapted outcomes to fit and report MRI data (23). The quality of the studies was assessed with a revised version of the items included in the OHBM (Organization for Human Brain Mapping) COBIDAS (Committee on Best Practice in Data Analysis and Sharing) report (24). A detailed description of the quality assessment criteria can be found in Figure 2, and the results of each rated article can be found in Table 1.

Data Analysis

We used the author-topic model approach as described by Ngo to discover coactivation patterns across the different experiments (20). The basic premise is that we wanted to identify underlying brain activation components that may be common across studies that have investigated trauma in children and adolescents and the brain regions that underpin these components; we were interested in how the different tasks used in different studies may cluster together in terms of the brain areas activated. As described by Ngo, the author-topic model approach is based on a method that is used for identifying topics from a corpus of text documents. In the current application to brain imaging, we took each experiment selected from our screening process, extracted the relevant experimental contrasts (from a whole-brain analysis), and considered each contrast as its own unique task category (20). Note that the method does not weight by the sample size of a study; all task categories in the model are considered equal.

The model parameters estimated are the probability that an experiment would recruit a coactivation pattern Pr(coactivation pattern|experiment) and the probability that a voxel would be involved in a coactivation pattern Pr(voxel|coactivation pattern); the model uses the coreset variational Bayes algorithm to estimate these parameters. We adapted the code freely made available by Ngo to run the author-topic model using our extracted fMRI coordinates (20). We ran the model multiple times assuming 1, 2, 3, 4, or 5 coactivation patterns and used the largest Bayesian inclusion criterion (BIC) value to identify the optimal number of coactivation patterns. To interpret the coactivation patterns, we inspected contrasts with Pr(coactivation pattern|experiment) above 0.75 proportional loading (from 0 to 1) and used GingerAle to develop z score

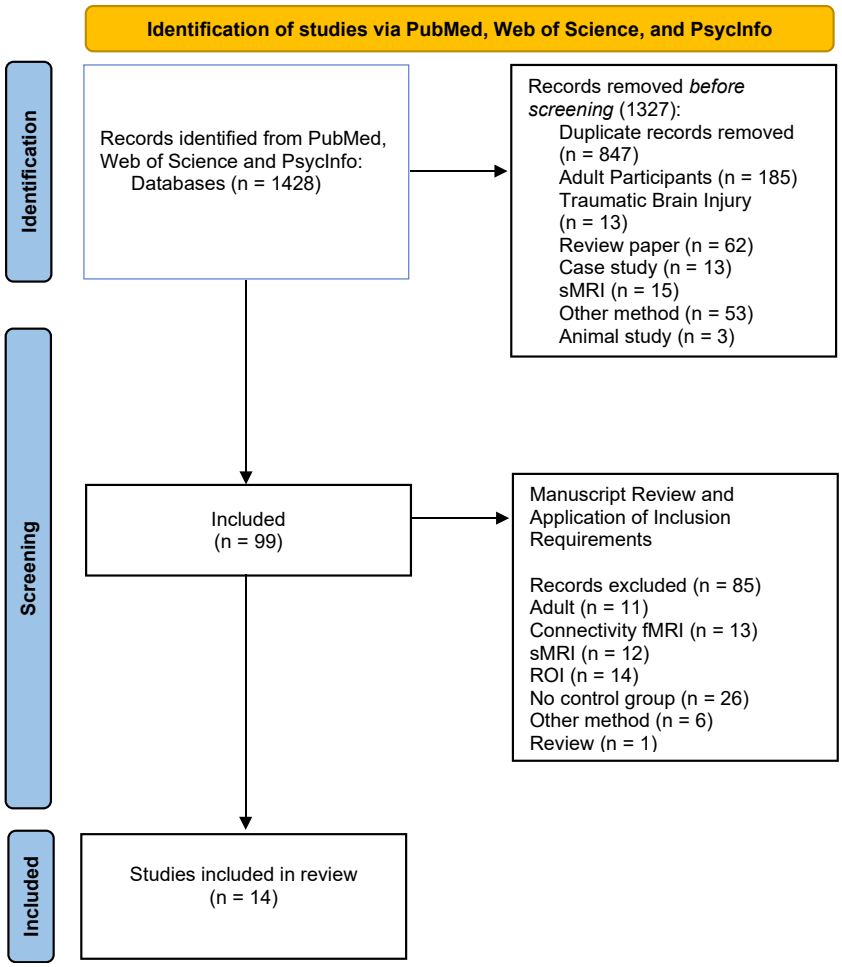

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart illustrating study identification, exclusion, and inclusion in the meta-analysis. Included searches of databases and registers only. fMRI, functional magnetic resonance imaging; ROI, region of interest; sMRI, structural MRI.

