Biologic Findings of Post-traumatic Stress Disorder and Child Maltreatment

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Current Psychiatry Reports 2003, **5:**108–117
Current Science Inc. ISSN 1523-3812

Child maltreatment is a serious problem in US society, affecting approximately three million children. Children and adolescents exposed to child abuse and neglect experience high rates of post-traumatic stress disorder (PTSD). In addition, they are at risk for comorbid mental illness. Biologic stress systems affected in trauma and in PTSD are complex. Findings in cognitive testing, neuroimaging, and affected pathways shed light on the consequences of child maltreatment. What is known about treatment and outcomes for children with history of maltreatment and maltreatment-related PTSD indicates the need for prevention, intervention, and treatment of children exposed to abuse and neglect. The following is a brief review of the most recent neurobiologic findings in child maltreatment and related PTSD.

Introduction and Background

Child maltreatment is a serious problem with consequences for the individual and society. Child maltreatment may include neglect, physical abuse, sexual abuse, and emotional or psychologic abuse. Children who are victims of maltreatment may experience chronic and multiple forms of abuse [1–4]. Child maltreatment is often a precursor to later mental illness [5]. In the US, an estimated three million children were reported for investigation to Child Protective Services in 1997 [6]. Of these cases, approximately one million were substantiated (a rate of 15 per 1000). It should be noted that less than 1% of the more than three million children referred were determined to be "false reports" [6]. Neglect is the most prevalent form of child maltreatment, followed in order by physical abuse, sexual abuse, and emotional abuse [6,7].

Maltreated children experience trauma at the hands of attachment figures whose role is to provide care and support. The interpersonal relationship contributes to the meaning and later sequelae of the trauma. Maltreated children are born with the ability to form attachments, but this may be disrupted by the experience of trauma [8••]. It has been well established in the literature that maltreated children are at risk to develop post-traumatic stress disorder (PTSD) (for review, *see* [8••]). Children exposed to traumas, such as maltreatment, are more likely to develop PTSD symptoms than adults [9].

Post-traumatic stress disorder is a disabling, chronic mental illness [10]. As described in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision*, criterion A of PTSD is exposure to an extreme traumatic stressor in which the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others, and responded with intense fear, helplessness, or horror (or, in children, disorganized or agitated behaviors) [11]. For diagnosis of PTSD, three clusters of categoric symptoms are present for more than 1 month after the experience of the traumatic event(s). These clusters include the following: 1) intrusive re-experiencing of the trauma(s) (criterion B); 2) persistent avoidance of stimuli associated with the trauma(s) (criterion C); and 3) persistent symptoms of increased physiologic arousal (criterion D) (Table 1).

Post-traumatic stress disorder is a common sequelae of child maltreatment, and is most often diagnosed immediately after disclosure [12,13]. Although the diagnostic picture of PTSD in children may be similar to adults [14], there are exceptions. In children younger than 4 years of age, identification of symptoms requires assessment of behavior rather than reliance on verbal reports [15,16]. This is necessary when considering the effect of the trauma on development and on the ability of the child to form a verbal narrative. The child may truly be unable to find the words to explain the trauma, because there is evidence of deactivation of Broca's area in response to traumatic stimuli [17]. Another important difference when considering a diagnosis of PTSD in children is the awareness that clinical and biologic findings in children who meet fewer than three clusters of symptoms may be equivalent [18]. For this reason, in addition to the frequently multiple and chronic types of maltreatment experienced by children, it may be reasonable to consider maltreated children as patients with complex PTSD or "disorders of extreme stress not otherwise specified" (for review, *see* [19]).

Table 1. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for post-traumatic stress disorder

Exposure and intense fear in response to a traumatic event that involved actual or threatened injury to self or others
Intrusive re-experiencing of the trauma
Persistent avoidance of traumatic stimuli and numbing of responsiveness
Persistent symptoms of increased physiologic arousal
Duration of symptoms greater than 1 month
Clinically significant distress
Many traumatized children have post-traumatic stress disorder or mood symptoms

(*Adapted from* American Psychiatric Press [11].)

