THE EFFECTS OF CHILD MALTREATMENT ON THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS

ELIZABETH VAN VOORHEES
ANGELA SCARPA
Virginia Polytechnic Institute and State University

Abnormal functioning of the hypothalamic-pituitary-adrenal (HPA) axis, a critical mammalian stress response system, has been associated with emotional responses such as anxiety and depression, as well as with behavioral and cognitive processes such as aggression, learning and memory deficits, and failure of response inhibition. This review examines the evidence for HPA axis dysregulation related to childhood maltreatment. It is concluded that child maltreatment may lead to disruptions in HPA axis functioning, and that factors such as age of maltreatment, parental responsiveness, subsequent exposure to stressors, type of maltreatment, and type of psychopathology or behavioral disturbance displayed may influence the degree and patterning of HPA disturbance.

Key words: *hypothalamic-pituitary-adrenal axis, corticotropin releasing factor, cortisol, child maltreatment*

THEORISTS HAVE POINTED to the need for a developmental psychobiological integration in the approach to understanding the effects of trauma on children (Pynoos, Steinberg, Ornitz, & Goenjian, 1997; Trickett & Putnam, 1993). One psychobiological system in particular, the hypothalamic-pituitary-adrenal (HPA) axis has been found to be involved in memory, learning, and emotions (Stansbury & Gunnar, 1994), and it appears to respond specifically to situations of psychological stress involving novelty, negative emotional valence, and feelings of lack of control (Biondi & Picardi, 1999; Lovallo, McCann, & Wilkinson, 1995). In addition, the HPA axis response has been found to be attenuated by responsive caregiving in children (Gunnar, 1993). Given these characteristics of the HPA axis, investigating this stress response system may contribute a great deal toward the goal of a developmental psychobiological integration of the childhood trauma literature. Moreover, the HPA axis seems to be involved in psychological and behavioral problems such as depression, post-traumatic stress disorder (PTSD), and aggression. In light of the strong correlation between childhood maltreatment and adult psychopathology (Horwitz, Widom, McLaughlin, & White, 2001; Widom, 1998), examination of the HPA axis also has the potential to illuminate our understanding of the mechanisms by which psychological trauma can contribute to psychopathology.

To facilitate such research, this review examines the literature on HPA axis functioning in childhood maltreatment with an eye toward identifying patterns that may be explored, as

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well as pointing out methodological issues that should be addressed in future investigations. This article is divided into three major sections. The first section provides a brief overview of the HPA axis, including each of the major hormones involved in its functioning and some of the hormones' behavioral, cognitive, and affective correlates. The second section reviews research on the effects of chronic maltreatment on the HPA axis of children, followed by an exploration of the longer-term consequences of child maltreatment reflected in the HPA functioning of adults who were maltreated as children. This section concludes with a brief review of some of the relevant animal literature on chronic stress and HPA functioning. The final section attempts to integrate the literature, make suggestions for future research, and identify some important methodological considerations.

KEY POINTS OF THE RESEARCH REVIEW

- Abnormal functioning of the HPA axis has been associated with emotional responses such as anxiety and depression, as well as cognitive and behavioral processes such as learning and memory deficits and failure of response inhibition.
- There is evidence that attachment status may have profound developmental effects on the reactivity of the HPA axis.
- Although substantial research has found HPA axis dysregulation in abused children, the nature of the disruption (i.e., increased or decreased ACTH in response to CRF, increased or decreased cortisol secretion) appears to be influenced by several factors: age of onset of abuse, parental responsiveness, continued exposure to stressors or maltreatment, type of maltreatment, and type of psychopathology or behavioral disturbance displayed.
- Early abuse may cause HPA axis hypersensitivity in some women, which may make them especially vulnerable to the effects of stress later in life. Continued exposure to stress may result in blunted HPA axis responding in those who develop depression.
- With regard to animal studies on extreme stress and HPA axis functioning, (a) chronic stress in early life may lead to long-term dysregulation of the HPA axis, (b) these stress-induced changes in HPA axis functioning may contribute to long-term alterations in mood and behavior, and (c) age of exposure and maternal responsiveness may both have profound effects on HPA axis response to extreme stress.

SECTION I: FUNCTIONING OF THE HPA AXIS

Overall Functioning

In its normal functioning, the HPA system is instrumental in coordinating an organism's response to stress. The system can be activated by a multitude of stressors, from physical insults such as surgery to psychological stimuli such as social stress, subordination, or perceived threat (Lopez, Akil, & Watson, 1999). When the HPA axis is activated, corticotropin releasing factor (CRF) is secreted from the hypothalamus, which stimulates the release of adrenocorticotropic hormone (ACTH) from the pituitary. ACTH, in turn, stimulates the release of glucocorticoids from the adrenal cortex. In addition to the direct negative feedback at the level of the hypothalamus and the pituitary, activation of glucocorticoid receptors on the hippocampus inhibit the HPA axis by reducing the release of CRF (Lopez et al., 1999; McEwen, 1994; Stansbury & Gunnar, 1994). CRF may also affect the stress reaction through other brain structures that ultimately activate the HPA axis, such as the amygdala (Graham, Heim, Goodman, Miller, & Nemeroff, 1999; Steckler & Holsboer, 1999). Finally, behavioral effects resembling depression and anxiety have been found to result from injections of CRF directly into the central nervous system of rodents and primates (Holsboer, von Bardeleben, Heuser, & Steiger, 1988; Owens & Nemeroff, 1991).

Glucocorticoids, referred to as cortisol in humans and primates and corticosterone in rodents, are the final product of the HPA axis. These steroid hormones terminate the stress response through feedback at various levels of the system. On initial activation of the system, glucocorticoids stimulate cortical arousal, increase energy, and improve the ability to concentrate. The delayed effects seem to involve a reversal of these actions, such that exposure to glucocorticoids during the span of a few days contributes to decreased energy, a decreased ability to concentrate, and depressed mood. Re-

searchers have suggested that the dual effects of glucocorticoids on the system may provide for an optimal response to the stressor at the time of exposure and then for the withdrawal required to recover from stress over time (Stansbury & Gunnar, 1994).

The presence of elevated levels of glucocorticoids has so consistently been associated with stress that it has come to be considered an indicator that a stress reaction has taken place. As suggested above, however, glucocorticoids not only may be the outcome of increased stress but also may contribute to the behavioral effects. For example, chronically high levels of glucocorticoids in rats have been found to increase the effects of central injections of CRF on anxiety-related behaviors (Lovallo & Thomas, 2000). One avenue by which glucocorticoids may modulate mood is through their effects on serotonergic receptors in the hippocampus, and possibly the cortex as well (Lopez et al., 1999; Lopez, Vazquez, Halmers, & Watson, 1997).

