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# Clinical Perspectives on Neurobiological Effects of Psychological Trauma[1]

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Physical trauma to the brain has always been known to affect brain functions and subsequent neurobiological development. Research primarily since the early 1990s has shown that psychological trauma can have detrimental effects on brain function that are not only lasting but that may alter patterns of subsequent neurodevelopment, particularly in children although developmental effects may be seen in adults as well. Childhood trauma produces a diverse range of symptoms and defining the brain's response to trauma and the factors that mediate the body's stress response systems is at the forefront of scientific investigation. This paper reviews the current evidence relating psychological trauma to anatomical and functional changes in the brain and discusses the need for accurate diagnosis and treatment to minimize such effects and to recognize their existence in developing treatment programs.

**KEY WORDS:** trauma; neurobiology; PTSD.

In 2001, approximately 5 million children in the United States were referred to state agencies for maltreatment (i.e. neglect, medical neglect, sexual abuse, physical abuse, and psychological maltreatment) (U.S. Department of Health & Human Services, 2003). Approximately 67% of these children were subsequently screened in to Child Protective Services and approximately 33% were screened out or referred to other agencies. Subsequent investigations found over 28% of these children were maltreated or at risk for maltreatment. According to the National Clearing House on Child Abuse and Neglect (2003), more than half of these children (57%) suffered neglect, 19% were physically abused, 10% sexually abused, 7% psychologically maltreated, and 2% medically neglected. Since most neglected and abused children never are reported to state or local authorities, these government statistics are considered vast underestimates and do not denote actual rates of child neglect and abuse (Hopper, 2002). Indeed, estimation rates of exposure to extreme emotional or physical trauma run as high as 3–5 million children each year (Perry, 1999; Perry and Azad, 1999; Schwarz and Perry, 1994). Depending on the nature, pattern, and number of traumatic events, 27–100% of these children subsequently develop physical, behavioral, social, psychological, cognitive, and emotional problems (Schwarz and Perry, 1994).

Emotional or physical trauma is believed to have distinct neurobiological sequelae. Understanding the developmental issues involved in the response, process, and adaptation to traumatic events is vital to understanding the neurobiological effects of childhood trauma. Children are particularly susceptible to developmental disorders related to trauma, however, the difficulty experienced by young children reporting trauma and the differential manifestation of symptoms across development makes the study of trauma's effects on children particularly complex. Stress and trauma are acknowledged as significant in precipitating psychiatric disorders, anxiety, and mood disorders (Yehuda, 2000) and the accommodation of childhood trauma often leads to psychopathology which can include depression, dissociation, anxiety, conduct disorder (Miller, 1995), and even attention deficit hyperactivity disorder (ADHD) (Donnelly et al., 1999; Perry, 1994; Weinstein et al., 2000). According to Perry (1994), childhood PTSD can become a developmental disorder. Many of the developmental problems (motor delays, language,

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impulsivity, dysphoria, disorganized attachment, hyperactivity, and attention) described in neglected children are caused by abnormalities in the brain (Perry, 2002). Understanding the sequelae of the neurobiological effects of childhood psychological trauma is vital to early detection, clinical phenomenology, and treatment. There may be contributions to understanding normal and abnormal neural development as well.

It was only within the decade of the 1990s that the evolution and rapid discoveries of the neurosciences have enabled us to address questions that were not even imagined a century before (Frank and Kupfer, 2000). Among these are the physical effects of psychological trauma on the developing brain. Childhood trauma produces a wide and diverse range of symptoms and defining the brain's response to trauma and the factors that mediate the body's stress response systems is at the forefront of scientific investigation.

## BRAIN DEVELOPMENT

The development of the human brain is dependent upon a complex interplay between environment and genetic potential. Cognitive, social, emotional, and physiological functioning are all mediated by the functional capacity of our neural systems (Perry, 2002). Although physical brain injury may well produce emotional disturbances and abnormalities in the amygdala, hippocampal, and temporal lobe; similar effects may also result from emotional trauma and neglect. Research has established that extreme stress and trauma are associated with harmful effects on the developing brain. Researchers have discovered high levels of glucocorticoids resulting from stress are harmful to the hippocampal area of the brain (Bremner and Narayan, 1998). According to Joseph (1996) "emotional trauma is not just a psychological event but a physiological experience" (p. 571). Psychological trauma and neglect may result in neural degeneration, neurochemical abnormalities, cerebral dysfunction, and neuroanatomical disconnection. More importantly, repeated and severe episodes of trauma and neglect can alter the functional and structural integrity of the brain. The immaturity of the limbic system and the neocortex make children more susceptible than adults to the overwhelming effects of trauma and emotional events (Joseph, 1996; Perry, 2002).

Much of neurodevelopment is activity dependent. In the developing brain, critical windows of development are dependent upon microenvironmental and environmental cues in order for neural systems to properly organize from their immature, undifferentiated form (Lauder, 1988; Perry, 1994; 2002; Perry and Pollard, 1998). Prolonged and repeated stress results in altered neurochemical and microarchitectural functioning. As van der Kolk (1993) noted, neurobiological abnormalities, including neuroendocrine disturbances have been linked to severe childhood trauma. Specifically, these abnormalities have been associated with the catecholamine, serotonin, and endogenous opiate systems.

Stress is defined as any event that disrupts the homeostasis or equilibrium of body systems. DeLongis et al. (1998) caution that relating a causal relationship between stress and long-term health raises several theoretical and methodological questions. As such, it is important that researchers realize stress in and of itself is not a unitary variable but "a system of interdependent processes, including appraisal and coping, which mediate the frequency, intensity, duration, and type of psychological and somatic response" (p. 486). As such, the body's stress response mechanisms subsequently activate several systems including the immune, neuroendocrine, peripheral autonomic nervous system, and the hypothalamic-pituitary axis with the release of cortisol, adrenocorticotropic hormone, and other neurochemicals designed to promote survival (Schwarz and Perry, 1994). The initial stress-response reaction initiated by the body's stress response alters brain function and structure to enable survival. If the stress response is of sufficient intensity, frequency, or duration, the compensatory stress response mechanisms may become maladaptive (overactivated or fatigued) and the individual is unable to return to pre-event homeostasis. The physiologic system reorganizes and these inhibitory or facilitatory alterations may lead to common PTSD symptoms (Perry and Pollard, 1998; Schwarz and Perry, 1994). While a child may experience a temporary change due to stress, the longer a child's stress-response is activated, the greater the likelihood of a "use-dependent" change in neural systems. A use-dependent change in neural systems occurs when an adaptive response to trauma persists beyond the time needed to respond to the trauma and subsequently becomes maladaptive and the stress-response systems fail to return to pre-event homeostasis. Limbic system hyperarousal is the most common of such prolonged responses (Fig. 1).

The more a neural system is activated the more a use-dependent change will occur (Perry et al., 1995). It is the catecholamines and glucocorticoids that are the first stage of defense to circumstances that threaten homeostasis (i.e. stress). Although it is imperative that an endocrine response to stress is activated when faced with provocative stimuli, exaggerated HPA activity or extended exposure to high glucocorticoid levels is also harmful

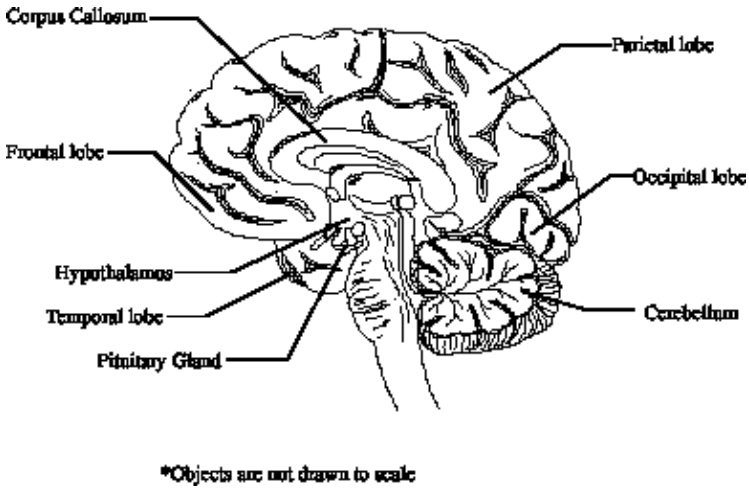


**Fig. 1.** The psychobiological stress response. Stress activates the hypothalamus secretion of CFR (corticotropin-releasing factor), dopamine, norepinephrine, serotonin, acetylcholine, and other secretagogues into the hypophysical-pituitary portal circulation which triggers the release of adrenocorticotropic hormone (ACTH) that activates the adrenocortical synthesis and glucocorticoids that block all nonessential functions, mobilizes energy, increases cardiovascular tone, and prepares the body for flight or fight.

(Meaney et al., 1996) to the developing brain. A prolonged traumatic stress response often results in abnormal timing, intensity, and pattern of catecholamine activity in a child's maturing brain (Perry, 1994, 2002). Sensitization occurs when neurochemical systems that mediate the brain's stress response become irreversible and change (i.e., become more sensitive to future stress-induced events). While sensitization may result from increased catecholamine activity in the mature brain of an adult, in a child's developing brain, neurotransmitters are a vital part in the brain's development, differentiation, synaptic proliferation, and neuronal migration. Putnam and Trickett (1997) also concur that understanding the effects of childhood maltreatment requires an understanding of biological mechanisms in conjunction with child development. Child development must be taken into account because maturation of neuroendocrine systems is dependent upon windows of vulnerability that are known to exist in human development.

