

Stress reactivity in war-exposed young children with and without posttraumatic stress disorder: Relations to maternal stress hormones, parenting, and child emotionality and regulation

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Abstract

The current study examined biomarkers of stress in war-exposed young children and addressed maternal and child factors that may correlate with children's stress response. Participants were 232 Israeli children aged 1.5–5 years, including 148 children exposed to continuous war. Similarly, 56 were diagnosed with posttraumatic stress disorder (PTSD) and 92 were defined as exposed-no-PTSD. Child cortisol (CT) and salivary alpha amylase (sAA), biomarkers of the hypothalamic–pituitary–adrenal and sympathetic–adrenal–medullary arms of the stress response, were measured at baseline, following challenge, and at recovery. Maternal CT and sAA, PTSD symptoms, and reciprocal parenting, and child negative emotionality and regulatory strategies were assessed. Differences between war-exposed children and controls emerged, but these were related to child PTSD status. Children with PTSD exhibited consistently low CT and sAA, exposed-no-PTSD displayed consistently high CT and sAA, and controls showed increase in CT following challenge and decrease at recovery and low sAA. Exposed children showed higher negative emotionality; however, whereas exposed-no-PTSD children employed comfort-seeking strategies, children with PTSD used withdrawal. Predictors of child CT included maternal CT, PTSD symptoms, low reciprocity, and negative emotionality. Findings suggest that high physiological arousal combined with approach strategies may be associated with greater resilience in the context of early trauma.

It is estimated that millions of the world's children are growing up amid political violence, continuous war, tribal and racial terrorism, genocide, military attacks on civilian locations, or guerrilla warfare (Belsky, 2008; Masten & Narayan, 2012). Others, such as children of combat soldiers in the United States, experience the aftermath of war-related trauma through a parent (McFarlane, 2009), while still others are exposed to a single act of terrorism, for instance, the September 11 attack (Chemtob, Nomura, & Abramovitz, 2008) or the Oklahoma City bombing (Pfefferbaum et al., 1999). Although systematic research is often difficult in zones of war, several studies have described children's response to war and terrorism across the globe, including Lebanon (Bryce, Walker, Ghorayeb, & Kanj, 1989), Gaza (Qouta, Punamaki, & El Sarraj, 2003), Israel (Laor, Wolmer, & Cohen, 2001), Kosovo (Lopes Cardozo, Kaiser, Gotway, & Agani, 2003), Bosnia–Hercegovina (Smith, Perrin, Yule, & Rabe-Hesketh, 2001), and Rwanda (Schaal, Jacob, Dusingizemungu, & Elbert, 2010). Studies indicate that political violence compromises children's mental health, leading to

anxiety, depression, posttraumatic symptoms, and conduct problems; that such problems tend to persist after the war has subsided; and that maternal factors, particularly the mother's well-being and support networks, function as resilience factors (Allwood, Bell-Dolan, & Husain, 2002; Feldman & Vengrober, 2011). However, very little research has focused on infants and young children exposed to political violence, and we are aware of no study that tested hormones, observed parenting, and temperamental dispositions in war-exposed young children.

In this study, we recruited a large cohort of infants and young children aged 1.5 to 5 years living in a zone of continuous war. Our goal was to examine children's physiological stress response and assess maternal and child factors that may correlate with variability in young children's stress response in the context of war exposure. Two neuroendocrine markers of stress were tested, cortisol (CT) and salivary alpha amylase (sAA), which are considered as biomarkers of the two arms of the stress response: the hypothalamic–pituitary–adrenal (HPA) and the sympathetic–adrenal–medullary (SAM) systems (Hellhammer, Wüst, & Kudielka, 2009; Nater & Rohleder, 2009). Functioning of these systems is thought to be shaped by a range of proximate conditions (Juster et al., 2011), and we examined the relations between children's stress response and several biological, parenting, and temperamental factors that have been linked with stress in

This study was supported by the NARSAD Independent Investigator Award (to R.F.) and German–Israeli Foundation Grant 1114-101.4/2010.

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young children. These include maternal CT and sAA, post-traumatic symptoms, and parenting style, and the child's reactivity and regulation. In addition to differences between exposed and nonexposed children, we were particularly interested in the differences between exposed children who developed posttraumatic stress disorder (PTSD) and those exposed to similar stressors who did not develop the disorder in an attempt to describe factors that may be associated with greater risk and resilience in the context of political violence.

Chronic Early Stress and Children's Stress Response

Chronic early stress initiates a cascade of physiological processes that alter the development of children's physiological stress systems (Gunnar & Quevedo, 2007; Heim, Plotsky, & Nemeroff, 2004; Teicher et al., 2003). Exposure to a variety of early stressors, such as maltreatment, poverty, or institutional rearing, may interfere with the development of neurotransmitters and brain systems regulating arousal and emotions (Weinstock, 2005), impair immune functioning and increase susceptibility to disease (Felitti et al., 1998; Graham, Christian, & Kiecolt-Glaser, 2006), increase the risk for behavior problems in childhood and mental illness in adulthood (Cicchetti & Toth, 1995; Fombonne, Wostear, Cooper, Harrington, & Rutter, 2001), and disrupt the development of social reciprocity and empathy (Decety, 2010). In light of research demonstrating links between early stress and children's stress physiology (Tarullo & Gunnar, 2006), the first goal of the current study was to examine biomarkers of the stress response in young children exposed to continuous war. However, because the response of individual children to stressful contexts varies widely, our second goal was to assess maternal and child factors that may correlate with variability in children's stress response within the group of war-exposed young children. Such data may be useful for the development of more specific interventions for this group.

Models on *allostatic load* (McEwen & Stellar, 1993) provided the theoretical framework for the study. Such models build on the concept of *allostasis* (the organism's adaptation to change) to describe the wear and tear caused by chronic stress that leads to persistent alterations in physiological systems (Juster et al., 2001). Across species, processes of allostatic load detail the ongoing trade-offs between the degree of stress and its persistence, the specific risks and resources embedded in the ecosocial niche, and differences related to the organism's dispositional response strategies (Korte, Koolhaas, Wingfield, & McEwen, 2005). Thus, in studying children exposed to continuous war, allostatic load models would suggest to take into account specific environmental resources and temperamental dispositions. In the current study, we focused on three maternal factors as indices of the risks and resources embedded in the child's ecology: the mother's stress hormone, PTSD symptoms, and reciprocal parenting. In addition, two factors were tested as markers of the child's temperamental dispositions: emotional reactivity and regulation strategies. Such multivariate approach is consistent with

Cicchetti and Rogosch (2009), who suggest that parental factors, parent and child biology, and temperamental dispositions should each be considered in research on young children exposed to chronic stress.

CT, SAA, and Early Exposure to Continuous War

The stress response involves the coordinated functioning of two major anatomically distinct systems: the SAM, which initiates the fight-or-flight response by increasing blood flow, respiration, cardiovascular activity, and the release of catecholamines (Nater & Rohleder, 2009), and the HPA system, which has a more gradual onset and is associated with physiological and behavioral withdrawal (Bauer, Quas, & Boyce, 2002; Tarullo & Gunnar, 2006). Whereas momentary stress induces immediate changes in each system, chronic stress exerts a lasting effect and may alter the balance between the functioning of the HPA and the SAM systems (Wolf, Nicholls, & Chen, 2008). It has been suggested that the assessment of basal levels, reactivity patterns, and functioning of both the HPA and the SAM systems may provide a fuller picture of the child's stress response under conditions of chronic stress (Del Giudice, Ellis, & Shirtcliff, 2011; Korte et al., 2005).

CT, the end product of activity of the HPA axis, is the most researched biomarker of the stress response; and its development in infancy is highly sensitive to the social context (Tarullo & Gunnar, 2006). Higher baseline levels and greater CT reactivity were found among children exposed to early stress, including maltreatment (Cicchetti & Rogosch, 2001), maternal postpartum depression (Essex, Klein, Cho, & Kalin, 2002; Feldman et al., 2009), or abuse (King, Mandansky, King, Fletcher, & Brewer, 2001). Studies have indicated that chronic stress impacts the body's response to trauma (De Bellis et al., 1999) and that ecological conditions may be related to the functioning of the HPA system following persistent exposure to traumatic conditions (Pervanidou, 2008).