Glucocorticoids may also have modulatory effects on the dopamanergic system. In one investigation (Lyons, Lopez, Yang, & Schatzberg, 2000), researchers found that chronic treatment with cortisol in squirrel monkeys led to a failure to inhibit goal-directed responses, very similar to performance failures associated with the administration of drugs known to decrease dopamine activity in the prefrontal cortex. Lyons et al. (2000) noted that individuals with psychotic depression, a subgroup of depressives with especially high levels of circulating glucocorticoids, as well as persons with Cushing's disease, both tend to perform poorly on tasks of attention and response inhibition.

In addition to the above-mentioned effects on emotion and behavior, it appears that glucocorticoids may have profound effects on learning and memory (Lupien & McEwen, 1997). Most of the research on the effect of glucocorticoids on learning and memory focuses on the hippocampus, an area of the brain central to contextual learning, as well as spatial, episodic, and declarative memory (Bremner, Southwick, & Charney, 1999; McEwen & Magarinos, 1997, 2001). McEwen and his colleagues (McEwen, 1982, 2001; McEwen & Magarinos, 1997, 2001) have done substantial work investigating the effects of stress-induced glucocorticoid elevations on hippocampally mediated learning and memory. It appears that there may be a U-shaped effect of glucocorticoids on hippocampal-related memory functioning (McEwen & Magarinos, 2001), such that basal levels of glucocorticoids are necessary for the proper functioning of learning mechanisms, but at stress levels they begin to interfere. Moreover, McEwen and his colleagues have found that high levels of glucocorticoids can lead to changes in the physical structure of the hippocampus by suppressing the growth or development of neurons. These changes may be associated with the observed learning and memory deficits.

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Glucocorticoids also modulate the formation of emotional memory. That is, long-term memory for emotional events may actually be enhanced by elevated levels of cortisol in humans (Buchanan & Lovallo, 2001). Furthermore, this effect may be mediated by glucocorticoid activity in specific areas of the amygdala (Lupien & McEwen, 1997).

In sum, the HPA axis has been associated with emotional responses such as anxiety and depressed mood, as well as with cognitive and behavioral processes (i.e., learning, memory, and failure of response inhibition). These responses may be modulated by functioning of the hippocampus and amygdala as well as through brain pathways that involve the neurotransmitters serotonin or dopamine.

HPA Axis Dysfunction

Stress-related HPA axis disruption also has been implicated in several psychiatric disorders that involve mood disturbance and cognitive impairment. As may be surmised from the above discussion, disruptions of HPA functioning can occur at any level along the axis. However, much of the research on HPA axis

dysregulation in mood and anxiety disorders distinguishes between two pathological states of glucocorticoid secretion: *hypercortisolism*, a relative overproduction of glucocorticoids, and *hypocortisolism*, a relative underproduction of glucocorticoids.

Hypercortisolism has been strongly associated in the literature with depression. Though not all depressed individuals exhibit elevated levels of cortisol production, a substantial percentage do, particularly those with melancholic and psychotic features (Evans, 1988). A review of the literature on hypercortisolism and mental illness (Krishnan, Nemeroff, & Carroll, 1989) and subsequent research conclude that CRF is hypersecreted in individuals with depression both in the hypothalamus and in other brain structures, and that this hypersecretion leads to blunting of ACTH response to CRF (Graham et al., 1999; Owens & Nemeroff, 1991). Furthermore, enlarged adrenal glands have been found in individuals with major depression (Nemeroff et al., 1992), probably due to high levels of ACTH. This may result in the overproduction of cortisol to stimulation by "normal" levels of ACTH (Holsboer et al., 1988).

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Glucocorticoid receptors have also been found to be decreased in both sensitivity and number in individuals with depression, which may be the result of down-regulation in response to the excessive production of cortisol. This glucocorticoid receptor insensitivity may prevent cortisol from functioning as effectively to "turn off" ACTH secretion at the level of the pituitary. Finally, individuals with depression tend not to suppress cortisol production in response to the administration of dexamethasone, a steroid that mimics the action of cortisol at the negative feedback receptors (Krishnan et al., 1989).

Although the connection between hypercortisolism and depression in adults is fairly well supported, this relationship has not been as thoroughly investigated in children. A recent study by Birmaher et al. (1993) examines the response to CRF administration among children ages 6 to 13 with major depression. Although Birmaher et al. found no differences in response to CRF administration between depressed and control children on measures of either ACTH or cortisol secretion, they did find interesting subgroup differences. A decrease in post-CRF ACTH levels was found in melancholic depressed children when compared to nonmelancholics, without a parallel decrease in post-CRF cortisol levels. As with adults, this could reflect a relative enlargement of the adrenal cortex in children with melancholic depression. In addition, baseline cortisol levels were found to be higher in both suicidal and melancholic depressed children relative to nonsuicidal and nonmelancholic children.

A few studies examine basal cortisol levels in children and adolescents with major depression. Some studies of prepubertal depressed children (Puig-Antich et al., 1989) and adolescents (Dahl et al., 1991) fail to show significant differences between depressed children and normal controls (Birmaher et al., 1992). A series of studies by Goodyer and colleagues (Goodyer et al., 1996; Goodyer, Herbert, Moor, & Altham, 1991), however, suggest that elevated cortisol levels in children and adolescents with depression may be related to the severity of the disorder, that cortisol levels decline on recovery, and that children may exhibit a similar flattening of the diurnal rhythm of cortisol secretion during depressive episodes as do adults. Furthermore, these researchers suggested that increased cortisol in depression may be associated with abnormal cognitive and emotional processes in children and adolescents.

Contrary to what is found in depression, research suggests that PTSD may be characterized by low levels of cortisol secretion (i.e., hypocortisolism). This has been observed both at baseline and in response to dexamethasone. Like depression, emotional and cognitive dysfunction in this disorder have been linked to

dysregulation of the HPA axis (Bremner et al., 1999; Yehuda, 1997, 1998). Also like in depression, there is evidence that CRF secretion is elevated in PTSD. In addition, CRF stimulation tests have found a blunted ACTH response to CRF administered to combat veterans with PTSD, in sexually abused girls, and in women with chronic pelvic pain and PTSD who have experienced sexual abuse (Yehuda, 1998). Also relevant, several of the symptoms of PTSD, including hypervigilance, exaggerated startle, avoidance behavior, and increased autonomic reactivity, are similar to those associated with increased CRF (Graham et al., 1999).

