Previous studies have revealed altered structural development of the frontal lobes and prefrontal cortex (PFC) in children with symptoms of posttraumatic stress disorder (PTSD). This study is the first to provide a detailed structural analysis of the PFC in children with and without PTSD symptoms. We compared gray and white matter volume in four subregions of the PFC between said groups, then explored whether volume was associated with PTSD symptom severity and functional impairment. PFC measurements were extracted from magnetic resonance imaging (MRI) data from a sample of 23 children (ages 7–14) with a history of trauma and symptoms of PTSD, who had undergone assessment for PTSD symptoms and functional impairment using the Child and Adolescent version of the Clinician-Administered PTSD Scale (CAPS-CA). These measurements were compared to data from an age-equivalent control group of 24 healthy children. Children with PTSD symptoms showed a significantly larger volume of gray matter in the delineated middle-inferior and ventral regions of the PFC than did control children. Decreased volume of gray matter in the dorsal PFC correlated with increased functional impairment scores. Results indicate that increased volume of the middle-inferior and ventral PFC may be associated with trauma and PTSD symptoms in children. Furthermore, the neuroanatomy of the dorsal PFC may influence the degree of functional impairment experienced by children with PTSD symptoms. Depression and Anxiety 23:17–25, 2006. © 2005 Wiley-Liss, Inc.
Investigation of morphological differences of the brain in children with PTSD symptoms holds particular promise for furthering our understanding of the biological mechanisms involved in the pathogenesis of chronic impairment following a traumatic event. To date, only a handful of studies have explored such factors in pediatric PTSD. Neurodevelopmental differences observed in children with PTSD symptoms have included decreased cranial and cerebral volumes when compared to matched control groups [Carrion et al., 2001; De Bellis et al., 1999, 2002a]. Studies from our laboratory have revealed an attenuation of the normal asymmetry of the frontal lobes [Carrion et al., 2001], mostly secondary to increased left frontal lobe volumes in children with PTSD symptoms. De Bellis and colleagues found significantly diminished volumes of total tissue and white matter of the prefrontal cortex in their sample of children with PTSD, as well as smaller midsagittal areas of the corpus callosum [De Bellis et al., 1999, 2002a], and increased volumes of gray matter in the superior temporal gyrus [De Bellis et al., 2002b].

These reports differ from the adult PTSD literature, which has focused on aberrant hippocampal morphology in the disorder [Bremner et al., 1995, 1997, 1999, 2003; Gilbertson et al., 2002; Stein et al., 1997; Villarreal et al., 2002]. Morphology of the hippocampus has been correlated with PTSD symptom severity [Gilbertson et al., 2002; Villarreal et al., 2002], and has provided a potential biological explanation for the working memory deficits observed in subjects with PTSD [Bremner et al., 1995, 1997; Jenkins et al., 1998; Vasterling et al., 1998]. The failure to replicate such findings in children suggests that the structural abnormalities associated with PTSD differ across the lifespan, and that the biological basis for pediatric PTSD may not invariably involve an aberrant hippocampal formation.

Within the broader PTSD literature and the field of cognitive neuroscience are indications that pathology of the prefrontal cortex (PFC) may be associated with many of the symptoms of cognitive and emotional dysfunction observed in PTSD. The PFC has been theorized to gate neural activity in other brain regions, thereby supporting a diverse array of mental processes through the activation, maintenance, and inhibition of activity in other structures [Shimamura, 2000]. Elzinga and Bremner [2002] have postulated that functional abnormality of the PFC may contribute to PTSD patients’ experience of working memory and attention deficits, emotional disinhibition, intrusive memories, and failure to inhibit irrelevant cognitions [for a complete review, see Elzinga and Bremner, 2002].