Sensitivity of the developing central nervous system (CNS) to traumatic stressors varies according to vulnerable periods of development. Early brain development is continually altered by environmental influences (Glaser, 2000). A child who is raised in an abusive, neglectful, or unpredictable environment may obtain a developing CNS catecholaminergic system that is dysregulated and poorly organized. Children are particularly vulnerable to stress and trauma due to the prolonged period of plasticity in the human brain's development. Studies have also shown that plasticity in the animal brain is a reflection of the ability of the environment to adapt the efficiency and sensitivity of neuroendocrine systems in mediating stress responses. Similarly, a child's brain develops new synapses in response to stimuli from the environment, which allows for maximal learning but increases vulnerability for the developing brain. Sensitive periods exist in which trauma and stress affect brain development in particular ways; this vulnerability may lead to permanent changes or deficits in cognitive abilities.

According to Perry (1997), the brain organizes from the bottom-up and inside-out as the more primitive and reactive (brainstem) functions of the brain are modulated by the subcortical and cortical areas. The greater part of the critical structural organization of the brain occurs during childhood. In the use-dependent organization of the developing brain, a child's developing brain experiences repetitive sensory experiences and neural system organization respond accordingly. Critical periods of development exist where specific sensory experiences are necessary for optimal development and organization of brain function. Studies have shown this use-dependent differentiation also occurs throughout the CNS (Craigg, 1967; Cummins and Livesey, 1979). Brain development will be affected differently at different points in development and outcome may vary depending upon a child's stage of CNS maturity at the time of trauma. While neural plasticity modulates a child's brain in response to needs and environment, with aging, the brain becomes less plastic

or less responsive to environmentally induced structural changes (assuming they remain external to the physiologic systems of the body). For example, the developmental effects of trauma occurring before age 4 results in a much higher likelihood of psychotic and prepsychotic symptomatology, while trauma occurring after age 4 (on average) tends to result in more anxiety and affective symptoms (Perry, 1994). According to Teicher et al. (1997), specific areas of a developing brain are particularly vulnerable to trauma and stress. These areas are primarily parts of the limbic system and include the amygdala, corpus callosum, and hippocampus, and the prefrontal cortex.

## THE LIMBIC SYSTEM AND THE SYSTEM RESPONSE

The limbic system stimulates the emotions that result in behavior vital for self-preservation and survival (van der Kolk, 1993). According to Teicher et al. (1996), "the prefrontal cortex, hippocampus, and amygdala are among the most plastic brain regions" (p. 65). These regions of the brain are particularly late maturing, with myelination really beginning to progress rapidly postpuberty but not completing this process until into one's 30s. Regions of the limbic system impact behavior, memory, emotional states, and learning (Teicher et al., 1996). Individuals exposed to severe trauma show abnormalities in the arousal mechanisms of the sympathetic nervous system, the endogenous opioid system, and the hypothalamic-pituitary-adrenocortical track. According to Donnelly et al. (1999), the dopamine (DA), epinephrine, and catecholamines norepinephrine (NE) are involved in frontal lobe activation, anxiety, reward dependence, working memory, thinking, perceiving, mood regulation, and arousal. Many of the behavioral, affective, and cognitive symptoms associated with trauma are the result of the release of norepinephrine in regions such as the cerebral cortex, hippocampus, and amygdala (Miller, 1995).

### Corpus Callosum

Information in the brain travels across hemispheres primarily but not exclusively via the corpus callosum (Joseph, 1996). The ability of the two hemispheres of the brain to share information is impacted by the lack of maturity of the corpus callosum in young children. Research suggests brain laterality is influenced by experiential factors and it is speculated that stress could impact hemispheric integration which could lead to psychopathology (Teicher et al., 1997). Joseph (1996) noted that "three conditions—lateralized specialization, frontal lobe inhibitory activity, and incomplete myelination of the callosum axons—can reduce the ability of the two hemispheres to communicate among [otherwise] normal, intact individuals" (p. 114). Lateral specialization of the brain results in processing or recognition of certain types of information more rapidly by the left or right half of the brain. The inability of one brain half knowing what is occurring in the other half serves a protective function for the linguistic consciousness and the brain by keeping it from becoming overwhelmed, however, intrapsychic conflict (i.e. conflicting feelings, thoughts, and actions) is a common side-effect (Joseph, 1996). Expression and perception of emotion, especially negative emotion, appears to be a specialization of the right hemisphere. Although some researchers theorize that positive emotions such as joy are in the left frontal lobe whereas the right frontal lobe is commonly associated with negative emotions such as sadness (Glaser, 2000), others suggest that all perception of emotion is a function of the right hemisphere (Teicher et al., 1996). Ultimately, most researchers will agree that under normal conditions the ability to evaluate, identify, and communicate affect is dependent upon interaction between both hemispheres of the brain. Since early brain development is vulnerable to stress and trauma, left and right hemispheric scrutiny is limited and subject to misinterpretation and interpretation. A study by Teicher et al. (1997) found evidence that abuse can affect hemispheric laterality and is associated with a reversal in left/right hemisphere asymmetry and left hemispheric abnormalities. Teicher et al. (1996) also found EEG abnormalities localized to the anterior and frontotemporal regions were three to four times more prevalent in patients with physical/sexual abuse histories. Results of the study suggest that greater left-sided dysfunction may be associated with childhood abuse. This, in turn, may result in a greater right hemispheric dependence and an enhanced reaction and perception to negative affect, in addition to unconscious storage of traumatic childhood memories.

### Prefrontal Cortex

The prefrontal cortex is responsible for inhibitory behaviors and integrating motor and speech activity with sensory information (Teicher et al., 1997). These executive functions control attention, working memory, and relevant information. The prefrontal cortex discriminates between externally and internally employed models of the world and impulsive behavior, inattention, lack of self-control,

and changes in personality can occur when the prefrontal cortex is damaged. According to Bremner et al. (1999), "human subjects with lesions of the prefrontal cortex show dysfunction of normal emotions and inability to relate in social situations that require correct interpretation of the emotional expressions of others" (p. 1788). This area of the brain is particularly susceptible to stress since it is not fully myelinated until the third decade of life (Teicher et al., 1997). According to Donnelly et al. (1999) exposure to stress is known to enhance dopamine turnover in areas of the brain including the prefrontal cortex (which has a disproportionate number of dopamine receptor sites), which can result in paranoia and hypervigilance. Altered dopaminergic functioning has been found in trauma victims and researchers speculate that common symptoms associated with PTSD may be a manifestation of dysregulation of dopamine function.

One area of focus is the catecholaminergic system, which plays a key role in the adaptation to stress and produces common symptoms of PTSD. Studies have shown that elevations of plasma cortisol levels, which reduce immunosuppression, are present in trauma victims. Trauma is believed to reduce NK cell activity (natural killer cells, which target cells using antibody dependent cell-mediated cytotoxicity—they also use perforin to kill cells in the absence of antibody), which may result in the symptoms of PTSD. Exposure to stressful events may affect children biochemically by activating the release of norepinephrine by the central noradrenegic neurons, resulting in pathophysiology of PTSD (Miller, 1995). The hypothalamic-pituitary-adrenal axis (HPA) is also vital in the physiological reaction to trauma by stimulating the adrenal cortical production of glucocorticoids.

## Amygdala

The amygdala is the part of the limbic system that provides emotional importance to the stimuli related to affective states. Giving significance to experience and associating it with larger schemes in addition to controlling sexual and aggressive behaviors are all functions of the amygdala. The amygdala perceives fear and sets off a response which might create a state of hyperarousal in children. More importantly, the amygdala plays a vital role in the formation of emotional memory. According to Joseph (1996) the hippocampal's relative immaturity at birth results in early memories (visual, tactile, gustatory, or emotional instead of cognitive or verbal) being created and stored within the amygdala, which is functional after a child's birth. The formation of emotional memories is primarily associated with the amygdala, whereas the establishment of cognitive and nonemotional memories is primarily the responsibility of the hippocampus (Joseph, 1996). This area of the brain is extremely sensitive to neuronal excitability when recalling emotional memories, especially in the absence of hippocampal participation. These early memories may be recalled through emotional disturbances and bodily sensations instead of the normal hippocampal retrieval mechanisms. The amygdala also plays a vital role in the development of condition fear responses and autonomic reactions that may be stored in early memory (Joseph, 1996). The amygdala mediates fear response and is sensitive to inhibitory inputs from the medial prefrontal dopaminergic system. This section of the brain is very sensitive, even to mild stressors and long-term potentiation of the amygdala may be related to learning abnormalities and the retrieval, storage, and encoding of traumatic memories.