However, studies employing metyrapone, a substance that prevents the production of cortisol from its precursors in the adrenal cortex, suggest that the mechanism of blunted ACTH response in PTSD may be different than in depression. On administration of metyrapone to normal volunteers, levels of ACTH secretion increase by a factor of 2 to 4. However, ACTH secretion was 4 times greater in response to metyrapone administration in combat veterans with PTSD than in normal controls. This suggests that contrary to the pituitary receptor insensitivity to cortisol found in major depression, individuals with PTSD may have a heightened pituitary glucocorticoid receptor sensitivity. In addition, glucocorticoid receptor numbers have been found to be increased in PTSD, in contrast to the decreased number found in major depression (Yehuda, 1998).

Reactions to the administration of dexamethasone also differ between depression and PTSD. Although cortisol response in PTSD victims to the normal dexamethasone administration of 1 mg is slightly lower or the same as in normal controls, Yehuda (1998) has found a significant decrease in cortisol release in PTSD victims to doses of .50 and .25 mg of dexamethasone. This finding suggests a hypersuppression of ACTH by dexamethasone and therefore, presumably also by cortisol, due to heightened glucocorticoid receptor sensitivity. Similar results have been found in adolescents with PTSD resulting from exposure to the Armenian earthquake of 1988 (Goenjian, Yehuda, Pynoos, & Steinberg, 1996).

A recent study by Kanter et al. (2001) suggests, however, that increased receptor sensitivity may not be the only mechanism by which cortisol secretion is reduced in PTSD. These researchers administered metyrapone to Vietnam veterans with PTSD and control participants to block cortisol synthesis and then reintroduced cortisol intravenously. Although baseline cortisol was found to be lower in the veterans with PTSD than in the control subjects, ACTH levels were not found to differ between the two groups in response to the intravenous reintroduction of cortisol. This suggests that increased glucocorticoid receptor sensitivity alone could not account for decreased cortisol secretion in individuals with PTSD. Kanter et al. suggested, however, that adrenal hyporesponsivity to ACTH, in combination with glucocorticoid receptor sensitivity, may produce such findings. Such a proposed mechanism would mean that the pattern of HPA axis dysfunction in PTSD (adrenal hyporesponsivity to ACTH and increased glucocorticoid receptor sensitivity) is opposite that found in depression (adrenal hyperresponsivity to ACTH and decreased glucocorticoid receptor sensitivity).

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Finally, some researchers have found evidence that PTSD is associated with decreased hippocampal volume in adults (Bremner et al., 1999). Yehuda (1997) suggested that although cortisol secretion appears to be decreased in PTSD, the increased glucocorticoid receptor sensitivity in PTSD may make hippocampal receptors especially vulnerable to the damaging affects of cortisol. Also, the persistent reexperiencing of traumatic events in the form of nightmares, flashbacks, and hyperarousal to traumatic cues may produce periodic elevations in cortisol levels that could result in hippocampal damage (McEwen & Magarinos, 2001). Such changes to hippocampal structure in PTSD have been associated with loss of cognitive function, especially hippocampally mediated memory functioning such as explicit

verbal memory (Bremner et al., 1999; Bremner, 2001).

It is relevant, however, that De Bellis and colleagues have not found the same decrease in hippocampal volume in traumatized children. In two independent samples of children and adolescents with PTSD, no decreases in hippocampal volume were observed in comparison with control participants (De Bellis Keshavan, et al., 1999; De Bellis, 2002). Furthermore, in a 2-year longitudinal study of 9 children with PTSD and 9 sociodemographically matched controls, no differences in hippocampal volume were detected during the course of the investigation (De Bellis, Hall, Boring, Frustaci, & Moritz, 2001). De Bellis et al. (2001) suggested possible explanations for the differences in findings between children and adults. First, adults with PTSD suffer from a high degree of comorbidity with other psychiatric disorders, including alcohol and substance abuse. Such comorbid disorders may contribute to the differences in hippocampal volume observed in adults. It is also possible that disclosure of abuse and the subsequent improvements in environmental circumstances may contribute to normalization of neural development in the hippocampus. When combined with the enhanced plasticity of the developing brain, these changes may "mask" the effects of the trauma in children.

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Apart from the findings of hypocortisolism in individuals with PTSD, some evidence has been found for decreased cortisol levels in aggressive children. Studies by McBurnett and colleagues (McBurnett, Lahey, Capasso, & Loeber, 1996; McBurnett, Lahey, Rathouz, & Loeber, 2000), for example, suggest that antisocial behavior characterized by early onset and overt aggression may be related to lower cortisol levels. Furthermore, a link has been found between the presence of antisocial personality disorder with a history of conduct disorder in fathers and low cortisol levels in their sons (Vanyukov et al., 1993). However, a review of the literature found only one study that examines the relationship between CRF levels and aggression in children (Susman et al., 1999), and this was in a special population (i.e., pregnant aggressive adolescents). In addition, no research, to the authors' knowledge, investigates dexamethasone suppression or metyrapone administration in aggressive children. As such, it is unclear whether the mechanism underlying the hypocortisolism observed in aggressive children is similar to that observed in PTSD.

SECTION II: HPA SYSTEM DISTURBANCE IN CHRONIC CHILDHOOD TRAUMA

The research reviewed above strongly suggests that disturbances of the HPA axis are related to mood dysregulation and cognitive dysfunction. This section will review evidence that suggests that child maltreatment can lead to such HPA axis dysfunction. Research suggesting the possibility of moderating factors in this relationship will also be explored.

Developmental Considerations: Attachment Security and Coping

Because perceived uncontrollability and unpredictability have been found to be powerful activators of the HPA system, the internalization of the feeling of security in one's environment and the perception of the ability to cope with environmental events are likely to be critical mediators of the HPA response to stress in children. Gunnar and colleagues (Gunnar, 1993, 1998; Hertsgaard, Gunnar, Erickson, & Nachmias, 1995) have conducted research that demonstrates that attachment status is, in fact, associated with children's responses to novel, frightening, or aversive stimuli.

Behaviorally inhibited children are one population where attachment status has been shown to modulate HPA functioning. Behaviorally inhibited children have been found to exhibit higher morning cortisol levels and higher cortisol reactivity to novel events than uninhibited children, and longitudinal studies demonstrate that they are at a higher risk for the development of anxiety disorders than their peers (Kagan, Reznick, & Snidman, 1988). However, Gunnar's work suggests that

attachment security may mediate the relationship between behavioral inhibition and HPA reactivity. In a study of 18-month-old toddlers and their mothers, it was found that only behaviorally inhibited toddlers in insecure attachment relationships exhibited elevations in cortisol in response to a series of novel events (Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996). Neither behaviorally inhibited toddlers in secure attachment relationships nor behaviorally uninhibited toddlers displayed such cortisol reactivity. Thus, the vulnerability of an inhibited temperament may be a liability only if the child is not provided with the caregiver support that allows him or her to feel safe in the face of potentially threatening stimuli.

