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# Default-Mode Network Abnormalities in Pediatric Posttraumatic Stress Disorder

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## Abstract

**Objective—**Resting-state functional magnetic resonance imaging (rs-fMRI) studies of adult posttraumatic stress disorder (PTSD) have identified default-mode network (DMN) abnormalities, including reduced within-network connectivity and reduced anti-correlation between the DMN and task-positive network (TPN). However, no prior studies have specifically examined DMN connectivity in pediatric PTSD, which may differ due to neurodevelopmental factors.

**Method—**29 youth with PTSD and 30 non-traumatized healthy youth of comparable age and sex completed rsfMRI. DMN properties were examined using posterior cingulate cortex (PCC) seed-based connectivity and independent component analysis (ICA).

**Results—**Contrary to adult studies, youth with PTSD displayed increased connectivity within the DMN, including increased PCC-inferior parietal gyrus connectivity, and age-related increases in PCC-ventromedial prefrontal cortex connectivity. Strikingly, youth with PTSD also displayed greater anti-correlation between the PCC and multiple nodes within salience and attentional control networks of the TPN. ICA revealed greater anti-correlation between the entire DMN and TPN networks in youth with PTSD. Furthermore, DMN and TPN connectivity strength were positively and negatively associated, respectively, with re-experiencing symptoms of PTSD.

**Conclusion—**Pediatric PTSD is characterized by heightened within-DMN connectivity, which may contribute to re-experiencing symptoms of PTSD and is consistent with the DMN's role in autobiographical memory. At the same time, greater anti-correlation between the DMN and attentional control networks may represent compensatory mechanisms aimed at suppressing trauma-related thought, a notion supported by the inverse relationship between TPN strength and

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re-experiencing. These findings provide new insights into large-scale network abnormalities underlying pediatric PTSD, which could serve as biomarkers of illness and treatment response.

**Keywords**

Pediatric PTSD; DMN; rs-fMRI; Connectivity

## INTRODUCTION

Pediatric posttraumatic stress disorder (PTSD) affects an estimated five percent of youth by age eighteen[1]. Pediatric PTSD has high comorbidity with other mental illnesses including anxiety disorders, depression, and attention-deficit/hyperactivity disorder (ADHD).[2] While there is a need to advance treatments for pediatric PTSD, progress remains hampered by an incomplete understanding of underlying brain mechanisms, which may differ from adult PTSD due to ongoing neurodevelopment.

Resting-state functional magnetic resonance imaging (rs-fMRI) allows assessment of intrinsic (i.e. task-free) functional networks[3] and is particularly suitable in pediatric populations. Resting state analyses consistently identify two main networks: the default mode network (DMN), involved in self-referential processes including autobiographical memory[4–6], and the task positive network (TPN), involved in attentional control and behavioral response via the salience, dorsal attention, and ventral attention sub-networks[7]. In healthy adults, the DMN and TPN operate in an anti-correlated fashion, indicative of functionally competing brain systems that switch during the processing of internal vs. external stimuli[8–11]. DMN hyperconnectivity and reduced DMN suppression/anti-correlation have been reported in psychopathology including schizophrenia and depression, suggesting that abnormal network strength and reciprocity may underlie difficulties in disengaging from internal stimuli such as delusional thought and depressive ruminations[11,12].

Studies in adult PTSD suggest abnormal DMN function and connectivity, including decreased within-DMN intrinsic connectivity[13–17], both decreased[13] and increased[16] DMN-TPN intrinsic anti-correlation, and reduced DMN suppression during task[17]. Together, these findings suggest that adult PTSD is characterized by both within and between-network abnormalities of the DMN, which may contribute to difficulties disengaging from trauma-related thought. However, no prior study has specifically examined DMN properties, including its relationship to attentional control networks, in pediatric PTSD. Thus, it remains unknown whether similar DMN abnormalities are present in pediatric as in adult PTSD, and whether the normal developmental pattern of the DMN is disrupted. Notably, DMN-TPN anti-correlation develops with age, going from positive connectivity in childhood to negative or anti-correlated connectivity by adulthood[18].

To address these knowledge gaps, we examined intrinsic network properties in a sample of youth with severe PTSD relative to non-traumatized healthy youth. First, we assessed DMN connectivity using seed-based connectivity of the posterior cingulate cortex (PCC), a key node of the DMN. Next, we used group independent component analysis (ICA) to examine large scale network differences within and between the DMN and TPN. Within these

analyses, we examined age-related effects cross-sectionally as an indicator of altered neurodevelopment in pediatric PTSD. We hypothesized that pediatric PTSD would be associated with disrupted within-DMN connectivity, and reduced anti-correlation between the DMN and TPN, bearing similarity to adult PTSD. Finally, we examined the relationship of DMN/TPN network properties to symptom severity using a multidimensional symptom approach, incorporating PTSD, anxiety, and depressive symptoms in this highly comorbid sample.

