Regular Article

The neurophysiological embedding of child maltreatment

Steven J. Holochwost[1,2] (iD), Guan Wang[3], Jacek Kolacz[4], W. Roger Mills-Koonce[3], J. Bart Klika[5] and Sara R. Jaffee[6]

[1]Palmer Wolf Corporation, 8A Francis Avenue, Cambridge, MA 02138, USA; [2]Andrus, 1156 North Broadway, Yonkers, NY 10701, USA; [3]School of Education, University of North Carolina Chapel Hill, 301K Peabody Hall, CB 3500, Chapel Hill, NC 27599-3500, USA; [4]Kinsey Institute, Indiana University, Lindley Hall, 150 South Woodlawn Avenue, Bloomington, IL 47405, USA; [5]Prevent Child Abuse America, 228 South Wabash Avenue, 10th Floor, Chicago, IL 60604, USA and [6]Department of Psychology, University of Pennsylvania, 425 S. University Avenue, Philadelphia, PA 19104, USA

Abstract

Maltreatment adversely impacts the development of children across a host of domains. One way in which maltreatment may exert its deleterious effects is by becoming embedded in the activity of neurophysiological systems that regulate metabolic function. This paper reviews the literature regarding the association between childhood maltreatment and the activity of three systems: the parasympathetic nervous system, the sympathetic nervous system, and the hypothalamic–pituitary–adrenal axis. A particular emphasis is placed on the extent to which the literature supports a common account of activity across these systems under conditions of homeostasis and stress. The paper concludes with an outline of directions for future research and the implications of the literature for policy and practice.

Maltreatment includes physical, sexual, and emotional abuse and neglect (Leeb, Paulozzi, Melanson, Simon, & Arias, 2008). In 2015, 683,000 children in the United States were victims of maltreatment (US Department of Health & Human Services, 2017), and while international estimates of maltreatment are variable, the World Health Organization notes that one in four adults report being physically abused as children (World Health Organization, 2017). While there are many ways by which maltreatment may exert its influence on child development, one avenue is the capacity of maltreatment to "get under the skin" (Lupien, King, Meaney, & McEwen, 2001), becoming embedded at multiple levels of biological organization, from genetic expression to cortical structure and function (Hertzman, 1999).

There is abundant evidence that speaks to the pernicious nature of maltreatment's influence in both the short and long term. Children who have been maltreated exhibit poorer performance on tasks of essential cognitive abilities, including working memory (DePrince, Weinzierl, & Combs, 2009), attention (Nolin & Ethier, 2007; Porter, Lawson, & Bigler, 2005), and inhibitory control (Pollak et al., 2010), and also display lower levels of academic achievement (Carrey, Butter, Persinger, & Bialik, 1995; DeBellis, Hooper, Spratt, & Woolley, 2009; Perez & Widom, 1994). Similar deficits in executive functions (Aas et al., 2012) and educational attainment (Jaffee et al., 2018; Majer, Nater, Lin, Capuron, & Reeves, 2010; Navalta, Polcari, Webster, Boghossian, & Teicher, 2006) have been observed among adults who

experienced maltreatment as children. Nor are the effects of maltreatment limited to cognitive development. Children who experience maltreatment exhibit worse health outcomes than their peers, including higher rates of obesity and poorer cardiovascular health (Rogosch, Dackis, & Cicchetti, 2011; Shalev et al., 2012), and these problems are also observed among adults who were maltreated as children (Miller, Chen, & Parker, 2011; Shalev et al., 2012; Tyrka et al., 2010). Mental health is also adversely impacted by maltreatment. Maltreatment is associated with higher rates of depression (Kessler, Davis, & Kendler, 1997; Nanni, Uher, & Danese, 2012), bipolar disorder (Agnew-Blais & Danese, 2016), psychotic disorders (Varese et al., 2012), posttraumatic stress disorder (PTSD) (Widom, 1999), as well as increased likelihood of substance use (Klanecky, McChargue, & Bruggeman, 2012; Madruga et al., 2011), self-injury (Lang & Sharma-Patel, 2011), and suicide in adulthood (Angelakis, Gillepsie, & Panagioti, 2018).

These pervasive, adverse effects of maltreatment have spurred research devoted to understanding the etiology of maltreatment's effects, including the neurophysiological embedding of maltreatment. Given maltreatment's nature as a toxic stressor (National Scientific Council on the Developing Child, 2005), researchers have placed particular emphasis on the activity of the systems that mediate the neurophysiological response to stress – the autonomic nervous system (ANS) and the hypothalamic–pituitary–adrenal (HPA) axis – and indeed dysregulation of these systems has been linked to many of the sequalae of maltreatment. For example, dysregulated ANS activity has been linked to poorer performance on measures of executive functions (Forte, Favieri, & Casagrande, 2019) and deficits in higher level cognitive functions among individuals with neurological impairments (Bassi & Bozzali, 2015); HPA axis function has also been associated with poorer performance on executive functions tasks in children

(Blair et al., 2011; Wagner et al., 2016) and lower levels of overall cognitive function in children (Suor, Sturge-Apple, Davies, Cicchetti, & Manning, 2015) and adults (Lee et al., 2007). Dysregulated ANS activity has been implicated in gastrointestinal illnesses (Kolacz & Porges, 2018; Kolacz, Kovacic, & Porges, 2019), while dysregulated HPA axis activity is associated with obesity in children (Rosmalen et al., 2005; Veldhorst et al., 2014) and adults (Jackson, Kirschbaum, & Steptoe, 2017). Dysregulated ANS activity has also been linked to poorer mental health, including depression in adolescents and adults (Kemp et al., 2010; Koenig, Kemp, Beauchaine, Thayer, & Kaess, 2016), as well as anxiety and PTSDs (Chalmers, Quintana, Abbott, & Kemp, 2014). Similarly, dysregulation of the HPA axis activity is associated with internalizing behaviors in children (Laurent, Gilliam, Wright, & Fisher, 2015) and depression in adults (Knorr, Vinberg, Kessing, & Wetterslev, 2010; Vreeburg et al., 2009), as well as a host of mental illnesses that typically manifest in adulthood: bipolar (Watson, Gallagher, Ritchie, Ferrier, & Young, 2004), psychotic (Karanikas, Antoniadis, & Garyfallos, 2014) and PTSDs (Goenjian et al., 1994), substance use (Sinha, 2008), nonsuicidal self-injurious behaviors (Larkin, Di Blasi, & Arensman, 2014), and suicide (O'Connor, Ferguson, Green, O'Carroll, & O'Connor, 2016).

The association between maltreatment and dysregulated neurophysiological activity, on one hand, and dysregulated neurophysiological activity and poorer cognitive function and reduced physical and mental health, on the other, outlines a model linking maltreatment to these outcomes via the dysregulation of the ANS and HPA axis. The purpose of this paper is to assess the evidence regarding the first association in this model by systematically reviewing studies that have examined the relation between maltreatment and the activity of these systems in childhood, in an effort to address two questions: (a) Does the literature support a particular account of ANS or HPA axis function under conditions of homeostasis and stress? That is, are these systems characteristically hyper- or hypoactive among children who have experienced maltreatment? And (b) to the extent that they are, can findings that are at odds with this account be explained either by methodological differences across studies or "third variables" such as gender, psychopathology, and genetics?

Maltreatment and the ANS

The ANS: Structure, function, and role in the stress response

The ANS lies outside (or is peripheral to) the central nervous system, and is divided into two branches: the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). Through efferent fibers originating in the brain and spinal cord, both branches of the ANS innervate tissues and organs throughout the body, collectively known as visceral effectors. Parasympathetic input to these effectors promotes anabolic activities such as extracting, conserving, and storing energy or allowing organs to rest and repair. Thus, parasympathetic input causes the bronchial muscles to constrict (limiting oxygen consumption), decreases the rate and strength of the heart's contraction (limiting blood flow), increases motility, tone, and gastric secretions of the stomach and intestines (encouraging digestion), and promotes glycogenesis in the liver (the storage of energy as glucose). However, under conditions of stress the activity of the PNS is reduced (or withdrawn), and the activity of the SNS increased. The net function of sympathetic activation is to free and direct metabolic resources in order to

support active defense behaviors. Sympathetic input dilates the bronchial muscles, allowing for increased oxygen intake, increases heart rate while dilating the vessels supplying blood to the skeletal muscles, inhibits digestion by reducing the motility, tone, and gastric secretions of the stomach and intestines, and promotes the liver's conversion of glycogen into glucose.

Altered ANS function following maltreatment

For most children, homeostatic ANS function will feature relatively high levels of PNS activity and relatively low levels of SNS activity; under situations of challenge, PNS activity will decrease and SNS activity will increase. But maltreatment may be expected to prompt alterations in ANS function under conditions of both homeostasis and stress. Under homeostatic conditions the most likely alteration of ANS activity for a maltreated child would be an increase in SNS activity, relative to a child not exposed to maltreatment, facilitating increased levels of vigilance to threat. Increases in SNS activity might be accompanied by decreases in PNS activity, in part due to the inhibitory inter-connections between the SNS and PNS, and in part because the context of maltreatment may offer reduced opportunities for states of calm engagement that are supported by relatively high levels of PNS activity. This configuration of ANS activity would be adaptive for a child who had been maltreated, at least in the short-term. However, in the long-term these elevated levels of SNS activity would strain children's cardiovascular function, a type of physiological burden that is often referred to as allostatic load (McEwen, 2005).

Under stressful conditions, two patterns of altered ANS activity are equally plausible. On one hand, exposure to a toxic stressor may recalibrate the autonomic stress response to a state of hyperreactivity, prompting large decreases in PNS activity and large increases in SNS activity in response to stress. While frequent recruitment of autonomic resources may impose a heavy allostatic load in the long term, in the immediate context these resources would support defensive behaviors necessary to ameliorate or escape an experience that may, in extreme cases, be life threatening. On the other hand, the experience of maltreatment may, over time, lead to down-regulation or hyporeactivity of the autonomic stress response. Such a response would feature smaller decreases in PNS activity and diminished increases in SNS activity. This could be indicative of a stress response that has become habituated to extreme adversity, or it could reflect the child's perception that a challenge posed by maltreatment is insurmountable. The latter possibility would recommend tonic immobility (playing dead), a last line of behavioral defense that is supported by an extreme reduction in SNS activity and that may, in part, be manifest in dissociative disorders associated with maltreatment (Putnam, 1993). The adaptivity of this hyporeactive recalibration would be inverse to that of a hyperreactive recalibration with respect to time: while hyporeactivity might avoid the long-term allostatic load imposed by frequent and large activations of the autonomic stress response, they also raise the possibility that in the short-term a child might not have the metabolic resources to support defensive or flight behaviors when they are absolutely needed.

Maltreatment and the HPA axis

The HPA axis: Structure, function, and role in the stress response

The HPA axis comprises three structures: the hypothalamus, the pituitary, and the adrenal glands. By secreting corticotropin-releasing factor, neurons of the paraventricular nucleus of the

hypothalamus signal the pituitary to secrete adrenocorticotropic hormone, which in turn prompts the synthesis and release of glucocorticoids – most notably, cortisol – into the blood stream. Cortisol and other glucocorticoids bind to glucocorticoid receptors throughout the body, increasing the levels of glucose in the blood (Munck & Náray-Fejes-Tóth, 1995) and suppressing immune function (Wiegers & Reul, 1998). Understanding the physiological function of the HPA axis does not a priori suggest what role it would play in the stress response. The "classical" account, first formulated by Hans Seyle (1950), focuses on the metabolism-enhancing functions of the HPA axis, a view that has become so well entrenched in the psychophysiological literature that activation of the HPA axis has become nearly synonymous with stress (Gunnar, 1992). However, the prolonged gap between the onset of a stressor and an HPA axis response led Munck, Guyre, and Hollbrook (1984) to propose a "revisionist" account, wherein the role of the HPA axis is to suppress previously activated neurophysiological defense mechanisms, including those associated with the SNS. Under certain conditions, both arguments may be correct. For brief stressors with a sudden onset, activation of the HPA axis is of limited utility, as the stressor will pass before the effects of activation are realized. But, as Sapolsky, Romero, and Munck (2000) point out, in social species such as our own, stressors are predictable, and thus activation of the HPA axis in anticipation of stressor onset can serve as a preparation for subsequent activation.

Altered HPA axis function following maltreatment

Given its role in the stress response, it is not surprising that research has assessed the association between maltreatment and alterations of HPA axis activity. Like research on alterations in ANS activity, studies of the HPA axis have examined altered function under conditions of both homeostasis and stress. However, unlike studies of ANS activity, investigations of HPA axis activity have had to accommodate the more complex profile of homeostatic HPA axis function, which features circadian or diurnal rhythms. The terms "basal" and "baseline" activity are alternatively used to refer to this homeostatic function. Elevated levels of morning HPA axis activity may be considered hyperactive, as may elevated levels of HPA axis activity prior to the onset of a stressor, regardless of when that activity is measured. In all but the youngest children, diurnal levels of HPA axis activity follow a predictable pattern, in which levels of activity peak shortly after waking and then gradually decrease over the course of the day. Therefore, attenuation of this decrease – a flatter diurnal trajectory – may also be classified as hyperactivity. However, *lower* levels of morning activity, when combined with flattened diurnal trajectories, can result in higher cumulative levels of HPA axis activity over the course of the day, and thus this pattern of HPA axis activity may too be indicative of hyperactivity (Miller, Chen, & Zhou, 2007).

The experience of maltreatment is most likely to engender hyperactivity across different components of homeostatic HPA axis activity. As noted above, one of the functions of the HPA axis may be to mobilize metabolic resources in anticipation of stressors that are predictable (Sapolsky et al., 2000). Maltreated children – particularly those who suffer frequent or repeated maltreatment – inhabit an environment in which highly stressful events are disproportionately likely to occur. As in the case of the ANS, elevated homeostatic activity of the HPA axis may be adaptive, in that it provides metabolic resources to support vigilance and active defense behaviors. However – and also as in

the case of the ANS – in the long-term elevated levels of HPA axis activity may impose a heavy allostatic load, inhibiting immune and cognitive function.

Maltreatment may also have the capacity to alter HPA axis reactivity to stress. One possibility is that maltreatment results in hyperreactivity of the HPA axis, or hypercortisolism. According to the glucocorticoid cascade hypothesis (Sapolsky, Krey, & McEwen, 1986), more frequent and pronounced increases in HPA axis activity and concomitant elevations in cortisol damage hippocampal receptors, interfering with the negative feedback loop that signals the paraventricular nucleus of the hypothalamus to cease secretion of corticotropin releasing factor. Hyperreactivity of the HPA axis may be adaptive for the maltreated child in the short term, providing resources to mitigate situations of extreme stress, but in the long term may impose an allostatic load. A second possibility is that maltreatment leads to hyporeactivity of the HPA axis, or hypocortisolism. According to this account, repeated exposure to the severe stress of maltreatment results in habituation of the HPA axis, which manifests as a blunted response to stress. The adaptive value of this alteration would be protection from the adverse effects of repeated or large spikes in HPA axis activity, but to the extent that this prevented a child from recruiting the full range of metabolic resources in the face of a truly existential threat, this alteration would be maladaptive.

Current study

Although these accounts of the potential associations between maltreatment and the altered function of the ANS and HPA axis are plausible, as of yet they have not been systematically evaluated in light of the literature. In the remainder of this paper we present the method and results for a systematic review of the associations between maltreatment and ANS and HPA axis activity in childhood. The results of our review are divided into two sections: the first reviews the literature on maltreatment and ANS function; while the second examines maltreatment and HPA axis activity. The separation of two systems does not accurately reflect reality – wherein the activity of these systems is closely coordinated – but it does reflect the literature, in which the activity of one system is measured typically in isolation.

Method

Search strategy

A protocol for reviewing the literature was developed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Shamseer et al., 2015). PsycInfo and Medline were searched concurrently using four different combinations of keywords. The first combination comprised ["maltreat*" OR "abuse" OR "neglect" AND "autonomic*" OR "ANS" OR "cardiac" OR "blood pressure"]. The second combination retained ["maltreat*" OR "abuse" OR "neglect"] but replaced the second set of keywords with ["autonomic," etc.] with a new set designed to yield studies that focused on the PNS. The third and fourth combinations retained the first set of keywords but replaced the second set with new keywords focused on the SNS and HPA axis, respectively. No date limitations were placed on the search results. The final search was completed on September 15, 2019. See Table 1 for a summary of keywords used in each iteration of the search.