Research on CT levels in childhood PTSD has shown inconclusive results. Several studies found that children with PTSD showed higher or comparable levels of CT to those of nonexposed controls (Carrion et al., 2002; De Bellis et al., 1999). Others reported lower baseline CT and blunted CT response in cases of PTSD. For instance, Pfefer, Altemus, Heo, and Jiang (2007) found lower baseline and flatter diurnal curves in children exposed to the 9/11 attack who developed PTSD as compared to those who did not develop psychopathology. Similarly, lower CT has been described in adults with PTSD following childhood-onset trauma (De Bellis et al., 1999). Gunnar and Vazquez (2001) described a phenomenon termed *hypocortisolism*, the paradoxical underreactivity of the HPA system in children exposed to early trauma or severe adversity, and argued that this blunted response should be examined in research on chronic early adversity. Recently, Badanes, Watamura, and Hankin (2011) found that young children growing in environments of high stress

showed low baseline CT and little diurnal variability, particularly when combined with maternal depression, and this hypocortisolism predicted greater risk for internalizing disorders. Consistent with models on allostatic load, the authors concluded that hypocortisolism in young children is a marker of allostatic load and that the combination of low and flat CT with chronic contextual stress may increase the risk for psychopathology.

Although much less research investigated sAA, and data on its source, role, and effects are still emerging, sAA has been suggested as a biomarker of the stress response that indexes SAM activity and is associated with plasma norepinephrine levels in response to stress (Nater & Rohleder, 2009). In contrast, Bosch, Veerman, de Geus, and Proctor (2011) argued that sAA is not a pure index of sympathetic activity and reflects both sympathetic and parasympathetic influences in ways that are still to be fully described. Notwithstanding this controversy, recent research examined sAA in relation to child health (Wolf et al., 2008), emotional reactivity (Spinrad et al., 2009), and attachment (Frigerio et al., 2009), and found links with stress-related processes. In general, no direct correlations emerged between CT and sAA (Granger, Kivlighan, el-Sheikh, Gordis, & Stroud, 2007), but associations were mediated by biological, genetic, or relational factors (Frigerio et al., 2009).

Several studies addressed the interaction of CT and sAA in predicting children's propensity for psychopathology. Higher CT was found to predict internalizing symptoms only among children high in sAA (El-Sheikh, Erath, Buckhalt, Granger, & Mize, 2008). Others found that the combination of low sAA and low CT predicted externalizing symptoms (Gordis, Granger, Susman, & Trickett, 2006), suggesting that hypoactivity of the two systems may index greater risk. Among adolescents exposed to Hurricane Katrina, the combination of high CT and high sAA indicated greater resilience and was associated with higher self-esteem (Vigil, Geary, Granger, & Flinn, 2010). Overall, research on stress biomarkers in children suggests that including CT and sAA in the context of developmental risk may provide a more comprehensive understanding of the child's stress response.

Maternal and Child Factors and Children's Stress Response

The most critical regulator of very young children's stress response is the mother (Hofer, 1995). Three maternal factors have been associated with young children's stress response: maternal stress physiology, maternal behavior, and maternal well-being. Animal studies have demonstrated the lifelong effects of maternal antenatal stress hormones, particularly CT, on the fetus's developing HPA axis through the maternal-placental-fetal neuroendocrine axis (Lightman, 2008; Wadhwa, 2005; Weinstock, 2005) and the programming of glucocorticoid gene expression in the amygdala, the hippocampus, and the hypothalamus (Fujioka, Fujioka, Ishida, Maekawa, & Nakamura, 2006; Welberg, Seckl, & Holmes, 2001). "Sen-

sitive" maternal behavior (i.e., more licking and grooming) has been shown to exert epigenetic effects on glucocorticoid receptor gene expression in the pup's hippocampus (Weaver et al., 2004), and maternal sensitivity has similarly been linked with more optimal HPA regulation in human infants (Haley & Stansbury, 2003). In addition, several studies reported correlations between levels of maternal and child's CT (Feldman, Singer, & Zagoory, 2010; Ruttle, Serbin, Stack, Schwartzman, & Shirtcliff, 2011; Sethre-Hofstad, Stansbury, & Rice, 2002) as well as maternal and child's sAA (Gordis, Margolin, Spies, Susman, & Granger, 2010), indicating that maternal stress biomarkers may serve as important correlates of the child's stress response.

Mother-child reciprocity describes the synchronous component in the maternal style, and longitudinal studies demonstrated the effects of reciprocal parenting on children's stress modulation and social growth (Feldman, 2007). Mother-child reciprocity has been associated with lower baseline CT in mother and child, and with quicker return to baseline following stress (Feldman et al., 2010). Similarly, higher maternal responsiveness was related to lower infant baseline CT (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996), whereas maternal psychopathology correlated with disruptions to the HPA response, expressed in child hypo- (Badanes et al., 2011) or hypercortisolism (Feldman et al., 2009). Overall, these studies suggest that the mother's stress hormones, reciprocal behavior, and psychopathology may each be associated with the child's CT and sAA.

In addition to maternal factors, children's temperamental reactivity and negative emotionality have shown to increase the risk for externalizing and internalizing symptoms in childhood (Sanson, Oberklaid, Pedlow, & Prior, 1991) and psychopathology in adolescence (Degnan, Almas, & Fox, 2010). In contrast, in addressing the effects of political violence on the development of psychopathology in children, Belsky (2008) suggested that under conditions of continuous war, high physiological arousal and temperamental reactivity do not necessarily index higher risk but may be an adaptive response to the stressful context. Similarly, it has been suggested that under conditions of uncertainty, high physiological arousal may function to maintain vigilance and may be considered an appropriate response to stress (Belsky & Pluess, 2009; Del Giudice et al., 2011). It is thus possible that among war-exposed young children, high temperamental reactivity and high physiological arousal, as expressed in higher levels of CT and sAA, may not necessarily correlate with greater risk for psychopathology.

The Current Study

In light of the above, the current study examined two sets of hypotheses: the first related to differences between war-exposed children and controls on physiological, maternal, and temperamental factors; the second assessing differences between war-exposed children who did or did not develop PTSD. Consistent with Cicchetti and Rogosch (2009), multiple

maternal and child biological and behavioral measures were collected. Children's stress response was indexed by two biomarkers: CT and sAA. Three maternal factors were examined as correlates of the child's stress response: maternal stress physiology indexed by the mother's CT and sAA, maternal reciprocity, and maternal PTSD symptoms. Three child temperamental factors were microcoded from a fear paradigm and similarly tested as correlates of the stress response: child negative emotionality and two emotion regulation strategies, comfort seeking and withdrawal.

With regard to the first set of hypotheses, we expected group differences on all of the aforementioned variables. War-exposed children were expected to show different levels of CT and sAA, more negative emotionality, and greater use of the two regulatory strategies. Mothers living in war zones were expected to report more posttraumatic symptoms, show lower reciprocity, and their stress physiology was expected to differ from that of controls. As to the second set of hypotheses, consistent with Badanes et al. (2011), we hypothesized that children diagnosed with PTSD would exhibit hypocortisolism, expressed in low baseline CT and minimal reactivity, and would select withdrawal strategies to regulate fear as compared to exposed children without PTSD. Finally, among all children, we expected that children's baseline CT and baseline sAA would be associated with the various maternal and child factors. Maternal biomarkers were expected to correlate with the parallel biomarker in the child, maternal reciprocity was expected to be associated with lower baseline CT, and maternal PTSD and child negative emotionality were expected to correlate with higher baseline CT. Because research on sAA as a stress biomarker is still emerging, we examined the relations between these variables and sAA without directional hypotheses.

Method

Participants

Participants included 232 children from 232 families aged 1.5 to 5 years ($M = 33.08$ months, $SD = 10.89$) and their mothers ($M = 31.27$ years, $SD = 5.55$, range = 22.3–47.4). The sample included 47.6% males and 47.1% firstborns. Maternal and paternal education averaged 3.88 ($SD = 1.44$) and 3.51 ($SD = 1.49$), respectively, on a scale of 1 (*elementary school*) to 4 (*college education*). Among mothers, 31.6% worked full time, 42.6% worked part time, and 11% were single mothers. All children lived with their mothers since birth with no prolonged separation. In order to assess the unique effects of war-related trauma, children were not included in the study if there were official records of maltreatment or family violence, mothers reported physical or sexual abuse, or the child suffered a severe motor vehicle accident or other major trauma other than war exposure.

One hundred and forty-eight families comprised the war-exposed group. These included children living in the same neighborhoods in the town of Sderot, Israel, which is located



Figure 1. (Color online) A map depicting the Israeli town of Sderot in relation to the Gaza Strip. Citizens of Sderot, Israel, live within a 10-km range of missile attacks from the Gaza Strip and have 15 s from the sound of alarm to enter sheltered settings.