Child Maltreatment and Risk for Comorbid Illness

Child and adolescent victims of maltreatment experience high rates of PTSD symptoms, depression, suicidal thoughts and behaviors, aggression, antisocial behaviors, and cognitive deficits (for review, *see* [8••]). Understanding the relationship between maltreatment and comorbid psychiatric illness may inform researchers of the psychobiology of these disorders. Later risk for development of comorbid mental health disorders is related to genetic and environmental factors. However, there is evidence that a history of trauma exposure in early childhood is an independent risk factor for later mental health and substance use disorders. For example, a study of twins discordant for child abuse exposure demonstrated that even after controlling for family background and parental psychopathology, the twin exposed to abuse suffered from an increased risk for adult psychopathology [20]. This was replicated in a recent study of an Australian volunteer twin panel. Twins exposed to childhood sexual abuse in pairs discordant for history of child sexual abuse had significantly greater risk for major depression, suicide attempt, conduct disorder, alcohol dependence, social anxiety, nicotine dependence, repeated sexual violence, and divorce [21].

It has been well established that early stress, such as that of child maltreatment, increases rates of major depressive disorder in children and adults (for review, *see* [22]). Furthermore, maltreated children with concurrent depression may experience higher rates of intrusive PTSD symptoms [23]. In a study of 3015 girls in grades five through 12, respondents to a survey who reported physical and sexual abuse or sexual abuse alone had higher rates of depressive symptoms [24]. A recent study showed that familial transmission of suicide attempt to offspring was more likely if the offspring or proband had a history of sexual abuse [25].

A history of childhood maltreatment may play a causal role in later alcohol and substance use problems (for review, *see* [26]). A study of 582 women with childhood histories of substantiated cases of childhood abuse and neglect suggested that a history of victimization in childhood was a cause of development of alcohol use disorders in women [27]. Patients recruited from an inpatient detoxification unit showed greater consequences of their use if they had a history of physical and sexual abuse [28]. Childhood abuse was more significantly associated with poor outcome of substance abuse in men. For women, the relationship of maltreatment to consequences of substance abuse was similar regardless of age of onset of the victimization. Finally, in a sample of 1478 women partners of male intravenous drug users, history of childhood sexual abuse correlated significantly with crack cocaine use (Fig. 1) [29].

The association between childhood maltreatment and personality disorder (PD) has been documented in a prospective study of adults maltreated as children [30]. In a multisite study of schizotypal, borderline, avoidant, and obsessive compulsive PD, patients with diagnosis of borderline PD reported the highest rates of trauma, particularly childhood sexual trauma, the highest rates of PTSD, and the earliest age of trauma exposure [31]. There is evidence that the severity of childhood sexual abuse is related to the development and severity of borderline PD [32].

Oppositional and attentional disorders have also been associated with a history of child maltreatment. In comparison with age and ethnicity matched controls, girls with attention deficit hyperactivity disorder (ADHD) combined type (n=93) were characterized by a history of documented abuse [33]. A study of consecutive child psychiatric outpatient admissions suggested that oppositional defiant disorder and ADHD diagnoses were associated with a history of physical or sexual abuse [34]. In addition, PTSD symptoms were more severe with coexistent ADHD and maltreatment. Thus, it is important to consider the relationship between cognitive and attentional factors associated with PTSD symptoms. This is discussed in greater detail herewith.

Biologic Stress Systems

Stress related to a traumatic exposure affects the neurotransmitter systems, the neuroendocrine system, and the immune system. Necessarily, these systems are interconnected to modulate response to routine stimuli, as well as acute and chronic stressors. The sympathetic nervous

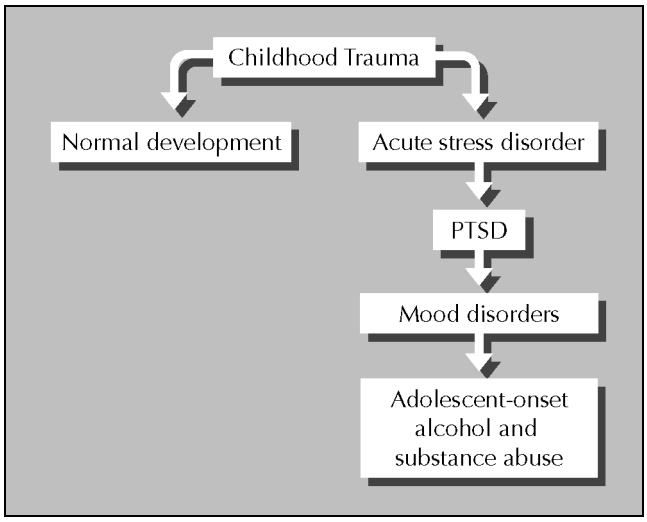

Figure 1. Algorithm of childhood trauma. PTSD—post-traumatic stress disorder.