In addition, children who spent their first 8 months of life or more in overcrowded Romanian orphanages and who thus, did not have the opportunity to develop appropriate attachment relationships, have been found to exhibit elevated levels of cortisol when compared to children who spent only their first 4 months in these orphanages (Gunnar, 2000). The degree of cortisol elevation in these children, as well as the degree of their cognitive and emotional impairment, was found to be associated with the length of time they spent in orphanages before being adopted into Canadian homes.

The research discussed above suggests that attachment security may have a profound effect not only on children's subsequent emotional development but also on the reactivity of their HPA systems to stress. These findings suggest that if disruptions to HPA axis functioning can be affected by maladaptive rearing environments that are not necessarily abusive, disruptions to this system may be especially profound in environments that also include overt physical or sexual maltreatment.

Studies With Maltreated Children

Kaufman (1991) published a preliminary examination of cortisol secretion in 56 seven- to twelve-year-old maltreated children, reporting an increase, rather than the normal decrease, in cortisol secretion from midmorning to midafternoon. Kaufman also found that those children who were both maltreated and met criteria for major depression were most likely to exhibit this cortisol abnormality. This finding was replicated and extended by Hart, Gunnar, and Cicchetti (1996) who examined cortisol levels in 131 maltreated and 66 nonmaltreated children attending a day camp. Maltreatment was defined as family involvement with child protective services, whether or not the child was individually identified as having been abused. Control children were recruited from families with similarly economically disadvantaged backgrounds. Overall, Hart et al. found that the maltreated children exhibited cortisol levels similar to nonmaltreated children in the morning but were likely to show less of a decrease from morning to afternoon. Within the depressed cohort, morning cortisol levels were lower in maltreated than nonmaltreated children, and some depressed maltreated children actually showed an atypical increase in cortisol levels from the morning to the afternoon. Finally, children with externalizing symptoms, regardless of maltreatment type, were found to have lower cortisol levels.

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In a follow-up to her 1991 study, Kaufman et al. (1997) investigated HPA axis functioning by administering the CRF stimulation test to 13 depressed maltreated, 13 depressed nonmaltreated, and 13 normal control children. Of the 13 depressed maltreated children, 8 also met criteria for PTSD secondary to their maltreatment. Contrary to the authors' expectation of finding decreased ACTH response to CRF administration in depressed-maltreated children, they found an overall *increase* in post-CRF ACTH release. Kaufman et al. found no differences in cortisol secretion. On further scrutiny of the data, these researchers observed that there was a bimodal distribution of ACTH response to CRF administration in the depressed maltreated children, with some being "ACTH responders" and some being "ACTH non-

responders." One factor emerged that distinguished the two groups: Those children that were ACTH responders were living in environments where they were exposed to continuing emotional maltreatment. Citing research with animals, Kaufman et al. noted that exposure to chronic stress, over time, appears to result in the return of ACTH responding to baseline, but that if a novel stressor is superimposed on the chronic stressor, ACTH response may be augmented. Thus, they hypothesized that the HPA axis of both subsets of children with histories of maltreatment may have exhibited compensatory HPA responses, but that those experiencing chronic adversity showed a heightened response to the continued emotional maltreatment.

Taken together, the pattern observed in depressed maltreated children suggests that they may show a decreased range of cortisol secretion during the diurnal cycle and if they are not reexposed to further maltreatment, blunted ACTH to CRF infusion. This pattern is similar to that found in depressed adults, with the exception that the overall hypercortisolism typically found in depressed adults was not observed.

Significantly greater concentrations of 24-hour urinary free cortisol were found in maltreated children compared to nonpsychiatric control children but not to children with overanxious disorder. PTSD symptoms were also found to positively correlate with concentrations of urinary free cortisol.

Others, however, have observed increases in basal cortisol in maltreated children (De Bellis et al., 1994; De Bellis, Baum et al., 1999). De Bellis et al. (1994), for example, examined 24-hour cortisol release as well as ACTH and cortisol response to CRF administration in 13 sexually abused girls compared to a control group matched for gender, age, race, family constellation, sexual development, and socioeconomic status. No significant differences were found in basal mean or CRF-stimulated cortisol release between the two groups, although a trend toward higher basal cortisol was found in sexually abused girls. The small number of subjects (13 per group) may have decreased the power needed to detect significant differences that may indeed have been present. The sexually abused girls also were found to have significantly lower mean basal and net CRF-stimulated ACTH levels than nonabused girls. In interpreting their results, De Bellis et al. suggested that hypersecretion of CRF associated with the stress of the maltreatment may have resulted in a down-regulation of pituitary CRF receptors, leading to a reduction in ACTH release. Similar to findings with depression, they speculated that this initial hypersecretion may have led to an enlargement of the adrenal cortex. Such adrenal enlargement may, in turn, have resulted in increased cortisol production in response to reduced ACTH. This would be consistent with the fact that the sexually abused girls had higher rates of dysthymia, suicidal ideation, and suicide attempts. As such, this group would be similar to the depressed maltreated ACTH nonresponders in Kaufman et al. (1997).

Another study of sexually abused girls also finds that these children exhibit significantly reduced mean basal and CRF-stimulated ACTH response, although the authors found no differences in mean basal or CRF-stimulated cortisol secretion (Putnam & Trickett, 1997). Unfortunately, it is unclear from the report how many subjects were administered the CRF-stimulation test in Putnam and Trickett's (1997) study, so it is difficult to interpret the data. However, in general, these findings seem to support the findings by De Bellis et al. (1994).

In a second study by De Bellis, Baum et al. (1999), a child maltreatment group (including neglect, physical abuse, sexual abuse, and emotional maltreatment) was compared to two control groups (i.e., nonmaltreated children with overanxious disorder and nonpsychiatric controls). At the time of the study, all participants were living in stable, nonabusive environments. Significantly greater concentrations of 24-hour urinary free cortisol were found in maltreated children compared to nonpsychiatric control children but not to children with overanxious disorder. PTSD symptoms were also found to positively correlate with concentrations of urinary free cortisol. Thus, although these maltreated children exhibited the hypercortisolism

associated with depression in adults, their PTSD symptoms were associated with *elevations* in cortisol levels, precisely opposite of what has been found in adults with PTSD. De Bellis et al. proposed a developmental hypothesis that the increased cortisol observed in the short-term may lead to enhanced negative feedback at the level of the pituitary in the long-term, which in turn could lead to the decreased cortisol levels seen in adult PTSD over time. These findings were replicated in a study by Carrion et al. (2002) in which salivary cortisol was found to be increased in a sample of 51 children with PTSD as compared to age- and gender-matched healthy controls.