10 kilometers from the Gaza border (see Figure 1 for map). Citizens of Sderot were exposed repeatedly to rocket attacks from Gaza over a period of several years, had only 15 s to enter protected spaces after hearing the alert sirens, and were exposed to frequent mortar shelling to which no alert signals were provided. Testing was conducted during a period of repeated rockets and missiles attacks (January 2006–October 2008). During this period, rocket attacks on Sderot occurred unpredictably and continuously several times a month, and all children were seen at least 1 month after the period in which these attacks have begun. Visits were not conducted during the day of the attack or within the next 2–3 days. Figure 1 presents a map of Sderot, Israel, and shows the close proximity to Gaza, particularly to the town of Bet Hanoun from which missiles were launched.

Eighty-four nonexposed children were recruited as controls from towns within the greater Tel-Aviv area that were equivalent to the town of Sderot in terms of population size, socioeconomic composition, and housing and employment opportunities. These areas were not exposed to missile attacks or acts of political violence during the study period, and controls were matched to the exposed group in age, gender, birth order (firstborn/late born), maternal and paternal age and education, and maternal employment and marital status. Prior to home visits, control families were screened by

phone for major traumatic events in the child's life (e.g., motor vehicle accidents and physical or sexual abuse), and those reporting such trauma were excluded. The study was approved by the institutional review board, and all mothers signed an informed consent.

Procedure

Children were visited at home for approximately 3.5 hr during the afternoon. Visits included hormone collection from mother and child, psychiatric diagnosis of child PTSD by interviewing mother when child was present, a series of mother-child interactions, a series of child emotion-eliciting paradigms, and a battery of self-report measures for mother. Following acquaintance, baseline saliva samples were collected from mother and child by mother placing a Salivette (Sarstedt, Rommelsdorf, Germany) in her own and in the child's mouth for 1 min (termed *baseline*). Following, mother and child were videotaped in several interactive episodes. To elicit the stress response, we used a detailed evocation of traumatic memories (see below), employed in research on CT reactivity in cases of PTSD (e.g., Smyth, Hockemeyer, & Tulloch, 2008), combined with a fear paradigm that involved the presentation of increasingly fearful novel objects adapted from the Lab-TAB (Goldsmith & Rothbart, 1996), consistent with research on CT reactivity in young children (Buss, Davidson, Kalin, & Goldsmith, 2004). A second salivary sample was collected from mother and child 20 min after the fear paradigm (termed *following challenge*), and a third set of samples from mother and child were collected 15 min thereafter (termed *recovery*). It is important to note that saliva collection was timed to the reactivity pattern of the HPA axis and not to that of the sAA. Our pilot study showed that it is not possible to draw more than three saliva samples from children at that age, and we selected to focus on the HPA axis as the central marker of the stress response. This should be noted as a study limitation with regard to the findings for sAA.

Psychiatric interview. Mothers in both the exposed and the control groups were interviewed when the child was present to diagnose child PTSD. Trained clinicians with a background in early childhood development and psychopathology visited families at home and diagnosed the child's PTSD using the Diagnostic Classification: Zero-to-Three (DC 0-3R; Zero to Three, 2005), which provides a validated tool for diagnosing psychiatric disorders in children 5 years and under (Chu & Lieberman, 2010). Clinicians conducted an extensive interview with the mother while the child was present and elicited detailed information on the nature of the trauma, the mother and child's proximity to the traumatic event, the child's emotional reaction to specific traumatic events, specific symptoms in the four symptom clusters (reexperiencing, avoidance, hyperarousal, and fears and aggression), and the child's developmental regression or arrest. Clinicians were supervised by a senior clinical child psychologist and a child psychiatrist, and cases were conferred every few weeks. In ad-

dition, formal observation of young children's reaction to trauma evocation is suggested as central to the diagnosis of PTSD at this age (Chu & Lieberman, 2010; Scheeringa, Zeanah, & Cohen, 2011), and the videos of mother and child during the evocation of traumatic memories were coded for maternal and child emotional behavior. Following the clinical interview, mothers were asked to rate the child's symptoms on a list of 58 posttraumatic symptoms that were compiled after a year of pilot study in Israeli and Palestinian war-exposed locations. In the pilot study, extensive interviews were conducted with parents, caregivers, and therapists living in war zones on the typical symptoms children at that age exhibit following repeated exposure to war-related violence (Feldman, Vengrober, & Hallaq, 2007). For each symptom, mothers rated if she had not notice the symptom in her child and, if she did, whether the child exhibited the symptom infrequently (once a week or less) or frequently (daily or every 2-3 days). Consistent with the DC 0-3R guidelines, PTSD was diagnosed if the child was exposed to a firsthand war-related trauma that was followed by verbal and/or nonverbal expression of intense fear or horror and exhibited at least 1 re-experiencing, 1 avoidance, and 2 hyperarousal symptoms described as occurring "frequently." According to the DC 0-3R criteria, both fears and aggression symptoms, and developmental regression are noted in detail during the diagnostic interview, but they are not included in the formal diagnosis of early childhood PTSD. PTSD was diagnosed in 56 of the exposed children (37.8%), and 92 children were defined as exposed-no-PTSD.

Control mothers were interviewed in a similar manner to the exposed group. Mothers were asked to describe events the child experienced as "traumatic," stressful, or emotionally difficult during the past few months; and the interview and symptom list followed the same procedure as the exposed group. Mothers described mildly "traumatic" events in the child's life, such as loss of a grandparent, illness in the family, and moving to a new neighborhood.

Detailed evocation of traumatic memories. Child was present in the room and situated near the mother when the clinician elicited detailed information on the traumatic experience. The clinician asked about the nature of the trauma, including the specifics of the trauma exposure, the child and family members' degree of exposure, and the child's emotional reaction to specific events, including the incidence of exposure; the child's proximity to the explosion; whether the child or family members were injured and how severely; the child's behavioral expression of fear, horror, and other emotions in response to each traumatic exposure; the specific symptoms the child expresses in the reexperiencing, avoidance, hyperactivity, and fears and aggression domains; and the nature of the developmental regression.

Mother-child free play. Mothers and children engaged in free play for 10 min. The experimenter placed a box of preselected

toys in front of mother, and instructions were “Play with your child as you normally do.”

Fear regulation. In this procedure, adapted from the Lab-TAB (Goldsmith & Rothbart, 1996), the experimenter puts on four masks of increasing fearfulness while the child is looking: clown, pet animal, scary animal, and ghost. The experimenter puts on each mask, calls the child’s name, and leaves it on for 10 s.

Maternal PTSD. Maternal PTSD symptoms were assessed with the Posttraumatic Diagnostic Scale (Foa, 1995). This scale provides symptom scores in the three major symptom clusters (reexperiencing, avoidance, and hyperarousal) and a general PTSD score with good reliability and validity.

Hormonal assays.

CT. Salivettes were kept cooled until thawed before being centrifuged at 4°C at 1000 × *g* for 15 min. The samples were then stored at –20°C until assayed. CT levels were assayed using a commercial ELISA kit (Assay Design, MI). Measurements were performed in duplicate according to the kit’s instructions. CT levels were calculated by using MatLab-7 according to the relevant standard curves. The intraassay and interassay coefficients are less than 10.5% and 13.4%, respectively. Missing values were estimated by the curve when one assessment was missing, and when two assessments were missing ($n = 21$, 9% for mothers and $n = 24$, 10% for children), the subject was taken out of the analysis.

sAA. The concentration of AA in saliva samples was determined by Salimetrics assay kit according to instructions. Most samples were diluted 1:100 prior to assaying. Samples exceed 400 U/ml were rerun at dilution of 1:500. Values too low to read at 1:100 dilution were rerun at dilution of 1:50.

The sAA concentration was calculated by the equation provided, taking into account appropriate dilution. Intraassay and interassay coefficient variances were 2.5 and 13.6, respectively.

Coding

Mother–child reciprocity. Interactions were coded using the Coding Interactive Behavior Manual, a global rating system for adult–child interactions with 45 codes aggregated into several composites. The system has shown adequate psychometric properties in multiple studies of healthy and high-risk populations at this age (Feldman & Eidelman, 2009; Feldman, Keren, Gross-Rozval, & Tyano, 2004; Feldman & Masalha, 2010). Two coders, trained to 90% reliability and blind to psychiatric information, coded. Reliability κ s on 40 interactions averaged 0.84 (range = 0.78–0.95). The *dyadic reciprocity* construct ($\alpha = 0.93$) was used, which includes the following codes: mother and child engage in give and receive interaction, mother adapts to child signals, and interactions are fluent and rhythmic.