Table 1. Summary of studies included in the review

Keyword Set 1 (fixed)	Keyword Set 2 (variable)	Records identified
"maltreat*" OR "abuse" OR "neglect"		
"maltreat*" OR "abuse" OR "neglect"	"autonomic*" OR "ANS" OR "cardiac*" OR "blood pressure"	602
"maltreat*" OR "abuse" OR "neglect"	"parasympathetic*" OR "PNS" OR "vagal" OR "arrhythmia" OR "interbeat" OR "heart rate variability" OR "HRV"	125
"maltreat*" OR "abuse" OR "neglect"	"sympathetic*" OR "SNS" OR "amylase" OR "ejection"	89
"maltreat*" OR "abuse" OR "neglect"	"hypothalamic*" OR "HPA" OR "cortisol"	459

Study selection

Together, the four iterations of the search yielded 1,275 papers; removing duplicate records reduced this number to 1,110 (for a diagram of the number of papers included at each stage of the review, see Figure 1). The records for these studies were compiled in a spreadsheet, and the titles and abstracts of each study were reviewed by the first author. Only those studies that met the following inclusion criteria were retained: (a) the paper had to report the results of an empirical study that examined the association between maltreatment (or the allegation of maltreatment) and some aspect(s) of ANS (including PNS and/or SNS) and/or HPA axis activity; (b) maltreatment could include any form of abuse or neglect perpetrated or alleged to have been perpetrated by a parent or primary caregiver, but excluded abuse perpetrated by others (e.g., a significant other), peer victimization, or exposure to violence, including inter-partner violence; (c) maltreatment must have occurred (or have been alleged to have occurred) during childhood (between ages 0 and 18 years); (d) the activity of neurophysiological system(s) must also have been measured during childhood; and (e) if maltreatment was included as part of an overall index of adversity the association between maltreatment (or its allegation) and neurophysiological activity must have been assessed independent of other aspects of adversity. This final criterion resulted in the exclusion of studies that examined the association between posttraumatic stress and neurophysiological activity except in those cases in which the trauma was due solely to maltreatment and/or the association between maltreatment and neurophysiological activity was examined independently of other factors that led to the posttraumatic stress.

A series of report characteristics were also applied as inclusion criteria. To be included in the review, we required that a study was: (a) empirical (which excluded letters, commentary, and case studies); (b) published in English; and (c) published in a peer-reviewed journal. The decision to include only papers published in English was based on prior research that suggests

doing so does not bias review results (Morrison et al., 2012), while the decision to include only peer-reviewed studies provided some assurance as to the quality of studies without requiring the use of potentially problematic assessment tools (Siddaway, Wood, & Hedges, 2019).

The application of these criteria yielded 103 papers. These papers were subject to full-text review by the first author. Approximately 40% of these papers were selected at random for an independent review by the second or third author (who each reviewed approximately half of these papers). After applying the criteria to the full texts, 55 papers remained. One paper (Koopman et al., 2004) was excluded not on the basis of the criteria, but rather because it was not clear whether neurophysiological activity was collected under conditions of homeostasis or challenge; six others were excluded because they extended the results of other papers that reported an association between maltreatment and neurophysiological activity. In each case, the two reviewers agreed about which papers should be included. Finally, the reference lists of the remaining papers were examined and the inclusion criteria applied by the first author. This yielded an additional six studies for inclusion in the review, for a total of 61 studies.

Data extraction and analysis

For each of these studies, the following information was extracted by the second author and entered into a form that included the following fields: (a) the type(s) of maltreatment; (b) the age at which maltreatment occurred; (c) the source(s) of information about maltreatment, where reported; (d) the age(s) at which neurophysiological data were collected, the neurophysiological system(s) assessed and the method for doing so; (e) the size and composition of the sample; and, where applicable, (f) the nature of the stressor(s) used to elicit a neurophysiological response. This form had been developed by the first author, who trained the second and third authors in its use. As data were entered into the form, the first author checked the entries and discussed them as needed with the second and third authors to ensure the reliability of data extraction. Data were then converted into a format for presentation in Table 2, using the fields from the form as the column headings for the table.

As is evident from the information presented in the table, the studies included in the review were heterogeneous with respect to nearly all aspects of study design, from the type(s) of maltreatment to sample size and composition to the neurophysiological system(s) from which data were collected and under what conditions. The extent of the heterogeneity precluded the possibility of conducting a meta-analysis. We therefore provide a systematic narrative synthesis of the literature that characterizes different associations between maltreatment and neurophysiological function in the context of methodological variations across studies.

Results

Altered ANS function following maltreatment

Nine studies have examined autonomic function under homeostatic conditions among maltreated children, with five of these reporting evidence of hyperactivity. Gooding and colleagues reported that maltreated adolescents (13–17 years) exhibited significantly higher resting diastolic blood pressure (a global measure of ANS activity) relative to nonmaltreated children (Gooding,
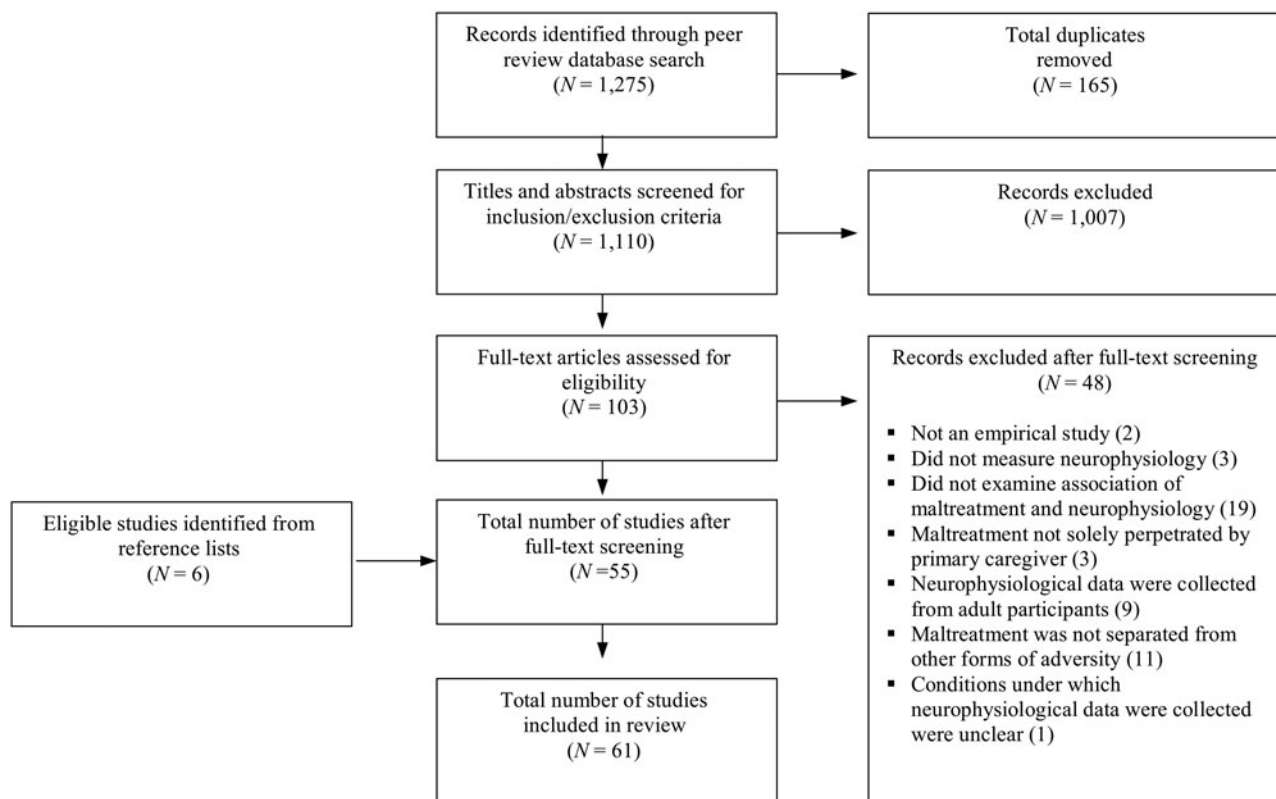
Figure 1. A depiction of the number of studies included at each stage of the literature review.

Milliren, Austin, Sheridan, & McLaughlin, 2016). Using more specific measures, Lunkenheimer and colleagues found that children (3–5 years) who had been physically abused exhibited lower levels of respiratory sinus arrhythmia (a measure of PNS activity; Lunkenheimer, Busuito, Brown, & Skowron, 2018); Skowron et al. (2011) reported a similar finding for children (3–5 years) who had been physically abused or neglected (Skowron et al., 2011). McLaughlin et al. (2015) found that Romanian children (13 years) who had been institutionalized exhibited shorter pre-ejection periods (an indication of higher SNS activity) at baseline compared to both noninstitutionalized children and children who had been moved from institutional to foster care. Among older females (12–16 years), one study found that a history of maltreatment was associated with lower levels of respiratory sinus arrhythmia, an index of PNS activity (Miskovic, Schmidt, Georgiades, Boyle, & MacMillan, 2009), although another study conducted with adolescent females (14–19 years) reported a trend towards *higher* levels of respiratory sinus arrhythmia among those who had been maltreated in the past year (Shenk, Putnam, & Noll, 2012).

While this is the only study of which we are aware to have yielded contrary findings, Gordis and colleagues did not find significant differences in respiratory sinus arrhythmia or skin conductance levels (a measure of SNS activity) between children and adolescents (9–16 years) who were maltreated and their peers (Gordis, Feres, Olezeski, Rabkin, & Trickett, 2010), just as Ford and colleagues found no differences in resting heart rate between abused children (6–19 years) and their peers (Ford, Fraleigh, Albert, & Connor, 2010). Similar findings were reported by Keeshin and colleagues, in that maltreatment was not

associated with levels of saliva alpha amylase (an index of ANS activity) among adolescents (12–17 years), although there was an association between saliva alpha amylase and the severity of PTSD symptoms, which may correspond to the severity of maltreatment (Keeshin, Strawn, Out, Granger, & Putnam, 2015).

Of the 12 studies that examined the function of the ANS among maltreated children in response to stress, seven reported evidence of hyporeactivity. Using the Trier Social Stress Task (TSST; Kirschbaum, Pirke, & Hellhammer, 1993), McLaughlin and colleagues found that a history of maltreatment was associated with reduced ANS reactivity, indexed by cardiac output, a global measure of overall ANS function, among adolescents (13–17 years; McLaughlin, Sheridan, Alves, & Mendes, 2014a). Studies employing other global measures (heart rate and blood pressure) have yielded similar results. Leitzke and colleagues found that children and adolescents (9–14 years) subjected to physical abuse did not exhibit an increase in systolic blood pressure in response to the TSST, whereas children who had not been maltreated did (Leitzke, Hilt, & Pollak, 2015). Analogous patterns of hyporeactivity in response to the TSST have been observed among maltreated adolescents (Gooding et al., 2016; McLaughlin et al., 2015) when diastolic blood pressure was used as a measure of ANS activity. Using more specific measures, McLaughlin and colleagues also found that maltreated adolescents exhibited blunted pre-ejection period response to the TSST relative to controls (McLaughlin et al., 2014a, 2015).

Among studies using stressors other than the TSST, two have yielded evidence that also supports the hyporeactivity account. Ford and colleagues reported that physically abused children

Table 2. Summary of studies included in the review

Study	Maltreatment Type(s)[a]	Maltreatment Age[b]	Maltreatment Source[c]	Participants Age at collection	Participants Composition (N)	Stressor	Measurement System(s)[d]	Measurement Method[e]	Findings Significant	Findings Nonsignificant
Alink et al. (2012)	Abuse (physical, emotional, sexual), Neglect	Childhood	Public records	6–9 years	Maltreated children (125), comparison children (111)	N/A	HPA axis	Morning (9 a.m.) and afternoon (4 p.m.) salivary cortisol collected at summer camp two times, one year apart.	Lower prosocial behavior and higher disruptive/aggressive behavior fully mediated the relation between maltreatment and lower morning cortisol levels a year later.	Withdrawn behavior did not mediate the relation between maltreatment and cortisol.
Bernard et al. (2010)	Unspecified maltreatment	Infancy	Public records	3–31 months	Maltreated children living with birth parents (155), maltreated children living with foster parents (184), comparison children (96)	N/A	HPA axis	Waking (8 a.m.) and bedtime (9 p.m.) salivary cortisol collected on two days at the child's home.	Maltreated children exhibited lower waking cortisol levels and flattened diurnal patterns of cortisol relative to controls. Maltreated children living with birth parents exhibited flatter diurnal patterns of cortisol relative to maltreated children living with foster parents.	
Bick et al. (2015)	Abuse (physical, emotional, sexual), Neglect (physical, emotional)	Adolescence	Self-report (CTQ[1])	14.5–19 years	Adolescents with histories of maltreatment (161), comparison children (45)	TSST-C[2]	HPA axis	Salivary cortisol samples were collected six times prior to, during, and after the stressor.[3]	Children who experienced moderate to severe physical neglect showed significantly higher levels of baseline cortisol, compared to children who experienced no or minimal levels of physical neglect. Sexual abuse was associated with greater cortisol reactivity at a level approaching significance.	Physical abuse/neglect and emotional abuse/neglect were not significantly associated with cortisol reactivity in response to the stressor.
Bruce et al. (2009)	Abuse (physical, emotional, sexual), Neglect (physical, supervisory)	Early childhood	Public records	3–6 years	Foster children (117), comparison children (60)	N/A	HPA axis	Morning salivary cortisol levels were collected at home 30 min after waking.	Physical neglect was related to lower morning cortisol relative to controls. Emotional abuse was related to higher morning cortisol relative to controls.	Physical abuse, sexual abuse, and supervisory neglect were not associated with significantly different cortisol levels, relative to controls.
Bugental et al. (2003)	Abuse (physical), Neglect (emotional)	Infancy	Self-report (CTS[4])	2 years	At-risk toddlers (44)	SSP[5]	HPA axis	Salivary cortisol samples were collected at baseline (40 m after arrival at the lab) and 20 m following the stressor.	Infants who experienced frequent maternal emotional withdrawal exhibited elevated baseline cortisol. Infants subjected to frequent corporal punishment displayed elevated reactivity.	

(Continued)

Table 2. (Continued.)

Study	Maltreatment			Participants			Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (N)	Stressor	System (s)[d]	Method[e]	Significant	Nonsignificant
Cicchetti and Rogosch (2001b)	Abuse (physical, emotional, sexual), Neglect	Childhood	Public records	6.5–11 years	Maltreated children (175), comparison children (209)	N/A	HPA axis	Morning (9 a.m.) and afternoon (4 p.m.) salivary cortisol collected at summer camp.	Children exposed to multiple forms of maltreatment (physical, sexual, emotional abuse and neglect) exhibited significantly higher morning cortisol levels relative to controls. A disproportionate number of children exhibiting high morning and afternoon cortisol levels had suffered multiple forms of maltreatment. The severity of sexual abuse was positively related to morning and afternoon cortisol levels.	No overall differences in morning or afternoon cortisol levels or diurnal trajectories were observed between maltreated children and controls. Developmental timing and chronicity of maltreatment were not related to morning cortisol levels.
Cicchetti and Rogosch (2001a)[6]	Abuse (physical, emotional, sexual), Neglect	Childhood	Public records	7–12 years	Maltreated children (167), comparison children (204)	N/A	HPA axis	Morning (9 a.m.) and afternoon (4 p.m.) salivary cortisol collected at summer camp.	Maltreated children with clinical internalizing problems displayed higher morning, afternoon, and overall cortisol levels relative to controls. Maltreated children with comorbid, clinical internalizing and externalizing problems were less likely to exhibit diurnal decreases in cortisol relative to controls.	No differences in morning, afternoon, or overall cortisol levels were observed between maltreated children without clinical internalizing problems and controls, regardless of whether controls had clinical internalizing problems.
Cicchetti et al. (2010)	Abuse (physical, emotional, sexual), Neglect	Early childhood	Public records	7–13 years	Early physical/sexual abuse (60), emotional abuse (205), comparison children (288)	N/A	HPA axis	Morning (9 a.m.) and afternoon (4 p.m.) salivary cortisol collected at summer camp.	Physical and sexual abuse accompanied by internalizing symptoms were associated with flattened diurnal cortisol relative to controls.	Neglect and emotional maltreatment were not significantly associated with diurnal cortisol.
Cicchetti et al. (2011)	Abuse (physical), Neglect (emotional)	Infancy	Public records	11–15 months	Maltreated infants (91), comparison infants (52)	N/A	HPA axis	Morning (10 a.m.) salivary cortisol		No difference was observed in morning cortisol between maltreated and nonmaltreated children.
DeBellis et al. (1994)	Abuse (sexual)	Childhood, adolescence	Public records (referral to Child Protective Services)	7–15 years	Sexually abused females (13), comparison females (13)	N/A	HPA axis	Plasma ACTH[7] and cortisol monitored before, during, and after evening (8 p.m.) ovine CRH[8] infusion. Urinary free cortisol was measured over 3 days prior to procedure.	Sexually abused females had lower baseline, stimulated, and total plasma ACTH than females in the the comparison group.	There were no significant differences in basal, stimulated, and total plasma cortisol secretion between groups. There were no significant differences in 24-hour urinary free cortisol measures.