Exposure to high levels of emotional arousal may negatively affect the hippocampus and the amygdala. Emotional stress, anxiety, and fear arouses the amygdala which releases large quantities of aminopeptide, corticotropin-releasing factor (CRF), which, in turn, potentiates autonomic and behavioral reaction to stress and fear. When stressed by restraint, cortisone levels dramatically increase and are released with the onset of stress to activate key systems in the body's stress-response mechanisms. This CRF secretion activates the release of adrenocorticotropic hormone (ACTH) from the pituitary. State-dependent memories may result in trauma-induced neurotransmitters, amygdala activation, and the development of abnormal neural pathways. Traumatic events may result in a diverse range of symptomology including harmful alterations in behaviors, emotions, and neurobiology. Additionally, aggression and inappropriate sexual activity may be linked to prolonged traumatization and childhood sexual abuse.

## Hippocampus

The hippocampus plays a crucial role in memory function, spatial learning, and behavior inhibition. The hippocampus is also known to play a critical role in anxiety and panic disorders (Teicher et al., 1997). Severe emotional trauma can result in the secretion of substances that overactivate the hippocampus. Hippocampal functioning is hindered when the amygdala receives a high level of stimulation. According to Joseph (1996) "when repetitively stressed and highly emotionally aroused, the hippocampus appears to become so aroused that it is essentially deactivated . . . [and] under conditions of extreme stress the hippocampus may be damaged with subsequent neural degeneration" (p. 586). While long-term exposure to stress is associated with alterations in neurotransmitter

systems and impairment in the hippocampal, according to Southwick et al. (1992) there is also evidence that "long-term potentiation has been found not only in the hippocampus but also in the lateral and basolateral nucleus of the amygdala" (p. 350). In animals, long-lasting increases in hippocampal synaptic responsivity impair behavioral learning and result in memory deficits. Hippocampal dysfunction affects the interpretation of incoming stimuli and inhibits proper categorization and evaluation of experiences. This can result in memories being experienced in a behavioral state or visual image (van der Kolk, 1993).

According to van der Kolk (1993), memories are fixed by myelinization. Until axons are myelinized the brain remains extremely plastic. Developmentally, this occurs at different ages and is the cause of amnesia in infants since the hippocampus is not fully myelinated until later in life (Jacobs and Nadel, 1985; Schachter, 1990; van der Kolk, 1993). According to van der Kolk (1993) "after the hippocampus is myelinized, the hippocampal localization system, which allows memories to be placed in their proper context in time and place, remains vulnerable to disruption by intense emotional states" (p. 227). With the maturing of the CNS, memory storage changes from primarily sensorimotor and perceptual to linguistic and symbolic representations of mental experience. Autonomic arousal results in access to memories that originated under similar arousal conditions. This intense autonomic arousal of memories influences interpretation of the traumatic event.

Stress produces deficits in memory resulting from damage to hippocampal neurons (Bremner et al., 1999). In addition to memory impairments, research has shown that cognitive impairments, lack of coping responses, and dissociation are also associated with hippocampal damage (Ratna and Mukergee, 1998). Deficits in short-term memory are also associated with the reduction in right hippocampal volume. A study by Bremner and Narayan (1998) found an 8% reduction in right hippocampal volume in PTSD patients. According to Joseph (1999), the hippocampus also plays a major part in storing and consolidating long-term memory. Additionally, Joseph (1999) postulates that,

> Although these substances are normally released as part of the "flight or fight" response, repeated or prolonged stress-induced secretory episodes of corticosteroids and enkephalins can injury the dentate gyrus and Ammon's horn and hyperactivate or kill hippocampal (as well as amygdala) pyramidal neurons–structures which normally display synaptic growth and dendritic proliferation in response to new learning. (p. 716)

According to Nutt (2000), when the hippocampus is damaged, the HPA system is changed from a normal negative feedback loop to a positive feedback loop. The resulting HPA system change increases the hippocampal's exposure to cortisol toxicity and results in reduced hippocampal volume. High glucocorticoid levels decrease hippocampal glucocorticoid receptors and result in increased feedback resistance and corticosterone secretion (Southwick et al., 1992). Many studies now show stress produces hippocampal dysfunction, atrophy (smaller volume as seen on QMRI), and deficits in declarative memory function (Bremner, 1998, Bremner et al., 1999; Nutt, 2000) due to the damaging effects of high levels of glucocorticoids on the hippocampus. Glucocorticoids disrupt cellular metabolism and increase hippocampal neuronal vulnerability to a variety of agents. The De Bellis et al. (1994) study found a 7% smaller cerebral volume in children suffering from PTSD (Glaser, 2000). Gurvitis et al. (1996) found an average 26% reduction in the left hippocampus and 22% reduction in the right hippocampus in Vietnam veterans with severe PTSD. Additionally, other studies (e.g. Ito et al., 1993, 1998; Teicher et al., 1993) found left frontal and temporal abnormalities on an EEG in addition to limbic system dysfunction in individuals with significant abuse histories.

According to Perry and Pollard (1998),

> As with central neurobiologic systems, stress, distress, and trauma alter HPA regulation (i.e., a new homeostasis has been induced by the stress). Abnormalities of the HPA axis have been noted in adults with PTSD. Chronic activation of the HPA system in response to stress has negative consequences. The homeostatic state associated with chronic HPA activation wears the body out. Hippocampal damage, impaired glucose utilization, and vulnerability to metabolic insults may result. Preliminary studies in a sample of abused children suggest similar hippocampal and limbic abnormalities. (pp. 41–42)

In animal studies a stress reaction produces increased glucocorticoid secretion leading to loss of hippocampal cells (Glaser, 2000). Studies also indicate a greater number of lymphocyte glucocorticoid receptors and a reduction in CRF which could account for the feedback inhibition of the HPA. The greatest number of type II glucocorticoid receptors is found in the hippocampus. During stress, HPA activation is inhibited by the hippocampus. Neural death is also linked to increased glucocorticoids. According to Sapolsky (1992), the CRF is released with the onset of stress to activate key systems in the body's stress-response mechanisms. This CRF secretion activates the release of adrenocorticotropic hormone (ACTH) from the pituitary. The ACTH, in turn, triggers the release of glucocorticoids and adrenocortical synthesis. Glucocorticoids quickly circulate, help mobilize energy from storage, block energy storage, increase cardiovascular tone,

and inhibit nonessential processes such as immunity, inflammation, reproduction, and growth. As stated by Sapolsky (1992), "there is a dose–response relationship between the severity of the stressor and the magnitude of the adrenocortical response" (p. 12). Adrenocortical activity is influenced by the amount of glucocorticoid concentrations in the bloodstream, which suggests that the adrenocortical axis has the ability to differentiate between different magnitudes of stressors. The long-term effects of chronic stress lead to excessive exposure to glucocorticoids. Studies involving rats have indicated neuronal loss in the hippocampal is connected with hypersecretion of glucocorticoids. According to Sapolsky (1992), "a major pacemaker of hippocampal neuron loss appears to be the extent of glucocorticoid exposure over the lifetime; excessive glucocorticoids can be neurotoxic to the hippocampus" (p. 113). In as little as 3 weeks, high glucocorticoid exposure will cause degeneration in neural dendrites. Additionally, excessive glucocorticoids can be neurodegenerative and disrupt normal development.

Recent studies have indicated that "there is growing evidence of hippocampal volume loss associated with chronic PTSD" (Bergherr et al., 1997, p. 39). Since this evidence suggests neuronal loss in the hippocampus is a consequence of acute stress and traumatization, it is imperative that clinicians identify children suffering from long-term traumatizations as soon as possible. According to a study conducted by Teicher et al. (1993, 1996), increased limbic system dysfunction is associated with abuse occurring before the age of 18. The authors caution however, that the study is correlational and does not establish a cause–effect relationship. Some authors even propose that limbic dysfunction may be hereditary and predispose a child to a greater risk of abuse (Table 1).

## Cortisol Levels

The stress-response of the developing brain results in an increase in neurotransmitter and hormone activity, which affects neuronal migration, synaptic proliferation, differentiation, and total brain development. Immediate response to stress includes the release of dopamine, norepinephrine, serotonin, and acetylcholine in the brain. This, in turn, stimulates the hypothalamus, pituitary gland, and adrenal glands, which release cortisol. Increased cortisol levels have been linked to brain alterations including thymus gland shrinkage, cell death, and hippocampal atrophy. Other effects include a reduction in lymphocytes in the blood leading to a weaker immune system (Sapolsky, 1996) and neuronal death (Munck et al., 1984). While acknowledging the damaging effects of high cortisol levels, Yehuda (2000) cautions that cortisol also serves a vital role in terminating the body's stress-response and is necessary to shutdown reactions that damage the brain. According to Yehuda (1997) "the major function of cortisol is to manage or contain the body's biological stress-response by stimulating the termination of the neural defense reactions that have been activated by stress" (p. 58). Munck et al. (1984) also asserts that cortisol works in a reparative fashion and actually shuts down other stress-related changes before more damage is caused. Originally, researchers thought the release of cortisol was dependent on the level of stressor experienced. Yet, according to Yehuda (2000),

> because of an increased number of glucocorticoid receptors on the pituitary, the normal stress response cascade is disrupted. Although ACTH stimulates the adrenal to release cortisol, cortisol acts at the level of the pituitary to shut off ACTH release from the pituitary, and ultimately less cortisol is made and released from the adrenal glands. (p. 267)