system or catecholamine system, the limbic-hypothalamic-pituitary-adrenal axis, and the serotonin system are the three major neurobiologic stress response systems implicated in mood, anxiety, and impulse control disorders (for review, *see* [35,36]). Arousal, stress response, emotional regulation, and development are dependent on these systems.

Trauma is perceived through all five senses. This information is posited in the corresponding cortical areas via the dorsal thalamus. Olfactory input has direct connections to the amygdala and entorhinal cortex. The primary sensory regions also project to the amygdala, an area of emotional regulation containing a central nucleus with pathways for anxiety- and fear-related behaviors [37,38]. Trauma is perceived as intense fear. Input from the visceral organs is received by the locus coeruleus, which contains the majority of noradrenergic neurons. Information from the locus coeruleus is relayed to the amygdala, entorhinal cortex, orbitofrontal cortex, hippocampus, and cingulate. Traumatic triggers (reminders of the trauma) may cause intrusive memories and PTSD symptoms of re-experiencing. The re-experienced fear engages the same pathways and traumatic anxiety ensues. Stimulation of locus coeruleus noradrenergic neurons increases norepinephrine in the following areas related to stress response, memory, and emotion: the locus coeruleus, hypothalamus, hippocampus, amygdala, and cerebral cortex, with simultaneous activation of the paragigantocellularis. The paragigantocellularis is an ancient part of the brain. It immediately stimulates the sympathetic nervous system, causing the "fight or flight" reaction, which is important for survival (for review, *see* [39]).

Thus, intense fear or anxiety activates the amygdala via the locus coeruleus, which, in turn, stimulates the hypothalamus, and corticotrophin-releasing hormone (CRH), also called corticotrophin-releasing factor, is released. Corticotrophin-releasing hormone causes the pituitary to secrete adrenocorticotropin, but CRH also stimulates cortical regions. In this manner, CRH functions as a hormone and a neurotransmitter [40]. Adrenocorticotropin results in release of cortisol from the adrenal gland, with feedback to the sympathetic nervous system, causing further activation (for review, *see* [41]). This results in tachycardia, hypertension, increased metabolic rate, hypervigilance, and increased levels of epinephrine, norepinephrine, and dopamine. Catecholamines contribute to dilation of the pupils, diaphoresis, renal inhibition, and decrease in peripheral blood flow. These symptoms, associated with intense fear, are the core symptoms of PTSD-related anxiety (Fig. 2).

The Hypothalamic-Pituitary-Adrenal Axis in Pediatric Post-traumatic Stress Disorder

Studies of maltreated children show evidence of elevation of CRH. These include studies of maltreated children with comorbid depression, which have shown dysregulation of the hypothalamic-pituitary-adrenal axis [42,43]. This was also true in girls with a history of sexual abuse and symptoms of dysthymia [44]. Children with PTSD as a result of maltreatment show evidence of increased catecholamine and cortisol activity. Neglected boys with comorbid depression had greater 24-hour urinary norepinephrine concentrations compared with control individuals [45]. Dysthymic girls with a history of sexual abuse showed greater 24-hour urinary catecholamine and catecholamine metabolite concentrations than non-maltreated subjects [46]. Medication-naïve children with maltreatment-related PTSD had significantly greater 24-hour urine concentrations of dopamine and norepinephrine compared with non-maltreated children with overanxious disorder and control individuals [47••]. These PTSD subjects also had higher concentrations of 24-hour urinary free cortisol compared with control individuals [47••]. Elevated morning cortisol was found in girls with a history of sexual abuse [48]. Carrion *et al.* [49] measured higher levels of salivary cortisol throughout the day in children with maltreatment-related PTSD symptoms. In this study, girls in the PTSD group had significantly higher levels of cortisol compared with boys with PTSD.