As such, the differences in PFC structure observed in children with PTSD symptoms may relate to functional alterations in both the PFC and connected brain regions, such as the amygdala and hippocampus, and thereby facilitate cognitive and emotional symptoms through a failure to regulate activity properly in those structures. Functional neuroimaging studies of adults with PTSD have provided support for this notion, with the majority of studies reporting either abnormal activation of the PFC or anterior cingulate (AC) during symptom provocation [Liberzon et al., 1999; Osuch et al., 2001; Shin et al., 1999, 2001], or concurrent functional differences in the PFC and functionally connected regions, including the amygdala [Rauch et al., 1996; Shin et al., 1997], hippocampus, and visual association cortex [Bremner et al., 1999]. Shin and colleagues [2004] recently reported that hypoactivity of the medial PFC is reciprocally related to hyperactivity of the amygdala during traumatic imagery in their sample of adults with PTSD. Furthermore, functional decreases in the medial PFC negatively correlated with measures of PTSD symptom severity. In summary, there is ample evidence to suggest that dysfunction of the PFC may contribute to the symptoms of PTSD, as well as the working memory and attention deficits that have been associated with the disorder.

The purpose of this study is twofold: (1) to determine whether the structure of the PFC differs in children with a history of trauma and posttraumatic stress symptoms (PTSS) when compared to healthy control children, and (2) to determine whether PFC structure predicts PTSD symptom severity and functional impairment. To determine whether one region of the PFC is uniquely different in structure or related to symptom severity and functional impairment, we applied a protocol to study four volumetric regions of the PFC (dorsal, middle-superior, middle-inferior, and ventral) and tested our hypotheses within each region. Using the pediatric sample previously reported by Carrion et al. [2001], we first compared gray and white matter volume in these four PFC regions between groups. Due to findings from our group and others suggestive of structural and functional abnormalities of the PFC and frontal lobe in PTSD, we hypothesized that prefrontal neuroanatomy would be particularly aberrant in children with PTSS. We then explored how regional PFC volume relates to PTSD symptom severity and functional impairment.

**METHODS**

**PARTICIPANTS**

The PTSS group was recruited by way of referrals from social service departments and mental health clinics in northern California. Each child met the following criteria for study inclusion: (1) a history of at least one exposure to significant interpersonal trauma, as defined by the DSM-IV [American Psychiatric Association, 1994]; (2) age 7 to 14 years; (3) at least 6 months had elapsed since the traumatic event(s); and (4) a minimum score of 12 on the PTSD Reaction Index [Nader et al., 1990]. Individuals with mental retardation, schizophrenia, autism, current substance...
dependence, and attributes known to confound the integrity of the imaging data (metal implants, traumatic head injury, epilepsy, and other neurological impairments) were excluded.

As reported in Carrion et al. [2001], 24 participants were included in the original sample. However, our current study excluded one participant who had three regional PFC volumes falling more than two standard deviations below the mean for the group. Therefore, our final PTSS group consisted of 23 participants, and included 13 boys and 10 girls. The mean age of the group was 11 years, with a range of 7 to 14 years. All participants were reported to be naive to psychotropic medication, with the exception of three participants for whom a complete medical history was not known or made available by their guardians. Traumatic events included separation and loss (55%), witnessing violence (40%), physical abuse (37%), sexual abuse (20%), physical neglect (12%), and emotional abuse (7%), and the majority of participants (55%) had experienced multiple traumatic events. Twelve participants met the diagnostic criteria for PTSD as assessed by the Clinician-Administered PTSD Scale for Children and Adolescents [CAPS-CA; Blake et al., 1990, 1995]. The other 11 participants demonstrated significant PTSD symptoms on the CAPS-CA but were subthreshold for the diagnosis of PTSD. Hence, we refer to the complete group as children with a history of trauma and PTSS.

The control group consisted of a sample of 24 typically developing children who had completed a clinical interview by a certified child psychiatrist to exclude significant psychiatric or neurological morbidity including PTSD. These control subjects also were used in the analyses reported in Carrion et al. [2001], and had been individually age and gender matched within 1.5 years of age to the original sample of 24 children with PTSD symptoms. Due to the exclusion of one participant with PTSS, the final sample for our current study consisted of 23 PTSS and 24 control participants.

PROCEDURE

Each child and legal guardian agreed to participate after reviewing board-approved consent forms that described the study. All participants with PTSS were evaluated with the following instruments:

1. The PTSD Reaction Index, a reliable and valid 20-item self-report that assesses PTSD symptom severity. The measure uses a 5-point Likert scale that prompts the subject to describe the frequency that symptoms are experienced (none to most of the time).
2. The CAPS-CA, a developmentally appropriate, structured clinical interview designed to evaluate the 17 PTSD symptoms described in the DSM-IV. The interview consists of standard questions, follow-up probes, and 5-point rating scales in which the children rate the frequency and intensity of their current and lifetime symptoms. Practice sessions and visual materials are included to aid children in accurately representing their experiences.