Although the damaging effects of high levels of cortisol are well documented, there is considerable debate over the inconsistent levels of cortisol (i.e. high vs. low) that have been found in victims of trauma. Yehuda (2000) postulates that neuroendocrine alterations (low cortisol levels, increased sensitivity, and larger than normal basal of glucocorticoid receptors) associated with PTSD are dissimilar to other stress responses and hippocampal atrophy in PTSD victims may actually be a function of increased glucocorticoid receptor sensitivity and not high levels of cortisol. According to Yehuda (2000), "the majority of the studies performed to date demonstrate that cortisol levels in PTSD are lower compared to those of other psychiatric groups and normal controls" (p. 269). Of the six studies of urinary cortisol levels done to date (1994), four found lower cortisol levels in psychiatric groups. Studies (e.g. De Bellis et al., 1994; Golier and Yehuda, 1998; Hart et al., 1995, 1996; Kaufman, 1991; Kaufman et al., 1997) suggest that lower cortisol levels are found in some children exposed to maltreatment, sexual abuse, neglect, and trauma. According to Glaser (2000), this is possibly due to an "enhanced negative feedback in the HPA axis" (p. 106). It is speculated that the HPA's lack of response to situations of stress may be related to the familiarity of the stress and a source of protection for the brains of vulnerable children. However, a study by De Bellis et al. (1999) found increased cortisol levels in children suffering from significant abuse and PTSD. Similar results were found in studies conducted by Pitman and Orr (1990) and Lemieux and Coe (1995). These results contradict studies finding lower cortisol levels in individuals suffering from PTSD (e.g. Mason et al., 1996; Yehuda et al., 1990, 1993, 1995). Yehuda et al. (1995) suggests these findings may be due to the immaturity of the HPA in children.

**Table 1.** Glossary of Neurostructural and Neurochemical Terms in Stress Response

| Term | Definition |
|---|---|
| Amygdala | Located in front of the hippocampus, it is the part of the limbic system that provides emotional importance to the stimuli related to affective states. Giving significance to experience and associating it with larger schemes in addition to controlling sexual and aggressive behaviors are all functions of the amygdala. More importantly, the amygdala plays a vital role in the formation of emotional memory. The amygdala also plays a vital role in the development of condition fear responses and autonomic reactions that may be stored in early memory. |
| Adrenocorticotropic hormone (ACTH) | Triggers the release of glucocorticoids and adrenocortical synthesis. Glucocorticoids quickly circulate, help mobilize energy from storage, block energy storage, increase cardiovascular tone, and inhibit nonessential processes such as immunity, inflammation, reproduction, and growth. |
| Catecholamines | The dopamine (DA), epinephrine, and norepinephrine (NE) are involved in frontal lobe activation, anxiety, reward dependence, working memory, thinking, perceiving, mood regulation, and arousal. They are major elements in the response to stress. |
| Corticotropin releasing factor (CRF) | Released with the onset of stress to activate key systems in the body's stress-response mechanisms. This CRF secretion activates the release of adrenocorticotropic hormone (ACTH) from the pituitary. Has an inhibitory effect of hippocampal functioning. |
| Cortisol | Most potent of the naturally occurring glucocorticoids, works as an anti-inflammatory agent released with the onset of stress and in addition to other neurochemicals, activates key systems in the body's stress-response mechanisms. Also serves a vital role in terminating the body's stress-response and is necessary to shutdown reactions that damages the brain. Has an inhibitory effect of hippocampal functioning. |
| Cortisone | A glucocorticoid that is likely a metabolite of hydrocortisone (s. cortisol). It influences the growth of connective tissue. |
| Hippocampal | Plays a crucial role in memory function, spatial learning, and behavior inhibition. Hippocampal dysfunction affects the interpretation of incoming stimuli and inhibits proper categorization and evaluation of experiences. This can result in memories being experienced in a behavioral state or visual image. |
| Hypothalamic-pituitary axis (HPA) | Vital in the physiological reaction to trauma by stimulating the adrenal cortical production of glucocorticoids. Overwhelming stress and traumatization are linked with the activation of the HPA. During stress HPA activation is inhibited by the hippocampal. Chronic activation has negative consequences and can wear the body out. |
| Limbic system | The limbic system governs the emotions vital for self-preservation, homeostasis, and basic needs. These regions of the brain are particularly late maturing, with myelination completing until into one's 30s. Regions of the limbic system impact behavior, memory, emotional states, attention, arousal, learning, and social and sexual behavior. |
| Neocortex | The arousal of the neocortex activates the amygdala and in turn, the neocortex become more receptive to processing sensory information which can lead to a state of attention, emotional arousal, or vigilance. |
| Norepinephrine | A neurotransmitter that plays a critical role in fight or flight reactions (automatic hyperarousal). Norepinephrine is released by the CNS which results in a cardiovascular response that allows for vigilance and focus on relevant stimuli, a total body mobilization that is necessary for survival. This reaction activates the area of the brain involved in attention, concentration, and arousal. Many of the behavioral, affective, and cognitive symptoms associated with trauma are the result of the release of norepinephrine in regions such as the cerebral cortex, hippocampus, and amygdala |
| Sympathetic nervous system (SNS) | Along with the HPA axis, the SNS is a major axis of stress response responsible for unconscious emergency responses. The SNS increases blood pressure and accelerates the heart rate in response to dangerous or stressful situations. This response serves a protective role and allows the body to prepare for "fight or flight." The long-term consequence is that the SNS becomes hyperreponsive in many individuals with PTSD. |
| Temporal lobe | Involved in complex visual, linguistic, auditory function, in addition to memory and emotional functioning. |

While studies have linked lower cortisol levels to chronic PTSD, Yehuda cautions that assessing levels of cortisol before and after traumatic events is necessary in order to establish that PTSD neuroendocrine alterations are due to the traumatic event and not pre-existing lower cortisol levels. Overwhelming stress and traumatization are linked with the activation of the HPA. According to Bergherr et al. (1997), the long-term effect of PTSD in individuals is associated with lower cortisol levels indicating "that PTSD is associated with increased HPA sensitivity

to feedback suppression by cortisol" (p. 35). Studies have demonstrated PTSD veterans have a greater number of glucocorticoid receptors, which is consistent with upregulation and often a secondary reaction to low cortisol. This is also associated with increased CRF hypersecretion.

## TRAUMA AND CHILDREN

According to Perry and Pollard (1998) neuropsychiatric disorders that are trauma related are affecting over 8 million children, approximately half of all children exposed to traumatic events (Schwarz and Perry, 1994). Often, these children are misdiagnosed with attention deficit disorder, oppositional defiant disorder, conduct disorder, anxiety, or a phobia (Perry and Azad, 1999). Life events that are stressful can also modify a wide array of immunological actions. An increase in the risk of illness and infectious disease is found in children where alterations in the immune system are stress induced. When stress-related mechanisms are activated, the brain reacts by responding in a way that promotes survival. If a traumatic event is prolonged or chronic, these protective mechanisms can become overactive causing a change in homeostasis.

The ability to regulate and modulate behavior increases as the brain develops (Perry et al., 1995) since the neurobiologic systems respond to stress in an age-related fashion that parallels developmental life tasks. "Traumatic events modify an adult's original state of organization or homeostasis but may be the original organizing experience for the child, thereby determining the foundational organization and homeostasis of key neural systems" (Perry and Pollard, 1998, p. 36). According to Pynoos et al. (1997) there are four periods in which the brain undergoes major structural changes. Additionally, these periods (which range from 15 months to 4 years, 6–10 years, puberty, and midadolescence) correspond with developmental growth in cognitive and emotional functions. What is harmful for a 2-year-old may not affect a 21-year-old and vice versa (Perry, 2002; Perry and Pollard, 1998). For example, not touching a newborn baby will result in severe traumatization but would have little effect on a 30-year-old. Neglect and abuse experienced by children early in life deprives the brain of experience-expectant maturation. For numerous children, abuse is not perceived as acutely traumatic because of its very chronic and predictable nature. Children who are commonly exposed to threatening or chaotic caregiving develop a use-dependent neurobiological response which results in a sensitized and dysfunctional stress-response system. The sensitization of the stress-response systems may result in anxiety, hyperactivity, impulsivity, hypertension, dysphoria, sleep problems, and tachycardia. These children often exhibit exaggerated reactivity due to a basal homeostatic level of constant anxiety. Although sensitized to traumatic events, these children are at a greater risk for developing stress-induced neuropsychiatric disorders when they get older as they exhibit maladaptive cognitive, behavioral, emotional, physiologic, and social problems (Perry and Pollard, 1998). Associated with a child's response to trauma are gender, developmental level, age, socioeconomic and family factors, and proximity. Developmental level and age impact a child's perception and comprehension of the trauma. Parental support and response to trauma are also predictive of a child's response to trauma and severity of trauma symptomology. Gender and locus of control can also affect a child's response and coping mechanisms (Amaya-Jackson and March, 1995; Perry and Azad, 1999; Pfefferbaum, 1997; Schwarz and Perry, 1994).