(Continued)

Table 2. (Continued.)

Study	Maltreatment			Participants		Stressor	Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (N)		System (s)[d]	Method[e]	Significant	Nonsignificant
de Punder et al. (2016)	Abuse (physical)	Early childhood	Public records	3–5 years	Maltreated children (35), comparison children (33)	N/A	HPA axis	Salivary cortisol collected at 9, 10, and 11 a.m.[9]	Total cortisol levels (indexed by AUC[10]) were positively related to the number and cumulative severity of instances of abuse.	
do Prado et al. (2017)	Abuse (physical, emotional, sexual), Neglect	Childhood	Self-report (CTQ[11])	13–17 years	Maltreated adolescents (30), comparison adolescents (27)	N/A	HPA axis	Cortisol concentrations were estimated from hair samples.	Early maltreatment experiences were associated with increased cumulative hair cortisol levels.	
Doom et al. (2014)	Abuse (physical, emotional, sexual), Neglect	Childhood, adolescence	Public records	5–13 years	Maltreated children (187), comparison children (154)	N/A	HPA axis	Salivary cortisol was collected at the same time every day at an after-school program one day per week for 20 weeks.	Maltreated children exhibited greater between-person variability in both initial cortisol levels and change in cortisol over time, relative to comparison children. The severity, timing, and number of subtypes of maltreatment predicted within-person cortisol variability. Children who experienced fewer types of maltreatment, less severe maltreatment, and less recent maltreatment displayed greater variability in cortisol levels over time.	
Doom et al. (2013)	Abuse (physical, emotional, sexual), Neglect	Childhood	Public records	8–11 years	Maltreated children (137), comparison children (110)	N/A	HPA axis	Salivary cortisol was collected 3 times a day over five days at summer camp.[12]	Maltreated children exhibited higher levels of cortisol than children who had not been maltreated. Girls who experienced less pervasive[13] or more recent maltreatment displayed higher levels of cortisol than girls with more pervasive or less recent maltreatment experiences.	Among boys, the pervasiveness and recency of maltreatment did not moderate the relation of maltreatment and cortisol.
Duval et al. (2004)	Abuse (sexual)	Adolescence	Diagnosis of PTSD[14] due to sexual abuse (DSM-IV)	12–20 years	Hospitalized inpatients with PTSD due to sexual abuse (14), comparison hospitalized adolescents without PTSD (14)	DST[15]	HPA axis	Salivary cortisol was assessed the morning prior to and at three times the day after the DST (8 a.m., 4 p.m., 11 p.m.)	Post-DST levels of ACTH were lower among maltreated adolescents at each time point following the DST.	No significant differences in cortisol at any time point (morning or post-DST) between maltreated adolescents with PTSD and adolescents who did not have PTSD.

(Continued)

Table 2. (*Continued.*)

Study	Maltreatment			Participants			Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (*N*)	Stressor	System (s)[d]	Method[e]	Significant	Nonsignificant
Ford et al. (2010)	Abuse (physical, sexual)	Childhood, adolescence	Public records, parent report, self-report	6–19 years	Maltreated children (134), comparison children (128)	Blood draw	ANS	Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP)	Children with a history of physical abuse were more likely to exhibit a decrease in both HR and SBP following the stressor than controls.	Children with a history of sexual abuse were no more likely to exhibit a decrease in both HR and SBP following the stressor than controls. Physical and sexual abuse were unrelated to resting HR.
Gerra et al. (2010)	Neglect	Adolescence	Self-report	14–19 years	187 adolescents (proportion maltreated not reported)	N/A	HPA axis	Blood ACTH and cortisol levels were collected in morning (8:30 a.m.)	Maternal and paternal neglect predicted higher cortisol levels. Paternal neglect predicted higher ACTH levels.	Maternal neglect was not related to ACTH.
Gooding et al. (2016)	Abuse (physical, emotional, sexual), Neglect (physical, emotional)	Childhood, adolescence	Self-report (CTQ, CECA[16])	13–17 years	Maltreated children (58), comparison children (87)	TSST, frustration task	ANS	SBP, DBP were measured prior to and following the stressors	Maltreated children exhibited significantly higher resting DBP than controls. Maltreatment was associated with reduced reactivity of SBP and DBP in response to stressors, relative to controls.	
Gordis et al. (2010)	Abuse (sexual, physical, emotional), Neglect	Childhood, adolescence	Public records	9–16 years	Maltreated children (234), comparison children (128)	Video clips depicting conflict situations	PNS, SNS	RSA (PNS) and skin conductance level (SCL; SNS) were measured at baseline and while viewing conflict videos.		Maltreatment was not associated with significant differences in RSA or SCL directly or as part of an interaction with gender at baseline or while watching the videos.
Gordis et al. (2008)	Abuse (physical, sexual), Neglect	Adolescence	Public records	9–14.5 years	Maltreated children (47), comparison children (37)	TSST	SNS, HPA axis	Salivary alpha amylase (SNS) and cortisol (HPA) were collected two times prior to the stressor and four times afterwards (at 0, 10, 20, and 30 min poststressor)	Maltreated children exhibited an inverse relation (i.e., asymmetry) in alpha amylase and cortisol responses to challenge, whereas the responses of controls were positively correlated.	
Gunnar et al. (2001)	Neglect	Infancy	Public records	6–12 years	Romanian orphans adopted after 8 months. (RO; 18), children adopted before 4 months. (EA; 15), Canadian born (CB) children (27)	N/A	HPA axis	Waking (15–30 m after waking), mid-day (11 a.m.–1 p.m.), and bedtime (8–9 p.m.) salivary cortisol collected on three days at child's home	RO children exhibited higher diurnal cortisol levels than EA or CB children. Longer institutionalization among RO children was associated with higher diurnal cortisol.	No differences in cortisol levels were observed between EA and CB children.

(*Continued*)

Table 2. (Continued.)

Study	Maltreatment			Participants		Stressor	Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (N)		System (s)[d]	Method[e]	Significant	Nonsignificant
Harkness et al. (2011)	Abuse (physical, emotional, sexual), Neglect (physical, emotional)	Childhood	Self-report (CECA)	12–21 years	Maltreated (3) and nonmaltreated adolescents (27) with no/ minimal depression; maltreated (8) and nonmaltreated adolescents (8) with mild/ moderate depression; maltreated (15) and nonmaltreated (10) adolescents with moderate/severe depression	TSST	HPA axis	Salivary cortisol collected at baseline, immediately before the stressor, after the stressor, and during an extended recovery period.	Mildly/moderately depressed, maltreated adolescents exhibited larger cortisol response (indexed by AUC) to stressor than comparably depressed, nonmaltreated adolescents. Moderately/severely depressed, maltreated adolescents displayed higher baseline cortisol than comparably depressed, nonmaltreated adolescents. Maltreated adolescents with mild/moderate or moderate/ severe depression displayed significantly higher baseline cortisol levels than maltreated adolescents with no/minimal depression.	Baseline cortisol levels did not differ between maltreated adolescents with mild/moderate depression and maltreated adolescents with moderate/severe depression.
Hart et al. (1995)	Abuse (physical, emotional, sexual), Neglect (physical)	Childhood	Public records	28– 75 months	Maltreated children (33), comparison children (8).	N/A	HPA axis	Morning salivary cortisol samples collected between 10:30 a.m. and 11:45 a.m. for 31 days at school.[17]	Maltreated children displayed lower cortisol on high-conflict days relative to controls.[18] Comparison children displayed significantly higher cortisol levels on high-conflict days than low-conflict days; maltreated children did not.	
Hart et al. (1996)	Abuse (physical, sexual), Neglect	Childhood	Public records	6–11 years	Maltreated children without depression (68), depressed, maltreated children (63), comparison children (66)	N/A	HPA axis	Salivary cortisol samples were taken daily at 10 a.m. and 4 p.m. on three consecutive days.	Depressed maltreated children had lower morning cortisol concentrations compared to nondepressed maltreated children and were more likely to show a rise rather than the expected decrease in cortisol from morning to afternoon.	Morning cortisol levels did not differ between maltreated children and controls.
Kaess et al. (2018)	Abuse (physical, emotional, sexual), Neglect	Childhood	Self-report (CTQ[19])	Time 1: 11– 13 years; Time 2: 14– 16 years	69 adolescents	N/A	HPA axis	Pituitary gland volume (PGV) was measured by magnetic resonance imaging at time 1. Cortisol awakening response (CAR) was calculated at time 2 using salivary cortisol measures collected at 3 points in time (waking, 30 min and 60 min after waking) on two consecutive days.	Higher levels of maltreatment predicted smaller CAR, but only among participants with a larger PGV volume.	

(Continued)

Table 2. (*Continued.*)

Study	Maltreatment			Participants		Stressor	Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (*N*)		System (s)[d]	Method[e]	Significant	Nonsignificant
Kaess et al. (2017)	Abuse (physical, emotional, sexual), Neglect	Childhood	Self-report (CTQ)	14–16 years (cortisol)	69 adolescents	N/A	HPA axis	Cortisol awakening response (CAR) was calculated in mid-adolescence using salivary cortisol measures collected at 3 points in time (waking, 30 min and 60 min after waking) on two consecutive days.	Higher childhood maltreatment significantly predicted smaller CAR.	
Kaufman et al. (1997)	Abuse (physical, sexual), exposure to extreme domestic violence	Childhood	Self-report, parent-report (PSS[20]), medical records	7–13 years	Depressed, abused children in stable environment (6), depressed, abused children in unstable environment (7), depressed nonabused children (13), comparison children (13)	1.0 µg/kg of human CRH given intravenously	HPA axis	Baseline and changes of ACTH and cortisol obtained at nine intervals from blood samples.	Depressed and abused children living in an unstable environment had significantly higher levels of peak and total ACTH following the administration of CRH relative to the other three groups of children.	No significant differences in ACTH were observed between the remaining groups of participants. No significant between-group differences were observed in baseline cortisol or cortisol reactivity following the administration of CRH.
Keeshin et al. (2014)	Abuse (sexual)	Adolescence	Medical records	12–17 years	Sexually abused adolescent girls (24), comparison adolescent girls (12)	N/A	HPA axis	Salivary cortisol was collected at home upon awakening, 30 min after waking, and in the late afternoon on three consecutive school days.	Among maltreated participants, more severe traumatic experiences prior to maltreatment and more severe PTSD symptoms following maltreatment were associated with smaller cortisol awakening response.	
Keeshin et al. (2015)	Abuse (sexual)	Adolescence	Medical records	12–17 years	Sexually abused adolescent girls (24), comparison adolescent girls (12)	N/A	ANS	Salivary alpha amylase (sAA) was collected at home upon awakening, 30 min after waking, and in the late afternoon on three consecutive school days.	Morning sAA levels were positively associated with the severity of PTSD symptoms among maltreated participants.	There were no significant between-group differences in levels of sAA.
Kertes et al. (2008)	Abuse (physical, sexual) Neglect (physical, social), combined with age at adoption to create index of deprivation	Infancy to middle childhood	Parent-report	7–11 years	International adoptees who had been in their adoptive homes for at least three years (164)	N/A	HPA axis	Salivary cortisol collected 30 min after waking (~7–8 a.m.) and 30 min before bedtime (or 8–9 p.m. if bedtime was after 9:30 p.m.) on three days at child's home.	Deprivation prior to adoption predicted growth delay, which in turn predicted elevated waking cortisol levels and a larger diurnal decrease in cortisol levels.	
King et al. (2001)	Abuse (sexual)	Childhood	Parent-report and public records	5–7 years	Abused girls (10), matched controls (10)	N/A	HPA axis	Salivary cortisol samples were collected between 9 and 11 a.m. prior to doctors' visits.	Maltreated children exhibited significantly lower morning cortisol levels relative to controls.	
Kočovská et al. (2013)	Abuse (physical, sexual), Neglect (physical, emotional)	Childhood	Adoption records (maltreated), public records and caregiver report (comparison)	9–12 years	Adopted children with a history of maltreatment and reactive attachment disorder (34), comparison children (32)	N/A	HPA axis	Salivary cortisol samples were collected in the morning (6–8 a.m.), at midday (12-2 p.m.), and in the evening (6–9 p.m.).	Maltreated children exhibited lower levels of cortisol across all measurements.	Diurnal slope of cortisol did not differ between groups (i.e., there was not a significant interaction between group and time).

(*Continued*)

Table 2. (*Continued.*)

Study	Maltreatment			Participants			Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (N)	Stressor	System (s)[d]	Method[e]	Significant	Nonsignificant
Kuhlman et al. (2015)	Abuse (physical, emotional)	Childhood, adolescence	Parent-report[21]	9–16 years	121 youths	SE-CPT[22]	HPA axis	Salivary cortisol samples were collected at home immediately after waking, 45 min after waking, before dinner, and immediately before bed on two consecutive weekdays. Salivary cortisol samples were collected in the lab 30 min prior to and immediately before the stressor and then six times following the stressor.	Physical abuse was associated with a more rapid reaction to the stressor, while emotional abuse was associated with delayed recovery following the stressor.	Maltreatment was not associated with waking or diurnal cortisol levels.
Leitzke et al. (2015)	Physical aggression, harsh parental discipline, corporal punishment	Childhood	Parent-report (CTSPC[23])	9–14 years	Maltreated children (34), comparison children (77)	TSST analog	ANS	Baseline SBP and change in SBP following stressor	Maltreated children did not exhibit an increase in SBP following the stressor, whereas comparison children did exhibit an increase.	
Linares et al. (2013)	Abuse (physical, emotional, sexual) Neglect (physical, emotional)	Infancy to adolescence	Self-report (CTQ)	14–17 years	Low-income, sexually active female adolescents (40) who experienced childhood sexual abuse (CSA+) and/or physical abuse by their partner (PA +).	AIVA[24]	HPA axis	Three salivary cortisol samples were collected in the lab prior to and during the stressor task.	CSA+ group displayed the greatest reactivity to the stressor compared with CSA- group after adjusting for PA. The PA+ group showed less reactivity to the stressor than PA- groups after adjusting for CSA. The PA+ group had higher levels of resting cortisol compared with PA- group.	
Lunkenheimer et al. (2018)	Abuse (physical, emotional, sexual), Neglect	Early Childhood	Public records	3–5 years	Maltreated children and mother dyads (68), comparison dyads (77)	Two dyadic puzzle tasks	PNS	RSA	Children who had been physically abused exhibited lower levels of resting RSA.	
MacMillan et al. (2009)	Abuse (physical, emotional, sexual) Neglect (emotional)	Childhood	Self-report (CEVQ, CTQ)	12–16 years	Maltreated female adolescents (67), control female adolescents (25)	TSST	ANS, HPA axis	HR (ANS) and salivary cortisol samples (HPA) were recorded 3 times prior to the TSST and 3 times after its onset.	Maltreated children exhibited a blunted cortisol response, relative to controls.	No between-group differences were observed in HR or cortisol levels prior to the onset of the stressor.
McLaughlin et al. (2014a)	Abuse (physical, emotional, sexual)	Childhood	Self-report (CTQ, CECA)	13–17 years	Maltreated adolescents (64), comparison adolescents (105)	TSST	ANS, SNS	Cardiac output (CO; ANS) and pre-ejection period (PEP; SNS)	Maltreatment history and the severity of maltreatment were associated with reduced CO reactivity in response to all three components of the TSST. Maltreated adolescents exhibited reduced PEP reactivity in response to the math component of the TSST relative to controls.	Maltreatment was unrelated to PEP reactivity in response to the preparation and speech components of the TSST.