The CAPS-CA provides severity scores for the three PTSD symptom clusters: re-experiencing, avoidance/numbing, and hyperarousal. It also yields a total symptom severity score, consisting of the sum of cluster subtotals. These CAPS-CA total scores were used in the present analyses. The CAPS-CA includes an additional subscale to assess the functional impairment that children may experience as a result of their symptoms. Specifically, this functional impairment measure probes children about the degree to which their symptoms affect (1) social functioning, (2) school performance, (3) general distress, and (4) experience of regressive behaviors. The clinician rates each child’s current functional impairment within these four areas on a scale of 1 to 4. The scores for these four domains were summed to yield a total functional impairment score.

The CAPS-CA was administered to participants by a board-certified child psychiatrist (VGC). Ten interviews were videotaped and scored by a developer of the instrument (Elana Newman), and an intraclass correlation coefficient of .97 was established between raters for CAPS-CA total scores. CAPS-CA total scores were available for all 23 participants with PTSS, and functional impairment scores were available for 21 of the participants with PTSS.

3. The Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present State and Lifetime version (K-SADS-PL), a semistructured clinical interview designed to identify Axis I disorders [Kaufman et al., 1997]. All 23 participants were interviewed with the K-SADS by a board-certified child psychiatrist (VGC) to assess comorbidity. Attention-deficit/hyperactivity disorder (ADHD) and major depressive disorder (MDD) are conditions that have been associated with altered PFC development in children [Casey et al., 1997; Castellanos et al., 1996; Nolan et al., 2002]. Therefore, coded variables were created that indicated the presence of comorbid ADHD or MDD in participants. These variables were used in post hoc analyses.

NEUROANATOMICAL EVALUATION

Magnetic resonance imaging (MRI) data was collected using a 1.5 Tesla G.E. Signa scanner (General Electric, Milwaukee, WI). A coronal three-dimensional (3D) spoiled gradient echo (SPGR) series was collected for each participant [repetition time (TR) = 35,
echo time (TE) = 6, flip angle 45°, number of excitations = 1, field of view (FOV) = 24, matrix = 256 × 192, 124 contiguous slices, 1.5 mm per slice.

Image analyses were conducted at the Stanford Psychiatry Neuroimaging Laboratory. Raw data was processed using Brainimage 5.x [Reiss, 2005]. Processing consisted of the removal of nonbrain voxels from the data, correction of bias field artifact, and repositioning of the brain using a standard stereotactic atlas template [Andreasen et al., 1996; Kates et al., 1999]. This procedure sets the template according to selected landmarks in the brain rather than warping the brain to fit a given template. Tissue was then segmented into gray matter, white matter, and cerebrospinal fluid (CSF) constituents, subdivided into the cerebral lobes, cerebellum, brain stem, and subcortical regions using an atlas-based parcellation algorithm [Kates et al., 1999; Reiss et al., 1998], and measured in cubic centimeters. Interrater reliabilities for all of the described procedures were ≥ .90, as obtained by the intraclass correlation coefficient.

To isolate the PFC, whole-brain images were uniformly positioned along a horizontal plane defined by landmarks on the anterior and posterior commissures by a single rater (AK) who was blind to diagnostic status. A coronal slice containing the initial appearance of the anterior corpus callosum was selected to mark the posterior boundary of the PFC for each subject. The PFC was divided into dorsal, middle-superior, middle-inferior, and ventral regions proportionally using a plane orthogonal to the interhemispheric fissure and parallel to the plane defined by the anterior and posterior commissures. Dorsal PFC divisions included Brodmann area (BA) 8 and a superior division of BAs 9 and 32. The middle-superior PFC included an inferior component of BA 9, and a superior component of BAs 10, 24, 32, and 46. The middle-inferior included an inferior component of BA 10, and a middle portion of BAs 24, 32, and 46. The ventral PFC included BA 11, an inferior portion of BA 32, and rostral BA 47 (see Fig. 1). Tissue in each region was segmented into gray matter, white matter, and CSF, and measured in cubic centimeters.