Hart, Gunnar, and Cicchetti (1995) examined the relationship between cortisol excretion and social competence in maltreated children between the ages of 47 and 75 months (3.9 to 6.3 years of age). In this study, maltreatment was defined as physical, sexual, or emotional abuse or as physical neglect. Cortisol levels were collected at a therapeutic preschool for maltreated children for a period of 31 days between the hours of 10:30 a.m. and 11:45 a.m. Cortisol levels for control children were collected by the same procedure at a separate preschool serving low socioeconomic status families. Hart et al. (1995) found that the control group exhibited significantly higher cortisol on high-conflict days than on low-conflict days, whereas the maltreated children did not. It was suggested that the cortisol response of the control children to high-conflict days was reflective of adaptive functioning and of a willingness to engage in social interaction despite conflict. This pattern of elevated cortisol on high-conflict days was not found in the maltreated children, possibly reflecting their tendency to withdraw from conflict, similar to socially incompetent children. However, Hart et al. went on to observe that maltreated children also did not exhibit increased cortisol on days where they did not withdraw but indeed, had to be physically restrained to calm them. Thus, rather than a tendency to withdraw and avoid conflict, it was suggested that these findings reflected an overall lack of cortisol "reactivity" to stress in maltreated children. It is equally possible to conclude, however, that aggressive behavior that may have required the restraint, and not maltreatment status per se, accounted for the lower cortisol levels. This interpretation would be consistent with findings indicating that aggressive children have lower levels of cortisol than their peers (McBurnett et al., 1996, 2000; Pajer, Gardner, Rubin, Perel, & Neal, 2001).

The above studies of HPA functioning in maltreated children show mixed results, with some indicating hypercortisolism, some a decreased range of cortisol reactivity and hypocortisolism, and still others no difference in cortisol responses. These mixed findings may reflect the diversity of psychological disorders and problems found in this population, including depression, PTSD, and aggressive behavior. A recent study by Cicchetti and Rogosch (2001) also may shed light on these conflicting findings, suggesting that type of maltreatment may show different patterns of cortisol responsivity. In Cicchetti and Rogosch's study, cortisol samples were collected at 9:00 a.m. and 4:00 p.m. on each day of a 5-day camp experience. The sample included 16 children who were both sexually and physically maltreated, 12 children who had been sexually but not physically maltreated, 49 children who had been physically but not sexually maltreated, 76 children who had been neglected but not physically or sexually maltreated, and 21 children who had suffered emotional maltreatment but no other form of abuse. The control group consisted of 209 nonmaltreated children from similarly deprived economic backgrounds. Overall, Cicchetti and Rogosch found no differences in morning and evening cortisol values between the maltreated and nonmaltreated groups and no evidence of differences in the patterns of diurnal change. However, they did find significant differences among the maltreatment groups. Children who had suffered the most pervasive abuse (i.e., those that were both phys-

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ically and sexually maltreated) exhibited the highest morning cortisol levels, consistent with findings of increased basal cortisol in De Bellis et al. (1994) and De Bellis, Baum et al. (1999). Severity of sexual abuse was found to explain the most variance in elevated morning cortisol levels in this group, and those children that had suffered sexual and not physical abuse also had significantly elevated morning cortisol levels when compared to normal controls and to other maltreatment groups. It is interesting that the physically abused group showed a trend toward *lower* morning cortisol levels than both the other maltreated children and the normal controls. Thus, these children showed a pattern of reduced cortisol secretion similar to what has been found in studies of aggressive children.

In the Cicchetti and Rogosch (2001) study, therefore, children showed different patterns of cortisol secretion based on their history of maltreatment. In addition to the type of maltreatment, however, it may be important that diagnostic status and attachment to caregivers be taken into consideration in interpreting cortisol data. Regarding diagnosis, none of the studies discussed above clearly distinguish maltreated children suffering from PTSD from children suffering from comorbid PTSD and depression or depression alone. In studies with adults, Yehuda (Griffin, Resick, & Yehuda, 2001) has found that adults suffering from "pure" PTSD tend to exhibit the characteristic reduced baseline cortisol secretion, but that adults with comorbid PTSD and depression may not. Thus, clarifying the specific pathology associated with the abuse suffered by maltreated children may be central in detecting the patterning of HPA axis dysregulation expressed. In the study by Cicchetti and Rogosch, for example, it could be that children experiencing sexual and physical abuse also have a tendency to respond with greater depression and thus, elevated cortisol. Conversely, children who have suffered physical but not sexual abuse may tend to respond with more PTSD symptomatology or aggression and thus, lower cortisol levels. Overall, it will be difficult to determine if children exhibit similar or different HPA axis patterning in response to maltreatment as do adults until such diagnostic distinctions are made.

In addition to the type of maltreatment, however, it may be important that diagnostic status and attachment to caregivers be taken into consideration in interpreting cortisol data.

Regarding attachment status, research suggests that secure attachment to a caregiver may mitigate some of the effects of stress on HPA axis functioning (Gunnar, 1993, 1998; Hertsgaard et al., 1995; Nachmias et al., 1996), and that continued exposure to emotional maltreatment may affect the manifestation of the disruption to the HPA system (Kaufman et al., 1997). However, the quality of the caregiver-child relationship has not been assessed in most studies of HPA axis functioning and child maltreatment. Again, such factors need to be taken into consideration before a clear understanding of the effects of maltreatment on HPA functioning in children can be achieved.

It is important to realize, however, as emphasized by Cicchetti and Rogosch (2001) in their most recent study, that it is unclear whether the dysregulated patterns of cortisol secretion found in maltreated children are permanent. Some of the research with animals has suggested that these abnormalities may be reversible, and that psychopharmacological treatment may be effective in reducing or reversing some of the damage to the HPA system that is observed (O'Brien, Skelton, Owens, & Nemeroff, 2001). Furthermore, the availability of attachment figures at critical periods of children's development may play a significant role in the effects of stress on behavior, cognitive disturbances, and HPA axis functioning (Gunnar, 2000). Although aberrant patterns of HPA activity suggest that maladaptive physiological responses are beginning to take place in maltreated children, the multitude of factors that could both contribute to and buffer children from the progression of this dysfunction suggest that permanent emotional and cognitive disturbance is not inevitable. Thus, although these children may all experience extreme stress at a vulnerable period, there is still considerable multifinality in their presentation.