maps of activation patterns for each cluster. These were then visualized via MRICron software (https://www.nitrc.org/projects/mricron/). We also considered whether we could draw out common themes in terms of the types of tasks/experiments that were grouped together in 1 coactivation pattern, which would enable us to describe the processes that may be associated with a given coactivation pattern.

RESULTS

A total of 1428 studies were identified during our initial search. Of these studies, 14 met our inclusion criteria; they examined the whole brain activated during task-based fMRI (Table 1). Across the 14 studies included, the group-level contrasts consisted of children with trauma histories compared to HCs. The current analysis showed what contrasts loaded into various regions of the brain during task-based fMRI for each study. The 14 studies included a total of 582 child participants (under age 18 years; range 8–20 years) (Table 1); 285 of the child participants had trauma histories, and 297 child participants were categorized as HCs.

According to the BIC output, the best model fit was achieved with 2 components (i.e., coactivation patterns), which demonstrated the largest BIC value of -1.0798×10 (Figure 3). A higher BIC score indicates that the model has a better fit. As can be seen from the *z* cluster maps (Figure 4), there were 2 main cluster regions. Components 1 and 2 activations are highlighted in the red scale (hot). The types of tasks found to load onto each component are illustrated (Figure 4, Table 2), and the theta weight loading (between 0 and 1) is included (Figure 4) to further demonstrate the task component loadings and to highlight where children with trauma histories showed alterations in brain activity.

Component 1: DMN, Affective Network, and Posterior Insula

We found blood oxygen level–dependent activation differences between children with trauma histories and HCs within regions associated with the DMN, posterior insula, and the affective network (limbic system) (see Table 3 and Figure 4). The first activation cluster peaked within the left lentiform nucleus of the putamen (Brodmann area [BA] 13) and extended into the claustrum, hippocampus, insula, thalamus, and the amygdala. Another cluster peak was present within the right lentiform nucleus of the putamen (BA 13) and extended into the

Experimental design and reporting
- Number of subjects
- Subjects approached
- Subjects consented
- Subjects refused to participate
- Subjects excluded
- Subjects participated and analysed
- Subjects diagnosed by clinical professional

Inclusion criteria and descriptive statistics
- Age
- Sex
- Race & ethnicity
- Handedness
- Education & SES
- IQ
- Exclusion criteria
- Clinical criteria
- Clinical instruments
- Matching strategy
- Population & recruitment strategy
- Neurocognitive measures

Ethical considerations
- Ethical approval
- Informed consent

Design specifications
- Design type
- Condition & stimuli
- Number of blocks, trials or experimental units
- Timing and duration
- Length of the experiment
- Design optimization
- Presentation software

Task specification
- Subject scanning order
- Condition
- Instructions
- Stimuli
- Randomization
- Stimulus presentation & response collection
- Run order

Power analysis
- Outcome
- Power parameters

Behavioural performance
- Variables recorded
- Summary statistics

Acquisition reporting
- Mock scanning
- Special accommodations
- Experimental personnel

MRI system description
- Scanner
- Coil
- Significant hardware modifications
- Software version

MRI acquisition
- Pulse sequence type
- Imaging type
- Essential sequence & imaging parameters
- Phase encoding
- Shimming
- Slice order & timing
- Slice position procedure
- Brain coverage
- Scanner side pre-processing
- Scan duration
- T1 stabilization

Preliminary quality control
- Motion Monitoring
- Incidental findings

Pre-processing reporting
- Software
- Software citation
- Brain extraction
- Segmentation
- Slice time correction
- Motion correction
- Gradient distortion correction
- Intensity correction
- Intensity normalization
- Artifact and structured noise removal
- Volume censoring
- Spatial smoothing