# METHOD

## Participants

Youth with PTSD and healthy youth were recruited from area mental health clinics and the community, respectively. Healthy participants were free of any history of trauma or mental illness. Exclusion criteria for all participants included IQ<70, unstable medical condition, MRI contraindication, and possibility of pregnancy. Additional exclusion criteria for the PTSD group included active suicidality, history of psychotic disorder, bipolar disorder, obsessive-compulsive disorder, recent (past 4 weeks) substance abuse or dependence, or use of psychotropic medication (past 4 weeks; 6 weeks for fluoxetine). A total of 119 youth were screened for study inclusion. Of these, 44 were excluded at initial assessment (subthreshold for PTSD, n=29; exclusionary diagnosis, n=7; active substance/medication use, n=3; no child memory of a traumatic event, n=3; MRI contraindication, n=1; other, n=1). Three additional youth met study criteria but were unable to complete MRI. Seventy-two participants completed the study, including 35 youth with PTSD and 37 healthy youth. Of these, 12 were excluded based on data quality described below. The final sample includes 29 youth with PTSD (18 females; $M_{age}$ = 14.6 yrs.) and 30 healthy youth (18 females, $M_{age}$ = 14.0 yrs). All participants provided written consent, or assent with caregiver consent when applicable. All procedures were approved by the University of Wisconsin Health Science Internal Review Board.

## Clinical and Behavioral Assessment

Clinical assessments for this study have been previously described[19,20]. A board-certified child and adolescent psychiatrist interviewed and screened all participants, incorporating both caregiver and youth reports. Psychiatric diagnoses and trauma exposure were assessed using the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS)[21]. PTSD was diagnosed using *DSM-IV* criteria by combination of the K-SADS and the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA)[22,23]. A PTSD diagnosis required at least five *DSM-IV* symptoms, including at least one from each symptom cluster following Cohen et al.[24] These criteria are slightly modified from adult criteria and were chosen to allow greater likelihood of study inclusion, yet maintain a relatively high symptom severity. Furthermore, youth fulfilling two vs. three symptom clusters do not differ in overall clinical impairment or distress[25]. Using these criteria, most youth in the group with PTSD (n=24 or 83%) met full standard *DSM-IV* criteria for PTSD. Of the remaining five participants with PTSD, three met criteria for two symptom clusters, and two met criteria for one symptom cluster. With regard to *DSM-5* criteria, an estimated 22 (76%) met the full diagnosis of PTSD using conservative criteria based on extrapolation

from *DSM-IV* symptoms[26]. Of the remaining seven participants, five met criteria for three symptom clusters, and two met criteria for two symptom clusters. PTSD severity was additionally examined using the University of California, Los Angeles (UCLA) PTSD Reaction Index (PTSD-RI)[27]. Since the CAPS-CA was not acquired for the first 7 participants with PTSD, PTSDRI scores were used in lieu of CAPS-CA for secondary analyses. Here, the greater of youth and caregiver report for each item was used[19,20], as this was most strongly correlated with CAPS scores, which represent the gold standard for PTSD assessment (r = 0.85, 0.74, and 0.60 for greater of youth/caregiver, youth only, and caregiver only, respectively). Depressive symptoms (past two weeks) were quantified with the Mood and Feelings Questionnaire (MFQ)[28]. Anxiety symptoms (past three months) were quantified with the Screen for Child Anxiety Related Emotional Disorders (SCARED)[29]. MFQ and SCARED scores were calculated using the average of youth and caregiver reports. Pubertal stage was assessed by self-report using the Tanner picturebased rating scale[30]. IQ was estimated using the Full-Scale IQ-2 component of the Wechsler Abbreviated Scale of Intelligence-II[31].

## Data Acquisition

Each participant underwent two mock scan sessions to familiarize them to the scanning environment and reduce motion. High-resolution T1 and rs-fMRI data were acquired using a 3.0T GE Discovery MR750 scanner with an eight-channel head coil (General Electric Medical Systems, Waukesha, WI). High-resolution T1 images were acquired using a BRAVO pulse sequence (with axial orientation, TE =3.18 ms, TR = 8.16 ms, TI = 450 ms, voxel size = 1 × 1 × 1 $mm^3$, 156 slices, flip angle = 12 degrees, FOV = 25.6 cm, and matrix size = 256 × 256). Rs-fMRI was acquired using an echo-planar imaging (EPI) pulse sequence (with sagittal orientation, TE = 22 ms, TR = 2150 ms, flip angle = 79 degrees, slice thickness = 3 mm, gap = 0.5 mm, 41 slices, FOV = 224 mm, and matrix size = 64 × 64, number of volumes = 147 [5min16s]). For rs-fMRI, participants were instructed to remain still with their eyes fixed on a cross.

## rs-fMRI Preprocessing

Preprocessing was carried out using AFNI[32]. Figure S1, available online, shows the preprocessing pipeline used for each research participant. The steps were: deletion of the first three volumes; despiking of rs-fMRI data; slice-timing correction; co-registration of T1 and EPI images, realignment of EPI volumes and normalization to Montreal Neurological Institute (MNI) template in a single step (final resolution 2mm isotropic for visualization with template underlay); spatial smoothing (6mm full width at half maximum [FWHM]); anatomy segmentation, nuisance regression (eroded white matter and cerebrospinal fluid masks, six motion parameters and their derivatives), temporal filtering (0.01–0.1Hz) along with motion censoring in a single step. Volumes were motion censored using a threshold of 0.25mm based on framewise displacement calculated using the Euclidean norm. Participants having ≥37 (25%) of volumes flagged by the censoring algorithm were excluded from the study, resulting in twelve exclusions (6 PTSD, 7 healthy). The average motion in all directions was calculated and compared across groups; no difference in motion was observed (Table S1, available online).