All of these studies suggest that traumatized children with or without PTSD manifest dysregulation of biologic stress response systems (for review, *see* [8••]). Similar dysregulation have also been shown in adults who suffer from PTSD. Adult combat veterans with PTSD have elevated levels of central CRH [50,51]. Additionally, adults with PTSD have elevated 24-hour urinary excretion of catecholamines, but lower 24-hour urinary-free cortisol than control individuals (for review, see [52]). Depressed women who were abused as children showed hypersensitivity of the limbic-hypothalamic-pituitary-adrenal axis and hyperarousal in response social stressors [53].

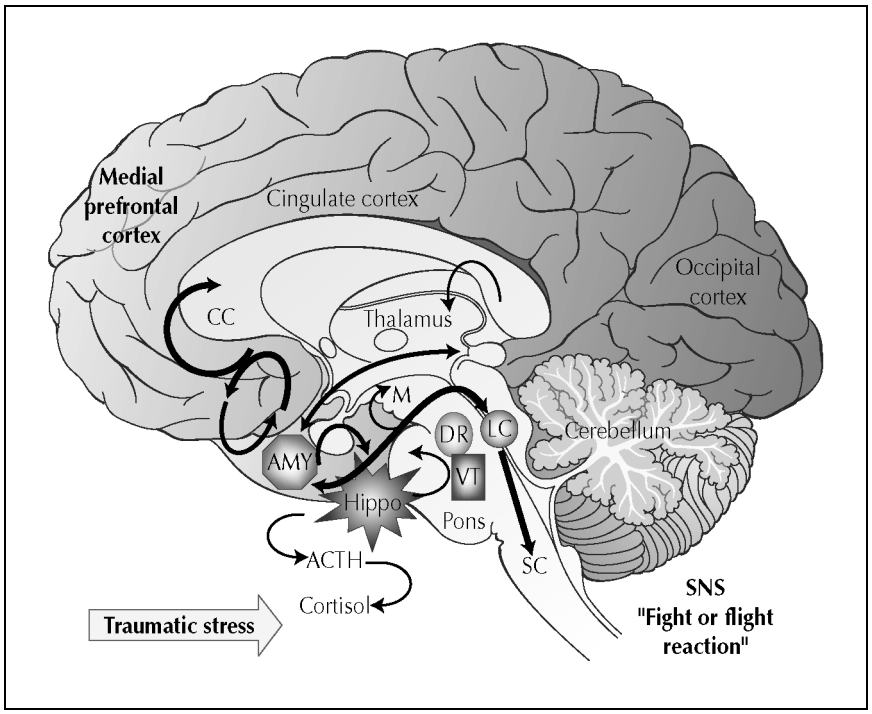

Figure 2. Biologic stress systems. ACTH—adrenocorticotropin; AMY—amygdala; CC—cerebral cortex; DR—dorsal raphe; Hippo–hippocampus; LC—locus coeruleus; M—medulla; SC—locus subcoeruleus; SNS—sympathetic nervous system; VT—ventral tegmental.

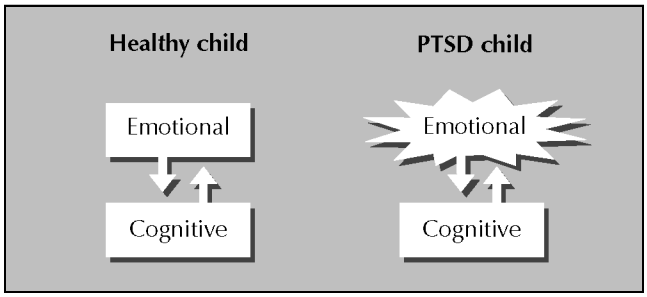

Figure 3. Cognitive findings. PTSD—post-traumatic stress disorder.

Cognitive Findings

Cognitive function measured by neuropsychologic testing has not been frequently reported in pediatric PTSD or in abused and neglected children. In a study of 14 child outpatients with PTSD secondary to maltreatment, children with PTSD showed more deficits in attention and abstract reasoning/executive function than sociodemographically matched control individuals [54]. Neuropsychologic testing has also suggested deficits in everyday memory in children and adolescents with PTSD [55]. Multiple reports of lower intelligence quotient (IQ) and academic performance exist (reviewed in [55]). In a magnetic resonance imaging (MRI) study by this author, the established relationship between IQ and intracranial volume was seen; however, verbal, performance and full-scale IQ negatively correlated with duration of child abuse that led to PTSD in maltreated children compared with control individuals (Fig. 3) [56••].