A response that serves a protective role is one that allows the body to prepare for "fight or flight." When homeostasis is threatened, the adrenal glucocorticoids and catecholamines serve as regulators of stress (Perry, 1994, 2002). Stress in the developing brain causes an increase in endogenous opiates and alters multiple neuroendocrine systems. Subsequently, the SNS increases blood pressure and accelerates the heart rate in response to dangerous or stressful situations. Norepinephrine is released by the CNS which results in a cardiovascular response that allows for vigilance and focus on relevant stimuli, a total body mobilization that is necessary for survival. This reaction activates the area of the brain involved in attention, concentration, and arousal.

Differing from the neurobiology of a hyperarousal response, activating the autonomic nervous system leads to a slowing of the heart and lowering of blood pressure which results in a dissociative state. The likelihood of a dissociative response increases when a child is unable to escape a frightening experience and/or experiences physical injury, pain, or torture. Perry et al. (1995) found a parasympathetic nervous system response (decreased heart rate and blood pressure, increases in circulating epinephrine) in girls and young children when a dissociative response occurs. Dissociation is a common response to trauma and occurs when infants/children abandon initial alarm behaviors and become compliant, passive, or show restricted affect. Common mental defense mechanisms such as avoidance, daydreaming, numbing, fantasy, fugue, catatonia, or fainting are often manifested (Perry and Pollard, 1998). Essentially, dissociation involves a disengagement from the external world and focus on the internal world. Adaptive styles of females and young children are more likely to involve dissociation, while males are more likely to respond from a reactive stance or fight or flight response that prepares them to flee or fight the perceived threat

(Perry et al., 1995). Additionally, females are more likely to internalize and males more likely to externalize symptoms (e. g., see Reynolds and Kamphaus, 1992). Differences in the adaptive stress response patterns of males and females are clearly seen in the incidence of childhood neuropsychiatric disorders. More males meet the criteria for externalizing disorders (conduct disorder, ADHD, oppositional defiant disorder), while females experience more internalizing disorders (anxiety, dissociative disorders, depression). Additionally, in adolescence, the ratio of neuropsychiatric disorders is three to one (male to female), yet the prevalence rates change to two to one (female to male) in early adulthood (Perry et al., 1995). The risk of developing PTSD is also three times greater in children exposed to traumatic experiences before age 11 as opposed to later years (Amaya-Jackson and March, 1995). The long-term consequence of "fight or flight" is that the SNS becomes hyperreponsive in many individuals with PTSD.

## POSTTRAUMATIC STRESS DISORDER

PTSD was included as distinct psychiatric syndrome in the 1980 publication of the DSM-III. PTSD is usually seen as a psychological disorder by clinicians and yet recent research indicates that PTSD also should be viewed from a biological perspective (Southwick et al., 1997). According to Pfefferbaum (1997), estimates for the prevalence of PTSD ranges from 1% to 14%. Perry (1994) states a conservative estimate of PTSD in children exceeds 15 million. Additionally, with the high number of children exposed to trauma, abuse, neglect, maltreatment, and violence, the number of children developing PTSD continues to grow each year. According to Pfefferbaum (1997), PTSD comprises three essential features and includes: "1) persistent re-experiencing of the stressor, 2) persistent avoidance of reminders of the event and numbing of general responsiveness, and 3) persistent symptoms of arousal" (p. 1503). These key characteristics are sometimes referred to as the holy trinity of PTSD symptoms and simply summarized as avoidance, arousal, and re-experience.

According to Southwick et al. (1997), recent studies strongly support the idea that psychological trauma can result in changes in the body's neurobiological stress response years after the original event. According to a review of clinical literature by Southwick et al. (1997), studies indicate that hyperresponsiveness and alterations in the SNS and HPA axis are provoked by original reminders of the trauma. The neurobiological dysfunction associated with PTSD includes the noradrenergic, dopaminergic, opiate, benzodiazepine, and hypothalamic-pituitary-adrenal axis. Increases in regional norepinephrine, locus coeruleus neuron responsiveness, dopamine and endogenous opiates release, elevated glucocorticoid levels, and decreased density of benzodiazepine receptors and opiate receptors are associated with the neurochemical system response to PTSD. These neurochemical reactions produced by stress result in hypervigilance, anxiety, analgesia, fear, hyperarousal, and behavioral responses that function together in an attempt to cope with imminent danger (Southwick et al., 1992). While these neurochemical responses may be beneficial initially, the long-term consequences are associated with PTSD. In addition to alterations in the brain of persons experiencing PTSD, including reduction in hippocampal volume, a study conducted by Canive et al. (1997) found gross structural abnormalities in individuals with PTSD. Using MRI FLAIR imaging sequences of patients with PTSD, Canive et al. (1997) found focal white matter lesions in the brain of the PTSD patients. The gross abnormalities of the PTSD patients were higher than a comparative neurologically normal group. The authors caution however, that the high comorbidity of alcohol and depression associated with PTSD in adults makes the exact factors involved difficult to assess. Similar research involving children with PTSD may be beneficial in resolving the comorbidity problem of alcohol and depression commonly found in adult patients.

## CHILDHOOD SEXUAL ABUSE

The psychological impact of childhood sexual abuse is associated with various physiological and psychobiological changes. According to Joseph (1999) "a clear relationship has been established between early childhood abuse, and the development of severe social emotional disturbances and limbic system injury, including child and adult onset psychopathology and dissociative abnormalities and posttraumatic stress disorder" (p. 721). Ratna and Mukergee (1998) noted in their research that 1 in 6 women are victims of childhood sexual abuse. Additionally, studies have shown 90% of 3–16 year olds who have been abused and 86% of adult survivors of sexual abuse to have PTSD symptoms or meet the PTSD diagnostic criteria (e.g. Mcleer et al., 1988; Rodriquez et al., 1996). According to Weinstein et al. (2000), "considerable research suggests the effects may be pervasive and long-lasting, leading to increased risk for adjustment difficulties and mental health problems in adulthood" (p. 362). Additionally, the most common cause of PTSD is childhood sexual abuse (Bremner et al., 1999).

Various studies (e.g. Bremner et al., 1997; Schacter et al., 1996; Stein et al., 1997) have also indicated a statistically significant decrease in hippocampal volume in the left side of adult survivors of severe childhood sexual

abuse. The decreased hippocampal volume was associated with the severity of PTSD. It is presumed that increased cortisol levels resulting from the abuse lead to physical hippocampal damage reflected in smaller hippocampal volume.

According to Glaser (2000), catecholamine levels were higher in girls who were sexually abused. Greater baseline (homeostasis) noradrenaline and dopamine levels have been found in abused children with PTSD (e.g. De Bellis et al., 1999). Duration of abuse was significantly correlated with the levels of noradrenaline and dopamine found.

A recent study by Shin et al. (1999) looked at whether childhood sexual abuse victims with and without PTSD exhibited differences in the anterior limbic and paralimbic areas of the brain during imagery of the traumatic event. The study consisted of 16 women, who experienced penetrative sexual abuse before age 16, 8 of who meet the criteria for PTSD. Subjects underwent two PET scans during which they recalled traumatic and neutral stimuli scripts. The study found that during neutral conditions, both groups experienced increased cerebral blood flow (CBF) in the anterior temporal poles and the orbitofrontal cortex, although the PTSD group exhibited the greatest increase. During the traumatic condition, the PTSD group had an increased heart rate and decreased CBF in the bilateral anterior frontal regions and left inferior frontal gyrus. Both groups exhibited CBF decreases in the visual cortex. The results suggest that although the two groups differ in patterns of activation among paralimbic regions, the recollection and imagery of traumatic events is accompanied by increased CBF to the anterior paralimbic region in individuals exposed to trauma (with or without PTSD).

A study by Stein et al. (1997) found hippocampal volume was significantly reduced in 21 women who were victims of childhood sexual abuse. The hippocampal volume on the left side was 5% smaller for the sexually abused group than sociodemographically similar women with no histories of abuse. Additionally, "the left-sided hippocampal volume correlated highly ($r_s = -0.73$) with dissociative symptom severity" (Stein et al., 1997, p. 951). Bremner et al. (1999) conducted a study in which women with PTSD who had also been victims of childhood sexual abuse "demonstrated increased activation in posterior cingulate, anterolateral prefrontal cortex (Brodmann's areas 6 and 9), and motor cortex . . . as well as deactivation in right hippocampal, fusiform/inferior temporal gyrus, supramarginal gyrus, and visual association cortex" (p. 1788). Features observed in PTSD including hippocampal damage, cognitive and memory impairment, and dissociation also frequently are observed in severe sexual abuse (Ratna and Mukergee, 1998).

## ADHD

Research indicates symptoms of hyperarousal in victims of trauma produces changes in the brain system that results in long-term hyperactivity. Trauma exposure may result in the failure to modulate aggression, impulsivity, and anger. This loss of drive regulation in externalizing disorders is associated with ADHD, social and cognitive impairments, and impulsive behavior which can lead to increased risk for trauma exposure and subsequently PTSD. The dysfunction of the prefrontal cortex is often what leads to the diagnosis of Attention Deficit Hyperactivity Disorder (ADHD). Stress activates the catecholamines (norepinephrine, epinephrine, and dopamine) and the sympathetic nervous system and the medulla receives messages of stress and/or fear from the hippocampus and the amygdala. The adrenal gland also secretes noradrenaline and adrenaline, which raises the heart rate, blood pressure, and sweating. According to Glaser (2000), prefrontal cortex dysfunction is linked to raised levels of dopamine and noradrenaline. Studies show that the long-term effects of chronic stress lead to excessive exposure to glucocorticoids. While glucocorticoids are a vital part of the survival stress-response, overexposure can result in a multitude of disorders. According to Miller (1995), "symptoms associated with traumatization, such as anxiety, startle response, hypervigilance, and avoidance of traumatization triggers seem to directly or indirectly reflect a long-lasting problem of modulation alarm and arousal" (p. 9).