### Connectivity Analysis: Seed-Based

DMN connectivity was calculated using a 4mm-radius sphere located in the PCC (MNI coordinates [RAI]: 2, 52, 26). Individual connectivity maps were converted from r to Z using a Fisher-Z transform. Group differences in connectivity were examined using an analysis of covariance (ANCOVA) in AFNI (3dttest++), with covariates including age, sex, and their interaction with group. Multiple comparison correction was performed using Monte Carlo simulation, which incorporates the estimated data smoothness to establish the likelihood of false positives of different cluster sizes[33]. The cluster threshold was 152 voxels at a voxel-wise threshold of $p$=.005, resulting in a corrected $\alpha$=0.05.

### Connectivity Analysis: Independent Component Analysis

Resting-state networks were identified using a spatial group independent component analysis, implemented in GIFT[34]. Data input to the ICA were first preprocessed by correcting for participant motion using rigid-body realignment of EPI volumes, correction for slice timing, alignment of EPI data to the T1-weighted structural image, transformation (linear affine and nonlinear) to MNI space, and spatial smoothing with a Gaussian kernel (FWHM 6mm). Within GIFT, dimensionality was first reduced using principal components analysis (PCA) at the individual level. Forty independent components were estimated at the group level using the Infomax algorithm[35]. Group data were then back-reconstructed to individual participants. ICA maps were thresholded using the default setting in GIFT.

The component representing the DMN (consisting of posterior cingulate/precuneus, lateral parietal cortex, and medial prefrontal cortex) and a component representing the TPN (dorsolateral prefrontal cortex, frontoinsular cortex, dorsal anterior cingulate/pre-supplementary motor area, intraparietal sulcus) were visually identified from the group results. Between-network functional connectivity was estimated by computing the correlation between these two ICA component time series for each participant. ANCOVA was then conducted in AFNI (3dttest++) to examine group differences in average network and between-network connectivity covarying for age and sex. Due to the targeted, exploratory nature of the three ICA analyses, additional adjustment for multiple comparisons was not applied.

### Post Hoc Analyses

Post hoc analyses were conducted on extracted cluster averages in *R* (R Core Team, 2014) to examine: (1) potential confounds in group differences, (2) relationships to PTSD, depression, and anxiety symptoms, and (3) relationship to trauma exposure within the PTSD group, covarying for age and sex. Given high rates of comorbid affective and anxiety disorders in our sample, we used a multidimensional symptom approach to examine the relationship between symptom measures and brain findings within the PTSD group. Specifically, we performed data reduction using PCA of PTSD, depressive, and anxiety symptoms from the PTSD-RI, MFQ, and SCARED in a slightly expanded sample of youth with PTSD (n=31) including all participants in the current study. This approach allows for avoidance of collinearity in symptom analysis and minimization of the number of statistical tests, though generalizability to other populations may be limited. For this reason, we also report standard symptom relationships in Supplemental Material (p.1, available online).

Items with low correlation coefficients in all components (< 0.4) and/or low measures of sampling adequacy (< 0.5) were removed. Principal component loadings for each item were rotated using the Varimax method with Kaiser normalization. Component inclusion was based on an eigenvalue ≥1.

Five components were extracted from the final iteration of PCA, explaining 74.8% of the total variance in symptom measures. Based on the items loading to each component, the five symptom domains included (with percent of total variance explained): social aversion (20.7%), hopelessness (18.0%), negative affect (14.1%), hyperarousal (12.0%), and re-experiencing (10.0%) (Table S2, available online). These five components reached significance for Bartlett's Test of Sphericity ($p < .0001$) and had a Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy = 0.609. The specific PTSD-RI, MFQ, and SCARED items loading into each component can be found in Supplement 1, available online. Component scores for each participant with PTSD were calculated and used in post hoc analyses.

## RESULTS

### Participant Characteristics

A summary of participant characteristics is shown in Table 1. The healthy and PTSD groups did not differ in age, IQ, female-to-male ratio, or pubertal stage. For the group with PTSD, the average PTSD-RI score was 47, which is indicative of severe PTSD. The most common index trauma was sexual abuse, followed by accident, traumatic death of a loved one, and witnessing domestic violence. Of the 29 participants with PTSD, 26 had comorbid psychiatric illness, most commonly depressive disorders (n=20).