Fear regulation. The fear episode was microcoded in 0.01-s frames using a computerized system for four categories of behavior, each including a set of mutually exclusive codes: gaze, affect, vocalization, and regulatory behavior, consistent with previous research (Feldman et al., 2009). Interrater reliability for 40 interactions averaged $\kappa = 0.82$ (range = 0.73–0.91). Three constructs were used as indices of temperamental emotional reactivity and regulation. *Negative emotionality* was the sum frequencies of the following codes: child expresses negative affect, child cries, and child emits fussy vocalizations. *Comfort seeking* was the sum frequencies of the child gazes to mother when seeing the scary object, child seeks maternal comfort, and proximity seeking. *Withdrawal* was the sum frequencies of gaze avert, child no talk, and child self-soothing behavior.

Results

The results are presented in two sections. In the first, we examine differences among the three groups (controls, exposed children with PTSD, and exposed-no-PTSD) on (a) child and maternal CT and sAA (b) maternal factors, including maternal PTSD and mother–child reciprocity, and (c) child temperament, including negative emotionality and regulatory strategies. To control for variability in child age, child age in months was entered in all analyses as a covariate. The second section presents two hierarchical regressions predicting child CT and sAA from maternal and child factors for the entire sample.

Differences among exposed children with PTSD, exposed children without PTSD, and nonexposed controls

Child and maternal biomarkers.

CT. A repeated-measure multivariate analysis of covariance (MANCOVA) with group (controls, exposed children with PTSD, and exposed-no-PTSD) and child gender as the between-subject factors and child age as a covariate was computed for the three measurements of CT (baseline, following challenge, and recovery). The results revealed an overall effect for measurement, Wilks $F(2, 201) = 7.18$, $p < .001$, effect size (ES) = 0.07. This suggests that CT changed across assessments for all children. An overall between-subject effect was found for group, $F(2, 201) = 16.58$, $p < .001$, ES = 0.17. This finding demonstrates that CT levels were different among the three groups. Means are presented in Table 1 and show that group differences in CT were significant for all three assessments: baseline, following challenge, and recovery. Finally, an interaction of CT and group was found, Wilks $F(4, 402) = 2.32$, $p = .042$, ES = 0.03. This interaction indicates that the pattern of change across the three assessments differed as a function of group. Among the two exposed groups, CT did not change across assessments in more than 10%, thus showing little reactivity to stress. Among controls, however, CT showed the typical increase–

Table 1. Biomarkers, mothering, and temperament in war-exposed children with PTSD, war-exposed children without PTSD, and nonexposed controls

	PTSD (a)		Ex-No-PTSD (b)		Controls (c)		Univariate	F
	M	SD	M	SD	M	SD		
Cortisol (nM)								
Baseline	6.09	1.89	8.01	2.18	6.66	1.70	16.04***	a < c < b
Following challenge	6.02	1.68	7.82	2.02	7.22	1.66	14.43***	a < c < b
Recovery	5.84	2.18	7.71	2.14	6.54	1.71	13.19***	a < c < b
Salivary alpha amylase (U/m)								
Baseline	11.02	16.41	16.65	19.82	5.53	4.36	4.62*	a, b > c
Following challenge	9.66	11.51	16.18	18.30	4.52	3.74	6.85**	b > a > c
Recovery	6.54	8.36	14.90	17.44	4.03	3.40	7.25**	b > a, c
Maternal factors								
PTSD symptoms ^a	6.82	11.80	3.64	7.47	0.58	3.01	11.36***	a > b > c
Reciprocity ^b	2.92	1.27	3.27	1.17	3.73	1.24	6.18**	a < b < c
Child temperament factors ^c								
Negative emotionality	0.93	1.77	0.86	1.59	0.27	0.66	3.86*	a, b > c
Comfort seeking	2.73	2.18	4.53	3.31	3.62	2.86	5.36**	b > a > c
Withdrawal	8.46	5.14	7.31	4.26	5.82	2.64	6.47**	a > b > c

Note: PTSD, posttraumatic stress disorder; Ex-No-PTSD, war-exposed children without PTSD.

^aAssessed by the Posttraumatic Diagnostic Scale.

^bThe numbers represent the frequencies during the fear paradigm.

^cThe numbers are coded on a scale of 1–5.

* $p < .05$. ** $p < .01$. *** $p < .001$.

decrease pattern (Figure 2). Stress reactivity scores were computed by subtracting the child's CT levels at baseline from the CT levels following challenge. The results indicated significantly greater stress reactivity among controls as compared to the exposed children, $F(2, 197) = 6.37, p < .01$, with no differences between the two exposed groups. Computing stress reactivity as regression coefficients (residuals resulting

from regressing baseline CT on CT levels following challenge) showed similar results, with higher reactivity found for controls as compared to the exposed groups, $F(2, 197) = 5.82, p < .01$. It thus appears that although exposed children with PTSD showed consistently low CT and exposed children without PTSD showed consistently high CT compared to controls, in both groups there was little reactivity

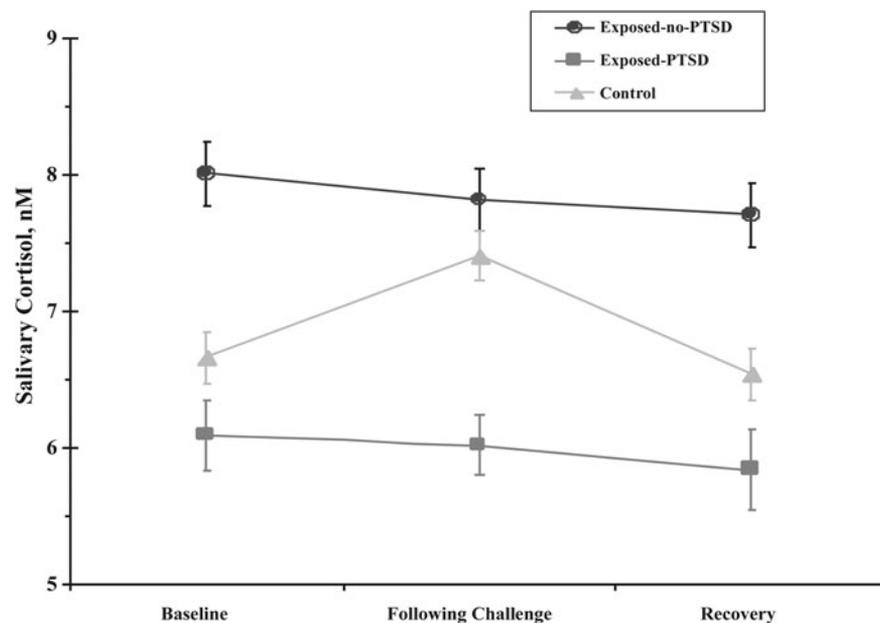


Figure 2. Cortisol at baseline, following challenge, and recovery in war-exposed children diagnosed with posttraumatic stress disorder (PTSD), war-exposed children without PTSD, and controls.

of the system in response to momentary stress or recovery of the system following induced stress.

A similar repeated-measure MANCOVA was computed for maternal CT in the three assessments. Mother's CT similarly showed a main effect for group, $F(2, 203) = 3.84$, $p = .04$, $ES = 0.04$. However, unlike the findings for children, differences were found only between the exposed and the control mothers and not between mothers of children with and without PTSD. Mothers in the two exposed groups displayed higher baseline CT ($M = 7.92$, $SD = 2.01$) than did mothers of controls ($M = 7.11$, $SD = 1.63$).

sAA. A repeated-measure MANCOVA with group (controls, exposed children with PTSD, and exposed-no-PTSD) and child gender as the between-subject factors and child age as the covariate showed no overall change across assessments, indicating that sAA did not change meaningfully across assessments. Possibly, because the reactivity patterns of sAA are quicker than those of CT, the timing of the collection did not allow for a clear reflection of sAA reactivity. A significant main effect was found for group, $F(2, 201) = 4.33$, $p = .03$, $ES = 0.04$. As seen in Table 1 and Figure 3, control children had the lowest sAA of all groups. Among exposed children, exposed-no-PTSD had significantly higher sAA in the following challenge and recovery assessments as compared to children with PTSD. No interaction effect was found.