STATISTICAL METHODS

Using SPSS 11 software, all data was first evaluated for normality. The distribution of gray matter revealed one prominent outlier: a PTSS participant with significantly smaller volumes than the group means for the middle-superior and middle-inferior PFC regions, and a different control participant had significantly larger volumes for the ventral PFC region. We accounted for regional outliers in our post hoc analysis.

An independent samples t-test revealed that the PTSS group had a significantly smaller mean total cranial gray matter volume ($t = 2.948; P = .005$) and mean total cranial white matter volume ($t = 3.482; P = .001$) than the control group. Hence, total cranial gray matter volume and total cranial white matter volume were used as covariates in the subsequent analyses. Two multivariate analyses of covariance (MANCOVAs) were used to determine whether the PTSS and control subjects exhibited significant volumetric differences in gray and white matter in the dorsal, middle-superior, middle-inferior or ventral PFC, while controlling for the statistical effects of total cranial gray or total cranial white matter volume.

Analyses of specific relationships between regional PFC volume, PTSD symptomatology, and functional impairment in the PTSS group were chosen based on the results of the previous analyses. Hierarchical linear regression analyses were used to determine the relationships between CAPS-CA total scores, functional impairment scores, and gray/white matter volumes in the regions of interest within the PFC. Either dorsal, middle-superior, middle-inferior, or ventral PFC gray/white matter volume were entered as a dependent variable in each equation. Total cranial gray/white matter volume was to be entered in the first block of the regression as a covariate, and both CAPS-CA total scores and functional impairment scores were entered as predictor variables in the second block.
RESULTS

CLINICAL ASSESSMENT

Within the PTSS group, the mean CAPS-CA total score was 44.0 (SD = 23.0). The mean functional impairment score was 5.8 (SD = 2.8).

The K-SADS data indicated that many children in the PTSS group had comorbid psychiatric conditions. Of these 23 participants with PTSS, 13.0% also met criteria for MDD, 4.4% for depressive disorder not otherwise specified, 13.0% for social phobia, 13.0% for ADHD, 8.7% for separation anxiety disorder, and 8.7% for simple phobia.

COMPARISON OF REGIONAL PFC VOLUME BETWEEN GROUPS

The MANCOVA analysis of gray matter volume revealed a significant effect of diagnostic status on the dependent variables [gray matter volume in the four PFC regions; Wilks’s λ = .732, F (4, 41) = 3.758; P = .011], while controlling for the effect of total cranial gray matter volume. Tests of between-subjects effects revealed that the regional gray matter volume of the middle-inferior [F (1, 44) = 12.089; P = .001] and ventral PFC [F (1, 44) = 7.348; P = .010] were significantly larger in the PTSS group. Regional gray matter volume of the dorsal [F (1, 44) = .171; P = .682] and middle-superior [F (1, 44) = 2.542; P = .118] PFC did not differ between groups (see Table 1). The MANCOVA analysis of white matter volume revealed no significant effect of diagnostic status on the dependent variables when controlling for the effect of total cranial white matter volume [Wilks’s λ = .964, F (4, 41) = .383; P = .819].

FUNCTIONAL IMPAIRMENT

Since our previous analyses revealed volumetric differences in PFC gray matter between groups, we focused our subsequent regression analyses exclusively on gray matter volume and its relationship to PTSD symptomatology and functional impairment. The first step of the hierarchical regression with the 21 PTSS participants with valid functional impairment scores revealed that total cranial gray matter was significantly correlated with the volume of gray matter in the dorsal PFC (β = .655; P = .001). This relationship remained significant (β = .553; P = .003) in the second step of the regression after functional impairment scores were entered into the equation. Functional impairment scores significantly predicted dorsal PFC gray matter volume (β = −.377; P = .031). The overall model accounted for approximately 76 % of the variance in dorsal PFC gray matter volume (r² = .756; 8.202; P = .052).