Studies of Adults Maltreated as Children

Information on the HPA system in adults who were maltreated as children is reviewed in an effort to examine the potential long-term affect of maltreatment on endocrine functioning. Based on research with animals, Heim, Newport, Bonsall, Miller, and Nemeroff (2001) have hypothesized that early overwhelming stress sensitizes the HPA axis to the effects of later stressors. Partially consistent with this notion, they found that adult women who had experienced maltreatment but who were not diagnosed with depression exhibited a higher ACTH response to CRF stimulation, a lower cortisol response to ACTH stimulation, and lower baseline cortisol levels than control women or abused women with depression. Heim et al. suggested that this could indicate a sensitized HPA axis in abused nondepressed women, in that there was evidence of hyperactive responding of the pituitary to CRF. A reduction in cortisol secretion in response to ACTH was also found, however, suggesting atrophy or deterioration of the adrenal cortex. This overall pattern of sensitized HPA axis functioning could leave these women vulnerable to the effects of later stress. This conclusion seems consistent with the findings of Kaufman et al. (1997), who noted that ACTH responders consisted of a subgroup of maltreated children who had been reexposed to maltreatment. On the other hand, the Heim et al. study reveals *decreased* ACTH responding to the CRF-stimulation test in abused women with depression, suggesting a reduction in or blunting of pituitary CRF receptors. These women also had a higher incidence of comorbid PTSD and reported greater levels of current life stress than did the abused women without depression. The authors concluded that the women's exposure to continued chronic stress in adulthood may have resulted in a persistent increase in CRF release, leading to the eventual down-regulation or desensitization of pituitary CRF receptors.

In a study of HPA axis responsivity to a public speaking and mental arithmetic stressor task in women abused as children, Heim et al. (2000) also found augmented HPA axis responding in the abused women as compared to controls. However, in this study, both ACTH and cortisol levels were higher in abused women than in controls, with the most pronounced response found in abused women with current depression. Heim et al. suggested that the different findings in this study from the CRF-stimulation study may reflect a hypersecretion of CRF in stressful situations among the abused women, and particularly among the depressed abused women. This excessive increase may have overridden the down-regulation of pituitary ACTH receptors hypothesized to account for the decreased ACTH response in depressed abused women after exogenous CRF administration (Heim et al., 2001).

Lastly, a study by Stein, Koverola, Hanna, Torchia, and McClarty (1997) finds that women who had suffered childhood sexual abuse exhibited an enhanced suppression of cortisol in response to a low dose (0.5 mg) of dexamethasone, similar to that found in combat veterans with PTSD. The authors suggested that this may be due to enhanced negative feedback of cortisol at the level of the pituitary due to sensitized glucocorticoid receptors.

Again, the results of the few studies of adults abused as children are mixed. Taken together, however, a picture emerges suggesting a hypersensitivity of the HPA axis in some women abused as children, which may, in turn, make them especially vulnerable to the effects of stress later in life. With time, however, down-regulation of pituitary CRF receptors and/or decreased negative feedback receptor sensitivity may lead to blunted HPA axis responding in those who develop depression. These latter findings are more consistent with the overall blunting of ACTH responding in studies of depressed maltreated children. These interpretations must be viewed with caution, however, as so few studies of adult survivors of abuse have been conducted,

The authors concluded that the women's exposure to continued chronic stress in adulthood may have resulted in a persistent increase in CRF release, leading to the eventual down-regulation or desensitization of pituitary CRF receptors.

and the majority have included only female samples.

Animal Studies

The research with humans reviewed above leaves unanswered several questions that can be addressed through animal studies. Three of these questions will be addressed here. First, the human research suggests that traumatic stress in childhood can lead to alterations in HPA functioning. However, it is conceivable that preexisting HPA axis abnormalities may lead to increased vulnerability to stress. Thus, the first question addressed here is, Given controlled genetic and environmental variables, can chronic stress result in long-term dysregulation of the HPA axis? Secondly, human research involving exogenous administration of HPA axis hormones such as cortisol suggests that temporary alterations of HPA functioning transiently affect mood and cognition. However, is there evidence that chronic, stress-induced HPA axis changes can result in long-term changes in mood and behavior? This question can be answered through the induction of chronic stress in otherwise tightly controlled animals, which are subsequently tested for both hormone levels and cognitive/affective and behavioral performance. Finally, what factors are involved in the various patterns of HPA axis response to chronic stress? Although the answer to this question remains unclear despite substantial animal research, there is some evidence that the age at which the stress occurs and the maternal response to her neonate's stress exposure may both have an impact. It is important to note, however, that although animal studies can help to fill gaps in the human literature, extrapolation of findings from animals to humans must be done with extreme caution.

Given controlled genetic and environmental variables, can chronic stress result in long-term dysregulation of the HPA axis? A great deal of research with both rats and monkeys suggests that the answer to the above question is yes. Maternal deprivation is commonly used as a stressful experience in studies of HPA axis functioning in neonatal rats. This procedure has been reliably found to result in HPA axis alterations in the neonate that may persist into later life. For example, it has been found that rat pups that were separated from their mothers for 1 hour per day for 9 days exhibited significantly higher corticosterone levels to further separation than the control pups (McCormick, Kehoe, & Kovacs, 1998). This suggests that chronic stress in neonatal rats may result in sensitization to the effects of later early-life stress.

There is also evidence that neonatal stress can have even longer term effects on HPA axis functioning in rats, perhaps persisting into adulthood. One recent study by Plotsky and Meaney (1993) examines basal and stress-induced CRF response in rats that had been separated for 3 hours a day from Perinatal Days 2 to 14. Plotsky and Meaney found increased basal levels of CRF in adult rats subjected to maternal separation when compared to controls, as well as increased CRF depletion in the hypothalamus (suggesting elevated levels of secretion) and increased corticosterone release in response to 20 minutes of restraint stress in adulthood. A second study also found increased basal and stress-induced ACTH release in response to foot shock in adult male rats exposed to 6 hours of maternal deprivation from Perinatal Days 2 to 20 as compared to controls, as well as increased CRF release in the hypothalamus and decreased pituitary CRF receptor binding (Ladd, Owens, & Nemeroff, 1996). Finally, a third study found that rats exposed to 4.5 hours of maternal deprivation during the first 3 weeks of life responded with *decreased* corticosterone release to restraint stress in adulthood (Ogawa et al., 1994). Although these results at first appear to conflict with the results of Plotsky and Meany, research by van Oers, de Kloet, and Levine (1997) suggests that the timing of stress may influence the endocrine alterations. For example, van Oers et al. found that 24-hour periods of maternal deprivation on Perinatal Days 3 to 4 produced adult rats with hyperreactive ACTH secretion in response to saline injection, whereas those deprived at Perinatal Days 7 to 8 or 11 to 12 exhibited a hyporeactive ACTH response to saline injection in adulthood. Thus, there is evidence that the stress of relatively long periods of maternal deprivation in the neonatal rat can result

in dysregulation of the HPA axis in adulthood, although the direction of the altered response may depend on factors such as age of exposure to the stressor.