A similar MANCOVA assessing maternal sAA for the baseline, following challenge, and recovery assessments showed an overall main effect for group, $F(2, 203) = 4.02$, $p = .03$, $ES = 0.04$. Again, differences in maternal sAA were found only between the exposed and nonexposed mothers, and not between mothers of children with and without PTSD. Mothers in the two exposed groups had higher sAA at baseline ($M = 17.36$, $SD = 14.22$) than did controls

($M = 5.89$, $SD = 4.41$), $F(1, 215) = 5.77$, $p = .004$, at the following challenge assessment, exposed: $M = 16.55$, $SD = 15.45$; controls: $M = 6.16$, $SD = 5.41$; $F(1, 215) = 5.09$, $p = .008$, and at recovery, exposed: $M = 13.66$, $SD = 16.51$; controls: $M = 5.71$, $SD = 5.42$; $F(1, 215) = 3.39$, $p = .03$.

Associations between maternal and child's biomarkers. In both CT and sAA, significant correlations emerged between maternal and child biomarkers at all assessments: Pearson r values for maternal and child CT were as follows: baseline, $r = .35$, following challenge, $r = .37$, and recovery, $r = .28$, $ps < .01$. Correlations between maternal and child sAA were as follows: baseline, $r = .58$, following challenge, $r = .51$, and recovery, $r = .34$, $ps < .001$. No significant correlations emerged between CT and sAA at any observation.

Maternal mental health and relational factors.

Maternal PTSD symptoms. A univariate analysis of covariance with group and child gender as the between-subject factors and child age as the covariate assessed group differences in mothers' PTSD symptoms. A main effect for group was found, $F(1, 229) = 11.36$, $p < .001$. As seen in Table 1, exposed mothers reported significantly more PTSD symptoms than did controls. However, mothers of children diagnosed with PTSD had more PTSD symptoms than did mothers of exposed children not diagnosed with the disorder.

Mother-child reciprocity. A similar analysis of covariance examined group differences in mother-child reciprocity. A main effect was found for group, $F(1, 229) = 4.27$, $p < .01$. Differences were found among the three groups, and means are presented in Table 1. As seen, control mothers and children showed higher reciprocity than did exposed

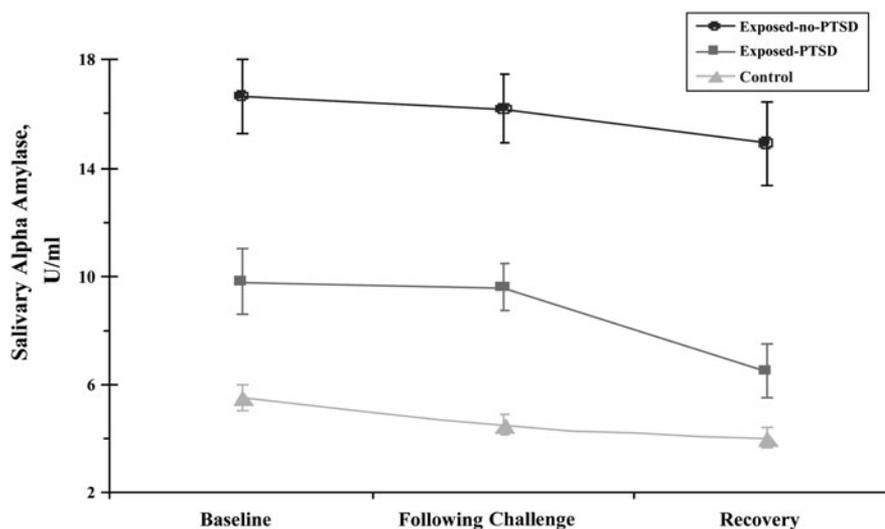


Figure 3. Salivary alpha amylase at baseline, following challenge, and recovery in war-exposed children diagnosed with posttraumatic stress disorder (PTSD), war-exposed children without PTSD, and controls.

Table 2. Predicting CT and sAA

Criterion Predictors	Baseline CT			Baseline sAA		
	Beta	ΔR^2	ΔF	Beta	ΔR^2	ΔF
Child age	-0.12	.02	2.06	0.09	.01	0.96
Mother education	0.11	.02	2.77	0.18*	.03	3.86*
Mother cortisol	0.36*	.05	4.75*	0.10	.01	2.75
Mother sAA	0.08	.01	0.86	0.33*	.06	5.36**
Maternal PTSD	0.29*	.04	4.29*	0.06	.00	0.31
Mother-child reciprocity	-0.25*	.03	3.97*	0.22*	.03	3.91*
Child negative emotionality	0.23*	.03	3.72*	0.12	.01	2.37
Child comfort seeking	-0.11	.01	1.22	0.34*	.05	4.52*
Child withdrawal	-0.25**	.04	5.19*	0.08	.00	0.83
R^2 total	.25, $F(9, 196) = 5.09, p < .001$.20, $F(9, 196) = 4.04, p < .001$		

Note: CT, child cortisol; sAA, salivary alpha amylase; PTSD, posttraumatic stress disorder.

* $p < .05$. ** $p < .01$.

dyads. However, mothers and children in the exposed-no-PTSD group showed higher levels of reciprocity as compared to mothers and children diagnosed with PTSD.

Child temperamental factors. MANCOVA assessing the three temperamental factors: negative emotionality, child comfort seeking, and child withdrawal, with group and child gender as between-subject factors and child age as covariate showed an overall effect for group, $F(1, 225) = 5.18, p = .02, ES = 0.05$. Exposed children exhibited more negative emotionality compared to controls. However, whereas exposed-no-PTSD children showed the highest levels of comfort seeking among all groups, children diagnosed with PTSD exhibited the highest levels of withdrawal (Table 1).

Predicting children's stress response

Prior to computing the regression models, correlations between predictor variables were examined with Pearson correlations. The results indicated that more maternal PTSD symptoms were associated with lower child CT ($r = -.18, p < .01$), lower mother-child reciprocity ($r = -.15, p < .05$), and higher child withdrawal ($r = .16, p < .05$). Higher reciprocity correlated with lower child CT ($r = -.20, p < .01$) and lower maternal CT ($r = -.19, p < .01$). In contrast, higher reciprocity correlated with greater child sAA ($r = .21, p < .01$) and greater maternal sAA ($r = .19, p < .01$). More child negative emotionality correlated with higher child CT ($r = .22, p < .01$), and more child withdrawal was related to lower child CT ($r = -.19, p < .01$). Higher child comfort seeking was related to higher child sAA ($r = .27, p < .001$) and higher maternal sAA ($r = .15, p < .05$).

Finally, two hierarchical regression equations were computed predicting children's baseline CT and sAA. Variables were entered in nine blocks in a theoretically determined order. In the first two blocks, child age in months and mother education were entered to partial out variance due to these

demographic factors. In the third and fourth blocks, maternal biomarkers (CT and sAA) were entered as predictors of the child's biomarkers. In the fifth and sixth blocks, maternal factors, including maternal PTSD symptoms and mother-child reciprocity, were entered. In the last three blocks, child temperamental factors, including negative emotionality, comfort seeking, and withdrawal, were entered. The results are presented in Table 2.

The results of the first model indicated that child CT was independently related to maternal CT, higher maternal PTSD symptoms, lower mother-child reciprocity, greater child negative emotionality, and lower withdrawal. The results of the second model showed that maternal sAA, higher mother-child reciprocity, and more child comfort seeking were each independently linked with child sAA. Overall, these models suggest that these two biomarkers of the stress response in children are related to components of the child's ecology, including maternal biomarkers, PTSD symptoms, and reciprocal parenting, to children's emotional reactivity, and to the strategies children use to regulate fear.

Discussion

The results of the current study are the first to address neuroendocrine markers of stress in infants and young children exposed to political violence and to describe biological, relational, maternal mental health, and child temperamental factors that correlate with children's stress response under such conditions. Overall, the findings point to differences between war-exposed children and controls on all factors tested. War-exposed children showed a different physiological stress response, as indexed by both CT and sAA, and tended to react with more negative emotions to the elicitation of fear. Mothers living in war zones reported more PTSD symptoms, were less reciprocal during interactions, and their stress physiology showed higher levels of CT and sAA. However, whereas some war-exposed children were diagnosed with

PTSD, others did not develop the disorder, and differences in child hormones, temperamental dispositions, and maternal well-being and relational behavior emerged between these two groups. In this context, it is important to note that because the study is cross-sectional and not longitudinal, no causal effects regarding the impact of prolonged war exposure on mother or child can be ascertained.