ADHD is difficult to assess and diagnose distinctly from several related disorders, yet numerous children are given the diagnosis. Comorbid conditions among children with PTSD are more likely because critical developmental windows and milestones are sensitive to changes in neurobiological activation and maturation which can be disrupted by trauma (Donnelly et al., 1999). According to Weinstein et al. (2000), part of the misdiagnosis problem is that other behavioral disorders, PTSD, and ADHD all have shared characteristics and symptoms between them (Table 2). Given the complications resulting from misdiagnosis, the challenge is for clinicians to pay increased attention to differential diagnosis in PTSD and ADHD. Donnelly et al. (1999) also notes that comorbidity between PTSD and externalizing disorders may result in the presentation of traditional features of ADHD including impulsivity, hyperactivity, irritability, restlessness, and distractibility. Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD) are also externalizing disorders that have become more prevalent with the increase in PTSD. The hyperarousal characteristic of PTSD, including anger or irritability, sleeplessness, and hypervigilance, makes it easy to misdiagnoses PTSD as ADHD or even

**Table 2.** Comorbitity Symptoms

| Posttraumatic Stress Disorder (PTSD) | Attention-Deficit/Hyperactivity Disorder (ADHD) | Oppositional Defiant Disorder (ODD) | Conduct Disorder (CD) |
|---|---|---|---|
| Anxiety | | | |
| Avoidance | | | |
| Social withdrawal | Rejection by peer | Social conflicts | |
| Increased arousal | Increased arousal | | |
| Sleeplessness | Sleeplessness | | |
| Recurrent nightmares | | | |
| Hyperviligance | Hyperactivity/hyperviligance | High motor activity | |
| Feeling constantly threatened | | | |
| Impaired relationships | Poor relationships | Poor relationships | |
| Exaggerated startle response | Exaggerated startle response | High reactivity | |
| Irritability | Mood lability/irritability | Mood lability | |
| Impulsive behavior | Impulsivity | Impulsivity | Impulsivity |
| Self-destructive behavior | | Disruptive Behavior | Disruptive Behavior |
| Outbursts of anger | Temper outbursts | Losing temper | |
| Hostility | Oppositional behavior | Hostile behavior | |
| Difficulty completing tasks | Difficulty completing tasks | | |
| Difficulty concentrating | Difficulty concentrating | | |
| Feelings of guilt | Poor self esteem | Low/high self-esteem | |
| Shame | | | |
| Hopelessness | | | |
| Despair | | | |
| Dissociative symptoms | Dysphoria | | |
| Feelings of ineffectiveness | Demoralization | | |
| Somatic complaints | | | |
| Auditory hallucinations | | | |
| Paranoid ideation | | | |
| Impaired affect modulation | | | |
| Feelings permanently damaged | | | |
| Loss of previous beliefs | | | |
| Change in personality characteristics | | | |

Bipolar Disorder if comprehensive history and trauma assessments are not routine components of ADHD assessment. According to Weinstien et al. (2000), "in fact, some literature suggests that sexually abused children may be at heightened risk for the development of PTSD, though they are more often diagnosed as ADHD than PTSD" (p. 361). In one study (Mcleer et al., 1994), 54% of sexually abused children with PTSD also met the criteria for ADHD diagnosis.

## ATTACHMENT

A securely attached child has the ability to regulate distress and anxiety by using his/her caregiver as a secure base. Gunnar et al. (1996) speculate that the negative effects of elevated glucocorticoids in children are countered by secure attachment relationships. Gunnar (1998) hypothesized that the primary buffer of the HPA axis is a secure attachment. One adaptive response to stress is for the body to increase serum cortisol. Serum cortisol suppresses the immune system and increases glucose in the body. The hypothalamic-pituitary-adrenal (HPA) axis is the pathway that connects the adrenal cortex and the brain. The adrenal cortex secretes cortisol and long-term elevation of cortisol levels may be harmful, especially early in life. A study by Gunnar and Nelson (1994) found the activity of the hippocampus was impeded by high cortisol levels. Sapolsky's (1996) finding of a correlation between hippocampus damage and excess cortisol, supports these conclusions. According to Donnelly et al. (1999), "in younger children these may manifest as attachment disorders, impaired social skills, aggressiveness, impulsivity, and sexualized behaviors, depending upon the nature of the trauma" (p. 206).

### Neuropsychological Assessment and Treatment

The growing number of children in America exposed to trauma is resulting in a public health crisis. Children who have been traumatized often show symptoms of other disorders as well as PTSD (Amaya-Jackson and March, 1995; Perry, 2002), thus, comorbidity often makes diagnosis difficult in traumatized children. Because PTSD symptoms mimic many other child disorders, children are often

misdiagnosed and mistreated. According to Schwarz and Perry (1994),

> In general, because youngsters rarely attribute symptoms to trauma and may be reluctant patients or poor historians, and because posttraumatic symptoms can be nonspecific, superimposed on, or mimic other childhood disorders, it is important to maintain a high level of suspicion regarding the posttraumatic cause of any presenting symptoms and include the possibility of trauma in differential diagnoses of most childhood symptoms. Thus, even when youngsters present without a history of trauma, it is nevertheless useful to inquire routinely . . . . (p. 319)

The authors go on to caution against suggestible questions and instruct that inquiry should consist of nonbiased and open-ended questions.

Early assessment, detection, and treatment are vital to halting the devastating neurobiological sequela that occurs in many victims of childhood trauma. Many of the treatments for children and adolescents suffering from PTSD parallel interventions used with adult PTSD victims (Putnam, 1996). However, differential diagnosis is crucial since disorders that can mimic PTSD in children (e.g., ADHD, conduct disorder, and other externalizing disorders; see Reynolds and Kamphaus, 2002, for a review) require a different set of treatments than PTSD. In fact, some of the treatments for the mimic disorders such as stimulant medication for ADHD can be harmful to children with PTSD and can aggravate their neuropsychological symptoms.

Differential diagnosis requires at a minimum a detailed history of development, broad-band behavior rating scales (e.g., Behavior Assessment System for Children; Reynolds and Kamphaus, 1992), assessment of cognitive and academic status (as school failure is common among childhood PTSD victims and can also be misdiagnosed as a learning disability), and specific neuropsychological measures of arousal and attention. Assessment of brain function using a broad band of neuropsychological instruments is justified on the basis of the developmental neurobiological effects of trauma. As we have noted, chronically elevated cortisol levels can have detrimental effects on several brain systems that are integral components of attentional and memory systems in particular. Tests of memory and of new learning should be used to assess the functional impact of these potential alterations in brain development. The presence of memory and learning problems in such children will dictate additional treatment options such as cognitive remediation and the development and implementation of memory prostheses. Without the proper diagnosis and prescription of these aids by the neuropsychologist, children may be denied their use in the schools. Comprehensive assessment thus must be the order of the day when encountering traumatized or suspected-traumatized children, and purely traditional psychological assessments of personality and emotion will be insufficient to elucidate accurate, effective treatments and to avoid actually designing treatment plans that violate the prime directive of health care: first, do no harm.

## CONCLUSIONS

The number of children exposed to traumatic events is continuing to increase. Last year alone, over 5 million children in the United States were referred to state agencies (National Child Abuse and Neglect Data System, 2003) for suspected maltreatment. Trauma leaves a severe and lasting impression on children (Amaya-Jackson and March, 1995) and society. Every day millions of children in the United States are exposed to stressors such as violence, neglect, abuse, deprivation, and acts of war. Contrary to what many would believe, the United States is characterized as the most violent nation among the industrialized world and child maltreatment in the United States is an epidemic (Putnam, 1996; U.S. Advisory Board on Child Abuse and Neglect, 1995). The vulnerability of children to trauma is more apparent now than ever before in our history.

The epidemic of childhood trauma could have significant implications for public policy (Bremmer and Narayan, 1998). The numerous children suffering from childhood neglect and maltreatment, trauma, and PTSD could affect educational, social, and health policies that will have far reaching implications for society. Hippocampal toxicity and its included deficits in scholastic performance will impair children throughout their lives. Early development of the brain is modified constantly by external stimuli and children are unusually sensitive to these deleterious effects of stress due to the plasticity of the developing brain.