Is there evidence that chronic, stress-induced HPA axis changes can induce long-term changes in mood and behavior? There is also evidence to suggest that stress-induced changes to HPA axis functioning in rats and primates does contribute to long-term alterations in mood and behavior. The most convincing research has involved stress-induced HPA changes and behavioral dysfunction in primates. Perhaps the most cited work in this regard is Coplan et al.'s (1996) study involving the effects of a variable foraging paradigm on the offspring of female bonnet macaques. Adult female bonnet macaques with infants approximately 17 weeks of age were exposed to one of three food availability conditions: consistently low foraging demand, requiring little effort to find adequate nutrition; consistently high foraging demand, requiring substantially more effort to obtain adequate nutrition; and variable foraging demand, where foraging demand varied between high and low, alternating every 2 weeks during a 12-week period. In contrast to the normal maternal behavior of the mothers in the low foraging demand and high foraging demand conditions, the mothers subjected to the uncertainty and stress of the variable foraging demand were observed to engage in "inconsistent and erratic, and sometimes dismissing rearing behavior" (Coplan et al., 1996, p. 1622) with their offspring. Compared to the offspring of the mothers in the other two conditions, the offspring of these mothers were found to be more reactive to stressful or novel environments immediately following the investigation and less social and more subordinate as young adults. Also, the variable foraging demand offspring were found to have significantly higher levels of CRF and significantly lower CSF cortisol levels than the high foraging demand or low foraging demand offspring years after the manipulation. Coplan et al. noted that this hormonal profile is similar to that observed in individuals with PTSD.

Another study finding both behavioral and hormonal abnormalities related to early adverse rearing used a peer-rearing versus mother-rearing paradigm (Fahlke et al., 2000). In this study, 97 infant rhesus macaques were randomly assigned to be reared with access to peers only (peer reared) or to be reared normally by their mothers (mother-reared controls) for the first 6 months of their lives. At 6 months old, the monkeys were subjected to four consecutive 4-day-long separations from either their mothers or their peers interspersed with 3-day-long reunion periods. Fahlke et al. (2000) found that the peer-reared monkeys exhibited higher cortisol secretion in response to the separation challenge than did the mother-reared monkeys. Those peer-reared monkeys with increased cortisol secretion also drank excessive amounts of alcohol as adults, and peer-reared monkeys overall were found to exhibit trait-like anxiety as demonstrated by increased clinging to one another, low levels of play, and increased self-directed behavior. Taken together, the animal research cited here is consistent with the possibility that chronic, stress-induced changes to HPA axis functioning can contribute to long-term disruptions of mood and behavior.

What factors are involved in the various patterns of HPA axis response to chronic stress? Finally, although it is unclear what factors are involved in the various patterns of HPA axis response to chronic stress, two have been addressed most clearly in the animal literature. The first, age at the time of the stressor, has been mentioned above. The second is the behavior of the mother toward the neonate after it is subjected to the stressor. Early researchers on stress in rodents commonly used a "handling" paradigm, whereby the neonatal rat was removed from its mother, handled for approximately 15 minutes, and returned to the home cage. These researchers often found a decreased behavioral and endocrine response to stress or novelty in adulthood in these neonatally handled animals, leading them to conclude that this procedure somehow afforded the manipulated neonates a more adaptive response (Levine, 1962). However, longer separation from the

Coplan et al. noted that this hormonal profile is similar to that observed in individuals with PTSD.

mother, as in the maternal deprivation paradigm, usually results in just the opposite response—increased behavioral reactivity, increased CRF release, and either increased or decreased ACTH and cortisol response to stress in adulthood (van Oers et al., 1997; van Oers, de Kloet, & Levine, 1998).

The factor that seems to account for the differences in handled versus separated pup responses is maternal behavior. It has been found that handled pups respond with increased ultrasonic vocalizations aimed at eliciting maternal care and when the pups are returned to their cages, their mothers respond with increased licking and grooming of the infants and increased "arched-back" nursing (Francis et al., 1996). A study examining the natural variations in licking and grooming behaviors among rat mothers found that the offspring of higher licking and grooming mothers showed reduced ACTH and corticosterone response to stress, increased glucocorticoid feedback sensitivity, and changes in CRF gene expression in both the hypothalamus and the hippocampus (Liu et al., 1997). High licking and grooming offspring have also been found to have increased levels of proteins involved in the growth of neural synapses in the hippocampus, as well as increased performance on spatial learning/memory tasks (Bredy, Weaver, Champagne, & Meaney, 2001). Finally, some of the endocrine effects of maternal deprivation on neonatal rats have been found to be reduced by stroking similar to that performed by rat mothers (Suchecki, Rosenfeld, & Levine, 1993; van Oers, de Kloet, Whelan, & Levine, 1998).

Taken together, these studies suggest that early in life, maternal interaction with neonates may serve to "set" HPA axis responsivity. Some researchers have postulated that this may be an adaptive process, as offspring are likely to live in the same environmental niche as their parents. Thus, through her behavior, a mother communicates to her infant much about the surroundings it will likely encounter. For example, if a bonnet macaque mother is subjected to the stressful environment of uncertain food availability, she will communicate that uncertainty to her infant through her less involved maternal behavior. The infant will then develop a stress response that is more attuned to threat than will an animal whose mother did not face such uncertainties regarding survival (Bredy et al., 2001).

Taken together, these studies suggest that early in life, maternal interaction with neonates may serve to "set" HPA axis responsivity.

In sum, although it is still unclear exactly what factors lead to which patterns of HPA system dysregulation, animal research suggests that maternal behavior in early life has a powerful effect on the functioning of the HPA axis overall and on buffering potentially negative effects of early trauma.