Total cranial gray matter volume was significantly related to middle-superior and middle-inferior PFC gray matter volume in the first and second steps of the regression analysis. However, the volume of the ventral PFC was not predicted by total cranial gray matter volume in any step of the regression. Functional impairment scores did not significantly predict the volume of gray matter in the middle-superior, middle-inferior, or ventral PFC. The relationship between middle-superior PFC gray matter volume and functional impairment scores approached significance (β = −.208; P = .052).

SYMPTOM SEVERITY

The first step of the hierarchical regression with the 23 PTSS participants with CAPS-CA total scores revealed a significant relationship between total cranial gray and dorsal PFC gray matter volume (β = .652; P = .001). This relationship remained significant in the second step of the analysis (β = .650; P = .001), and the relationship between CAPS-CA total scores and dorsal PFC gray matter was not significant (β = .009; P = .957).

Total cranial gray matter volume was significantly related to middle-superior and middle-inferior PFC gray matter volume in the first and second steps of the regression analysis. Again, the volume of the ventral PFC was not predicted by total cranial gray matter volume in any step of the regression. CAPS-CA total scores did not significantly predict the volume of gray matter in the middle-superior, middle-inferior, or ventral PFC.

POST HOC ANALYSES

We reran our MANCOVA study of gray matter volume in the middle-inferior and ventral PFC after excluding the remaining outliers that fell above the mean in each data set (one participant in each set). The main effect of diagnostic status remained significant [Wilks’s λ = .793, F (2, 41) = 5.341; P = .009], as did our previous findings of larger volumes of gray matter in the middle-inferior [F (1, 42) = 8.202; P = .007].

Table 1. Regional PFC gray matter volumes

<table>
<thead>
<tr>
<th>PFC Region</th>
<th>M</th>
<th>SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSS</td>
<td>12.58</td>
<td>4.15</td>
<td>.682</td>
</tr>
<tr>
<td>Control</td>
<td>14.53</td>
<td>4.35</td>
<td></td>
</tr>
<tr>
<td>Middle-superior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSS</td>
<td>28.37</td>
<td>3.61</td>
<td>.118</td>
</tr>
<tr>
<td>Control</td>
<td>29.00</td>
<td>3.20</td>
<td></td>
</tr>
<tr>
<td>Middle-inferior</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSS</td>
<td>32.38</td>
<td>3.42</td>
<td>.001</td>
</tr>
<tr>
<td>Control</td>
<td>31.54</td>
<td>3.36</td>
<td></td>
</tr>
<tr>
<td>Ventral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSS</td>
<td>27.27</td>
<td>7.28</td>
<td>.010</td>
</tr>
<tr>
<td>Control</td>
<td>23.52</td>
<td>7.31</td>
<td></td>
</tr>
</tbody>
</table>

*P values reflect the results of the MANCOVA, which controls for the statistical effects of total cranial gray matter volume.
and ventral PFC \(F(1, 42) = 7.056; P = .011\) in children with PTSS.

As stated, pediatric MDD and ADHD are conditions that have been associated with altered PFC development. We reran our original MANCOVAs of gray matter volume in the middle-inferior and ventral PFC with a coded variable indicating either comorbid ADHD or MDD entered as an additional covariate. The main effect of PTSS status on the dependent variables remained significant when covarying for ADHD \(\lambda = .759, F(4, 40) = 3.179; P = .023\) as did findings of larger gray matter volumes in the middle-inferior \(F(1, 43) = 11.906; P = .001\) and ventral PFC \(F(1, 43) = 4.906; P = .032\) in children with PTSS. Similarly, the main effect of group remained significant when covarying for MDD \(\lambda = .757, F(4, 40) = 3.211; P = .022\) and gray matter volumes in the middle-inferior \(F(1, 43) = 10.290; P = .003\) and ventral PFC \(F(1, 43) = 6.327; P = .016\) remained larger in the PTSS group.

We then ran three post hoc analyses that tested the relationship between functional impairment and dorsal PFC volume in the PTSS group when accounting for comorbid ADHD and MDD, and participants with subthreshold PTSD. In the first two analyses, the relationship between increased functional impairment scores and smaller dorsal PFC volumes remained significant when a coded variable indicating either comorbid ADHD \(\beta = - .379, P = .033\) or MDD \(\beta = - .555, P = .037\) was entered as an additional covariate in the first block of the original regression. In the third analysis, the relationship between functional impairment and dorsal PFC gray matter volume was not significant when the original regression was rerun using only the 10 subjects that had met CAPS-CA criteria for PTSD and had valid functional impairment scores \(\beta = - .501; P = .124\).