Exposed-no-PTSD children exhibited the highest levels of CT at each of the three assessments (baseline, following challenge, and recovery) as well as consistently high sAA in these same assessments. Such co-occurrence of high CT and high sAA has been linked with lower adaptation and higher externalizing and internalizing symptoms in studies that assessed the interactive effects of the two biomarkers (e.g., El-Sheikh et al., 2008). Nevertheless, “adaptation” is a context-specific construct that receives its meaning only in relation to the demands of specific ecologies. In the context of repeated missile attacks that leave only a few seconds to enter sheltered spaces and continue unpredictably over the course of several years, it is possible that a consistently aroused physiology may be a more adaptive by-product of the allostatic process. As seen, higher CT and higher sAA were also found in the exposed mothers, who needed to maintain constant vigilance for the safety of themselves and their child. In addition to highly aroused stress response, exposed-No-PTSD children employed more approach, comfort seeking emotion regulation strategies as compared to all other groups and had mothers who were more reciprocal as compared to mothers of children with PTSD. Possibly, within the limited resources available to mothers during extended periods of war, children who turn more naturally for help and seek the mother’s assistance more actively would receive more involved parenting, which in turn may be associated with greater resilience. At the same time, it is also possible that when the mother is better able to provide reciprocal parenting, the child learns to use the mother for the regulation of distress. Within a cross-sectional design, it is not possible to determine whether the child’s approach tactics shaped the mother’s reciprocal style or vice versa.

In contrast to the exposed-no-PTSD group, children diagnosed with PTSD showed hypocortisolism, expressed in low baseline CT levels and blunted reactivity. These findings are consistent with the description of hypocortisolism in young children exposed to severe trauma by Gunnar and Vazquez (2001), with the findings that following the 9/11 attack children diagnosed with PTSD showed blunted CT reactivity (Pfeffer et al., 2007), and with the results that young children growing in highly stressful environments show hypocortisolism and that such low CT was considered a marker of allostatic load (Badanes et al., 2011). Although the mechanisms leading from early adversity to HPA hypoactivity are not fully understood, these authors suggest that hypocortisolism may have been the body’s response to periods of very high HPA reactivity and that the allostatic process functioned to maintain equilibrium by hypoactivity, similar to the findings reported for animals following prolonged maternal deprivation (Hofer, 1995). Both exposed groups showed minimal CT reactivity,

perhaps suggesting that continuous war may be associated with reduced responsiveness to momentary environmental stressors possibly as a result of lengthy exposure to highly stressful challenges that upregulate the system’s reactivity. Among the children with PTSD, there was an additional and significant decrease in physiological and behavioral reactivity, which was not observed in the exposed-no-PTSD group. Although these children displayed high negative emotionality during the fear paradigm, they used withdrawal tactics to regulate emotions, expressed in gaze aversion, termination of verbal dialogue, and self-soothing behavior. It is of interest that although these children exhibited at least two hyperarousal symptoms in order to receive a diagnosis of childhood PTSD, their stress physiology and regulatory tactics reflected hypoactivation and withdrawal. In parallel, mothers of children with PTSD reported the highest levels of PTSD symptoms and engaged in the lowest levels of reciprocal interactions as compared to all other groups. It is possible that these children did not learn to turn to their mothers for regulating distress or adapted the posttraumatic avoidant strategies of their mothers, but future longitudinal studies are required to examine this issue in depth.

The two types of physiological and behavioral response in children echo the writings of Spitz (1946) and Bowlby (1969), similarly formulated on the basis of their experience with war-exposed children during World War II. According to these authors, during periods of prolonged war, when the attachment system is in jeopardy, children first react by increasing physiological and behavioral arousal (the “separation” protest response) in order to force the mother back into her regulatory role. When the mother’s physical or emotional absence continues, the separation response, which is typically short-lived, turns into “loss,” characterized by hypoactivity of physiological and behavioral systems that support engagement with the world. The work of Hofer (1995) in animal models details a similar process. When the mother’s physical proximity, which functions to regulate the pup’s physiology in a system-specific fashion, is removed, pups first react by increasing arousal and agitation. As separation continues, this hyperactivity turns into hibernation-like disengagement. Although our study is cross-sectional and we do not suggest that the children diagnosed with PTSD experienced a period of high arousal prior to the period of hypoactivity, these perspectives provide a conceptual framework to the findings that children’s response to prolonged periods of war may be observed in either hyper- or hypoactivity of the child’s physiological and behavioral systems.

The results of the regression models indicate that children’s baseline CT levels were independently related to maternal baseline CT, lower maternal reciprocity, greater maternal psychopathology, higher child negative emotionality, and lower child withdrawal. The concordance between maternal and child CT has been previously reported in infants and young children (Feldman et al., 2010; Ruttle et al., 2011; Sethre-Hofstad et al., 2002), and such “endocrine fit” is thought to stem from genetic, epigenetic, and social interac-

tive sources. The findings relating child CT to maternal psychopathology, lower interactive sensitivity, and greater negative emotionality is consistent with much previous research suggesting that components of the child's ecology are related to the physiological stress response (Cicchetti & Rogosch, 2001; De Bellis et al., 1999; Haley & Stansbury, 2003; Tarullo & Gunnar, 2006). Consistent with Cicchetti and Rogosch (2009), the findings point to the independent associations between the mother and child's biology, relationship, and temperament with children's stress reactivity under conditions of chronic stress. Future research is thus needed to fully understand the neurobiology of stress in the context of political violence and assess multiple sources of influence on the development of psychopathology using longitudinal and experimental designs.

The current findings are the first to assess sAA in war-exposed young children and their mothers and add to the rapidly growing literature on this biomarker and its correlates. Most research on sAA considers it as an index of SAM activity, although this assumption is still controversial and requires further validation. Similar to CT, the data show that maternal and child sAA showed concordance at each assessment, findings consistent with previous research on sAA in adolescence (Gordis et al., 2010). Child baseline sAA was related to mother-child reciprocity and the use of comfort-seeking strategies. In addition, maternal sAA similarly correlated with reciprocity and child comfort seeking. Research has pointed to the associations between sAA with more optimal mother-child relationships and with positive emotionality and approach behavior in young children. For instance, Frigerio et al. (2009) found that secure attachment, combined with genetic polymorphisms on the serotonin transporter linked polymorphic region gene and gamma-aminobutyric acid receptor subunit alpha-6 gene, predicted sAA in 12- to 18-month-olds; Fortunato, Dribin, Granger, and Buss (2008) showed links between sAA and positive affect and approach behavior in toddlers; and Spinrad et al. (2009) reported correlations between sAA and lower dispositional anger in preschoolers. The findings show correlations between sAA and child approach strategies and more positive social interactions, but much further research on sAA is required to assess its biological underpinnings and predictive utility.

Limitations

The limitations of the study are important to consider in the interpretation of the findings. Due to the cross-sectional nature of the study, it is important to emphasize that no causal

relationships can be inferred and longitudinal follow-up is required to address predictive relations between components of the young child's ecology and developmental outcome under conditions of political violence. The timing of the saliva collection was set to the reactivity of the HPA axis and did not accommodate the response patterns of sAA, and this should be considered in the interpretation of the sAA results. Children were collected across a wide age range (1.5–5 years), and although age was controlled in the analyses, children were at different developmental stages and a more narrow focus on specific developmental periods would be an important next step. Similarly, children's stress response is shaped by multiple factors, including living conditions, number of children, and availability of caregiving; although we matched war-exposed and control children on multiple demographic factors, some unknown or unmeasured variable could have influenced the results. Taken into consideration life-span and developmental psychopathology perspectives (Cicchetti & Rogosch, 2009; Juster et al., 2011), it would be important to follow both groups of exposed children and determine whether the exposed-no-PTSD group is more resilient across development. The lack of father data is an important drawback that precludes a fuller investigation of the child's rearing ecology and functioning during periods of war. In addition, generalizability of the findings to other regions of political violence should be examined, in light of the facts that there were very few casualties across the period of exposure, no father absence or direct exposure to fighting, no real shortage of food or basic supplies, and fighting was limited to a small region of the country. Finally, a more in-depth assessment of the neurobiology of stress, including stress genes and stress-related neural networks, would have provided a more comprehensive picture of the ways in which war exposure shapes the physiological stress response in young children.

Conclusion

Future research is required to assess genetic, brain, and behavioral markers of risk and resilience among children exposed to war-related trauma. Although millions of the world's children are growing up amid armed conflict, research detailing its impact on infants and young children is critically lacking. Such research should chart context-specific pathways of risk and resilience in order to build theoretical models and culturally sensitive interventions that can target the effects of war on children's physiological stress and psychological distress.