(Continued)

Table 2. (*Continued.*)

Study	Maltreatment			Participants			Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (*N*)	Stressor	System (s)[d]	Method[e]	Significant	Nonsignificant
McLaughlin et al. (2015)	Neglect[25] (physical, emotional, social)	Childhood	Public records	13 years	Romanian children in institutional care (RI; 43), Romanian children moved to foster care (RF; 48), comparison Romanian children (RC; 47)	TSST, peer evaluation task, frustration task	PNS, SNS, HPA axis	HR, SBP, DBP (ANS), RSA (PNS), PEP (SNS), salivary cortisol, DHEA-S (HPA) collected at baseline and during tasks.	RI exhibited elevated baseline PEP relative to RF and RC. RI exhibited blunted HR, DBP, and PEP reactivity during the speech portion of TSST, blunted DBP during the preparation portion, and blunted DBP and PEP during math portion relative to RF and RC. RI exhibited blunted cortisol reactivity across all portions of TSST compared with RF.	No between-group differences were observed in baseline HR, SBP, DBP, RSA, cortisol or DHEA-S.
Miskovic et al. (2009)	Maltreatment (unspecified)	Childhood, adolescence	Public records, self-report	12–16 years	Females with a history of maltreatment (38), comparison females (24)	N/A	PNS	Baseline RSA was collected at two time points 6 months apart	RSA was lower among females who had been maltreated at time 2 relative to members of the comparison group.	No between-group differences were observed in RSA at time 1.
Negriff et al. (2015)[26]	Abuse (physical, sexual, emotional), Neglect	Childhood	Public records	9–12 years[27]	Maltreated children (303), comparison children (151).	TSST-C	HPA axis	Salivary cortisol was collected six times: 90, 45, and 10 min prior to the stressor and 10, 20, and 30 min after the stressor.	Maltreatment was associated with blunted HPA axis reactivity to stress among boys.	Maltreatment was unrelated to HPA axis reactivity among girls.
Oosterman et al. (2010)	Abuse (physical, sexual) Neglect	Childhood	Case records	26–88 months	Children in foster care (60)	SSP	PNS, SNS	RSA (PNS), PEP (SNS)	Neglected children exhibited greater PEP reactivity than children who had not been neglected. Neglected children and children with disordered attachment showed smaller RSA reactivity (reduced withdrawal) than children with ordered attachment.	No associations were observed between physical or sexual abuse and PEP or RSA reactivity.
Peckins et al. (2015)[28]	Abuse (physical, sexual, emotional), Neglect	Childhood	Public records	9–16 years (data were collected at four ages)[29]	Maltreated children (303), divided into a sexual/physical abuse group and a nonsexual/physical abuse group, comparison children (151).	TSST-C	HPA axis	Salivary cortisol was collected six times at each age: 90, 45, and 10 min prior to the stressor and 10, 20, and 30 min after the stressor. Patterns of HPA axis reactivity at each age were classified as blunted, moderate, or elevated.	Maltreated children were more likely to be classified as exhibiting a blunted cortisol response than controls at ages 2 and 3. This pattern of findings was consistent across children who had experienced sexual/physical abuse and those who had not.	At age 4 there were no differences in profile membership between maltreated children and controls.

(*Continued*)

Table 2. (Continued.)

Study	Maltreatment Type(s)[a]	Age[b]	Source[c]	Participants Age at collection	Composition (N)	Stressor	Measurement System(s)[d]	Method[e]	Findings Significant	Nonsignificant
Pollak et al. (2005)	Abuse (physical)	Childhood	Public records	4–5 years	Maltreated children (11), nonmaltreated controls (22)	A recorded conversation containing three episodes of anger status (active, unresolved, resolved)	ANS	HR and SCL were collected during the stressor.	Maltreated children exhibited greater overall HR deceleration during the unresolved anger episode than controls. Controls displayed a significantly larger increase in SCL during the active anger period than maltreated children. Maltreated children displayed a large increase in SCL mid-way through the unresolved anger period, whereas nonabused controls displayed a decrease. Maltreated children did not display a recovery of HR during the resolution period, while controls did.	
Puetz et al. (2016)	Abuse (physical), Neglect (physical, emotional), abandonment	Childhood	Public records, interviews[30]	8–14 years	Maltreated children (25), comparison children (26)	N/A	HPA axis	Salivary cortisol samples were collected at home three times a day (30 min after awakening, 30 min before lunch, and 30 min before going to sleep) on two consecutive days.	Maltreated children exhibited lower morning cortisol levels and flattened diurnal trajectories relative to controls.	
Quevedo et al. (2017)	Abuse (physical, sexual), Neglect	Childhood, adolescence	Other-report (K-SADS[31])	11–19 years	Maltreated adolescents (35), comparison adolescents (20)	N/A	HPA axis	Salivary cortisol samples were collected three times a day (upon waking, 30 min after waking, and 60 min after waking) on four nonconsecutive days.	Maltreated adolescents who were also depressed exhibited a larger cortisol awakening response compared to adolescents who had not been maltreated. Maltreated adolescents who were depressed and who displayed elevated levels of dorsal anterior cingulate cortex (dACC) activity during processing of negative self-descriptors[32] exhibited larger awakening responses than depressed adolescents who were not maltreated.	Maltreated adolescents who were depressed and who displayed low levels of dACC activity did not exhibit different awakening responses than depressed adolescents who were not maltreated.
Rinnewitz et al. (2018)	Abuse (physical, sexual) Neglect	Childhood, adolescence	CECA-Q[33]	12–17 years	Adolescent females with nonsuicidal self-injury (NSSI) behaviors (30)	Cold pressor task	HPA axis, ANS	Salivary cortisol samples were collected before and 15 min after task. HR and heart rate variability (HRV) were measured before and throughout the task.	More severe maltreatment was associated with higher levels of cortisol and larger decreases in HRV during and following the task.	

(Continued)

Table 2. (*Continued.*)

Study	Maltreatment			Participants			Measurement		Findings	
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (*N*)	Stressor	System (s)[d]	Method[e]	Significant	Nonsignificant
Saxbe et al. (2012)	Abuse (physical)	Adolescence	Maternal and paternal self-report[34]	15 years	Adolescents (54)	A conflict discussion task between adolescents and parents	HPA axis	Five saliva cortisol samples were collected: at baseline (after a relaxing video), immediately post discussion (40 min), and again at three additional time points (50 min, 60 min, and 80 min post discussion).	Adolescents' conflict discussion rating interacted with family aggression in predicting AUC$_i$,[35] such that adolescents with low family aggression exhibited increased cortisol reactivity when the discussion featured more conflict, whereas adolescents with high family aggression exhibited lower cortisol reactivity when he discussion featured more conflict.	Adolescents' conflict discussion rating and its interaction with family aggression were not significantly associated with AUC$_g$.[36] Adolescents' conflict discussion rating and family aggression were not independently associated with AUC$_i$.
Shenk et al. (2010)	Abuse (sexual)	Childhood	Public records	13–23 years	Sexually abused females (52), comparison females (77)	Timed, mental rotation task.	ANS, HPA axis	Vagal tone (PNS), waking salivary cortisol (HPA).	Sexually abused females were significantly more likely to exhibit vagal withdrawal and a blunted cortisol response (as indexed by AUC) than controls 7 years after documented abuse. Sexually abused females were also more likely to exhibit an asymmetrical physiological response, defined as vagal withdrawal above the mean and a cortisol response below the mean.	
Shenk et al. (2012)	Abuse (physical, sexual), Neglect (physical)	Adolescence	Public records	14–19 years	Females who had been maltreated in past year (51), females who had not been maltreated in the last year (59)	Affect recognition task, videos of parent-adolescent conflict	PNS, HPA axis	RSA (PNS), salivary cortisol from five samples collected prior to, during, and following the challenge task.	RSA was higher under conditions of homeostasis and challenge among maltreated females than among females who had not been maltreated at a level approaching significance.	There were no significant between-group differences in cortisol under conditions of homeostasis or challenge.
Şimşek et al. (2015)	Sexual abuse	Childhood, adolescence	Public records	8–17 years	Maltreated children (44), comparison children (42)	N/A	HPA axis	Blood cortisol samples were obtained between 10 and 12 a.m.	Cortisol levels were significantly higher among children who had been sexually abused than children who had not been abused. Recency of abuse was positively associated with cortisol levels.	ACTH levels were higher among children who had been sexually abused than children who had not been abused at a level approaching significance.

(*Continued*)

Table 2. (Continued.)

| Study | Maltreatment | | | Participants | | | Measurement | | Findings | |
	Type(s)[a]	Age[b]	Source[c]	Age at collection	Composition (N)	Stressor	System (s)[d]	Method[e]	Significant	Nonsignificant
Skowron et al. (2011)	Abuse (physical), Neglect (physical)	Early Childhood	Public records	3–5 years	Physically abused preschoolers (17); physically neglected preschoolers (26), comparison children (33)	Teaching task[37]	PNS	RSA	Maltreated children exhibited lower baseline RSA levels relative to comparison children.	There were no significant between-group differences in the slopes indexing change in children's RSA from baseline to task.
Skowron, Cipriano-Essel, Gatzke-Kopp, Teti, and Skowron et al. (2014)	Abuse (physical, emotional), Neglect (physical, emotional)	Early childhood	Public records	3–5 years	Maltreated children (78), comparison children (83)	Mother-infant block construction task, delayed gratification and locked box frustration task	PNS	RSA was collected prior to and during the block construction and frustration tasks.		There were no significant between-group differences in RSA during any task.
Sturge-Apple et al. (2012)	Neglect (emotional)	Infancy	Maternal report, observer ratings[38]	2 years	Toddlers from at-risk families (201)	SSP, SPAT[39]	HPA axis	Salivary cortisol samples were collected once at baseline (within 15 min of arriving at the lab) and twice poststressor (15–25 min and again 35–50 min).	Higher levels of emotional neglect (and interparental violence) were associated with higher baseline cortisol and lower reactivity to the strange situation task.	
Sullivan et al. (2013)	Neglect (physical, supervisory)	Childhood	Public records, parent-report[40]	6–9 years	Neglected children (30), comparison children (34)	Self-evaluation tasks[41]	HPA axis	Salivary cortisol samples were collected at baseline (10 min after arrival), and 20 and 35 min after the completion of the last failed puzzle task.	Neglected children exhibited higher baseline cortisol levels than controls. Neglected children exhibited a steeper decline in cortisol levels from baseline than controls.	
Sumner et al. (2014)	Abuse (physical, emotional, sexual)	Childhood	Self-report (CTQ, CECA)	13–17 years	Maltreated adolescents (61), comparison adolescents (97)	TSST	HPA axis	Salivary cortisol samples were collected at baseline, 15 min after the start of the speech portion of TSST and 15 min into recovery period.	Maltreated adolescents exhibited lower levels of cortisol 15 min after TSST began and during the recovery period than non-maltreated group.[42] Maltreated adolescents with one or more G alleles of rs110402 had a significantly reduced cortisol response (as indexed by AUC) than those in the nonmaltreated group.	There was no significant difference in cortisol levels between maltreated group and control group in baseline cortisol.
Trickett et al. (2014)	Abuse (physical, emotional, sexual), Neglect	Childhood	Public records	9–12 years	Maltreated adolescents (303), comparison adolescents (151)	TSST	HPA axis	Six salivary cortisol samples collected throughout the task: two before and four after the stressor.	Maltreated children showed a blunted response to the stressor as compared with controls. This attenuated response was especially pronounced for those who were physically and/or sexually abused.	

(Continued)

Table 2. (*Continued.*)

Study	Maltreatment Type(s)[a]	Maltreatment Age[b]	Maltreatment Source[c]	Participants Age at collection	Participants Composition (*N*)	Stressor	Measurement System (s)[d]	Measurement Method[e]	Findings Significant	Findings Nonsignificant
Trickett et al. (2010)	Abuse (sexual)	Childhood	Public records	6–30 years (data were collected at 5 ages)[43]	Abused females (84), comparison females (89)	N/A	HPA axis	Waking (9–10 a.m.) cortisol samples were collected at each age of assessment. The first three samples were blood cortisol, the final two were salivary samples[44].	At initial assessment, cortisol levels were significantly higher among abused participants. After controlling for depression and anxiety, abused participants maintained higher levels of waking cortisol over the 13 years in which data were collected.	
Usta et al. (2016)	Abuse (sexual)	Childhood, adolescence	Interview (K-SADS-PL[45])	12–18 years	Sexually abused female adolescents with PTSD (20), comparison adolescents (20)	N/A	HPA axis	Dehydroepiandro-sterone sulphate (DHEA-S) and cortisol levels were collected from blood samples between 8 a.m. and 9 a.m.	Female adolescents who had been sexually abused and diagnosed with PTSD had higher cortisol to DHEA-S ratios relative to comparison adolescents.	There were no between-group differences in cortisol levels.
White et al. (2017)	Abuse (physical, emotional, sexual), Neglect	Childhood, adolescence	Public records	3–16 years	Maltreated children and adolescents (245), comparison group (292)	N/A	HPA axis	Cortisol concentrations were estimated from hair samples.	Maltreated children exhibited lower cortisol concentrations than controls beginning between 9 and 10 years of age. Chronicity and the number of types of maltreatment experienced were associated with lower cortisol concentrations.	
Wismer Fries et al. (2008)	Neglect (emotional)	Infancy and toddlerhood	Parent report	54 months	Institutionalized children who had been adopted (18), comparison children living with biological parents (21)	Interaction with parent or unfamiliar adult during computer game similar to "Simon Says"	HPA axis	Waking (21 min after child awoke) urine samples were collected on eight mornings: four on "typical" days, two on days prior to the first experimental session, and two on days between the two experimental sessions.	After interacting with their foster parents, institutionalized children's cortisol levels were significantly higher than controls. Institutionalized children subjected to severe neglect exhibited higher baseline cortisol levels and higher levels after interacting with their foster parent than institutionalized children who had experienced less severe neglect.	Basal cortisol did not differ between institutionalized and control children.

[a]Specific types of abuse and/or neglect are listed for studies where that information was provided.
[b]Approximate age(s) at which maltreatment occurred.
[c]When provided by the authors, specific measures used for self-report are listed. When the authors specified the approach taken to classify children as maltreated using public records, that approach is listed.
[d]Hypothalamic–pituitary–adrenal (HPA) axis, autonomic nervous system (ANS), parasympathetic nervous system (PNS), sympathetic nervous system (SNS).
[e]When approximate times of collected were reported by the authors, those are included in the table. When mean times of collection are reported (regardless of whether these included indices of dispersion such as standard deviations) the mean time of collection is reported to the nearest hour.
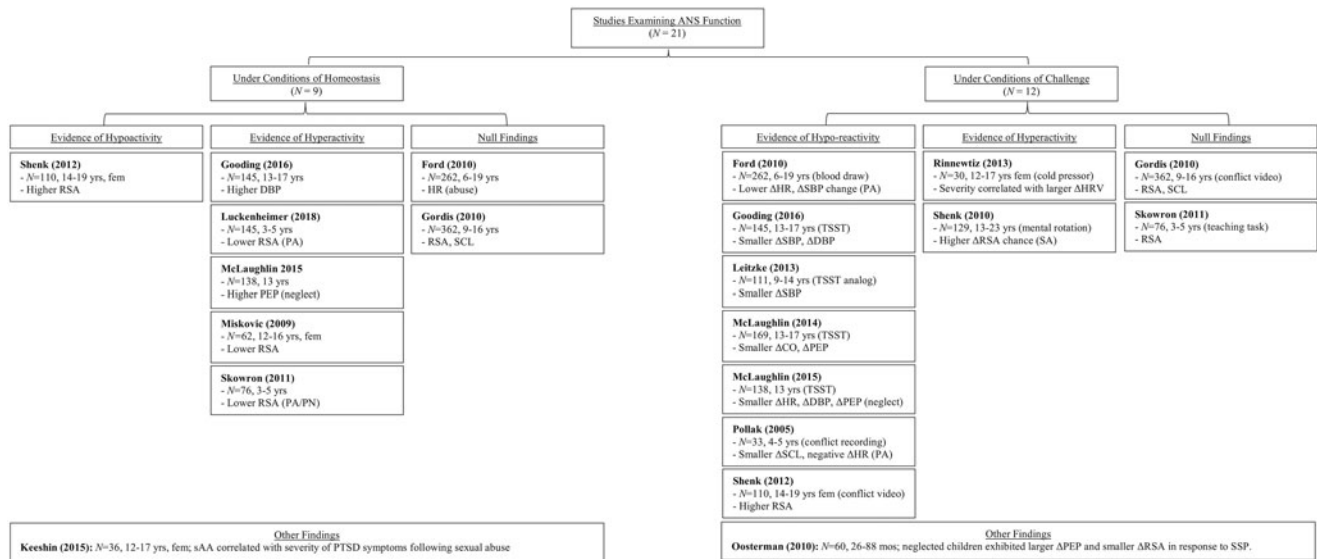
Figure 2a. A graphical summary of the literature examining the association between maltreatment and autonomic nervous system function.