Cognitive function is dependent on the prefrontal cortex. This area is active in executive tasks, such as planning [57], decision making, working memory, and attention [58], and responds in dangerous and unknown circumstances [59]. The medial prefrontal cortex may inhibit limbic system activation in fear, with influence on the amygdala [38]. Elevated catecholamines, including norepinephrine and dopamine, in experiences of severe stress can interfere with this programmed inhibition, which allows unchecked activation of the limbic pathways [60]. Interruption of prefrontal inhibition of the amygdala may cause characteristic PTSD symptoms. The anterior cingulate cortex, a region of the medial prefrontal cortex, interrupts conditioned fear responses, and has been implicated in the pathophysiology of PTSD (for review, *see* [61]). Intrusive memories with resultant anxiety and disrupted concentration that is characteristic of PTSD may indicate loss of anterior cingulate function.

Positron emission tomography studies provide further evidence for medial prefrontal and anterior cingulate disruption in adult PTSD. Positron emission tomography investigations of Vietnam War combat veterans with PTSD showed a lower level of blood flow to the anterior cingulate during traumatic reminder exposure to combat imagery compared with those without PTSD [62]. Similarly, women with PTSD as a result of sexual abuse in childhood showed less anterior cingulate blood flow during traumatic reminder imagery [63] and during recalled memories of sexual abuse [64] than that observed in women with similar history who did not have PTSD. In the studies, PTSD subjects had activation of the amygdala and not the medial prefrontal cortex, whereas those without PTSD showed the reverse. Clearly, such invasive studies cannot be done in children. However, MRI has allowed a noninvasive, safe method to observe and measure brain structure and development in children.

Magnetic resonance imaging studies of traumatized children are discussed herewith.

Neuroimaging Findings

Magnetic resonance imaging has allowed comparison of healthy children and those exposed to trauma, including abuse and neglect. This is a relatively new area of study, and a handful of studies have been published with results that indicate adverse brain development as a consequence of abuse and neglect resulting in PTSD or subsyndromal symptoms of PTSD. In a study of 44 maltreated children and adolescents with PTSD and 61 matched control individuals, findings included intracranial volume decrease by 7% and total brain volume decrease by 8% in PTSD subjects compared with control individuals. In addition, PTSD subjects showed decreased total mid-sagittal area of the corpus callosum and enlarged right, left, and total lateral ventricles in PTSD-diagnosed subjects compared with control individuals [56••]. Decreased subregions of the corpus callosum were previously reported in physically abused and neglected children who were not evaluated for PTSD compared with psychiatrically ill non-maltreated control individuals [65]. Boys with PTSD had smaller measurements of the corpus callosum, and a trend for smaller total brain volume compared with girls with PTSD [56••]. Boys may be more vulnerable to the effects of severe stress on brain structures than girls. Nonetheless, adverse effects were found regardless of gender. In this study, earlier onset of abuse and longer duration of abuse correlated with smaller intracranial volume. These findings not only suggest disrupted brain development in patients with maltreatment-related PTSD, but also indicate that adverse effects may be greater with exposure to trauma in early childhood. The correlation of lower intracranial volume with longer duration of abuse suggests that recurrent and chronic abuse may have a collective, harmful effect on brain development (Fig. 4).

Another study by Carrion *et al.* [66] substantiated many of these findings. Children with PTSD or subthreshold PTSD symptoms demonstrated smaller total brain and cerebral volumes when compared with healthy age- and gender-matched archival control individuals. In addition, attenuation of frontal lobe asymmetry in children with maltreatment-related PTSD was also observed in comparison with control individuals [66]. These studies did not match for IQ or for low socioeconomic status, which may also influence brain volume. Another study of 28 psychotropic-naïve children and adolescents with maltreatment-related PTSD showed smaller intracranial, cerebral and prefrontal cortex, prefrontal cortical white matter, and right temporal lobe volumes in comparison with 66 sociodemographically matched healthy control individuals [67]. Compared with control individuals, subjects with PTSD had decreased areas of the corpus callosum and its subregions (2,4,5, 6, and 7), and larger