### DMN Connectivity Abnormalities in Pediatric PTSD: Seed-Based Analysis

Using the PCC seed, the DMN was consistently present in participants from both groups (Figure 1). A summary of seed-based connectivity findings can be found in Table 2. Within the DMN, youth with PTSD showed increased connectivity between the PCC and left inferior parietal gyrus (IPG, Brodmann area [BA] 40). Youth with PTSD also showed reduced (more anti-correlated) connectivity between the PCC and multiple regions associated with the task-positive network (Figure 1). These regions included the right intraparietal sulcus (IPS, BA 40), right inferior frontal gyrus extending into the insular cortex (IFG, BA 6/22), and dorsal anterior cingulate cortex/pre-supplementary motor area (dACC/pre-SMA, BA 32/24). Similar effects were observed for the left IPS and IFG at lower cluster extent thresholds (Figure S2, available online). Finally, a group by age interaction was present for connectivity within the DMN. Specifically, PCC connectivity to the ventromedial prefrontal cortex (vmPFC, BA 11) decreased with age in healthy youth, but increased with age in youth with PTSD (Figure S3, available online).

### DMN Connectivity Abnormalities in Pediatric PTSD: Independent Component Analysis

ICA results are summarized in Figure 2. Components for the DMN and TPN were identified across the entire sample, showing similarity to seed-based connectivity patterns. Analysis of extracted, average network connectivity strength for each component revealed no overall

differences in DMN or TPN strength between healthy youth and those with PTSD. However, consistent with seed-based findings, youth with PTSD displayed reduced (more anti-correlated) connectivity between the DMN and TPN components compared to healthy youth (−0.29 and −0.12, respectively, $t_{53} = -2.25$, $p = .029$).

To facilitate comparison between the seed-based and ICA connectivity findings, the overlap was examined between seed-based clusters and the DMN and TPN component maps derived from ICA. Here, the IPS, IFG, and dACC clusters derived from the seed-based analysis overlapped closely with the TPN component (91%, 93%, and 99.6% respectively) but showed no overlap with the DMN component. Conversely, the IPG and vmPFC clusters overlapped the DMN component (23.9% for both) but showed no overlap with the TPN component.

### Post Hoc Analyses

To examine potential confounds in group main effects, post hoc analyses were conducted on average PCC and ICA connectivity, adjusting for age, sex, IQ, and past exposure (in months) to alpha-agonists, selective serotonin reuptake inhibitors (SSRIs)/serotonin–norepinephrine reuptake inhibitors (SNRIs), and stimulants. All group main effects remained significant within these models ($p < .05$). Additionally, age-related increases in PCC-vmPFC connectivity in the PTSD group remained significant with adjustment for time elapsed since trauma ($\beta = 0.261$, $t_{21} = 3.186$, $p = .004$).

Next, the relationship between connectivity measures and symptom dimensions was examined within the group with PTSD, adjusting for age and sex. For the PCC seed analysis, PCC–IPG connectivity was positively associated with re-experiencing symptoms ($\beta = 0.433$, $t_{21} = 2.229$, $p = .037$; Figure 3). Additionally, PCC–cerebellum connectivity was negatively associated with social aversion symptoms ($\beta = -0.460$, $t_{21} = -3.425$, $p = .002$). For the ICA analysis, average TPN connectivity strength was negatively associated with reexperiencing symptoms ($\beta = -0.445$, $t_{21} = -2.418$, $p = .025$; Figure 3). Connectivity between the DMN and TPN was positively associated (trend level) with symptoms of hopelessness ($\beta = 0.386$, $t_{21} = 2.032$, $p = .055$). No significant relationship was observed between connectivity measures and negative affect or hyperarousal symptom dimensions.

Finally, the relationship between connectivity measures and trauma exposure measures (time elapsed since index trauma, index trauma type, number of trauma types endorsed) was examined within the group with PTSD, adjusting for age and sex. PCC–IPG connectivity was significantly associated with index trauma type ($F_{7,21} = 3.751$, $p = .008$), such that youth with interpersonal index traumas had greater connectivity relative to accident index trauma ($t_{21} = -3.211$, $p = .004$). No significant relationships were observed with time elapsed since index trauma or trauma load.

## DISCUSSION

To our knowledge, this is the first reported study to examine DMN properties, including their relationship with task-positive networks, in pediatric PTSD. Contrary to expectations and reports in adult PTSD, our findings revealed greater connectivity within the DMN in

pediatric PTSD. Greater within-DMN connectivity (PCC to IPG connectivity) was further associated with re-experiencing symptoms, suggesting that a network known to underlie self-referential processing may also contribute to intrusive trauma-related thought in youth. At the same time, youth with PTSD showed abnormal anti-correlation between the DMN and task-positive attentional control networks, a pattern bearing similarity to healthy adults. TPN connectivity strength, in turn, was inversely correlated with re-experiencing symptoms, directly implicating attentional control networks in the suppression of trauma-related thought in youth. Together, these novel findings suggest striking abnormalities in brain networks underlying self-referential thought and attentional control in pediatric PTSD, which may offer important targets for intervention in afflicted youth.

Surprisingly, we found no evidence for weaker connectivity within the DMN in pediatric PTSD, which stands in stark contrast to studies of adult PTSD[13–17]. On the contrary, our findings revealed increased within-DMN connectivity in pediatric PTSD, specifically between the PCC and IPG. Furthermore, youth with PTSD showed age-related increases in connectivity between the PCC and vmPFC, suggesting that within-DMN connectivity strength may become even more pronounced over the course of development in trauma-exposed youth with PTSD. In addition to these group differences, post hoc analyses revealed that PCC–IPG connectivity was positively associated with re-experiencing symptoms, but unrelated to anxiety, depressive, or other PTSD symptoms. This is particularly intriguing given the role of these regions, and the DMN more generally, in autobiographical memory retrieval as well as envisioning future scenarios[6]. Thus, increased connectivity within the DMN may underlie, in part, the persistence of trauma-related memory and worry in affected youth.