Studies Examining ANS Function (N = 21)

Under Conditions of Homeostasis (N = 9)

Evidence of Hypoactivity
- Shenk (2012): N=110, 14-19 yrs, fem; Higher RSA

Evidence of Hyperactivity
- Gooding (2016): N=145, 6-19 yrs; Higher DBP
- Luckenheimer (2018): N=145, 3-5 yrs; Lower RSA (PA)
- McLaughlin 2015: N=138, 13 yrs; Higher PEP (neglect)
- Miskovic (2009): N=62, 12-16 yrs, fem; Lower RSA
- Skowron (2011): N=76, 3-5 yrs; Lower RSA (PA/PN)

Null Findings
- Ford (2010): N=262, 6-19 yrs; HR (abuse)
- Gordis (2010): N=362, 9-16 yrs; RSA, SCL

Under Conditions of Challenge (N = 12)

Evidence of Hypo-reactivity
- Ford (2010): N=262, 6-19 yrs (blood draw); Lower ΔHR, ΔSBP change (PA)
- Gooding (2016): N=145, 13-17 yrs (TSST); Smaller ΔSBP, ΔDBP
- Leitzke (2013): N=111, 9-14 yrs (TSST analog); Smaller ΔSBP
- McLaughlin (2014): N=169, 13-17 yrs (TSST); Smaller ΔCO, ΔPEP
- McLaughlin (2015): N=138, 13 yrs (TSST); Smaller ΔHR, ΔDBP, ΔPEP (neglect)
- Pollak (2005): N=33, 4-5 yrs (conflict recording); Smaller ΔSCL, negative ΔHR (PA)
- Shenk (2012): N=110, 14-19 yrs fem (conflict video); Higher RSA

Evidence of Hyperactivity
- Rinnewitz (2013): N=30, 12-17 yrs fem (cold pressor); Severity correlated with larger ΔHRV
- Shenk (2010): N=129, 13-23 yrs (mental rotation); Higher ΔRSA chance (SA)

Null Findings
- Gordis (2010): N=362, 9-16 yrs (conflict video); RSA, SCL
- Skowron (2011): N=76, 3-5 yrs (teaching task); RSA

Other Findings: Keeshin (2015): N=36, 12-17 yrs, fem; sAA correlated with severity of PTSD symptoms following sexual abuse

Other Findings: Oosterman (2010): N=60, 26-88 mos; neglected children exhibited larger ΔPEP and smaller ΔRSA in response to SSP.
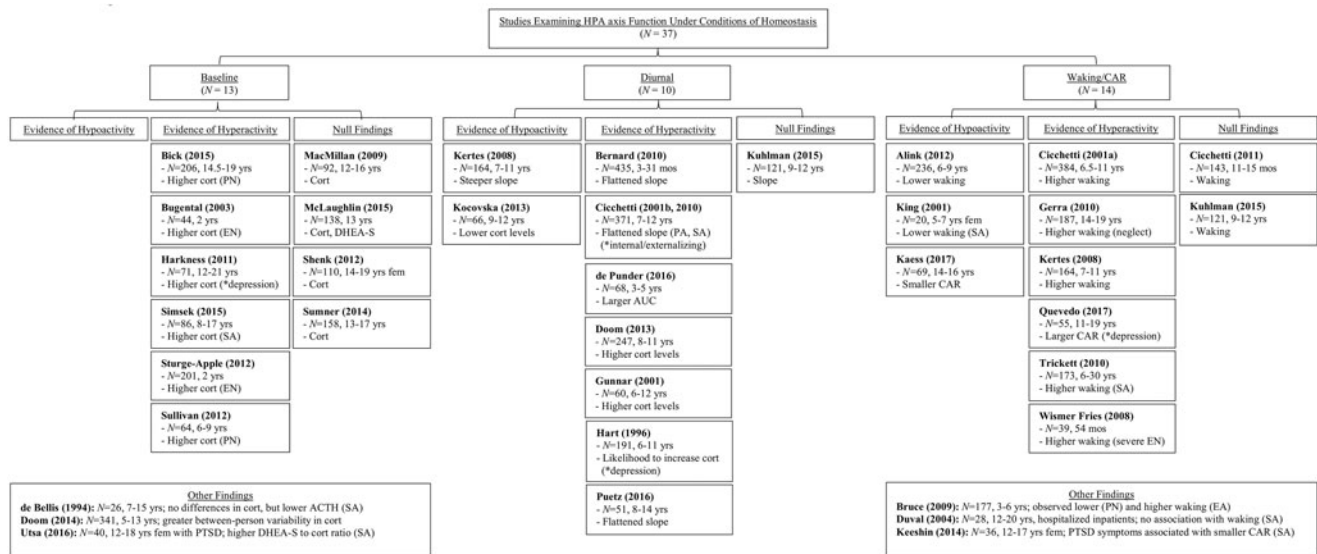
Figure 2b. A graphical summary of the literature examining the association between maltreatment and HPA axis function under conditions of homeostasis.

Studies Examining HPA axis Function Under Conditions of Homeostasis (N = 37)

Baseline (N = 13)

Evidence of Hypoactivity — (none)

Evidence of Hyperactivity
- Bick (2015): N=206, 14.5-19 yrs; Higher cort (PN)
- Bugental (2003): N=44, 2 yrs; Higher cort (EN)
- Harkness (2011): N=71, 12-21 yrs; Higher cort (*depression)
- Simsek (2015): N=86, 8-17 yrs; Higher cort (SA)
- Sturge-Apple (2012): N=201, 2 yrs; Higher cort (EN)
- Sullivan (2012): N=64, 6-9 yrs; Higher cort (PN)

Null Findings
- MacMillan (2009): N=92, 12-16 yrs; Cort
- McLaughlin (2015): N=138, 13 yrs; Cort, DHEA-S
- Shenk (2012): N=110, 14-19 yrs fem; Cort
- Sumner (2014): N=158, 13-17 yrs; Cort

Diurnal (N = 10)

Evidence of Hypoactivity
- Kertes (2008): N=164, 7-11 yrs; Steeper slope
- Kocovska (2013): N=66, 9-12 yrs; Lower cort levels

Evidence of Hyperactivity
- Bernard (2010): N=435, 3-31 mos; Flattened slope
- Cicchetti (2001b, 2010): N=371, 7-12 yrs; Flattened slope (PA, SA) (*internal/externalizing)
- de Punder (2016): N=68, 3-5 yrs; Larger AUC
- Doom (2013): N=247, 8-11 yrs; Higher cort levels
- Gunnar (2001): N=60, 6-12 yrs; Higher cort levels
- Hart (1996): N=191, 6-11 yrs; Likelihood to increase cort (*depression)
- Puetz (2016): N=51, 8-14 yrs; Flattened slope

Null Findings
- Kuhlman (2015): N=121, 9-12 yrs; Slope

Waking/CAR (N = 14)

Evidence of Hypoactivity
- Alink (2012): N=236, 6-9 yrs; Lower waking
- King (2001): N=20, 5-7 yrs fem; Lower waking (SA)
- Kaess (2017): N=69, 14-16 yrs; Smaller CAR

Evidence of Hyperactivity
- Cicchetti (2001a): N=384, 6.5-11 yrs; Higher waking
- Gerra (2010): N=187, 14-19 yrs; Higher waking (neglect)
- Kertes (2008): N=164, 7-11 yrs; Higher waking
- Quevedo (2017): N=55, 11-19 yrs; Larger CAR (*depression)
- Trickett (2010): N=173, 6-30 yrs; Higher waking (SA)
- Wismer Fries (2008): N=39, 54 mos; Higher waking (severe EN)

Null Findings
- Cicchetti (2011): N=143, 11-15 mos; Waking
- Kuhlman (2015): N=121, 9-12 yrs; Waking

Other Findings: de Bellis (1994): N=26, 7-15 yrs; no differences in cort, but lower ACTH (SA). Doom (2014): N=341, 5-13 yrs; greater between-person variability in cort. Utsa (2016): N=40, 12-18 yrs fem with PTSD; higher DHEA-S to cort ratio (SA)

Other Findings: Bruce (2009): N=177, 3-6 yrs; observed lower (PN) and higher waking (EA). Duval (2004): N=28, 12-20 yrs, hospitalized inpatients; no association with waking (SA). Keeshin (2014): N=36, 12-17 yrs fem; PTSD symptoms associated with smaller CAR (SA)

and adolescents (6–19 years) were more likely to exhibit *decreases* in the global ANS measures of heart rate and systolic blood pressure in response to a blood draw procedure than their peers (Ford et al., 2010), though it is important to note these changes may have been indicative of syncope (fainting), which can accompany a blood draw in some individuals. Similarly, Pollak and colleagues reported that maltreated children (4–5 years) exhibited reduced SNS reactivity and heart rate *de*celeration in response to angry background conversations (Pollak, Vardi, Bechner, & Curtin, 2005). However, two studies employing stressors other than the TSST support an account of *hyper*reactive ANS function. Shenk and colleagues found that female adolescents (13–23 years) who had been sexually abused were more likely than controls to display reductions of respiratory sinus arrhythmia in response to a timed cognitive task (Shenk, Noll, Putnam, & Trickett, 2010), a finding similar to that reported by Rinnewitz et al. (2018), who observed a positive association between the severity of maltreatment and the magnitude of the reduction in heart rate variability in response to a cold pressor task among a sample of maltreated adolescent females (12–17 years) exhibiting nonsuicidal self-injurious behaviors (Rinnewitz et al., 2018). Oosterman and colleagues reported mixed findings, reporting that while neglected children (26–88 months) exhibited larger increases in the pre-ejection period in response to the Strange Situation (Ainsworth, Blehar, Waters, & Wall, 1978) compared to children who had not been neglected, they also exhibited smaller decreases in respiratory sinus arrhythmia (Oosterman, De Schipper, Fisher, Dozier,
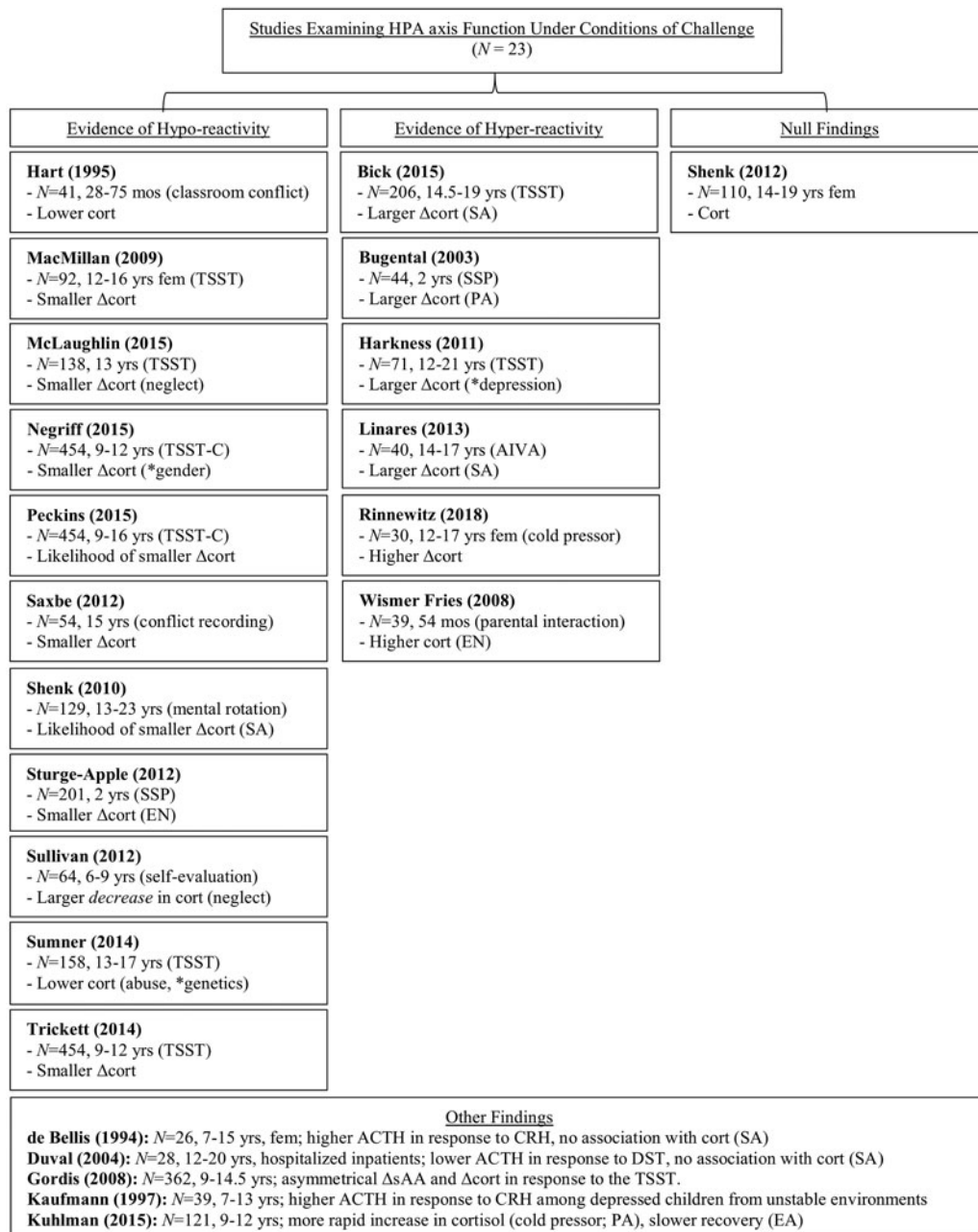
Figure 2c. A graphical summary of the literature examining the association between maltreatment and HPA axis function under conditions of challenge.

& Schuengel, 2010). Two other studies found no association between maltreatment and the response to different challenges (conflict videos in the case of Gordis et al., 2010 and a teaching task in the case of Skowron et al., 2011). Figure 2a summarizes the literature on altered ANS function under conditions of maltreatment.

Altered HPA axis function following maltreatment

Altered HPA axis function under conditions of homeostasis

Thirty-seven studies have examined HPA axis function under conditions of homeostasis. Thirteen of these examined HPA axis activity prior to the onset of stressor (i.e., baseline function), of which six reported an association between maltreatment and HPA axis hyperactivity. In two of these studies, frequent maternal emotional withdrawal (Bugental, Martorell, & Barraza, 2003) and maternal emotional neglect (Sturge-Apple,, Davies, Cicchetti, & Manning, 2012) were associated with elevated levels of salivary cortisol prior to participation in the Strange Situation Procedure (Ainsworth et al., 1978) among young children (aged 2 years). Studies of older children have yielded similar results: Bick and colleagues reported that adolescents (14.5–19 years) who experienced moderate to severe physical neglect exhibited significantly higher levels of cortisol prior to participating in the Trier Social Stress Task for Children (TSST-C; Buske-Kirschbaum et al., 1997) compared to adolescents with no or minimal levels of physical neglect (Bick et al., 2015), while school-aged children (6–9

years) who had been physically neglected exhibited higher cortisol levels prior to participating in a self-evaluation task than children who had not been neglected (Sullivan, Bennett, & Lewis, 2013). In a study of children and adolescents (ages 8–17 years), Şimşek and colleagues found that those who had been sexually abused exhibited higher levels of resting cortisol than children and adolescents who had not been abused (Şimşek, Yüksel, Kaplan, Uysal, & Alaca, 2015). Harkness and colleagues examined psychopathology together with maltreatment status, and found that depressed adolescents who had been maltreated exhibited higher cortisol levels prior to the TSST than comparably depressed adolescents who had not been maltreated (Harkness, Stewart, & Wynne-Edwards, 2011). Although six studies that examined baseline cortisol found no evidence of differences as a function of maltreatment (DeBellis et al., 1994; MacMillan et al., 2009; McLaughlin et al., 2015; Shenk et al., 2012; Sumner, McLaughlin, Walsh, Sheridan, & Koenen, 2014; Usta, Tuncel, Akbas, Aydin, & Say, 2016), two of these did report differences in biomarkers related to cortisol. De Bellis and colleagues reported lower levels of adrenocorticotropic hormone among sexually abused children and adolescents (7–15 years), while Utsa and colleagues found higher cortisol-to-dehydroepiandrosterone sulphate ratios among sexually abused adolescents with symptoms of posttraumatic stress (Usta et al., 2016).