Statistical modelling & inference
- Dependent variable: Data submitted to statistical modelling
- Independent variables
- Model type & setting
- Inference: Contrast/effect
- Inference: Statistic type
- Inference: P-value computation
- Inference: Multiple testing correction

Results reporting
- Effects tested
- Extracted data
- Tables of coordinates
- Thresholded maps
- Unthresholded maps
- Spatial features

TOT/84

Figure 2. Revised version of the items included in the OHBM (Organization for Human Brain Mapping) COBIDAS (Committee on Best Practice in Data Analysis and Sharing) report (24). MRI, magnetic resonance imaging; SES, socioeconomic status; TOT, total.

globus pallidus, thalamus, hippocampus, posterior cingulate, caudate, insula, and claustrum. Participants with trauma histories demonstrated increased activation in component 1 compared to HCs during tasks pertaining to emotion processing (words and faces) and social tasks. However, HCs activated this system more than children with trauma histories during tasks pertaining to memory and reward processing (see Tables 2 and 3 and Figure 4).

Component 2: Central Executive Network

We also found blood oxygen level–dependent activation differences between children with trauma histories within regions associated with the CEN (see Tables 2 and 4 and Figure 4). The first peak of the activation coordinates fell within the left middle frontal gyrus (BA 8, 9) and extended into the left and right hemispheres and the bilateral superior frontal gyri. The second coordinate peak fell within the left superior temporal gyrus (BA

Table 1. Description of Studies Included in the Meta-Analysis, Recruitment Criteria, Demographic Information, and Quality Rating According to the OHBM COBIDAS Report Criteria

Author	Participants, *n*	Age, Years	Task	Contrast	Quality/84
PTSS					
Carrión *et al.* (7)	16 PTSS and 11 HC	10–17	Verbal declarative memory task	Retrieval > control	60
Carrión *et al.* (8)	16 PTSS and 14 HC	10–16	Go/NoGo task	NoGo > Go	63
Garrett *et al.* (9)	23 PTSS and 23 HC	10–16	Implicit emotional facial expressions task	Phase × emotion	70
CM					
Crozier *et al.* (5)	29 CM and 45 HC	8–17	Emotional oddball task	Fear > scrambled targets	68
Puetz *et al.* (10)	21 CM and 19 HC	10–14	Emotional Stroop task	Rejection words > neutral words	65
McCrory *et al.* (11)	34 CM and 33 HC	10–14	ABM recall	Positive ABM recall > negative ABM recall	67
Marusak *et al.* (12)	14 CM and 16 HC	9–16	Emotional conflict task	Incongruent > congruent trials; postincongruent incongruent > postcongruent incongruent trials	64
Gerin *et al.* (13)	20 CM and 21 HC	10–15	Problematic passive avoidance task	Approached stimuli > expected value; avoided stimuli > expected value; punishment feedback > prediction error	67
Hart *et al.* (14)	20 CM and 27 HC	12–20	Emotion discrimination task	Fear > fixation; fear > happy	64
Hoffmann *et al.* (15)	41 CM and 34 HC	10–14	Balloon analog risk task	Observed > alone; peer pressure > observed; win > loss	68
Lenow *et al.* (16)	14 CM and 16 HC	12–16	Trust learning task	Unexpected take > expected take	67
PTSD					
Calderon-Delgado *et al.* (17)	22 PTSD and 22 HC	9–14	Emotional word processing task	Positive > neutral; negative > neutral	61
Dégeilh *et al.* (18)	10 PTSD and 10 HC	13–18	Self-reference processing task	self-negative > semantic; self-positive > semantic	70
Yang *et al.* (19)	5 PTSD and 6 HC	12–14	Perception and imagery recall task	Perception earthquake > perception neutral; imagery earthquake > imagery neutral	52

The number of criteria reported in each article from the COBIDAS report was totaled and is presented out of the total number of criteria.

ABM, autobiographical memory; CM, child maltreatment; COBIDAS, Committee on Best Practice in Data Analysis and Sharing; HC, healthy control children; OHBM, Organization for Human Brain Mapping; PTSD, posttraumatic stress disorder; PTSS, posttraumatic stress symptoms.