According to Schwarz and Perry (1994), "PTSD may be preventable" and public education can help prevent violence and children's expose to trauma. Accurate and comprehensive diagnostic studies of children referred for ADHD and related symptoms must be the standard of practice or many such individuals will be misdiagnosed with ADHD instead of recognizing their status as individuals with PTSD. Mistreatment with stimulants may then exacerbate the symptoms and lead to more detrimental outcomes long-term (Schwarz and Perry, 1994). Unfortunately, many managed care companies refuse to certify comprehensive diagnostic services for such referrals. Given the complexities of comorbidity generally and of the long-term consequences of undiagnosed and untreated—or mistreated—PTSD, professionals engaged in diagnosis where PTSD may be an issue will need to be acquainted

with the empirical support for comprehensive diagnostic services to substantiate the need for approval and provision of these necessary services

The need to move beyond traditional psychological assessments for children exposed to trauma is crucial, given the costs of misdiagnosis. Neuropsychologists must be utilized when working with children who have been exposed to trauma as the ability to attenuate the neurobiological impact of childhood trauma is dependent upon the awareness, recognition, and understanding of the devastating effects of trauma. In addition to traditional psychological assessments, specific neuropsychological measures of arousal and attention must be utilized before effective and accurate treatment can occur.

## REFERENCES


Amaya-Jackson, L., and March, J. S. (1995). Posttraumatic stress disorder. In: March, J. S. (ed.), *Anxiety Disorders in Children and Adolescents* Guilford, New York, pp. 276–300.

Bergherr, T., Bremner, J. D., Southwick, S.M., Charney, D. S., and Krystal, J. H. (1997). Neurobiological perspectives on trauma and aging. *J. Geriatr. Psychiatry* **30**(1): 27–59.

Bremner, J. D. (1998). Neuroimaging of posttraumatic stress disorder. *Psychiatr. Ann.* **28**(8): 445–450.

Bremner, J. D., and Narayan, M. (1998). The effects of stress on memory and the hippocampus life cycle: Implication for childhood development and aging. *Dev. Psychopathol.* **10**: 871–885.

Bremner, J., Narayan, M., Staib, L. H., Southwick, S. M., McGlashan, T., and Charney, D. S. (1999). Neural correlates of memories of childhood sexual abuse in women with and without posttraumatic stress disorder. *Am. J. Psychiatry* **156**(11): 1787–1795.

Bremner, J., Randall, P. L, Vermetten, E., Staib, L., Bronen, R., Mazure, C., Capelli, S., McCarthy, G., Innis, R., and Charney, D. (1997). Magnetic resonance imaging-based measurement of hippocampal volume in post-traumatic stress disorder related to childhood physical and sexual abuse—a preliminary report. *Biol. Psychiatry* **41**(1): 23–22.

Canive, J. M., Lewine, J. D., Orrison, W. W., Edgar, C. J., Provencal, S. L., Davis, J. T., Paulson, K., Graeber, D., Roberts, B., Escalona, P. R., and Calais, L. (1997). MRI reveals gross structural abnormalities in PTSD. *Ann. N. Y. Acad. Sci.* **821**: 512–515.

Craigg, B. G. (1967). The density of synapses and neurons in the motor and visual areas of the cerebral cortex. *J. Anat. (Lond.)* **101**: 639–654.

Cummins, R. A., and Livesey, P. (1979). Enrichment-isolation, cortex length, and the rank order effect. *Brain Res.* **178**: 88–98.

De Bellis, M. D., Baum, A. S., Birmaher, B., Keshavan, M. S., Eccard, C. H., Boring, A. M., Jenkins, F. J., and Ryan, N. D. (1999). Developmental traumatology Part I: Biological stress systems. *Biol. Psychiatry* **45**(10): 1259–1270.

De Bellis, M., Chrousos, G., Dorn, L., Burke, L., Helmers, K., Kling, M., Trickett, P., and Putnam, F. (1994). Hypothalamic-pituitary-adrenal axis disregulation in sexually abused girls. *J. Clin. Endocrinol. Metab.* **78**(2): 249–255.

DeLongis, A., Folkman, S., and Lazarus, R. S. (1988). The impact of daily stress on health and mood: Psychological and social resources as mediators. *J. Pers. Soc. Psychol.* **54**: 486–495.

Donnelly, C. L., Amaya-Jackson, L., and March, J. S. (1999). Psychopharmacology of pediatric posttraumatic stress disorder. *J. Child Adolesc. Psychopharmacol.* **9**(3): 203–220.

Frank, E., and Kupfer, D. (2000). Peeking through the door to the 21st century. *Arch. Gen. Psychiatry* **57**(1): 83–85.

Glaser, D. (2000). Child abuse and neglect and the brain—a review. *J. Child Psychol. Psychiatry* **41**(1): 97–116.

Golier, J., and Yehuda, R. (1998). Neuroendocrine activity and memory-related impairments in post-traumatic stress disorder. *Dev. Psychopathol.* **10**(4): 857–869.

Gunnar, M. R. (1998). Quality of early care and buffering of neuroendocrine stress reactions: Potential effects on the developing brain. *Prev. Med.* **27**(12): 208–211.

Gunnar, M. R., Brodersen, L., Nachmias, M., Buss, K., and Rigatuso, J. (1996). Stress reactivity and attachment security. *Dev. Psychobiol.* **29**(3): 191–204.

Gunnar, M. R., and Nelson, C. A. (1994). Event-related potentials in year-old infants: Relations with emotionality and cortisol. *Child Dev.* **65(1)**: 80–94.

Gurvitis, T., Shenton, M., Hokama, H., Ohta, H., Lasko, N., Gilbertson, M., Orr, S., Kikinis, R., Jolesz, F., McCarley, R., and Pitman, R. (1996). Magnetic resonance imaging (MRI) study of hippocampal volume in chronic combat related posttraumatic stress disorder. *Biol. Psychiatry* **40**: 1091–1099.

Hart, J., Gunnar, M., and Cicchetti, D. (1995). Salivary cortisol in maltreated children: Evidence of relations between neuroendocrine activity and social competence. *Dev. Psychopathol.* **7**(1): 11–26.

Hart, J., Gunnar, M., and Cicchetti, D. (1996). Altered neuroendocrine activity in maltreated children related to symptoms of depression. *Dev. Psychopathol.* **8**(1): 201–214.

Hopper, J. (2002). Child Abuse: Statistics, Research, and Resources. Retrieved September 14, 2002, from http://www.jimhopper.com/abstats

Ito, Y., Teicher, M. H., Glod, C. A., and Ackerman, E. (1998). Preliminary evidence for aberrant cortical development in abused children. A quantitative EEG study. *J. Neuropsychiatr. Clin. Neurosci.* **10**(3): 298–307.

Ito, Y., Teicher, M. H., Glod, C. A., and Harper, D., Magnus, E., and Gelbard, H. (1993). Increased prevalence of electrophysiological abnormalities in children with psychological, physical and sexual abuse. *J. Neuropsychiatry* **5**(4): 401–408.

Jacobs, W. J., and Nadel, L. (1985). Stress-induced recovery of fears and phobias. *Psychol. Rev.* **92**(4): 512–531.

Joseph, R, (1996). *Neuropsychiatry, Neuropsychology, and Clinical Neuroscience* (2nd edn.), Williams & Wilkins, Baltimore.

Joseph, R. (1999). The neurology of traumatic "dissociative" amnesia: Commentary and literature review. *Child Abuse Negl.* **22**(8): 715–727.

Kaufman, J. (1991). Depressive disorders in maltreated children. *J. Am. Acad. Child Adolesc. Psychiatry* **30**(2): 257–265.

Kaufman, J., Birmaher, B., Perel, J., Dahl, R. E., Moreci, P., Nelson, B., Wells, W., and Ryan, N. D. (1997). The cortcotropin-releasing hormone challenge in depressed abused, depressed nonabused, and normal control children. *Biol. Psychiatry* **42**(8): 669–679.

Lauder, J. M. (1988). Neurotransmitters as morphogens. *Prog. Brain Res.* **73**: 365–388.

Lemieux, A. M., and Coe, C. L. (1995). Abuse-related posttraumatic stress disorders: Evidence for chronic neuroendocrine activation in women. *Psychosom. Med.* **57**(2): 105–115.

Mason, J. W., Giller, E. L., Kosten, T. R., Ostroff, R. B., and Podd, L. (1996). Urinary-free cortisol levels in posttraumatic stress disorder patients. *J. Nerv. Ment. Disord.* **174**: 145–159.

McLeer, S. V., Callaghan, M., Henry, D., & Wallen, J. (1994). Psychiatric disorders in sexually abused children. *J. Am. Acad. Child Adolesc. Psychiatry*, **33**(3): 313–319.

McLeer, S. V., Deblinger, E., Atkins, M. S., Foa, E. B., and Ralphe, D. L. (1988). Posttraumatic stress disorder in sexually abused children. *J. Am. Acad. Child Adolesc. Psychiatry* **27**(5): 650–654.

Meaney, M. J., Bhatnagar, S., Larocque, S., McCormick, C. M., Shanks, N., Sharma, S., Smythe, J., Viau, V., and Plotsky, P. M. (1996). Early environment and the development of individual difference in the hypothalamic-pituitary-adrenal stress response. In Pfeffer, C. (ed.), *Severe Stress & Mental Disturbance in Children*, American Psychiatric Press, Washington, DC.

Miller, W. M. (1995). Stress adaptation in children: Theoretical models. *J. Contemp. Psychol.* **25**(1): 5–14.

Munck, A. W., Guyre, P. M., and Holbrook, N. J. (1984). Physiological functions of glucocorticoids in stress and their reaction to pharmacological actions. *Endocr. Rev.* **5**(1): 24–44.