References

- Allwood, M. A., Bell-Dolan, D., & Husain, S. A. (2002). Children's trauma and adjustment reactions to violent and nonviolent war experiences. *Journal of the American Academy of Child & Adolescent Psychiatry*, 41, 450–457.
- Badanes, L. S., Watamura, S. E., & Hankin, B. L. (2011). Hypocortisolism as a potential marker of allostatic load in children: Associations with family risk and internalizing disorders. *Development and Psychopathology*, 23, 881–896.
- Bauer, A. M., Quas, J. A., & Boyce, W. T. (2002). Associations between physiological reactivity and children's behavior: Advantages of a multi-system approach. *Journal of Developmental and Behavioral Pediatrics*, 23, 102–113.

- Belsky, J. (2008). War, trauma and children's development: Observations from a modern evolutionary perspective. *International Journal of Behavioral Development, 32*, 260–271.
- Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin, 135*, 885–908.
- Bosch, J. A., Veerman, E. C. I., de Geus, E. J., & Proctor, G. B. (2011). Alpha amylase as a reliable and convenient measure of sympathetic activity: Don't start salivating just yet! *Psychoneuroendocrinology, 36*, 449–453.
- Bowlby, J. (1969). *Attachment and loss: Vol. 1. Attachment*. New York: Basic Books.
- Bryce, J. W., Walker, N., Ghorayeb, F., & Kanj, M. (1989). Life experiences, response styles and mental health among mothers and children in Beirut, Lebanon. *Social Science Medicine, 28*, 685–695.
- Buss, K. A., Davidson, R. J., Kalin, N. H., & Goldsmith, H. H. (2004). Context-specific freezing and associated physiological reactivity as a dysregulated fear response. *Developmental Psychology, 40*, 583–594.
- Carrion, V. G., Weems, C. F., Ray, R. D., Glaser, B., Hessel, D., & Reiss, A. L. (2002). Diurnal salivary cortisol in pediatric posttraumatic stress disorder. *Biological Psychiatry, 51*, 575–582.
- Chemtob, C. M., Nomura, Y., & Abramovitz, R. A. (2008). Impact of conjoined exposure to the World Trade Center attacks and to other traumatic events on the behavioral problems of preschool children. *Archives in Pediatric Adolescent Medicine, 162*, 126–133.
- Chu, A. T., & Lieberman, A. F. (2010). Clinical implications of traumatic stress from birth to age five. *Annual Review of Clinical Psychology, 6*, 469–494.
- Cicchetti, D., & Rogosch, F. A. (2001). The impact of child maltreatment and psychopathology on neuroendocrine functioning. *Development and Psychopathology, 13*, 783–804.
- Cicchetti, D., & Rogosch, F. A. (2009). Adaptive coping under conditions of extreme stress: Multilevel influences on the determinants of resilience in maltreated children. *New Directions for Child and Adolescent Development, 124*, 47–59.
- Cicchetti, D., & Toth, S. L. (1995). A developmental psychopathology perspective on child abuse and neglect. *Journal of the American Academy of Child & Adolescent Psychiatry, 34*, 541–565.
- De Bellis, M. D., Baum, A. S., Birmaher, B., Keshavan, M. S., Eccard, C. H., Boring, A. M., et al. (1999). A.E. Bennett Research Award. Developmental traumatology: Part I. Biological stress systems. *Biological Psychiatry, 45*, 1259–1270.
- Decety, J. (2010). The neurodevelopment of empathy in humans. *Developmental Neuroscience, 32*, 257–267.
- Degnan, K. A., Almas, A. N., & Fox, N. A. (2010). Temperament and the environment in the etiology of childhood anxiety. *Journal of Child Psychology and Psychiatry, 51*, 497–517.
- Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). The adaptive calibration model of stress reactivity. *Neuroscience and Biobehavioral Review, 35*, 1562–1592.
- El-Sheikh, M., Erath, S. A., Buckhalt, J. A., Granger, D. A., & Mize, J. (2008). Cortisol and children's adjustment: The moderating role of sympathetic nervous system activity. *Journal of Abnormal Child Psychology, 36*, 601–611.
- Essex, M. J., Klein, M. H., Cho, E., & Kalin, N. H. (2002). Maternal stress beginning in infancy may sensitize children to later stress exposure: Effects on cortisol and behavior. *Biological Psychiatry, 52*, 776–784.
- Feldman, R. (2007). Parent–infant synchrony and the construction of shared timing: Physiological precursors, developmental outcomes, and risk conditions. *Journal of Child Psychology and Psychiatry, 48*, 329–354.
- Feldman, R., & Eidelman, A. I. (2009). Biological and environmental initial conditions shape the trajectories of cognitive and social–emotional development across the first years of life. *Developmental Science, 12*, 194–200.
- Feldman, R., Granat, A., Pariente, C., Kanety, H., Kuint, J., & Gilboa-Schechtman, E. (2009). Maternal depression and anxiety across the postpartum year and infant social engagement, fear regulation, and stress reactivity. *Journal of the American Academy of Child & Adolescent Psychiatry, 48*, 919–927.
- Feldman, R., Keren, M., Gross-Rozval, O., & Tyano, S. (2004). Mother–child touch patterns in infant feeding disorders: Relation to maternal, child, and environmental factors. *Journal of the American Academy of Child & Adolescent Psychiatry, 43*, 1089–1097.
- Feldman, R., & Masalha, S. (2010). Parent–child and triadic antecedents of children's social competence: Cultural specificity, shared process. *Developmental Psychology, 46*, 455–467.
- Feldman, R., Singer, M., & Zagoory, O. (2010). Touch attenuates infants' physiological reactivity to stress. *Developmental Science, 13*, 271–278.
- Feldman, R., & Vengrober, A. (2011). Post-traumatic stress disorder in infants and young children exposed to war-related trauma. *Journal of the American Academy of Child & Adolescent Psychiatry, 50*, 645–658.
- Feldman, R., Vengrober, A., & Hallaq, E. (2007). *Mother–child relationship, child symptoms, and maternal well-being in Israeli and Palestinian infants and young children exposed to war, terror, and violence*. Paper presented at the 13th meeting of the European Society for Child and Adolescent Psychiatry, Florence, Italy.
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., et al. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine, 14*, 245–258.
- Foa, E. B. (1995). *Posttraumatic Stress Diagnostic Scale manual*. North Brunswick, NJ: National Computer Systems.
- Fombonne, E., Wostear, G., Cooper, V., Harrington, R., & Rutter, M. (2001). The Maudsley long-term follow-up of child and adolescent depression: 2. Suicidality, criminality and social dysfunction in adulthood. *British Journal of Psychiatry, 179*, 218–223.
- Fortunato, C. K., Dribin, A. E., Granger, D. A., & Buss, K. A. (2008). Salivary alpha-amylase and cortisol in toddlers: Differential relations to affective behavior. *Developmental Psychobiology, 50*, 807–818. doi: 10.1002/dev.20326
- Frigerio, A., Ceppi, E., Rusconi, M., Giorda, R., Raggi, M. E., & Fearon, P. (2009). The role played by the interaction between genetic factors and attachment in the stress response in infancy. *Journal of Child Psychology and Psychiatry, 50*, 1513–1522.
- Fujioka, A., Fujioka, T., Ishida, Y., Maekawa, T., & Nakamura, S. (2006). Differential effects of prenatal stress on the morphological maturation of hippocampal neurons. *Neuroscience, 141*, 907–915.
- Goldsmith, H., & Rothbart, M. (1996). *The Laboratory Temperament Assessment Battery (Lab-TAB): Locomotor version 3.0 technical manual*. Madison, WI: University of Wisconsin, Department of Psychology.
- Gordis, E. B., Granger, D. A., Susman, E. J., & Trickett, P. K. (2006). Asymmetry between salivary cortisol and alpha-amylase reactivity to stress: Relation to aggressive behavior in adolescents. *Psychoneuroendocrinology, 31*, 976–987.
- Gordis, E. B., Margolin, G., Spies, L. A., Susman, E. J., & Granger, D. A. (2010). Interparental aggression and parent–adolescent salivary alpha amylase symmetry. *Physiology & Behavior, 100*, 225–233.
- Graham, J. E., Christian, L. M., & Kiecolt-Glaser, J. K. (2006). Stress, age, and immune function: Toward a lifespan approach. *Journal of Behavioral Medicine, 29*, 389–400.
- Granger, D. A., Kivlighan, K. T., el-Sheikh, M., Gordis, E. B., & Stroud, L. R. (2007). Salivary alpha-amylase in biobehavioral research: Recent developments and applications. *Annals of the New York Academy of Sciences, 1098*, 122–144.
- Gunnar, M., & Quevedo, K. (2007). The neurobiology of stress and development. *Annual Review of Psychology, 58*, 145–173.
- Gunnar, M. R., Brodersen, L., Nachmias, M., Buss, K., & Rigatuso, J. (1996). Stress reactivity and attachment security. *Developmental Psychobiology, 29*, 191–204.
- Gunnar, M. R., & Vazquez, D. M. (2001). Low cortisol and a flattening of expected daytime rhythm: Potential indices of risk in human development. *Development and Psychopathology, 13*, 515–538.
- Haley, D. W., & Stansbury, K. (2003). Infant stress and parent responsiveness: Regulation of physiology and behavior during still-face and reunion. *Child Development, 74*, 1534–1546.
- Heim, C., Plotsky, P. M., & Nemeroff, C. B. (2004). Importance of studying the contributions of early adverse experience to neurobiological findings in depression. *Neuropsychopharmacology, 29*, 641–648.
- Hellhammer, D. H., Wüst, S., & Kudielka, B. M. (2009). Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology, 34*, 163–171.
- Hofer, M. A. (1995). Hidden regulators: Implication for a new understanding of attachment, separation, and loss. In S. Goldberg, R. Muir, & J. Kerr (Eds.), *Attachment theory: Social, developmental, and clinical perspectives* (pp. 203–230). Hillsdale, NJ: Analytic Press.
- Juster, R.-P., Bizik, G., Picard, M., Arseneault-Lapierre, G., Sindi, S., Trepanier, L., et al. (2011). A transdisciplinary perspective of chronic stress in relation to psychopathology throughout life span development. *Development and Psychopathology, 23*, 725–776.
- King, J. A., Mandansky, D., King, S., Fletcher, K. E., & Brewer, J. (2001). Early sexual abuse and low cortisol. *Psychiatry and Clinical Neuroscience, 55*, 71–74.