At present, it remains unclear why these current findings differ from adult PTSD, where studies have consistently shown reduced within-DMN connectivity[13–17]. One possibility is that trauma exposure during childhood may have different effects on the DMN compared to adult trauma. However, reduced DMN connectivity has been reported even in adults with PTSD due to childhood trauma[14]. Another alternative is that neural representations of re-experiencing are different between youth and adults with PTSD. However, prior studies of adult PTSD have not shown any clear relationship between reduced DMN connectivity or PTSD severity. A related possibility, then, is that reduced within-DMN connectivity in adult PTSD actually represents a delayed, compensatory decrease in DMN connectivity that may serve to counteract reexperiencing symptoms. These hypotheses would clearly require further testing in future studies, including longitudinal examination of youth with PTSD into adulthood. While the current DMN findings do differ from adult PTSD, it is worth noting that increased within-DMN connectivity has been consistently reported in both youth and adults with major depressive disorder[12], discussed further below.

In addition to within-DMN connectivity differences, our study revealed prominent abnormalities in connectivity between the DMN and task-positive networks in pediatric PTSD. Specifically, in the seed-based analysis, youth with PTSD showed abnormal anti-correlation between the PCC and nodes of the salience network (dACC/SMA), dorsal attention network (IPS), and ventral attention network (IFG/insula). In adults, these networks are normally anti-correlated with the DMN at rest[8–10]. However, this pattern may

be different in children, in whom DMN-TPN connectivity is either positive or only slightly negative[18], as observed in our healthy youth. The salience, ventral attention, and dorsal attention subnetworks of the TPN subserve stimulus detection, attentional redirection, and attentional maintenance, respectively, for external tasks[7]. Crucial to the functioning of these networks in attentional control is the suppression of the DMN (and vice versa for self-referential thought). As such, anti-correlation between the DMN and TPN appears to represent functional competition between these networks. Notably, our findings revealed that TPN connectivity strength was inversely related to re-experiencing symptoms, suggesting that the magnitude of coupling in attentional networks may confer a greater ability to suppress trauma-related thought. In light of this, greater DMN-TPN anti-correlation in pediatric PTSD may represent a compensatory mechanism to suppress unwanted thought, perhaps reflecting early maturation of these networks towards adult connectivity patterns. While DMN-TPN anti-correlation was not directly associated with re-experiencing, it was associated with symptoms of hopelessness, suggesting that anti-correlation of these networks could underlie perceptions of symptom controllability when attempting to engage in outward-focused tasks.

Given the high comorbidity of depressive disorders in our sample, it is worth noting that major depressive disorder (MDD) has also been associated with DMN abnormalities. A recent meta-analysis showed that adult MDD is characterized by increased within-DMN connectivity, but that DMN-TPN connectivity may be either increased or decreased depending on the TPN subnetwork examined[12]. While less is known about DMN properties in pediatric depression, studies to date consistently implicate increased anterior DMN connectivity, which is further associated with symptom severity and rumination[36]. Surprisingly, we found relatively few associations with depressive symptoms and DMN measures in our sample, with the possible exception of DMN-TPN anti-correlation and hopelessness noted above. On the other hand, the use of a PCC (and not anterior DMN) seed may have precluded more depression-specific findings. In either case, our findings suggest that pediatric PTSD may share some commonality with depression in terms of hyperconnectivity within the DMN, and which may contribute to the pathological persistence of self-referential thought in both disorders, namely depressive rumination and traumatic reexperiencing. Clearly, future studies would be merited to explore DMN abnormalities both common and specific to depression and PTSD, and whether symptom improvement is associated with normalization of DMN connectivity.

While our study presents novel findings of abnormal intrinsic network connectivity in pediatric PTSD, it is not without limitations. First, this study did not include trauma-exposed healthy youth, which will be important in fully teasing apart the effects of trauma versus PTSD. However, our post hoc analyses suggest differential relationships of symptom and trauma exposure measures with network connectivity, which has the benefit of examining these variables within participants. Second, group differences are based on cross-sectional data, and we are not able to determine whether network abnormalities are premorbid traits, acquired following trauma exposure, or with the development of PTSD or its comorbidities. Future studies employing a longitudinal design will be needed to examine these possibilities. Third, while our symptom dimension analyses suggest specificity of effects to re-experiencing symptoms of PTSD, future work examining resting state networks across

multiple diagnostic groups (e.g. depression only, PTSD only) will be needed to fully explore diagnostic specificity vs. commonality. Fourth, while the exploratory ICA analysis confirms the seed-based results, these two analyses may not be completely independent given that DMN and TPN components were identified visually with a priori knowledge of the seed-based results. Finally, the PCA symptom dimensions were generated from a relatively small sample for the purposes of data reduction and may not generalize to other study populations.