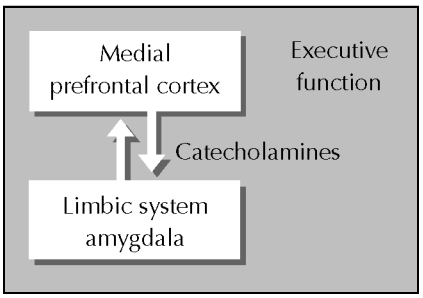

Figure 4. Neuroimaging findings.

frontal lobe cerebrospinal fluid volumes than control individuals after adjustment for cerebral volume. Again, total brain volume positively correlated with age of onset of trauma causing PTSD (smaller volumes with earlier onset of trauma) and negatively correlated with duration of abuse (longer duration of abuse with smaller volumes). Another significant gender by group effect was found; maltreated boys with PTSD had larger ventricular volumes than maltreated girls with PTSD.

An interesting common feature of these studies is that, unlike findings in adult PTSD, in all three cross-sectional studies and one longitudinal pediatric PTSD study [68], no hippocampal differences were seen. In a study of children and adolescents with alcohol use disorders, a subanalysis of those subjects with and without PTSD who misused alcohol showed decreased hippocampal volume in the group with PTSD [69]. Concerning and marked global adverse effects are observed in children with PTSD symptoms secondary to abuse and neglect. Findings of decreased intracranial volumes and cerebral volumes in maltreated children with PTSD are worthy of further exploration. These findings may implicate neuronal loss, disruption of neuronal growth, or interference with neuronal replacement and migration. Abnormalities of brain development may play a causal role in cognitive and developmental deficits, as well as pervasive emotional and behavioral problems, which many maltreated children with PTSD symptoms express. These results provide indirect evidence that PTSD in maltreated children may be regarded as a complex environmentally induced developmental disorder [8••]. An important task for future research in developmental traumatology is the pursuit of longitudinal studies that may begin to identify the pathway from trauma exposure to resilience, as well as to abnormalities of brain structure, psychopathology, and cognitive deficits.

N-acetyl-aspartate

N-acetyl-aspartate (NAA) is considered to be a marker of neuronal health or integrity. Low levels of NAA are associated with neuronal damage or loss (for review, *see* [70]). This is seen in stroke and has been measured in schizophrenia. N-acetyl-aspartate is measured via magnetic resonance spectroscopy. This is a measure that can be used safely in children to assess neurochemistry of the developing brain. N-acetyl-aspartate is measured via the N-acetyl

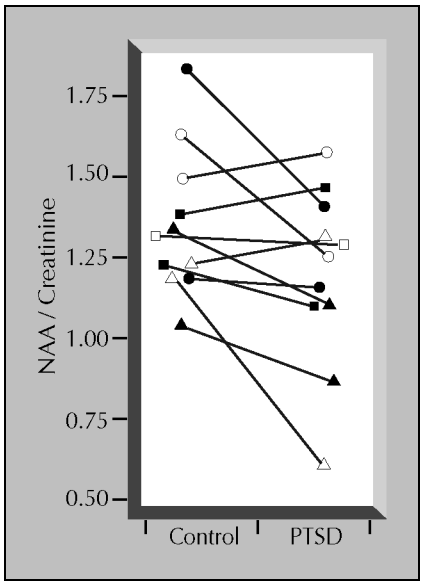

Figure 5. Anterior cingulate N-acetyl-aspartate (NAA) in maltreated children with post-traumatic stress disorder (PTSD) and control individuals (6 boys/5 girls, matched pairs, age 4 to 15 years; paired T test=2.24, degree of freedom=10; $P<0.05$).

signal in the proton (1H) spectrum. A study of 11 children with maltreatment-related PTSD suggested that maltreated children and adolescents with PTSD have lower NAA/creatine ratios compared with control individuals matched for age, race, socioeconomic status, and IQ [71]. These findings suggested loss of neuronal integrity in the anterior cingulate region of the medial prefrontal cortex. There was no difference observed in boys versus girls. Adult neuroimaging studies support this finding in that they provide evidence for dysfunction of the medial prefrontal cortex and anterior cingulate gyrus in adult PTSD [72,73]. These findings may indicate that the anterior cingulate is affected in adult and pediatric PTSD. This may be important to the pathology of this disorder, because the anterior cingulate is involved in the extinction of responses to conditioned fear (Fig. 5).