National Child Abuse and Neglect Data System (2003). Report retrieved December 15, 2003, from http://www.acf.hhs.gov/programs/cb/publications/cmreports.htm

National Clearing House on Child Abuse and Neglect Information (2003). Child Maltreatment 2001: Summary of Key Findings. Retrieved December 15, 2003, from http://www.calib.com/nccanch

Nutt, D. J. (2000). The psychobiology of posttraumatic stress disorder. *J. Clin. Psychiatry* **61**(5): 24–32.

Perry, B. C. (2002). Childhood experience and the expression of genetic potential: What childhood neglect tells us about nature and nurture. *Brain Mind* **3** 79–100.

Perry, B. D. (1994). Neurobiological sequelae of childhood trauma: PTSD in children. In Murburg, M. (ed.), *Catecholamine Function in Posttraumatic Stress Disorder: Emerging Concepts.* Progress in Psychiatry Series #42, American Psychiatric Press, Washington, DC, pp. 233–255.

Perry, B. D. (1997). Incubated in terror: Neurodevelopmental factors in the 'cycle of violence.' In Osofsky, J. (ed.), *Children, Youth and Violence: The Search for Solutions* Guilford, New York, pp. 124–148.

Perry, B. D. (1999). Effect of traumatic events on children. *Interdiscip. Educ. Ser.* **3**(2): 1–22.

Perry, B. D., and Azad, I. (1999). Posttraumatic stress disorders in children and adolescents. *Curr. Opin. Pediatr.* **11**: 310–316.

Perry, B. D., and Pollard R. (1998). Homeostasis, stress, trauma, and adaptation. *Child Adolesc. Psychiatr. Clin. North Am.* **7**(1): 33–51.

Perry, B. D., Pollard, R., Blakley, T., Baker, W., and Vigilante, D. (1995). Childhood trauma, the neurobiology of adaptation, and "use-dependent" development of the brain: How "states" become "traits." *Infant Men. Health J.* **16**: 271–291.

Pfefferbaum, B. (1997). Posttraumatic stress disorder in children: A review of the past 10 years. *J. Am. Acad. Child Adolesc. Psychiatry* **36**(11): 1503–1511.

Pitman, R. K., and Orr, S. P. (1990). Twenty-four hour urinary cortisol and catecholamine excretion in combat-related posttraumatic stress disorder. *Biol. Psychiatry* **27**(2): 245–247.

Putnam, F. W. (1996). Posttraumatic stress disorder in children and adolescents. *Am. Psychiatr. Press Rev. Psychiatry* **15**: 447–467.

Putnam, F. W., and Trickett, P. K. (1997). Psychobiological effects of sexual abuse. *Ann. N. Y. Acad. Sci.* **821**: 150–159.

Pynoos, R. S., Steinberg, A. M., Ornitz, E. M., and Goenjian, A. K. (1997). Issues in the developmental neurobiology of traumatic stress. *Ann. N. Y. Acad. Sci.* **821**: 176–193.

Ratna, L., and Mukergee, S. (1998). The long term effects of childhood sexual abuse: Rationale for and experience of pharmacotherapy with nefazodone. *Int. J. Psychiatr. Clin. Pract.* **2**: 83–95.

Reynolds, C. R., and Kamphaus, R. W. (1992). *The Behavior Assessment System for Children*, American Guidance Service, Circle Pines, MN.

Reynolds, C. R., and Kamphaus, R. W., (2002). *The Clinician's Guide to the Behavior Assessment System for Children*, Guilford, New York.

Rodriquez, N., Ryan, S. W., and Rowan, A. B. (1996). Posttraumatic stress disorder in a clinical sample of adult survivors of childhood sexual abuse. *Child Abuse Negl.* **20**(10): 943–952.

Sapolsky, R. (1992). *Stress, the Aging Brain, and the Mechanisms of Neuron Death*, MIT Press, Cambridge, MA.

Sapolsky, R. (1996). Why stress is bad for your brain. *Science* **273**: 749–750.

Schacter, D. L. (1990). Toward a cognitive neuropsychological awareness: Implicit knowledge and anosognosia. *J. Clin. Exp. Neuropsychol.* **12**(1): 155–178.

Schacter, D. L., Koutstaal, W., and Norman, K. A. (1996). Can cognitive neurosciences illuminate the nature of traumatic childhood memories? *Curr. Opin. Neurobiol.* **6**(2): 207–214.

Schwarz, E. D., and Perry, B. D. (1994). The post-traumatic response in children and adolescent. *Psychiatr. Clin. North Am.* **2**(17): 311–326

Shin, L. M., McNally, R. J., Kosslyn, S. M., Thompson, W. L., Rauch, S. L., Alpert, N. M., Metzger, L. J., Lasko, N. B., Orr, S. P., and Pitman, R. K. (1999). Regional cerebral blood flow during script-driven imagery in childhood sexual abuse-related PTSD: A PET investigation. *Am. J. Psychiatry* **156**(4): 575–584.

Southwick, S. M., Krystal, J. H., Johnson, D. R., and Charney, D. S. (1992). Neurobiology of posttraumatic stress disorder. *Review of Psychiatry* **11**: 347–367.

Southwick, S. M., Morgan, C. A., Bremner, A. D., Grillon, C. G., Krystal, J. H., Nagy, L. M., and Charney, D. S. (1997). Noradrenergic alteration in posttraumatic stress disorder. *Ann. N. Y. Acad. Sci.* **821**, 125–141.

Southwick, S. M., Yehuda, R., and Charney, D. S. (1997). Neurobiological alterations in PTSD: Review of the clinical literature. In Fullerton, C. S., and Ursano, R. J. (eds.), *Posttraumatic Stress Disorder: Acute and Long-Term Responses to Trauma and Disaster* American Psychiatric Press, Washington, DC, pp. 241–266.

Stein, M. B., Koverola, C., Hanna, C., Torchia, M. G., and McClarty, B. (1997). Hippocampal volume in women victimized by childhood sexual abuse. *Psychol. Med.* **27**: 951–959.

Teicher, M., Glod, C., Surrey, J., and Swett, C. (1993). Early childhood abuse and limbic system ratings in adult psychiatric outpatients. *J. Neuropsychiatr Clin. Neurosci.* **5**(3): 301–306.

Teicher, M. H., Ito, Y., Glod, C. A., Anderson, S.L., Dumont, N., and Ackerman, E. (1997). Preliminary evidence for abnormal cortical development in physically and sexually abused children using EEG coherence and MRI. *Ann. N. Y. Acad. Sci.* **821**: 160–175.

Teicher, M. H., Ito, Y., Glod, C. A., Schiffer, F., and Gelbard, H. A. (1996). Neurophysiological mechanisms of stress response in children. In Pfeffer, C. (ed.), *Severe Stress and Mental Disturbance in Children*, American Psychiatric Press, Washington, DC.

U.S. Advisory Board on Child Abuse and Neglect (1995). A nation's shame: Fatal child abuse & neglect in the United States. Retrieved December 15, 2003, from http://www.ems-c.org/cfusion/resource DetailNew.cfm?id=1388226222.

U.S. Department of Health and Human Services, Administration on Children, Youth, and Families (2003). *Child Maltreatment 2001,* U.S. Government Printing Office, Washington, DC.

van der Kolk, B. (1993). Biological considerations about emotions, trauma, memory, and the brain. In Ablon, S. L., Brown, D., Khantzian, E. J., and Mack, J. E. (eds.), *Human Feelings: Explorations in Affect Development and Meanings*, Analytic Press, Hillsdale, NJ.

Wallen, S., Callaghan, M., Henry, D., and Wallen, J. (1994). Psychiatric disorders in sexually. *J. Am. Acad. Child Adolesc. Psychiatry* **33**: 313–319.

Weinstein, D., Staffelbach, D., and Biaggio, M. (2000). Attention-deficit hyperactivity disorder and posttraumatic stress disorder: Differential diagnosis in childhood sexual abuse. *Clin. Psychol. Rev.* **20**(3): 359–378.

Yehuda, R. (1997). Sensitization of the hypothalamic-pituitary-adrenal axis in posttraumatic stress disorder. *Ann. N. Y. Acad. Sci.* **821**: 57–73.

Yehuda, R. (2000). Cortisol alterations in PTSD. *International Handbook of Human Response to Trauma* Plenum, New York, pp. 265–283.

Yehuda, R., Boisoneau, D., Mason, J. W., and Giller, E. L. (1993). Glucocorticoid receptor number cortisol excretion in mood, anxiety, and psychotic disorder. *Biol. Psychiatry* **34**: 18–25.

Yehuda, R., Kahana, B., Binder-Brynes, K., Southwick, S., Mason, J., and Giller, E. (1995). Low urinary cortisol excretion in holocaust survivors with posttraumatic stress disorder. *Am. J. Psychiatry* **152**(7): 982–986.

Yehuda, R., Southwick, S. M., Nussbaum, G., Wahby, V., Giller, E. L., and Mason, J. W. (1990). Low urinary cortisol excretion in patients with posttraumatic stress disorder. *J. Nerv. Ment. Disord.* **178**(6): 366–369.