One study that examined baseline HPA axis activity did so by assessing cortisol levels at the same time of day over the course of 20 weeks, and focused on the degree of variability in cortisol levels over time. The authors found that there was a greater degree of between-person variability in cortisol among children and adolescents (5–13 years) who had been maltreated than among their comparison-group peers. Moreover, among children who had been maltreated, the experience of fewer types of maltreatment, less severe maltreatment, and less recent maltreatment were all associated with greater within-person variability in cortisol levels over time (Doom, Cicchetti, & Rogosch, 2014).

Ten studies that have examined the association between maltreatment and HPA axis function have focused on diurnal activity. Eight of these reported an association between maltreatment and diurnal hyperactivity. For example, Bernard and colleagues found that infants and toddlers (3–31 months) who had been maltreated exhibited lower waking cortisol levels and flattened slopes of cortisol throughout the day, which, as discussed above, is indicative of hyperactivity (Bernard, Butzin-Dozier, Rittenhouse, & Dozier, 2010). Bernard also found that maltreated children living with their birth parents exhibited flatter slopes than those living with foster parents. These findings are similar to those reported by Gunnar and colleagues: children (6–12 years) who had been Romanian orphans and who had been adopted after 8 months of age exhibited higher diurnal cortisol levels than orphans who had been adopted before 4 months of age. Moreover, among the Romanian orphans, those who remained in institutionalized care for longer periods of time exhibited higher diurnal cortisol levels (Gunnar, Morison, Chisholm, & Schuder, 2001). Puetz and colleagues observed similar results, reporting that school-aged children (8–14 years) who had been maltreated exhibited lower waking cortisol levels and flattened diurnal cortisol slopes, relative to their comparison-group peers (Puetz et al., 2016). Among younger children (3–5 years), de Punder and colleagues found that the total amount of cortisol produced over the course of the day was positively correlated with the number and cumulative severity of instances of abuse children had experienced (de Punder et al., 2016). Similar findings were reported by Doom

and colleagues, though the authors also found that among maltreated females (8–11 years), more recent or *less* pervasive maltreatment was associated with higher cortisol levels (Doom, Cicchetti, Rogosch, & Dackis, 2013). Finally, as was the case in studies examining cortisol levels prior to the onset of a stressor, psychopathology may reinforce the association between maltreatment and diurnal HPA axis activity. In a series of studies with a sample of school-aged children (6–13 years), Cicchetti and colleagues found that those who had been maltreated and who displayed comorbid internalizing (Cicchetti, Rogosch, Gunnar, & Toth, 2010; Cicchetti, Rogosch, & Oshri, 2011) or externalizing symptoms (Cicchetti & Rogosch, 2001a) exhibited flattened diurnal cortisol patterns relative to controls. Moreover, among school-aged children (6–11 years) who had been maltreated, those with comorbid depression were more likely than those without depression to display an increase in cortisol levels over the course of the day, rather than the typical decrease (Hart, Gunnar, & Cicchetti, 1996). Two of the ten studies that examined the association between maltreatment and diurnal activity found evidence of *hypo*activity. Kertes and colleagues found that maltreatment, operationalized as cumulative deprivation prior to placement in foster care, was associated with higher levels of HPA axis activity after children (7–11 years) had been living with their foster families for at least three years (Kertes, Gunnar, Madsen, & Long, 2008). Kočovská reported that children (9–12 years) who had been maltreated prior to adoption and who exhibited reactive attachment disorder were compared to children who had not been maltreated, adopted, or diagnosed with an attachment disorder (Kočovská et al., 2013).

An additional 14 studies have focused on waking or morning levels of cortisol as an aspect of homeostatic HPA axis activity. Five of these reported an association between maltreatment and hyperactivity. Young children (54 months) who had been severely emotionally neglected while in institutional care exhibited higher morning levels of cortisol relative to their peers who had not been maltreated (Wismer Fries, Shirtcliff, & Pollak, 2008). Among school-aged children (6.5–11 years), exposure to maltreatment (Cicchetti & Rogosch, 2001b) and neglect prior to adoption (Kertes et al., 2008) were associated with elevated waking cortisol levels, while a history of neglect was associated with higher waking cortisol among adolescents (14–19 years; Gerra et al., 2010). Finally, one longitudinal study found sexually abused females exhibited higher levels of waking cortisol at their initial assessment (which occurred when participants were between 6 and 16 years of age) than girls who had not been abused, and also maintained higher levels of waking cortisol as over the 13 years of the study (Trickett, Noll, Susman, Shenk, & Putnam, 2010). However, two studies have not found an association between maltreatment and waking cortisol levels. For example, Cicchetti and colleagues found no difference in morning cortisol levels among maltreated infants (11–15 months) and their peers (Cicchetti et al., 2011), while Kuhlman and colleagues reported similar findings among children and adolescents (9–16 years) who had been physically or emotionally abused (Kuhlman, Geiss, Vargas, & Lopez-Duran, 2015). Duval and colleagues reported that there were no differences in morning cortisol between adolescents (12–20 years) with PTSD due to sexual abuse and their peers who were not diagnosed with PTSD, but it is important to note that these adolescents were hospitalized at the time of the study (Duval et al., 2004).1988

Moreover, the results of two other studies suggest that certain types of maltreatment may be associated with lower waking or

morning cortisol levels, and that gender and psychopathology may be implicated in the broader association between maltreatment and cortisol levels. For example, while Trickett and colleagues found that sexually abused girls (ages 6–16 years) exhibited higher waking cortisol than girls who had not been abused (Trickett et al., 2010), King and colleagues observed that in a mixed-gender sample of children (ages 5–7), sexual abuse was associated with lower waking cortisol levels compared to controls (King, Mandansky, King, Fletcher, & Brewer, 2001). Moreover, Alink and colleagues found that among school-aged children (6–9 years), the experience of maltreatment was associated with lower morning cortisol levels measured one year later, but that this relation was fully mediated by externalizing behaviors (Alink, Cicchetti, Kim, & Rogosch, 2012). Differential results by maltreatment type were reported by Bruce and colleagues in their work with a single sample of young children (3–6 years): children who had been exposed to emotional abuse exhibited higher morning cortisol levels relative to their peers who had not been maltreated, whereas those who had experienced physical neglect exhibited lower levels (Bruce, Fisher, Pears, & Levine, 2009).

In four studies (two of which used the same data) cortisol was measured at multiple time points in the morning, allowing for an examination of the association between maltreatment and the cortisol awakening response (CAR). This response is characterized by an initial elevation in cortisol levels that occurs within 1–2 hr after waking, and that typically precedes the diurnal decline in HPA axis activity observed throughout the remainder of the day (Pruessner et al., 1997). According to the CAR anticipation hypothesis, larger CARs in anticipation of daily stressors may be adaptive (Schulz, Kirschbaum, Pruessner, & Hellhammer, 1998). In two of these four studies, both of which were conducted with a single sample of maltreated adolescents, Kaess and colleagues examined maltreated adolescents' CARs when they were 14–16 years old. Overall, higher levels of maltreatment in childhood were associated with smaller awakening responses in adolescence (Kaess et al., 2017). However, in subsequent analyses of these same data, this association was found to hold only among those participants who were found to have a larger pituitary gland in early adolescence (11–13 years; Kaess, Whittle, O'Brien-Simpson, Allen, & Simmons, 2018). Two other studies have also reported an association between maltreatment and the awakening response that was contingent on other factors. Keeshin and colleagues observed an inverse relation between the magnitude of the awakening response and the severity of both posttraumatic stress symptomatology following maltreatment and traumatic experiences prior to maltreatment among adolescents (12–17 years; Keeshin, Strawn, Out, Granger, & Putnam, 2014). In contrast, Quevedo and colleagues reported an association between maltreatment and *larger* awakening responses, but only among adolescents (11–19 years) who were depressed (as compared to adolescents who had not been maltreated; Quevedo, Doty, Roos, & Anker, 2017). Among depressed adolescents, the association between maltreatment and a larger awakening response was contingent upon elevated levels of dorsal anterior cingulate cortical activity during negative self-description (Quevedo et al., 2017).

Although the studies reviewed in this section thus far varied substantially in their methodology, those that assessed cortisol did so by assaying bodily fluids (typically saliva and occasionally blood). However, two studies examined cortisol concentrations in hair, which is thought to reflect cumulative or life stress (Karlén,

Ludvigsson, Frostell, Theodorsson, & Faresjö, 2011). Consistent with this account, do Prado and colleagues found that adolescents who experienced maltreatment early in childhood exhibited higher levels of hair cortisol than their peers (do Prado, Grassi-Oliveira, Daruy-Filho, Wieck, & Bauer, 2017). However, in another study, White et al. (2017) reported that children who had been maltreated exhibited lower cortisol concentrations than their peers, a finding the authors linked to variations in the chronicity and number of types of maltreatment (White et al., 2017).

Altered HPA axis function under conditions of challenge

Twenty-three studies have examined the association between maltreatment and HPA axis activity under conditions of challenge with children across a range of ages and employing a variety of stressors. Two of these studies were conducted with school-aged children and adolescents using the TSST as the stressor and reported an association between maltreatment and hyperreactivity of the HPA axis. Trickett and colleagues observed a blunted cortisol response to the TSST among maltreated school-aged children (9–12 years), relative to controls, and found that this attenuated response was especially pronounced among children who had been sexually and/or physically abused (Trickett, Gordis, Peckins, & Susman, 2014). In their work with Romanian adolescents (age 13 years), McLaughlin and colleagues reported similar findings: adolescents who had remained in institutional care as young children exhibited a blunted cortisol response to the TSST compared to their peers who had been moved to foster care (McLaughlin et al., 2015).

Four additional studies of school-aged children and adolescents that employed the TSST have also found evidence of hyporeactivity, but in those studies these findings were contingent upon age, gender, or genetic factors. For example, in a longitudinal study, school-aged children who had been maltreated were no more likely to exhibit a blunted cortisol response to the TSST-C (the variant of the TSST for children) than controls when cortisol was initially measured at 9–12 years. However, at the second and third measurements, taken 1 and 3 years later, maltreated children did exhibit a blunted response, though they did not do so at the final assessment, which occurred 7 years after the first (Peckins, Susman, Negriff, Noll, & Trickett, 2015). Two studies suggest that hyporeactivity is contingent upon the combination of age and gender. In an exclusively female sample, adolescents (12–16 years) who had been maltreated exhibited a blunted cortisol response to the TSST relative to controls (MacMillan et al., 2009). However, within a mixed-gender sample of school-aged children (9–12 years), Negriff and colleagues found that maltreatment was associated with blunted cortisol response to the TSST among males (9–12 years), but not among females of the same age (Negriff, Saxbe, & Trickett, 2015). Finally, one study that accounted for genetic factors found that while maltreated adolescents (13–17 years) exhibited blunted responses to the TSST relative to their peers at the trend level, only among those maltreated adolescents with one or more G alleles of the rs110402 polymorphism on the gene CRFR1 (which codes for corticotropin releasing factor receptor 1) was the magnitude of the response *significantly* smaller (Sumner et al., 2014).

Five studies employing a variety of stressors other than the TSST have also yielded evidence of HPA axis hyporesponsivity among maltreated children and adolescents. For example, Saxbe and colleagues found that adolescents (age 15 years) who had experienced higher cumulative family aggression (physical

abuse) produced less cortisol across the course of a laboratory-based conflict discussion with their parents when that discussion featured higher levels of conflict (Saxbe, Margolin, Spies Shapiro, & Baucom, 2012). Hyporesponsivity to conflict was also observed among maltreated children (age 28–75 months) by Hart and colleagues, who reported that on days featuring high levels of peer social conflict, children who had been maltreated displayed lower cortisol levels relative to their peers. Moreover, whereas children who had not been maltreated displayed higher levels of cortisol on high-conflict days over the course of a month, maltreated children displayed similar cortisol levels regardless of daily conflict (Hart, Gunnar, & Cicchetti, 1995). Shenk and colleagues found that females (age 13–23 years) who had been sexually abused were significantly more likely to exhibit a blunted cortisol response to a timed mental rotation task than controls 7 years after maltreatment occurred (Shenk et al., 2010), while Sullivan and colleagues observed that physically neglected children (6–9 years) exhibited a steeper decline in cortisol levels during a series of self-evaluation tasks than their peers (Sullivan et al., 2013). Among younger children, Sturge-Apple, Davies, Cicchetti, and Manning (2012) found maternal emotional neglect predicted a smaller cortisol response to the Strange Situation among maltreated toddlers (age 2 years) than their peers.

In contrast, six of the 23 studies that have examined HPA axis activity in response to challenge have yielded evidence that the HPA axis is *hyper*reactive to stress. For example, Bick et al. (2015) found that adolescents (14.5–19 years) who had been sexually abused exhibited greater cortisol reactivity to the TSST than their peers at a level approaching significance. Harkness and colleagues reported similar results: maltreated adolescents (12–21 years) who were depressed exhibited larger cortisol responses (as indexed by the area under the curve) to the TSST than depressed adolescents who had not been maltreated (Harkness et al., 2011). Evidence of hyperreactivity has also been found using stressors other than the TSST. For example, whereas Saxbe and colleagues found that adolescents (15 years) who had experienced physical abuse exhibited a reduced cortisol response to a high-conflict discussion with their parents (Saxbe et al., 2012), Wismer Fries and colleagues noted larger cortisol responses during interactions between young children (54 months) who had been neglected while in institutionalized care and their foster mothers than those observed among controls (Wismer Fries et al., 2008). And whereas Trickett and colleagues found that children (9–12 years) who had been physically or sexually abused exhibited especially small reactions to the TSST (Trickett et al., 2014), Linares and colleagues observed that adolescents (14–17 years) who had been sexually abused exhibited the largest cortisol response to completing the Attitudes toward Interpersonal Violence Assessment (Reese-Weber, 2008) relative to their peers and after controlling for physical abuse by their partner (Linares, Shrout, Nucci-Sack, & Diaz, 2013). A similar finding was reported by Rinnewitz et al. (2018): more severe maltreatment was associated with larger increases in cortisol in response to a cold pressor task among female adolescents (12–17 years) who exhibited nonsuicidal self-injurious behaviors (Rinnewitz et al., 2018). Burgental and colleagues reported that toddlers (2 years) who had experienced frequent corporal punishment displayed larger cortisol responses to the Strange Situation (Ainsworth et al., 1978) than their peers (Bugental et al., 2003), in contrast to Sturge-Apple et al. (2012), who found that toddlers who had experienced emotional neglect exhibited smaller cortisol responses to the Strange Situation.

Duval and colleagues found that hospitalized adolescents diagnosed with PTSD due to sexual abuse exhibited lower levels of adrenocorticotropic hormone (but not cortisol) following a dexamethasone suppression test than their hospitalized peers without PTSD (Duval et al., 2004); de Bellis and colleagues reported similar findings for adrenocorticotropic hormone (but again, not cortisol) following an infusion of corticotropin-releasing hormone (DeBellis et al., 1994). Although these are not stressors per se, the administration of pharmacological agents is a commonly used approach to assess the reactivity of the HPA axis. Finally, two studies found no association between maltreatment and the magnitude of the HPA axis response to challenge (Kuhlman et al., 2015; Shenk et al., 2012), though Kuhlman and colleagues did observe more rapid increases in cortisol in response to the cold pressor task among adolescents who had been physically abused and slower recovery following the task among emotionally abused adolescents (Kuhlman et al., 2015). The literature on altered HPA axis function following maltreatment is summarized in Figures 2b and 2c.