22) and expanded into the left middle temporal gyrus, supramarginal gyrus, and insula (reaching BAs 22, 39, 13, 43, 40, and 41). The last coordinate peak fell within the right middle frontal gyrus (BA 8) and expanded into the superior frontal gyrus and precentral gyrus (reaching BA 9). Component 2 was activated more for child participants with trauma than for HCs during reward tasks and trauma perception; HCs activated component 2 more than participants with histories of trauma on tasks pertaining to emotions (words and faces) and on social tasks (see Tables 2 and 4 and Figure 4).

DISCUSSION

Our main findings revealed 2 clusters in the brain that were associated with trauma histories. The first component activated included the DMN, posterior insula, and affective networks (including the limbic system) while the second component activated the CEN; these findings are consistent with our hypotheses with the exception of not detecting activation within the SN. Largely, our study revealed that children with trauma histories hyperactivated the DMN, posterior insula, and affective networks during emotionally laden tasks and tasks pertaining to the self. This differs from what we observed in HCs, who activated the CEN for emotion and social tasks more than children with a trauma history. HCs also activated the DMN, posterior insula, and affective networks more for memory and reward-processing tasks than children with trauma histories, whereas the children with trauma histories activated the CEN during reward processing more than HCs. Interestingly, we also found that children with trauma histories simultaneously activated the DMN, affective network, posterior

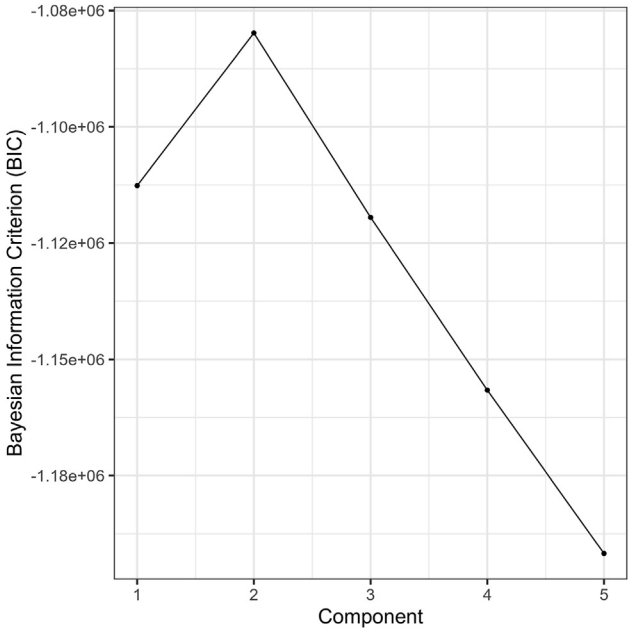

Figure 3. Bayesian information criterion (BIC) estimate of cognitive components. Better models are associated with a higher BIC. Our BIC spiked at 2 components.

insula, and the CEN more than HCs during tasks that pertain to active trauma recall. This suggests different activation patterns in the brain during trauma-neutral tasks than during tasks that incorporate the active processing of traumatic stimuli. It also indicates that one's brain and behavioral responses differ in response to trauma triggers more than during neutral situations that do not reference one's trauma.

Our results are consistent with symptom profiles and previous review studies of brain networks conducted with children with trauma histories. Previous studies have indicated that the functional connectivity of the amygdala and the ventral medial prefrontal cortex are abnormal in children with PTSD (25,26). This is consistent with our results, which indicate hyperactivation of the DMN, limbic regions, and the posterior insula during nontrauma-associated emotion-processing tasks and decreased activation of the CEN. However, our findings take these results further by specifying abnormalities in affective processing in children with trauma histories and indicating network patterns that characterize our results.

First, blunting within the CEN was observed for tasks pertaining to all aspects of affective processing (including words and emotional faces), and hyperactivation was found within the DMN, posterior insula, and affective network. There were no differences for contrasts of differing emotional states, but blunting was found within limbic regions associated with memory in children with trauma histories. Limbic blunting is consistent with previous studies that have suggested less activation in the parahippocampal gyrus and hippocampus during memory tasks, such as the verbal declarative memory task, in children with trauma histories (7). They also show weaker activation than HCs when retrieving words from memory.