- Korte, S. M., Koolhaas, J. M., Wingfield, J. C., & McEwen, B. S. (2005). The Darwinian concept of stress: Benefits of allostasis and costs of allostatic load and the trade-offs in health and disease. *Neuroscience and Biobehavioral Reviews*, *29*, 3–38.
- Laor, N., Wolmer, L., & Cohen, D. J. (2001). Mothers' functioning and children's symptoms 5 years after a SCUD missile attack. *American Journal of Psychiatry*, *158*, 1020–1026.
- Lightman, S. L. (2008). The neuroendocrinology of stress: A never ending story. *Journal of Neuroendocrinology*, *20*, 880–884.
- Lopes Cardozo, B., Kaiser, R., Gotway, C. A., & Agani, F. (2003). Mental health, social functioning, and feelings of hatred and revenge of Kosovar Albanians one year after the war in Kosovo. *Journal of Traumatic Stress*, *16*, 351–360.
- Masten, A. S., & Narayan, A. J. (2012). Child development in the context of disaster, war, and terrorism: Pathways of risk and resilience. *Annual Review of Psychology*, *63*, 227–257.
- McEwen, B. S., & Stellar, E. (1993). Stress and the individual: Mechanisms leading to disease. *Archives of Internal Medicine*, *153*, 2093–2101.
- McFarlane, A. C. (2009). Military deployment: The impact on children and family adjustment and the need for care. *Current Opinion in Psychiatry*, *22*, 369–373.
- Nater, U. M., & Rohleder, N. (2009). Salivary alpha-amylase as a non-invasive biomarker for the sympathetic nervous system: Current state of research. *Psychoneuroendocrinology*, *34*, 486–496.
- Pervanidou, P. (2008). Biology of post-traumatic stress disorder in childhood and adolescence. *Journal of Neuroendocrinology*, *20*, 632–638.
- Pfeffer, C. R., Altemus, M., Heo, M., & Jiang, H. (2007). Salivary cortisol and psychopathology in children bereaved by the September 11, 2001, terror attacks. *Biological Psychiatry*, *61*, 957–965.
- Pfefferbaum, B., Nixon, S. J., Tucker, P. M., Tivis, R. D., Moore, V. L., Gurwitch, R. H., et al. (1999). Posttraumatic stress responses in bereaved children after the Oklahoma City bombing. *Journal of the American Academy of Child & Adolescent Psychiatry*, *38*, 1372–1379.
- Qouta, S., Punamaki, R. L., & El Sarraj, E. (2003). Prevalence and determinants of PTSD among Palestinian children exposed to military violence. *European Child and Adolescent Psychiatry*, *12*, 265–272.
- Ruttle, P. L., Serbin, L. A., Stack, D. M., Schwartzman, A. E., & Shirtcliff, E. A. (2011). Adrenocortical attunement in mother-child dyads: Importance of situational and behavioral characteristics. *Biological Psychology*, *88*, 104–111.
- Sanson, A., Oberklaid, F., Pedlow, R., & Prior, M. (1991). Risk indicators: Assessment of infancy predictors of pre-school behavioural maladjustment. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *32*, 609–626.
- Schaal, S., Jacob, N., Dusingizemungu, J. P., & Elbert, T. (2010). Rates and risks for prolonged grief disorder in a sample of orphaned and widowed genocide survivors. *BMC Psychiatry*, *10*, 55.
- Scheeringa, M. S., Zeanah, C. H., & Cohen, J. A. (2011). PTSD in children and adolescents: Toward an empirically based algorithm. *Depression and Anxiety*, *28*, 770–782.
- Sethre-Hofstad, L., Stansbury, K., & Rice, M. A. (2002). Attunement of maternal and child adrenocortical response to child challenge. *Psychoneuroendocrinology*, *27*, 731–747.
- Smith, P., Perrin, S., Yule, W., & Rabe-Hesketh, S. (2001). War exposure and maternal reactions in the psychological adjustment of children from Bosnia-Herzegovina. *Journal of Child Psychology and Psychiatry*, *42*, 395–404.
- Smyth, J. M., Hockemeyer, J. R., & Tulloch, H. (2008). Expressive writing and post-traumatic stress disorder: Effects on trauma symptoms, mood states, and cortisol reactivity. *British Journal of Health Psychology*, *13*, 85–93.
- Spinrad, T. L., Eisenberg, N., Granger, D. A., Eggum, N. D., Sallquist, J., Haugen, R. G., et al. (2009). Individual differences in preschoolers' salivary cortisol and alpha-amylase reactivity: Relations to temperament and maladjustment. *Hormones and Behavior*, *56*, 133–139.
- Spitz, R. (1946). Anaclitic depression. *Psychoanalytic Study of the Child*, *2*, 313–342.
- Tarullo, A. R., & Gunnar, M. R. (2006). Child maltreatment and the developing HPA axis. *Hormones and Behavior*, *50*, 632–639.
- Teicher, M. H., Andersen, S. L., Polcari, A., Anderson, C. M., Navalta, C. P., & Kim, D. M. (2003). The neurobiological consequences of early stress and childhood maltreatment. *Neuroscience & Biobehavioral Reviews*, *27*, 33–44.
- Vigil, J. M., Geary, D. C., Granger, D. A., & Flinn, M. V. (2010). Sex differences in salivary cortisol, alpha-amylase, and psychological functioning following Hurricane Katrina. *Child Development*, *81*, 1228–1240.
- Wadhwa, P. D. (2005). Psychoneuroendocrine processes in human pregnancy influence fetal development and health. *Psychoneuroendocrinology*, *30*, 724–743.
- Weaver, I. C., Cervoni, N., Champagne, F. A., D'Alessio, A. C., Sharma, S., Seckl, J. R., et al. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience*, *7*, 847–854.
- Weinstock, M. (2005). The potential influence of maternal stress hormones on development and mental health of the offspring. *Brain Behavior, and Immunology*, *19*, 296–308.
- Welberg, L. A., Seckl, J. R., & Holmes, M. C. (2001). Prenatal glucocorticoid programming of brain corticosteroid receptors and corticotrophin-releasing hormone: Possible implications for behaviour. *Neuroscience*, *104*, 71–79.
- Wolf, J. M., Nicholls, E., & Chen, E. (2008). Chronic stress, salivary cortisol, and alpha-amylase in children with asthma and healthy children. *Biological Psychology*, *78*, 20–28.
- Zero to Three. (2005). *DC:0-3R: Diagnostic classification of mental health and developmental disorders of infancy and early childhood* (rev.). Washington, DC: Author.