In summary, the present findings revealed abnormal default mode network properties in pediatric PTSD that appear to differ markedly from adult PTSD. Namely, youth with PTSD showed increased connectivity within the DMN, which may directly contribute to re-experiencing of traumatic memory and is consistent with the DMN's role in autobiographical memory and rumination. On the other hand, youth with PTSD showed greater anti-correlation between the default mode and attentional control networks, which may reflect a compensatory mechanism to reduce trauma-related thought through opposition of the DMN. These intrinsic network patterns point to potential neural targets for therapeutic interventions that aim to regulate traumatic re-experiencing in youth. In particular, future studies might examine whether psychotherapy such as trauma-focused cognitive-behavioral therapy is capable of reducing connectivity within the default mode network, and whether such therapies may also further strengthen attentional control networks to reduce symptoms of PTSD in afflicted youth.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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### Clinical Guidance

- Youth with PTSD show abnormal functional connectivity of the brain's default mode network (DMN), which is involved in self-related thought and autobiographical memory.
- Youth with PTSD have abnormally increased connectivity within the DMN, which may contribute to reexperiencing of traumatic memory
- Youth with PTSD also have greater opposing connectivity between the DMN and attentional control networks, which may to help them to "switch out" of the DMN and suppress traumatic memory
- These default mode network abnormalities are quite different from adult PTSD and highlight the importance of studying brain networks in PTSD developmentally

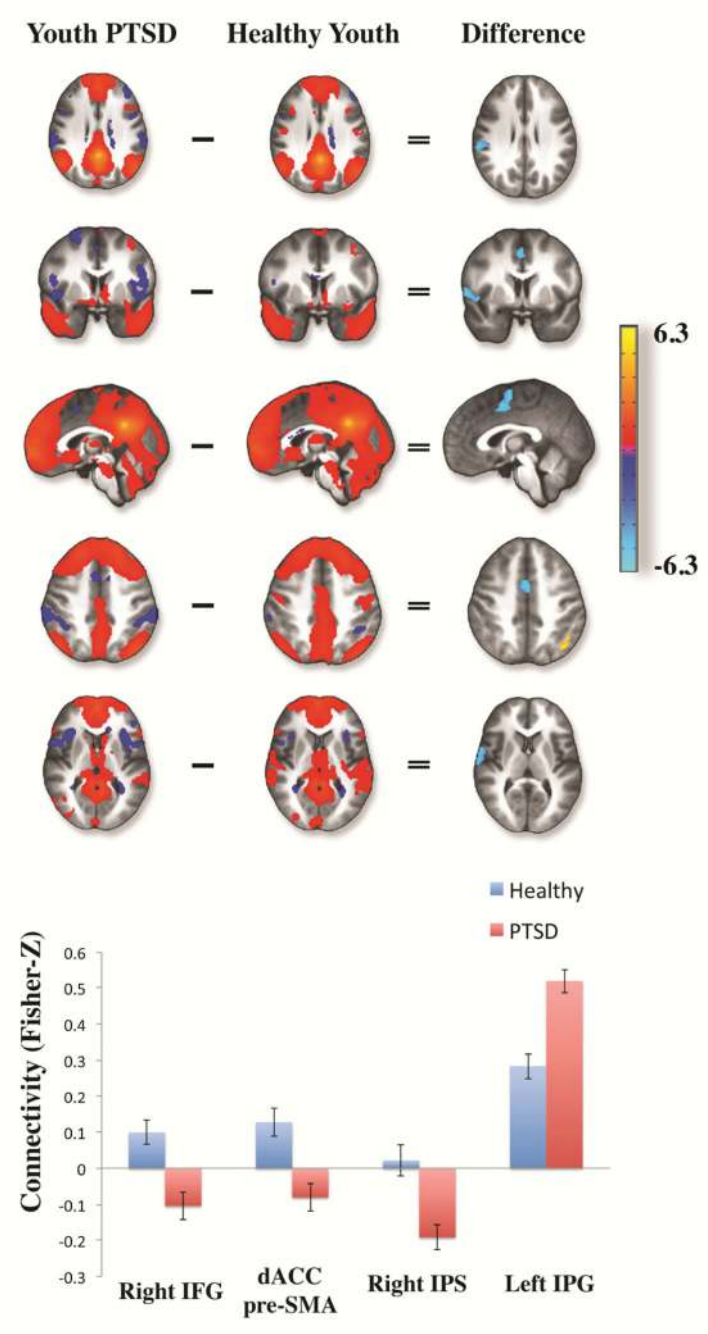


**Figure 1.**

Default mode network (DMN) connectivity differences between youth with posttraumatic stress disorder (PTSD) and healthy youth in the posterior cingulate cortex (PCC) seed-based connectivity analysis. Note: Respective group maps are shown as well as group connectivity differences, adjusting for age and sex. Youth with PTSD showed increased connectivity within the DMN (PCC-left inferior parietal gyrus [IPG]), but also greater anti-correlation between the PCC and multiple nodes of attentional control networks (right inferior frontal gyrus [IFG]/insula, right intraparietal sulcus [IPS], dorsal anterior cingulate cortex [dACC]/

pre-supplementary motor area [SMA]). Maps are shown at a voxelwise $p$=.005 and minimum cluster extent of 152 voxels. "-" represents a subtraction operation; "=" represents the results of the subtraction operation; "*" represents significant differences between youth with PTSD and healthy youth for the bar graph data.