Different effects were found during active trauma cue threat processing within limbic regions. Adolescents with PTSD showed greater activation in the parahippocampal gyrus and hippocampus when performing the memory task during imagery recall of their own experienced trauma (19), and children with trauma had greater activation in limbic regions when processing emotional words than when processing neutral words in situations where the child's traumatic experience was incorporated into the experimental task (17). Therefore, children with trauma histories showed greater activation than HCs in both the CEN and the DMN/affective network during tasks that activated their experience of trauma; the brains of children with trauma behaved differently when viewing traumatic threat-related stimuli compared to when performing everyday cognitive functions such as memory and affective processing.

We also found blunting in reward processing in children with trauma histories within the DMN, posterior insula, and affective network and increased processing within the CEN. Our results

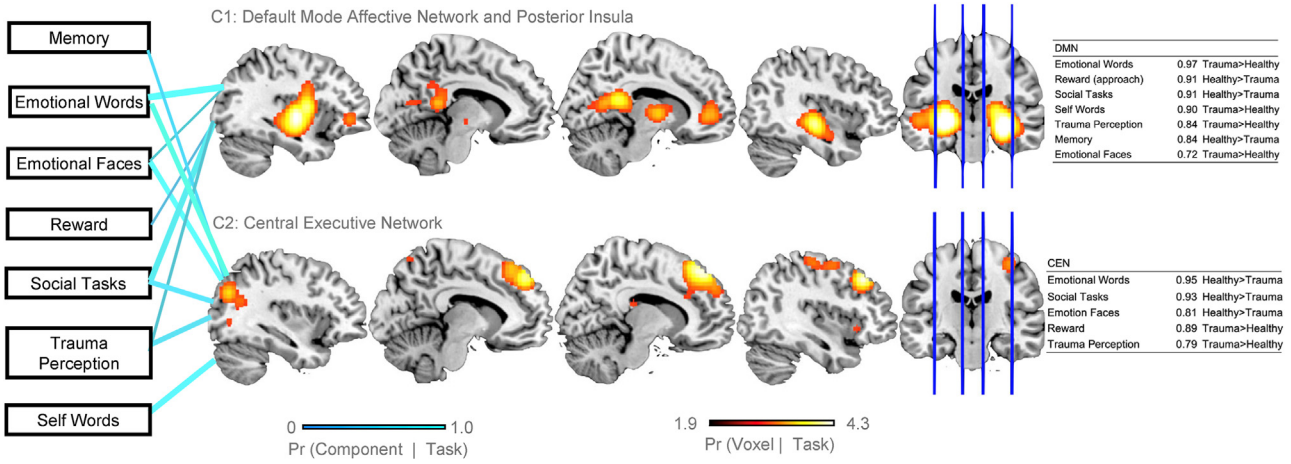

Figure 4. Components of childhood trauma. Estimates for the 2-component model. Lines connect each task type to components based upon the strength of the loading (a theta weight value between 0 and 1.0) of a particular task category onto each component. Each component is represented by a separate *z* cluster map thresholded at 1.9 minimum to 4.3 maximum cluster correction. The loadings of different task categories, highest theta weights for each category, and the group-level diagnostic contrasts are displayed on the right. C, component; Pr, probability.

Table 2. Loading of Diagnostic Contrasts Onto Components

Component	Healthy Children > Trauma	Trauma > Healthy Children
CEN	Emotional words Emotional faces Social tasks	Trauma perception Reward
DMN/Affect/pI	Reward Memory	Emotional words Self-words Trauma perception Emotional faces

Affect, affective network; CEN, central executive network; DMN, default mode network; pI, posterior insula.

are consistent with adult studies, which have indicated that reward deficits are reported in adults with PTSD (27,28), and with a study that found that reward-processing deficits were associated with childhood neglect and threat during adolescence (29). These findings suggest a potential pathway of influence for the development of anhedonia and demotivation symptoms in children and young people who have experienced trauma histories (30).