Discussion

Summary and interpretation

Summary: Altered ANS function following maltreatment

Five of the nine studies that examined the association between maltreatment and ANS function under homeostatic conditions reported hyperactivity. These studies varied in the type(s) of maltreatment, how maltreatment was measured (self-report or public records), sample age and composition, and the way in which autonomic function was assessed. The one study that reported an association between maltreatment and ANS hypoactivity (Shenk et al., 2012) did not differ substantially along these dimensions, and indeed was quite similar in terms of sample composition (adolescent females) and method of ANS measurement (RSA) to another study reporting hyperactivity (Miskovic et al., 2009). Therefore, it is not possible to attribute these differences to methodological causes.

Seven of the 12 studies that examined the association between maltreatment and the autonomic response to stress reported evidence of hyporeactivity. These studies varied widely in types of maltreatment and the ways in which autonomic response was indexed, but with two exceptions (Ford et al., 2010; Pollak et al., 2005) they featured samples comprising adolescents. In this respect they were similar to the two studies that reported an association between maltreatment and ANS *hyper*reactivity (those by Rinnewitz et al., 2018 and Shenk et al., 2010). What appears to differentiate these two studies from those that reported ANS hyporeactivity is the nature of the stressor employed. In all but one case (Ford et al., 2010), the studies that reported hyporeactivity employed a psychosocial stressor, either the TSST (in four studies) or a conflict recording or video (in two cases). However, the two studies that reported hyperreactivity used a physical (Rinnewitz et al., 2018) or cognitive challenge (Shenk et al., 2010) as the stressor. The nature of the stressor may also account for the complex pattern of results reported by Oosterman et al. (2010), in which smaller decreases of respiratory sinus arrhythmia (indicative of PNS hyporeactivity) and larger increases in pre-ejection period (corresponding to SNS hyperreactivity) were observed among young children who had been neglected. The particular stressor employed in this study – caregiver separation – was unique, and while speculative, one could

argue that the hyperactive SNS response exhibited by children with a history of neglect may be attributable to sensitization among these children to disengaged caregiver behavior.

Summary: Altered HPA-axis function following maltreatment

Among the 37 studies that examined the function of the HPA axis under conditions of homeostasis, 17 reported an association between maltreatment and elevated levels of HPA-axis function, with particularly consistent findings among studies that defined homeostatic function as HPA axis activity prior to the onset of a stressor (i.e., baseline function) or activity measured over the course of the day. None of the 13 studies that examined the association between maltreatment and baseline function reported evidence of hypoactivity; six reported an association between maltreatment and hyperactivity. Although these studies varied considerably in how maltreatment was measured and the ages of the participants (which ranged from 2–21 years across studies), they were consistent in two respects: in each case, salivary cortisol was used to index HPA axis activity, and, in four of the six studies, physical or emotional neglect was the type of maltreatment associated with hyperactivity. While the four studies that reported no association between maltreatment and HPA axis activity also measured that activity via salivary cortisol, two of these (McLaughlin et al., 2014a; Sumner et al., 2014) did not include children who had been neglected, raising the question of whether the association between maltreatment and baseline HPA axis activity may vary by maltreatment type as an avenue for future research (see below). Seven of the ten studies that examined diurnal function also reported evidence of hyperactivity, and these studies varied widely in the type(s) of maltreatment assessed, the manner in which maltreatment was reported, and the size and composition of the sample. The two studies that reported evidence of hypoactivity (Kertes et al., 2008; Kočovská et al., 2013) did not differ from the other studies in these respects, but they did differ substantially in other ways. In the case of Kertes and colleagues, there was at least a three-year gap between the experience of maltreatment (prior to foster placement) and the assessment of HPA axis activity (following foster placement); for Kočovská et al. (2013), children who had been maltreated and adopted were compared against children who had *not* been adopted. Therefore, in both cases variations in children's experience in foster care settings following maltreatment may explain findings of hypoactivity.

The literature is less consistent where homeostatic function is defined as waking or morning cortisol. Six studies – five of which examined waking levels of cortisol and one of which assessed the CAR – found evidence of HPA axis hyperactivity; three studies (two waking, one CAR) found evidence of hypoactivity, and two studies found no association between maltreatment and waking cortisol levels. Although these studies varied widely in terms of type(s) of maltreatment, reporting method, and sample size and composition, there is no apparent link between a particular aspect of this variation and a given pattern of findings. There is, however, a potential methodological explanation for the studies that reported an association between maltreatment and hypoactivity (Alink et al., 2012; Kaess et al., 2017; King et al., 2001). In all three of these studies, only those samples required to index waking cortisol or the CAR were collected. It is therefore possible that these lower, early levels of cortisol were followed by elevated levels throughout the remainder of the day, which, together with lower waking cortisol, would constitute a flattened diurnal slope indicative of hyperactivity.

The literature indicates that the HPA axis is hyporeactive to stress, with 11 of the 23 studies that have examined the association between maltreatment and reactivity yielding evidence of hyporeactivity, compared to six that reported evidence of hyperreactivity. The literature is most consistent among studies that used the TSST (or the TSST-C) to assess reactivity among school-age children or adolescents; six of the eight studies that fit this description reported hyporeactivity. Comparing studies in which the stressor and/or ages of children in the sample varied were more likely to yield discrepant results.

Consider, for example, findings reported by Trickett et al. (2014), wherein physically or sexually abused children (ages 9–12) exhibited a blunted response to the TSST, and those findings reported by Linares et al. (2013), in which adolescents (ages 14–17) who had been sexually abused displayed a hyperreactive response to the Attitudes toward Interpersonal Violence Assessment (Reese-Weber, 2008). These differences might be attributable to the different nature of the stressors employed in the two studies – a social-evaluative task (the TSST) versus a questionnaire (the Attitudes toward Interpersonal Violence Assessment) – or the way in which physical abuse was handled in the analyses: as a component of maltreatment by Trickett or covariate controlled for by Linares.

However, it is also possible that these differences instead reflect genuine heterogeneity in the association between types of maltreatment and altered patterns of HPA axis reactivity to stress that may be, in part, contingent upon age; adolescence may constitute a developmental shift, in which the association between sexual abuse and reactivity changes from hypo- to hyperreactivity. Extending this account to include the interaction between age and gender may help to explain discrepancies in the association between maltreatment and waking or morning cortisol. Though Trickett et al. (2010) found that sexually abused girls who ranged in age from 6–16, but who were, on average, pre-adolescents (*M* age = 11 years), exhibited higher waking cortisol levels than girls who had not been abused, King et al. (2001) reported that sexual abuse was associated with lower waking cortisol levels in a mixed-gender sample of younger children (ages 5–7). It is therefore possible that adolescence is a point of inflection in the association between sexual abuse and homeostatic function of the HPA axis (defined as waking or morning cortisol), and that the timing of this switch is contingent upon gender, and, specifically, the gender-associated differences in the onset of adrenarche.

Interpretation

As this summary makes clear, the literature regarding the neurophysiological embedding of maltreatment is complex. Nevertheless, it supports an account in which maltreatment is associated with hyperactivity of the ANS and HPA axis under conditions of homeostasis and hyporeactivity to stress. While the fact that a single account of altered function applies to both systems is surprising given the methodological variability across studies, this account makes good neurophysiological and evolutionary sense.

Consider first the consistencies between this account and our understanding of neurophysiological function as it occurs in situ: while our review reflected the literature, in that it devoted separate sections to the ANS and HPA axis, within any individual these systems operate in close concert, and their coordination is facilitated by mutually inhibitory and excitatory connections among systems. Therefore, while Gordis and colleagues found that maltreated children were more likely to exhibit

"asymmetrical" patterns of multisystem neurophysiological activity, in general patterns of multisystem activity are likely to be congruent or symmetrical, both under conditions of homeostasis and challenge (Gordis, Granger, Susman, & Trickett, 2008). Our review indicates that these idiographic patterns of multisystem activity are mirrored at the level of the sample.

This same person-centered perspective can also elucidate why homeostatic hyperactivity of the ANS or HPA axis may be associated with hyporeactivity to challenge: within an individual, homeostatic ANS or HPA axis activity provides a restrictive or permissive context for the activity of that system in response to stress. For example, hyperactivity of the ANS or HPA axis under homeostatic conditions may restrict the reactivity of that system in response to challenge, in accordance with the law of initial values and together with the fact that activity is bound by certain physiological limits. Within the meta-sample of studies reviewed here, we may be observing the same phenomenon at work, as indicated by studies that report hyperactivity under homeostatic conditions and hyporeactivity of the ANS (e.g., Gooding et al., 2016) or HPA axis (e.g., Sturge-Apple et al., 2012).

From an evolutionary perspective, hyperactivity of the ANS and HPA axis under conditions of homeostasis may serve two adaptive purposes: first, increased activity of the sympathetic branch of the ANS and the HPA axis provides the metabolic resources required to cope with an environment in which threats are extreme and severe – that is, the environment of maltreatment. Second, ANS hyperactivity corresponds to *reduced* activity of the PNS. As noted above, higher levels of homeostatic PNS activity foster a state of calm engagement with the environment, and, as such, higher levels of baseline PNS activity are generally considered a promotive factor for development. However, there is evidence that the association between high levels of baseline PNS activity and developmental outcomes is contingent upon the nature of the developmental environment, such that in environments marked by higher levels of adversity – including environments characterized by negative parenting behaviors – high levels of baseline PNS activity are associated with poorer developmental outcomes (cf., Conradt, Measelle, & Ablow, 2013). This is entirely consistent with polyvagal theory (Porges, 1992): if higher levels of PNS activity foster engagement with the developmental environment and that environment is marked by adversity, higher PNS activity is essentially opening the child to the full experience of that adversity.

Reductions in PNS activity as part of an overall pattern of ANS hyperactivity – and the concomitant closing off of the child to the environment – would therefore be adaptive for a child exposed to maltreatment, at least in the short term. The long-term problem with reduced homeostatic PNS activity is that the PNS evolved to support interaction with the environment under nonthreatening conditions by modulating metabolic output, and one way to accomplish this is through the reduction of parasympathetic activity. A maltreated child, for whom levels of homeostatic PNS activity are already reduced, has an inhibited ability to further decrease PNS activity, and therefore must draw on other systems to facilitate environmental interaction – namely, the SNS and HPA axis – even in the absence of threat. While this may be effective in the short term, this strategy cuts against the grain of our evolutionary heritage, in which the resources of the SNS and HPA axis are recruited only after those offered by recruiting the PNS are exhausted (Jackson, 1958). If a maltreated child is drawing on the resources of the SNS and HPA axis in their interactions with the environment under homeostatic conditions, the ranges

of potential system response under conditions of challenge will be reduced. By again applying a person-centered perspective we can see that the blunted neurophysiological response to stress common among maltreated children may be less an adaptation to maltreatment than a consequence of how maltreatment recalibrates homeostatic neurophysiological function.

As we noted at the outset of this paper, the capacity of maltreatment to become embedded in the activity of multiple neurophysiological systems may partially explain its adverse effects on child development. The alterations in neurophysiological function reported in the research reviewed here suggest a multitude of specific pathways that may link maltreatment to developmental outcomes. For example, maltreatment is associated with hyperactivity of the HPA axis activity under conditions of homeostasis, resulting in elevated levels of cortisol. Elevated cortisol levels may imperil neurological development, particularly in areas of the brain that develop more slowly over childhood, such as the prefrontal cortex (Gunnar & Quevedo, 2007; Heim & Nemeroff, 2001), and indeed maltreatment is associated with reduced volume in this area of the brain (DeBellis, 2001). The prefrontal cortex is the putative seat of executive functions, and children who have been maltreated exhibit poorer performance on measures of this core set of cognitive abilities (DePrince et al., 2009; Nolin & Ethier, 2007; Pollak et al., 2010; Porter et al., 2005). Thus, it is possible to delineate a path from maltreatment to HPA axis hyperactivity and elevated levels of cortisol to impeded development of the prefrontal cortex to poorer performance on measures of executive functions, or more generally from maltreatment to neurophysiological function to neurological development to cognitive outcomes. Although this path is certainly suggested by prior research, to date no study of which we are aware has empirically assessed its viability. An important direction for future research is to specify and then test these extended mediation models using longitudinal data, and the literature provides ample basis on which to formulate models connecting maltreatment to a multitude of adverse outcomes associated with maltreatment, from psychopathology (through altered HPA axis activity, immune function, and inflammatory response) to emotion regulation (through ANS hyporesponsivity and reward processing).

Future directions

Although at present the literature supports a certain association between maltreatment and altered neurophysiological function, that literature is hardly exhaustive; as can be seen in Figure 3, our knowledge about the association between maltreatment and neurophysiological function for any particular period of development is based on results from a small number of studies. Clearly there is a need for additional research designed to replicate and expand upon the findings presented in this paper in order to advance our understanding of the association between maltreatment and neurophysiological function. Here we offer two sets of suggestions that may help build that understanding as efficiently as possible, as well as one particular question for future research to address.

One suggestion concerns the analyses we conduct and how we report findings. Given their sample sizes, most studies of maltreatment focus on overall relations between maltreatment and neurophysiological function (i.e., main effects), rather than exploring relations that may be contingent on third factors (interaction effects). However, modest conditional relations
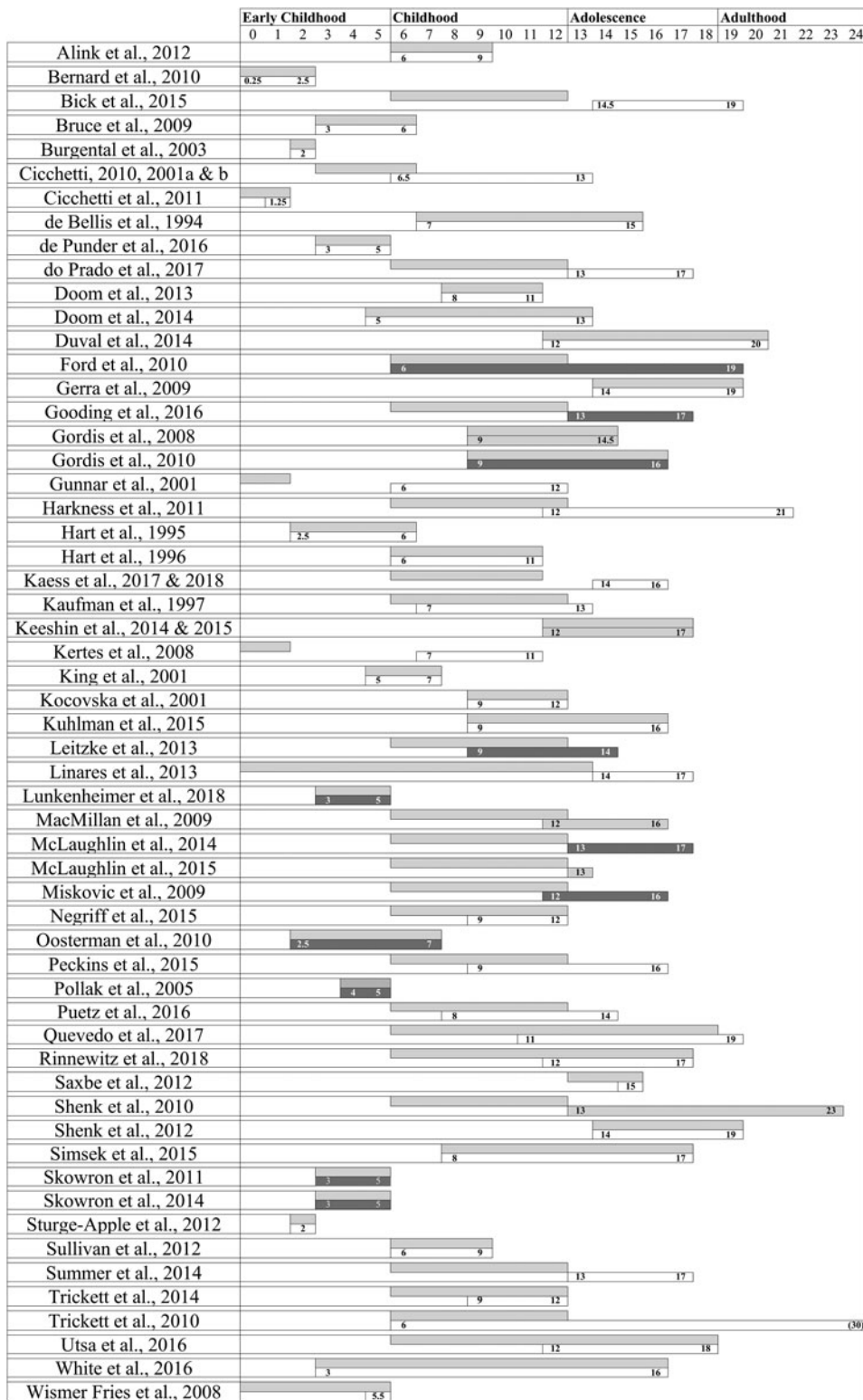
Figure 3. A graphical summary of the literature reviewed in this paper. For each study, the top, gray bar indicates the approximate ages at which maltreatment was reported to have occurred, while the bottom bar indicates the range of ages at which the function of the ANS (dark gray, white numerals), HPA axis (white, black numerals), or both (light gray, black numerals) were assessed. The bounds of the range during which neurophysiological function was assessed are indicated in Arabic numerals.

between maltreatment and neurophysiological function that do not achieve statistical significance ($r \sim [.10–.30]$) due to power constraints may nevertheless be of practical significance for other researchers; so too might the knowledge that the relation between maltreatment and neurophysiological function is essentially orthogonal in the presence of a particular third factor. It would therefore benefit the field if investigators reported the results of exploratory data analyses in supplementary materials, even – or perhaps especially – when the results of those analyses are not significant. The exact analyses performed would of course depend on the study, but reporting associations between maltreatment and neurophysiological function by the

type, severity, and recency of maltreatment, as well as relevant third factors, would be ideal.