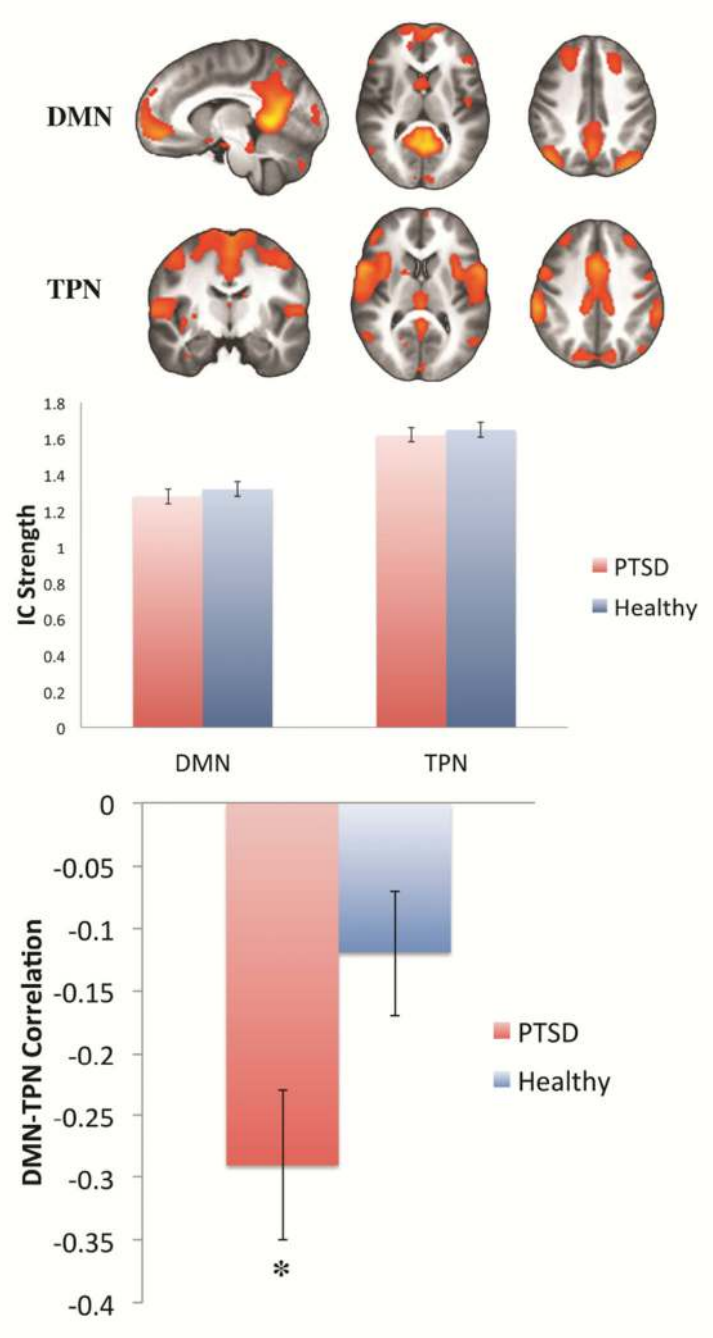


**Figure 2.**

Independent component analysis of default-mode network (DMN) and task-positive network (TPN) connectivity in youth with posttraumatic stress disorder (PTSD) and healthy youth. Note: PTSD and healthy youth did not differ in overall DMN and TPN connectivity strength, but show reduced overall connectivity between the DMN and TPN. DMN and TPN component maps are shown in the top panel. In the middle panel, bar graphs show the average connectivity strength for each group, for each of the two components. The bottom

panel shows the correlation between the DMN and TPN components for each group. Error bars represent standard error of the mean. IC = independent component. * $p < .05$.