In contrast to decreased activation for memory and reward processing within the DMN, limbic regions, and the posterior insula in children with trauma, we found hyperactivity for posterior insula activation in children during the processing of emotionally laden and social tasks. The posterior insula is involved in bottom-up processing of internal body cues (interoceptive senses) directly from the body including heart rate, breathing, the need to defecate and urinate, affective (slow c fiber) touch, orgasm, hunger, and satiety (31). It receives connections from the periphery of the body through the thalamus and shares connections with other regions involved in sensory processing such as the intraparietal lobule. The posterior insula also connects to and transmits stimuli pertaining to the body to the mid-insula, which shares connections to limbic regions and regions of the DMN and influences emotion, reward, self, and other processing (31). Disturbed activation within the posterior to mid-insula on tasks that do not directly and intentionally probe interoceptive senses suggests that interoceptive disturbances in the detection and processing of sensory cues directly from the body may contribute to the disturbances in emotion, self, and social-emotional processing commonly observed in children with trauma histories. Thus, hyperactivation of the posterior insula may be due to dampened internal bodily processing, and thus the child's developing brain may require more cognitive resources to process their internal states. This assertion is supported by a recent study that reported impaired interoceptive detection in young adults with a history of childhood trauma (32), a link between trauma exposure and reduced heart rate variability (33), and a dampened startle response in those with a history of childhood trauma (34,35).

Table 3. Local Maxima Coordinates Generated for Cluster 1

Region	Cluster Size	Peak *Z*	Side	BA	MNI Coordinates x	y	z
Left Globus Pallidus	15,880	5.53	L	13	−26	−14	−4
Claustrum	–	4.09	R	–	−32	−2	10
Hippocampus	13,208	5.25	R	13	30	−18	−10
Globus pallidus	–	4.11	R	–	22	−12	4
Putamen	–	3.88	R	–	22	−4	4
Posterior cingulate	–	3.6	R	29	10	−44	16

In regions with more than 1 cluster of activation, coordinates are listed for the cluster with highest activation. Number of voxels and peak activation are listed only for main clusters; activation is not listed for local maxima regions within clusters.

BA, Brodmann area; L, left; MNI, Montreal Neurological Institute; R, right.

Our results also indicate that children with trauma histories demonstrated decreased activation of the CEN during affective and social processing. In adolescents, empathy improves as prefrontal capacities and associated cognitive empathy develop with increasing age (36). Thus, a lack of recruitment of CEN capacities during social processing may influence mentalizing and empathy deficits noted in people who have experienced trauma (37,38).

Our findings are consistent with adult studies that suggest a decoupling of central executive and default mode activation in adults with PTSD (39). However, the SN plays an active role in the switching between central executive and default mode activation (39), but we did not find abnormal activation of the SN—namely the anterior insula and dorsal anterior cingulate cortex—in our child participants who have trauma histories. Developmental differences between children and adults may explain why we detected deficits in the posterior insula but not in regions of the SN. Substantial brain development occurs during childhood and throughout adolescence. Several of the brain regions encompassed within the DMN, posterior insula, and limbic regions—especially those involved in bottom-up sensory processing—primarily develop prenatally and during early childhood (40,41). However, the prefrontal regions of the CEN and the more anterior portions of the insula involve top-down processing and substantially develop and change in response to puberty and throughout adolescence and early adulthood (41). Specifically, because the anterior insula and dorsal cingulate cortex develop later during childhood than the posterior insula, this could reflect developmental differences in trauma symptom development. Our results indicating posterior insula deficits but not deficits within the anterior insula suggest that the detection of bodily cues—but not the awareness of one's interoceptive abilities—may be affected by childhood trauma, which indicates that treatments that directly address deficits in receiving information from the body may be more effective than the cognitive processing of one's awareness of their own body and emotions in childhood PTSD.