**DISCUSSION**

In this investigation we studied regional volume of the PFC in children with a history of trauma and PTSS. Our analyses revealed that children with PTSS exhibited a significantly larger gray matter volume of the middle-inferior and ventral regions of the PFC (BA 11; inferior BAs 10, 24, 32; rostral BA 47) than did healthy control children. These results remained significant following the post hoc exclusion of a PTSS group outlier in each region, and after controlling for the variance associated with comorbid MDD and ADHD, conditions that have been associated with PFC morphology [Casey et al., 1997; Castellanos et al., 1996; Nolan et al., 2002]. White matter volume did not differ between groups. Further analyses revealed a negative correlation between dorsal PFC gray matter volume (BA 8, dorsal BAs 9 and 32) and functional impairment scores after controlling for variance associated with total cranial gray matter volume. Post hoc analyses further controlled for the effects of comorbid ADHD and MDD, and confirmed that the relationship between dorsal PFC volume and functional impairment was not associated with these conditions. No significant relationships were found between CAPS-CA scores and gray matter volume in any of the four PFC regions.

Findings of increased gray matter in the middle-inferior and ventral PFC in the PTSS group suggested that aberrant development of these regions, which together comprise the inferior “half” of the PFC, is associated with the experience of childhood trauma and posttraumatic stress. The nature of this association is difficult to determine, as there were no relationships found between regional PFC gray matter volume and PTSD symptom severity, as measured by the CAPS-CA. The ventral PFC, which includes the orbitofrontal cortex (OFC), is involved in social–emotional functioning [Roberts, 1998] and the learning of positive and negative reinforcements [Damasio, 1998] by way of its reciprocal connections with the amygdala. The middle-inferior PFC included the rostral portion of the AC, which is a region that has also been implicated in both social functioning and fear conditioning [Hamner et al., 1999]. When startled with noise and electric shocks, patients with OFC lesions exhibit enhanced event-related potential (ERP; P3) amplitudes in posterior brain regions, and fail to inhibit their reactivity over time when compared with patients with dorsolateral PFC lesions and normal control subjects [Rule et al., 2002]. Similarly, animal studies show a marked increase in fear reactivity or weakened extinction with lesions to the medial PFC, including the AC [Morgan and Le Doux, 1995]. This supports the notion that regions within the inferior PFC, such as the OFC and AC, are involved in the neural modulation of emotional responses to adverse stimuli, and dysfunction in these regions may result in a potentiated emotional response and a failure to extinguish conditioned fear over time, as is observed in PTSD. As such, aberrant morphology of middle-inferior and ventral PFC gray matter in the PTSS group suggests one biological mechanism by which emotional inhibition may be disordered in children with, or at risk for, PTSD. This interpretation is consistent with those of previous investigators, in particular, based on their observations of functional differences in medial prefrontal and orbitofrontal regions during symptom provocation in adults with PTSD [Bremner et al., 1999; Shin et al., 1997, 2004].

The volume of the ventral region of the PFC was disproportionately large in PTSS children. Despite the fact that the mean total cranial gray matter volume of this group was significantly smaller than that of the control group, the unadjusted mean volume of the ventral PFC gray matter was larger than that of the control group (see Table 1). The results of the regression analyses further revealed that the volume of the ventral PFC was the only PFC region that was not related to total cranial gray matter volume in the PTSS group. Hence, our results suggest atypical neurode-
loration of the ventral PFC in children with PTSS. The abnormal size of the ventral PFC in this group may reflect use-dependent cortical development, resulting from high levels of activity from corticolimbic circuits during the posttrauma period of stress. An alternative hypothesis is that aberrant neurodevelopment in ventral and middle-inferior PFC regions serve as premorbid risk factors for pediatric PTSD.