Serotonin, Post-traumatic Stress Disorder, and Major Depression

The serotonin system is a stress response system that may activate anxiogenic and anxiolytic pathways in addition to its relationship to major depression. Serotonin is a component of multisystem neuronal communication [74]. Serotonergic inputs from the brainstem raphe nuclei communicate with the prefrontal cortex and the central and basolateral nuclei of the amygdala. The serotonergic system is innervated by CRH neurons in the midline raphe and overlap of the CRH and serotonin processes in the dorsal-lateral subnucleus. There is also an association of the serotonergic neurons with the cerebral microvasculature and the ependymal lining [40]. These findings are consistent with animal studies suggesting that serotonergic neurons respond to chronic stress [75,76]. Serotonin has been implicated in compulsive behaviors and emotional regulation. Low serotonin function is associated with impulsive aggression, self-injurious behavior (SIB), and suicidal behavior (for review, *see* [77]).

Post-traumatic stress disorder in adults is associated with low levels of serotonin. For example, studies of combat veterans with PTSD show low paroxetine binding in platelets [78] and in platelet-poor plasma compared with control individuals [79]. Paroxetine binding is considered a measure of serotonin uptake. In postmortem studies of suicide victims, there is evidence of decreased serotonin 1A receptors in the pontine raphe [80]. Interaction with CRH and with the noradrenergic system [81] suggests that dysregulation of serotonin increases the risk for comorbid major depression in PTSD. This is supported by the finding that trauma-exposed individuals with diagnosis of PTSD have a significantly higher risk for onset of major depressive disorder than trauma exposed individuals without PTSD [82]. Furthermore, abnormalities of the serotonergic and noradrenergic system may be related to SIB and symptoms of borderline PD that are often comorbid with PTSD and related to prolonged victimization [77]. Post-traumatic stress disorder secondary to trauma exposure may contribute to abnormalities of serotonin regulation. In this manner, PTSD may contribute to major depression, impulsive aggression, and suicidal behavior via common pathways as genetic vulnerability to dysregulation of CRH and serotonin.

The Neurobiology of Anti-anxiety and Antidepressant Medications in Post-traumatic Stress Disorder

The goal of medication management of child and adolescent PTSD is down-regulation of biologic stress systems, so that the frontal cortex can effectively inhibit traumatic reminder anxiety and catecholamine response. In this manner, children may be better able to engage in learning, therapy, and routine activities. Anti-anxiety and antidepressive medications, which dampen the activity of biologic stress systems in combination with psychotherapy and social interventions, may contribute to the clinical improvement of traumatized children. There is evidence of the efficacy of the serotonin reuptake inhibitors (SSRIs), sertraline [83] and fluoxetine [84] in adult PTSD. Fluoxetine treatment decreases symptoms of PTSD and is also associated with decreasing central CRH levels in depressed adults [85]. Although there are no randomized studies of SSRI treatment in children with maltreatment related PTSD, *Practice Parameters for the Treatment of Pediatric PTSD*, published by the American Academy of Child and Adolescent Psychiatry, state that SSRIs are the first-line medication treatment for child and adolescent PTSD, particularly in the setting of PTSD comorbid with major depression [86••]. There is also evidence that clonidine effects symptoms of PTSD, such as those secondary to maltreatment, by decreasing the activity of the noradrenergic locus coeruleus [87]. In a case report of a 7-year-old boy, clonidine treatment was associated with remission of PTSD symptoms and an increased anterior cingulate NAA/creatine ratio from baseline [88].