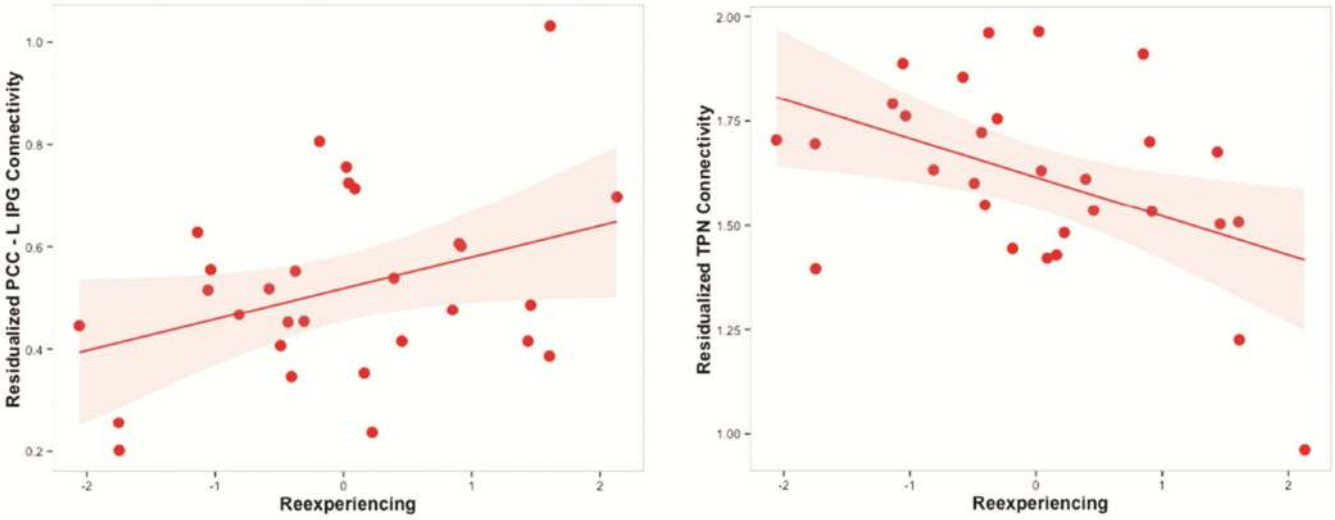


**Figure 3.**

Re-experiencing symptoms are related to default mode network (DMN) and task-positive network (TPN) connectivity strength in youth with posttraumatic stress disorder (PTSD). Note: Left panel: within the DMN, connectivity between the posterior cingulate cortex (PCC) and inferior parietal gyrus (IPG; derived from the seed-based analysis) predicts greater re-experiencing symptom severity. Right panel: TPN connectivity strength (derived from independent component analysis [ICA]) predicts lower re-experiencing symptom severity. Scatterplot values are adjusted for age, sex, and other symptom dimensions.

## Table 1

Participant Characteristics

| | Healthy | PTSD |
|---|---|---|
| Sample Size | 30 | 29 |
| Sex | 18 F, 12 M | 18 F, 11 M |
| Age (years) | 14.0 [2.3] | 14.6 [2.6] |
| IQ | 109 [12] | 102 [12] |
| Tanner stage | 3.3 [1.3] | 3.4 [1.3] |
| Handedness | 27 R, 3A | 23 R, 5 L, 1 A |
| PTSD Duration (months) | -- | 46 [38] |
| PTSD-RI | -- | 47 [14] |
| CAPS-CA | -- | 70 [21] |
| MFQ | 3 [2] | 30 [21] |
| SCARED | 7 [5] | 38 [23] |
| Index Trauma (n) | -- | Sexual abuse (13) |
| | | Accident (6) |
| | | Traumatic death of loved one (7) |
| | | Witness of domestic violence (4) |
| | | Physical abuse (1) |
| Comorbid Diagnosis (n) | -- | Major Depressive Disorder (17) |
| | | ADHD (7) |
| | | Generalized Anxiety Disorder (8) |
| | | Social Anxiety Disorder (4) |
| | | Separation Anxiety Disorder (4) |
| | | Depressive Disorder NOS (3) |
| Past Psychiatric Medication (n) | -- | SSRI/SNRI (8) |
| | | Stimulant (8) |
| | | Alpha-2 agonist (2) |

Note: The groups did not significantly differ in age, IQ, or Tanner stage. The Clinician-Administered PTSD (posttraumatic stress disorder) Scale for Children and Adolescents (CAPS-CA) was not obtained for the first seven participants with PTSD.

Values in brackets represent standard deviation.

A = Ambidextrous; ADHD = attention-deficit/hyperactivity disorder; F = Females; L = Left handed; M = Males; MFQ = Mood and Feelings Questionnaire; PTSD-RI = PTSD Reaction Index; R = Right handed; SCARED = Screen for Child Anxiety Related Emotional Disorders; SNRI = serotonin–norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

**Table 2**

Significant Clusters Observed in the Posterior Cingulate Cortex (PCC) Seed-Based Connectivity Analysis

| Contrast | Region | BA | Network | x | y | z | Peak T | # Voxels |
|---|---|---|---|---|---|---|---|---|
| Healthy > PTSD Youth | Right IFG | 6, 22 | TPN | −66 | 6 | 6 | −4.55 | 300 |
| | dACC / pre-SMA | 6, 24 | TPN | −2 | 6 | 60 | −4.32 | 282 |
| | Right IPS | 40 | TPN | −60 | 26 | 32 | −3.76 | 200 |
| PTSD > Healthy Youth | Left IPG | 40 | DMN | 46 | 56 | 54 | 4.55 | 188 |
| Group × Age: PTSD > Healthy Youth | MFG | 11 | DMN | 6 | −62 | −14 | 4.67 | 163 |
| | Cerebellum | -- | -- | −26 | 70 | −30 | 3.92 | 205 |

Note: The peak coordinates are in Montreal Neurological Institute (MNI) space (RAI orientation). Peak T statistics are derived from the contrast posttraumatic stress disorder (PTSD) – Healthy.

BA = Brodmann Area; dACC = dorsal anterior cingulate cortex; DMN = default-mode network; IPG = inferior parietal gyrus; IPS = inferior parietal sulcus; Pre-SMA = pre-supplementary motor area; TPN = task-positive network; vmPFC = ventromedial prefrontal cortex.

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