SECTION III: CONCLUSIONS

Based on this review of the literature, it is possible to conclude that childhood maltreatment is, in fact, related to disruptions to HPA axis functioning, and that these disruptions may have important implications for vulnerability to psychopathology in maltreated children. Although research is far from conclusive, it appears that changes can be observed in children not long after severe or prolonged exposure to maltreatment, and that these changes may persist into adulthood. Moreover, these findings occur despite the wide variation in methodologies and maltreatment characteristics/experiences of participants in these studies. First, CRF stimulation studies and stressor tasks suggest that increases in CRF release from the hypothalamus may be common among maltreated children and adults maltreated as children. CRF receptors on the pituitary may then become either sensitized or desensitized, leading to changes in ACTH production. Finally, changes in the adrenal glands, including enlargement or atrophy, and increases or decreases in the sensitivity of cortisol negative feedback receptors on the pituitary may also affect the functioning of the system. The direction of effects at different points along the axis may differ depending on various factors such as age of onset of the stressor, parental responsiveness, repeated exposure to stressors, type and characteristics of maltreatment, and type of psychopathology or behavioral disturbance displayed.

Several factors may interact to influence the direction and patterning of the HPA axis dysregulation, some of which have not been adequately considered in studies to date. One such factor to be considered is the relationship of the child with an attachment figure or figures. Both animal and human studies suggest that a mother's interaction with her child can have profound implications for the way that the child's HPA axis responds to extreme stress (Dawson & Ashman, 2000; Gunnar, 2000; Nachmias et al., 1996). Furthermore, it is clear that not all maltreated children are victimized by their primary caregiver or are insecurely attached to their parents, and these factors must be taken into consideration when examining the relationship between the experience of maltreatment and HPA axis functioning. The findings of Kaufman et al. (1997) that maltreated children exposed to continued emotional maltreatment had a different HPA axis profile than those in safer environments supports the contention that the availability of stable attachment figures can influence the functioning of this physiological system.

Both age at the time of abuse and type of maltreatment are also factors that need to be considered in future investigations. Research with rats suggests that the patterning of HPA axis dysregulation may be affected by the age at which the trauma takes place (Ogawa et al., 1994; Plotsky & Meaney, 1993; van Oers et al., 1997), and it is possible that age and developmental status may play a role in the affect of trauma on human children as well. Cicchetti and Rogosch's (2001) study suggests that HPA axis patterning may differ according to the type of maltreatment experienced, such that sexual abuse and sexual abuse combined with physical abuse may produce hypercortisolism, whereas physical abuse may lead to hypocortisolism. The interaction of type of maltreatment, HPA axis functioning, and diagnostic status may be an important area for future investigations. Finally, it is important that more longitudinal studies of maltreated children and more studies with adults maltreated as children be undertaken to determine the long-term effects of child maltreatment on HPA axis functioning and its relation to psychopathology.

Next, most of the work with HPA axis functioning in children examines baseline cortisol levels or reactions to dexamethasone tests. Although animal research (Fahlke et al., 2000; McCormick et al., 1998; Plotsky & Meaney, 1993), and some research with human adults (Heim et al., 2000), suggests that HPA axis reactivity to stressors may be affected by a history of extreme trauma, this has not been investigated in children. This is potentially a very important area for research in that physiological overreactivity or underreactivity to stressors may play a role in the development of difficulties in peer relationships. Studies by Goodyer, Herbert, and Altham (1998) and Goodyer, Herbert, Tamplin, and Altham (2000), for example, certainly suggest that this may be the case.

In addition, substantial research investigates the relationship between aggression and cortisol secretion, although only one (Scarpa, 1997) considers the interaction of maltreatment, aggression, and HPA axis functioning directly. This is a potentially fruitful area of inquiry for several reasons. First, because there is a strong association between aggression and maltreatment (Dodge, Bates, & Pettit, 1990; Widom, 1989) and because both maltreatment and aggression are associated with dysregulated HPA axis functioning (De Bellis et al., 1994; De Bellis, Baum et al., 1999; Hart et al., 1995; Kaufman, 1991; McBurnett et al., 1996, 2000), it is tempting to suggest that maltreatment may contribute to a physiological state that makes a child more vulnerable to aggressive behavior. Alternatively, it is possible that a child with a dysfunctional HPA system may behave inappropriately and aggressively, thereby increasing the chances of maladaptive parenting practices. Whatever the direction of causality, it appears from the research on aggression and cortisol functioning that the relationship is complex and warrants further investigation.

In sum, HPA axis functioning in maltreated children is an area with great potential to contribute to our understanding of the effects of trauma on physiological functioning and on vulnerability to psychopathology. In particular, it seems that changes in HPA functioning in maltreated children may contribute to manifestations of depression, PTSD, and aggressive be-

havior. Findings of blunted ACTH and increased basal cortisol in sexually abused girls seem consistent with findings typically observed in depressed adults. Findings of reduced cortisol in physically abused and other maltreated children, on the other hand, are more consistent with those typically observed in adults with PTSD or aggressive children.

The literature also suggests that the physiological changes and consequent disturbance in mood or behavior that occur subsequent to child maltreatment can be potentially long lasting but not necessarily permanent if protective practices from significant caregivers are put into place. As such, it is important that greater clarity is attained in understanding the relationships among child maltreatment, HPA functioning, and psychopathology. It is hoped that the research reviewed herein will provide a springboard for future refined investigations that address the gaps and limitations in methodology to date.

IMPLICATIONS FOR PRACTICE, POLICY, AND RESEARCH

Practice

- A great deal of psychological literature supports the importance of family relationships, social support, and secure attachment in helping children recover from the effects of maltreatment. The possibility that these factors may also have an effect at the level of the HPA axis, a physiological stress response system, bolsters their importance as targets for intervention with abused children.

Policy

- Evidence that stable, secure attachment may mitigate effects of extreme stress on the HPA axis, and that continued emotional stress may result in further disruptions of this system, points to the need for stability and permanency in safe foster care placements and expediency in adoption proceedings.

Research

- The role of the child's relationship with attachment figures as potentially moderating the effect of abuse on HPA axis functioning should be more fully explored.
- Timing of abuse and type of maltreatment should be considered in future research on HPA axis functioning and abuse.
- Cortisol reactivity to stressors, in addition to baseline cortisol secretion, warrants examination in future research.
- The impact of HPA axis dysregulation in cognitive functioning in children is a potentially important area of research that has not been addressed.

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Elizabeth Van Voorhees, M.A., is a graduate student in clinical psychology at Virginia Polytechnic Institute and State University (Virginia Tech). Her primary areas of research interest are psychobiological and psychosocial causes and consequences of aggressive behavior and violent victimization and the use of the animal-human bond in interventions for children and adults with emotional and behavioral problems.

Angela Scarpa, Ph.D., is an associate professor of psychology in the clinical child program area at Virginia Polytechnic Institute and State University (Virginia Tech). She has 15 years of experience in the study of aggression/violence in terms of its causes and the consequences of violence victimization.