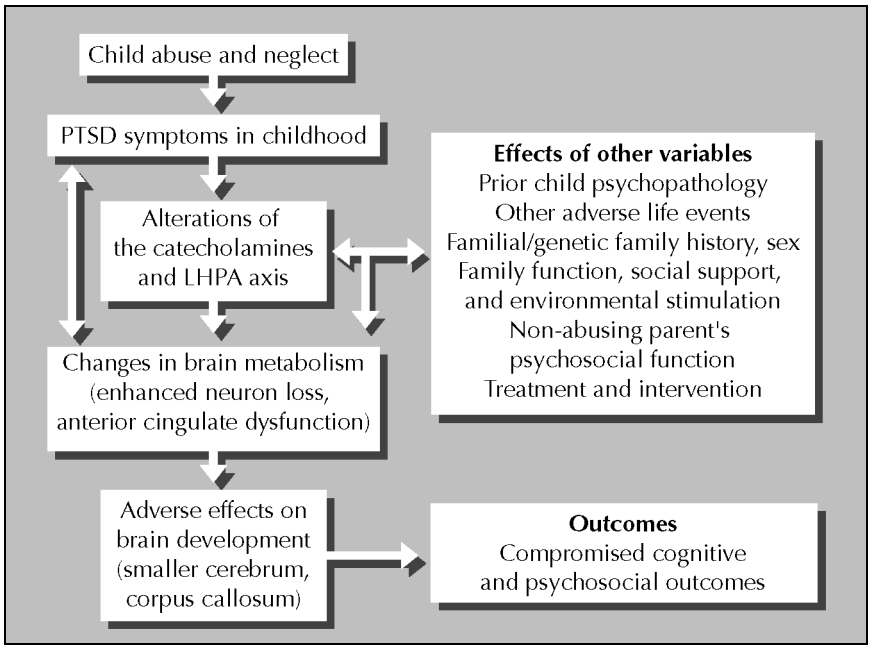

Figure 6. Algorithm for the neurobiology of hope. LHPA—limbic-hypothalamic-pituitary-adrenal; PTSD—post-traumatic stress disorder.

The Neurobiology of Hope

Not all children exposed to childhood maltreatment and other forms of trauma go on to develop PTSD. In the children who develop the sequelae of child abuse and maltreatment, there is evidence that adverse effects may be reversible. It may be possible to repair or regrow damaged and lost neurons. A capacity for primate neurogenesis in the hippocampus and frontal cortex has been observed [89,90]. There is evidence that environmental stress and resultant adrenal steroids inhibit this neurogenesis [91,92]. Effective treatment of maltreatment-related PTSD and depression is an important area for future investigations regarding therapeutic reversibility. Early psychosocial and treatment interventions may theoretically prevent and improve adverse effects. Support in times of stress may partially normalize biologic stress systems responses. For example, quality of childcare is associated with a buffering of hypothalamic-pituitary-adrenal axis to stress [93]. Placement in a preventative intervention setting with consistent response and training with regard to the needs of abused and neglected children may improve behavior and neuroendocrine activity [94]. When removed from extremely neglectful and abusive environments, maltreated children with severe psychiatric symptoms and marked delays were capable of accelerated rates of improvement, including remission of severe psychopathology and normalization of cognitive function [95–97].

Cognitive-behavioral therapy has shown significant promise in the treatment of traumatized children. In sexually abused children, treatment with cognitive-behavioral therapy models directed at the child and the non-offending parent have provided greater symptom remission than non-directive therapy (for review see [98••]). In theory, medications may improve global brain functioning and alleviate PTSD and depressive symptoms through removing the stress mediated inhibition on the rate of cortical neurogenesis. This may lead to therapeutic reversibility of the adverse brain developmental effects of maltreatment. These treatments offer hope for improved function in children who suffer the sequelae of child abuse and neglect. Finally, it should be noted that the biologic effects of PTSD and child maltreatment are some of the few preventable contributors to child psychopathology, cognitive impairment, and developmental disorder. The professional community should be tireless in their pursuit of safe and healthy environments for children (Fig. 6).

Conclusions and Future Studies

The need for further studies of the causes, psychobiologic consequences, sequelae, prognosis, and treatment of child maltreatment and related PTSD symptoms cannot be overstated. Clinicians will be best informed by longitudinal studies that further explore the biologic findings outlined herewith. Treatments with cognitive-behavioral therapy models appropriate for child victims of maltreatment have been effective. Data regarding the efficacy and mechanism of effect of medications in these children are needed. Studies have traditionally looked at cross-sectional data about children or outcome measures in adult survivors. In the future, researchers will be able to do more work in the area of treatment outcomes with child patients.

Acknowledgments

This work was supported by National Institute of Mental Health grant 5 K08 MHO1324-02 (Principal Investigator: Michael D. De Bellis, MD) and a 1998 National Alliance

for Research on Schizophrenia and Depression Young Investigators Award (Principal Investigator: Michael D. De Bellis, MD).

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- •• Of major importance

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