Age also plays an important role in the way that childhood trauma affects the brain. However, our study was unable to specifically account for changes in age because we were implementing a data-driven, machine learning meta-analytic approach. It is possible that SN deficits may be present in the older participants of the study compared to the younger children. Additionally, the fact that we were unable to specifically examine the influence of biological sex on the impact that trauma plays on the developing brain may impact our results because one of our previous studies showed opposite effects within the brain for males and females who had experienced child maltreatment, and specifically within the ventral anterior insula, a key region of the insula for emotional processing and interoceptive awareness (42,43). The fact that we were unable to consider sex effects within the ventral anterior insula may

Table 4. Local Maxima Coordinates Generated for Cluster 2

Region	Cluster Size	Peak *Z*	Side	BA	MNI Coordinates		
					x	y	z
Medial Frontal Gyrus	10,536	5.20	L	8	0	46	42
Superior Temporal Gyrus	3888	4.01	L	22	−52	−48	14
Middle Frontal Gyrus	2160	3.66	R	8	38	28	10

In regions with more than 1 cluster of activation, coordinates are listed for the cluster with highest activation. Number of voxels and peak activation are listed only for main clusters; activation is not listed for local maxima regions within clusters.

BA, Brodmann area; L, left; MNI, Montreal Neurological Institute; R, right.

have contributed to our lack of SN recruitment. Additionally, adult studies have also shown that brain activation within the SN varies depending upon hypoactive and hyperactive PTSD symptoms, meaning that dissociative symptoms (hypoactive) and arousal/reappraisal symptoms (hyper) are associated with more chronic and acute trauma symptoms, respectively, and demonstrate different responses within the SN and the medial prefrontal cortex (44,45). Thus, our sample may also include children with both symptom types, which may cancel out any activation deficits within the SN, thus further leading to our lack of results.

Limitations

One key limitation is that of the 1428 studies that were initially identified for this meta-analysis, only 14 were eligible for inclusion. This shows how limited the research is on childhood trauma using whole-brain task-based fMRI. Another limitation is that the type of trauma and maltreatment (i.e., interpersonal vs. natural disaster) experienced by the participants, age of trauma, trauma dosage, and chronicity were not measured and were unable to be controlled for in our analyses. The type of trauma that a person experiences, the age and pubertal stage when a child experiences trauma, and the extent of one's stress (i.e., allostatic load of a high traumatic load verses a low dose) differentially impact the brain (46–48). This could pose an issue for our study because children and young people who participated in the studies may have experienced different levels and types of traumas because brain effects are likely to differ depending on trauma dosage, age of the traumatic experience, type of trauma, and the chronicity of the trauma (48,49). Additionally, because we are implementing machine learning analyses that are data driven, our approach does not allow for covariates or the ability to control for specific factors, such as age or sex effects. Age effects may be extremely relevant to our results because substantial changes occur from childhood throughout adolescence as our study expands from school-age children to young adults (8–20 years), although most of the studies included participants from the ages of 10 to 17. Lastly, our study examined activation patterns from across various tasks, and some task types were examined more than others, which may have affected some of the nuances of our results. Nonetheless, our tool was designed to identify convergence among more than 1 task type and across varying brain areas, so our results need to be interpreted with the understanding that they arose from the pooling together of brain activation patterns from regions across the entire brain and also varying task types.

Conclusions

The aim of this investigation was to find evidence of consistent neural substrates in children who have experienced childhood trauma. Our findings demonstrated that children with trauma histories demonstrated hyperactivation in comparison to HCs within brain regions associated with the DMN, posterior insula, and affective network during tasks pertaining to affective, self-other processing and decreased activation in these regions for memory processing and reward. Instead, the CEN was recruited during reward tasks, and deficits were seen compared to HCs in emotion and social-emotional processing; no abnormal activation patterns were detected within the SN, a network that is associated with trauma in adults and has been suggested to be associated with trauma histories in child samples.

The results of our study appear to reveal a common neurodevelopmental cognitive substrate that underlies having a trauma history during childhood. It suggests a potential imbalance in bodily and cognitive processes that may influence emotions, learning, memory, and problems with self-other processing (50). Furthermore, activation patterns within the brain appear different during trauma triggering; the non-triggered brain state demonstrates evidence of activation deficits for bodily processing (interoceptive sensory processing) and self-other processing. Thus, the development and/or implementation of treatments that target interoception, affective, and self-other processing in children with trauma histories may be beneficial and should be explored in future studies.

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ARTICLE INFORMATION

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