Our data did not reveal a relationship between regional PFC volume and PTSD symptom severity, as measured by CAPS-CA total scores. Shin and colleagues [2004] found a relationship between medial PFC function and symptom severity during symptom provocation. Therefore, it is possible that measures of PFC function, rather than structure, would elucidate a relationship between PFC regions and symptom severity in our sample.

Among our children with PTSS, those with the most reduced dorsal PFC gray matter volume received higher functional impairment scores on the CAPS-CA (see Fig. 2). As previously stated, the CAPS-CA measure of functional impairment reflects children’s reported difficulties with current school and social functioning, subjective distress, and tendency toward regressive behaviors. In a previous investigation of 59 children with PTSD symptoms (which included the present sample), our group found that participants with subthreshold PTSD symptoms reported as much functional impairment as did subjects with a full PTSD diagnosis [Carrion et al., 2002]. Therefore, PTSD symptoms and functional impairment are not linearly related, and they may be influenced by different biological processes.

Difficulties with school and social functioning, distress, and regressive behavior are likely to reflect disturbed emotional states involving anxiety and negative affect. Our data suggest that processes supported by the dorsal PFC are involved in the occurrence of such emotional states, despite our understanding of the role of the ventral PFC in emotional regulation. Since the dorsal PFC is primarily involved in information processing and executive function, our results indicate that children’s adjustment following traumatization may be related to differences in cognitive function, reflecting a “top-down” process. Liotti and Mayberg (2001) proposed a model of emotional regulation in which cortical areas involved in perception, evaluation, attention and memory for emotional stimuli, such as the dorsal PFC (BA 9 specifically), would inhibit emotional responses via reciprocal connections with the ventral PFC. Furthermore, Ochsner and colleagues [2002] found that cognitively reappraising an adverse event in unemotional terms was associated with dorsal and lateral PFC regional cerebral blood flow (rCBF) increases, and rCBF decreases in the OFC and amygdala, indicating that the dorsal PFC is involved in actively reducing anxiety. Thus, children with a less developed dorsal PFC may be predisposed to experiencing functionally impairing emotional states, and may be less likely to engage in cognitive coping strategies that promote adjustment, such as reappraisal.

Children with PTSD have demonstrated performance deficits on cognitive tasks involving executive function and attention [Beers and De Bellis, 2002], as well as working memory [Moradi et al., 1999], which are processes supported by the dorsal PFC. Recently, Clark and colleagues [2003] reported that the dorsal PFC (BAs 8 and 9) was less active in adults with PTSD than in control subjects during working memory tasks. This supports the notion that in PTSD, dysfunction of the dorsal PFC and a diminished cognitive performance coexist as associated features of the disorder.

As PTSD symptom severity and functional impairment do not exhibit a linear relationship, it is believed that functional impairment scores can provide collateral and clinically important information about children’s PTSD that is distinct from their PTSD symptoms. We therefore recommend that future studies continue to utilize the functional impairment measure on the CAPS-CA.

Our study was not without limitations. The small sample size was the primary limitation to this study. Detailed demographic information, such as parent income data, was not available for our archived sample of control children and posed a limitation on our ability to compare groups. Furthermore, our sample included participants that varied according to age and developmental level (middle childhood to adolescence), as well as trauma type (i.e., sexual abuse vs. witnessing violence) and trauma exposure (single or multiple encounters), which prevents the generalization of our findings. Last, our participants varied according to symptom severity, with only 12 participants meeting the DSM-IV diagnostic criteria for PTSD. In our post hoc analysis, the relationship between functional impairment and dorsal PFC gray matter volume was
nonsignificant among the 10 subjects with a full PTSD diagnosis and functional impairment. However, the standardized $\beta$ in the post hoc analysis was actually larger than in the whole group analysis, and it is likely that the reduced sample size did not yield adequate power to detect a significant relationship.

CONCLUSION

Neurobiological investigations of children with PTSS inform our understanding of the impact of trauma exposure and early life stress on child development. Our findings suggest aberrant PFC morphology in children with a history of trauma and PTSS. These volumetric differences do not appear to relate directly to PTSD symptom severity. Further investigation will be required to understand the nature of these differences and their relationship to the experience of trauma, posttraumatic stress, and functional impairment.

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REFERENCES