The second suggestion concerns how we collect data. One suggestion is for researchers to come to some agreement regarding which stressors to employ in their studies. When different studies employ different stressors, comparing results across studies becomes difficult, even when children are of similar ages. While it may not be necessary for researchers to agree on a specific task or procedure, selecting tasks of a similar nature would facilitate the comparison of results. For example, the results of two studies that employ social evaluation tasks, even if both are not the TSST, may be quite comparable, whereas the results obtained using a social evaluation task and a stressor of another nature – be it a timed cognitive task, a conflict discussion, or completing a sensitive questionnaire – may not be. Another suggestion would be for researchers to simultaneously measure the function of the PNS, SNS, and HPA axis. It is common to study these systems in isolation, and the literature reflects that fact. But, as noted above, the activity of these systems is highly coordinated, and therefore studying the activity of one system without examining the function of the remaining systems may lead researchers to draw erroneous conclusions about the activity of the measured system with relation to maltreatment. In short, the activity of the unmeasured system or systems constitutes a crucial third factor that may moderate the relation of maltreatment and the activity of the measured system (see Holochwost, Kolacz, & Mills-Koonce, under review, for an elaboration of this argument).

Finally, there is one specific question for future research highlighted by the literature. Where both ANS and HPA axis activity are concerned, the results of prior research suggest that possibility that certain specific types of maltreatment – and, in particular, neglect and abuse – may be associated with different alterations in neurophysiological function. As McLaughlin and colleagues note, it is possible that abuse, which constitutes a threat or presence of a negative environmental input, may be associated with different neurophysiological sequalae than neglect or deprivation, which may be defined as the absence of positive environmental inputs (McLaughlin, Sheridan, & Lambert, 2014b). Although this framework is compelling and well-grounded in research with animal models, its validation would require comparing the results of studies in which the broad type of maltreatment varied but other aspects of maltreatment, as well as other key third factors such as child age and gender, were either held constant procedurally or adjusted for statistically. At present, the literature does not include a sufficient number of studies that fit this description and would therefore allow this framework to be tested, but as the literature continues to expand testing this explanation for different patterns of neurophysiological function will become possible.

Implications for policy and practice

The findings of this review suggest that maltreatment has the capacity to dysregulate multiple neurophysiological systems, and that the sequalae of childhood maltreatment may persist into adulthood. This underscores the need for policy and practice to focus on "upstream" efforts designed to prevent maltreatment from occurring in the first place. Home visitation is the most commonly employed approach in prevention efforts (Klika, Lee, & Lee, 2018), and while key differences exist across home visiting models, there is general consensus that intervening with families as early possible is critical to building parents' capacity to create a safe, stable, and nurturing environment.

A number of different home visitation approaches have been found to re-organize neurophysiological systems to more regulated patterns of activity (Boparai et al., 2018; Slopen, McLaughlin, & Shonkoff, 2014). However, while these approaches are widely considered examples of innovative practice, they have not as of yet been adopted for broad implementation by policy makers and practitioners. This may reflect a commendable desire to await consistent results from replication before implementing a given program at scale, as well as realities of bureaucratic inertia and budgetary constraints. But to some extent the fact that innovative approaches with strong evidence of effect have not been widely implemented is attributable to the barriers that impede the translation of research findings into policy and practice.

These barriers include policy makers' and practitioners' limited access to subscription-based academic journals and even more restricted time to read the articles that appear in them. To their credit, publishers have worked to remove some of these barriers by making certain papers open access, while universities have created centers to distill and disseminate research findings. But these efforts cannot overcome the misalignment between academic research conducted in highly controlled settings with relatively small convenience samples and the needs of policy makers and practitioners for findings that are generalizable to the families in their communities. One solution is to use extant data; it is not uncommon for states and large municipalities to have access to data from larger and more representative samples than any researcher could reasonably hope to collect. However, state and local agencies often lack the time to plumb these data for the relevant findings they may hold, and, in some cases, procedures to ensure that the data being collected are of acceptable quality for research purposes. These are areas in which researchers can provide guidance, but to do so effectively will require forging long-term, collaborative relationships among researchers, practitioners, and policy makers. Creating and sustaining these relationships will require investments on the part of professional organizations and funders, but those investments will have the potential to pay dividends in the form of improved outcomes for children and families.

References

Aas, M., Steen, N. E., Agartz, I., Aminoff, S. R., Lorentzen, S., Sundet, K., … Melle, I. (2012). Is cognitive impairment following early life stress in severe mental disorders based on specific or general cognitive functioning? *Psychiatry Research*, 198, 495–500. doi:10.1016/j.psychres.2011.12.045

Agnew-Blais, J., & Danese, A. (2016). Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: A systematic review and meta-analysis. *Lancet Psychiatry*, 3, 342–349.

Ainsworth, M. S., Blehar, M. C., Waters, E., & Wall, S. (1978). *Patterns of attachment: A psychological study of the strange situation.* Oxford, England: Erlbaum.

Alink, L. R. A., Cicchetti, D., Kim, J., & Rogosch, F. A. (2012). Longitudinal associations among child maltreatment, social functioning, and cortisol regulation. *Developmental Psychology*, 48, 224–236. http://dx.doi.org/10.1037/a0024892

Angelakis, I., Gillepsie, E. L., & Panagioti, M. (2018). Childhood maltreatment and adult suicidality: A comprehensive systemic review with meta-analysis. *Psychological Medicine*, 49, 1–22. http://dx.doi.org/10.1017/S0033291718003823.

Bassi, A., & Bozzali, M. (2015). Potential interactions between the autonomic nervous system and higher-level functions in neurological and neuropsychiatric conditions. *Frontiers in Neurology*, 6, 182. https://doi.org/10.3389/fneur.2015.00182.

Bernard, K., Butzin-Dozier, Z., Rittenhouse, J., & Dozier, M. (2010). Cortisol production patterns in young children living with birth parents vs children placed in foster care following involvement of Child Protective Services. *Archives of Pediatrics & Adolescent Medicine*, 164, 438–443. doi:10.1001/archpediatrics.2010.54

Bernstein, D. P., Fink, L., Handelsman, L., Foote, J., Lovejoy, M., Wenzel, K., … Ruggiero, J. (1994). Initial reliability and validity of a new retrospective measure of child abuse and neglect. *American Journal of Psychiatry*, 151, 1132–1136. http://dx.doi.org/10.1176/ajp.151.8.1132

Bick, J., Nguyen, V., Leng, L., Piecychna, M., Crowley, M. J., Bucala, R., … Grigorenko, E. L. (2015). Preliminary associations between childhood neglect, MIF, and cortisol: Potential pathways to long-term disease risk. *Developmental Psychobiology*, 57, 131–139. http://dx.doi.org/10.1002/dev.21265

Bifulco, A., Brown, G. W., & Harris, T. O. (1994). Childhood experiences of care and abuse (CECA): A retrospective interview measure. *Journal of Child Psychology and Psychiatry*, 35, 1419–1435.

Bifulco, A., Brown, G. W., Lillie, A., & Jarvis, J. (1997). Memories of childhood neglect and abuse: Corroboration in a series of sisters. *Journal of Child Psychology and Psychiatry*, 38, 365–374.

Blair, C., Granger, D. A., Willoughby, M., Mills-Koonce, R., Cox, M., Greenberg, M. T., … FLP Investigators. (2011). Salivary cortisol mediates effects of poverty and parenting on executive functions in early childhood. *Child Development*, 82, 1970–1984. doi:10.1111/j.1467-8624.2011.01643.x

Boparai, S. K. P., Au, V., Koita, K., Oh, D. L., Briner, S., Harris, N. B., & Bucci, M. (2018). Ameliorating the biological impacts of childhood adversity: A review of intervention programs. *Child Abuse & Neglect*, 81, 82–105. https://doi.org/10.1016/j.chiabu.2018.04.014

Bremner, J. D., Bolus, R., & Mayer, E. A. (2007). Psychometric properties of the early trauma inventory–self report. *The Journal of Nervous and Mental Disease*, 195, 211–218. https://doi.org/10.1097/01.nmd.0000243824.84651.6c

Bruce, J., Fisher, P. A., Pears, K. C., & Levine, S. (2009). Morning cortisol levels in preschool-aged foster children: Differential effects of maltreatment type. *Developmental Psychobiology*, 51, 14–23. http://dx.doi.org/10.1002/dev.20333

Bugental, D. B., Martorell, G. A., & Barraza, V. (2003). The hormonal costs of subtle forms of infant maltreatment. *Hormones and Behavior*, 43, 237–244. https://doi.org/10.1016/s0018-506x(02)00008-9

Buske-Kirschbaum, A., Jobst, S., Wustmans, A., Kirschbaum, C., Rauh, W., & Hellhammer, D. (1997). Attenuated free cortisol response to psychosocial stress in children with atopic dermatitis. *Psychosomatic Medicine*, 59, 419–426. https://doi.org/10.1097/00006842-199707000-00012

Carrey, N. J., Butter, H. J., Persinger, M. A., & Bialik, R. J. (1995). Physiological and cognitive correlates of child abuse. *Journal of the American Academy of Child and Adolescent Psychiatry*, 34, 1067–1075. doi:10.1097/00004583-199508000-00017

Chalmers, J. A., Quintana, D. S., Abbott, M. J., & Kemp, A. H. (2014). Anxiety disorders are associated with reduced heart rate variability: A meta-analysis. *Frontiers in Psychiatry*, 5, 80. https://doi.org/10.3389/fpsyt.2014.00080.

Cicchetti, D., & Rogosch, F. A. (2001b). Diverse patterns of neuroendocrine activity in maltreated children. *Development and Psychopathology*, 13, 677–693.

Cicchetti, D., & Rogosch, F. (2001a). The impact of child maltreatment and psychopathology on neuroendocrine functioning. *Development and Psychopathology*, 13, 783–804.

Cicchetti, D., Rogosch, F. A., Gunnar, M. R., & Toth, S. L. (2010). The differential impacts of early physical and sexual abuse and internalizing problems on daytime cortisol rhythm in school-aged children. *Child Development*, 81, 252–269. http://dx.doi.org/10.1111/j.1467-8624.2009.01393.x

Cicchetti, D., Rogosch, F. A., & Oshri, A. (2011). Interactive effects of corticotropin releasing hormone receptor 1, serotonin transporter linked polymorphic region, and child maltreatment on diurnal cortisol regulation and internalizing symptomatology. *Development and Psychopathology*, 23, 1125–1138. http://dx.doi.org/10.1017/S0954579411000599

Conradt, E., Measelle, J., & Ablow, J. C. (2013). Poverty, problem behavior, and promise: Differential susceptibility among infants reared in poverty. *Psychological Science*, 24, 235–242. http://dx.doi.org/10.1177/0956797612457381

Davies, P. T., Cummings, E. M., & Winter, M. A. (2004). Pathways between profiles of family functioning, child security in the interparental subsystem, and child psychological problems. *Development and Psychopathology*, 16, 525–550. doi:10.10170S0954579404004651

DeBellis, M. D. (2001). Developmental traumatology: The psychobiological development of maltreated children and its implications for research, treatment, and policy. *Development and Psychopathology*, 13, 539–564.

DeBellis, M. D., Chrousos, G. P., Dorn, L. D., Burke, L., Helmers, K., Kling, M. A., … Putnam, F. W. (1994). Hypothalamic-pituitary-adrenal axis dysregulation in sexually abused girls. *The Journal of Clinical Endocrinology and Metabolism*, 78, 249–255.

DeBellis, M. D., Hooper, S. R., Spratt, E. G., & Woolley, D. P. (2009). Neuropsychological findings in childhood neglect and their relationships to pediatric PTSD. *Journal of the International Neuropsychological Society*, 15, 868–878. doi:10.1017/ S1355617709990464

DePrince, A. P., Weinzierl, K. M., & Combs, M. D. (2009). Executive function performance and trauma exposure in a community sample of children. *Child Abuse & Neglect*, 33, 353–361. doi:10.1016/j.chiabu.2008.08.002

de Punder, K., Overfeld, J., Dörr, P., Dittrich, K., Winter, S. M., Kubiak, N., … Heim, C. (2016). Exposure to child maltreatment is associated with elevated stress and immune mediators in children aged 3–5 years. *Psychoneuroendocrinology*, 71, 39–40. 10.1016/j.psyneuen.2016.07.105

Doom, J. R., Cicchetti, D., & Rogosch, F. A. (2014). Longitudinal patterns of cortisol regulation differ in maltreated and nonmaltreated children. *Journal of the American Academy of Child and Adolescent Psychiatry*, 53, 1206–1215. http://dx.doi.org/10.1016/j.jaac.2014.08.006

Doom, J. R., Cicchetti, D., Rogosch, F. A., & Dackis, M. N. (2013). Child maltreatment and gender interactions as predictors of differential neuroendocrine profiles. *Psychoneuroendocrinology*, 38, 1442–1454. http://dx.doi.org/10.1016/j.psyneuen.2012.12.019

do Prado, C. H., Grassi-Oliveira, R., Daruy-Filho, L., Wieck, A., & Bauer, M. E. (2017). Evidence for immune activation and resistance to glucocorticoids following childhood maltreatment in adolescents without psychopathology. *Neuropsychopharmacology*, 42, 2272–2282. http://dx.doi.org/10.1038/npp.2017.137

Duval, F., Crocq, M. A., Guillon, M. S., Mokrani, M. C., Monreal, J., Bailey, P., & Macher, J. P. (2004). Increased adrenocorticotropin suppression following dexamethasone administration in sexually abused adolescents with posttraumatic stress disorder. *Psychoneuroendocrinology*, 29, 1281–1289.

Ford, J. D., Fraleigh, L. A., Albert, D. B., & Connor, D. F. (2010). Child abuse and autonomic nervous system hyporesponsivity among psychiatrically impaired children. *Child Abuse & Neglect*, 34, 507–515. http://dx.doi.org/10.1016/j.chiabu.2009.11.005

Forte, G., Favieri, F., & Casagrande, M. (2019). Heart rate variability and cognitive function: A systematic review. *Frontiers in Neuroscience*, 13, 710. https://doi.org/10.3389/fnins.2019.00710.

Gerra, G., Zaimovic, A., Castaldini, L., Garofano, L., Manfredini, M., Somaini, L., … Donnini, C. (2010). Relevance of perceived childhood neglect, 5-HTT gene variants and hypothalamus–pituitary–adrenal axis dysregulation to substance abuse susceptibility. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 153B, 715–722. http://dx.doi.org/10.1002/ajmg.b.31038

Goenjian, A. K., Najarian, L. M., Pynoos, R. S., Steinberg, A. M., Manoukian, G., Tavosian, A., & Fairbanks, L. A. (1994). Posttraumatic stress disorder in elderly and younger adults after the 1988 earthquake in Armenia. *American Journal of Psychiatry*, 151, 895–901. doi:10.1176/ajp.151.6.895

Gökler, B., Ünal, F., Pehlivantürk, B., Çengel Kültür, E., Devrim Akdemir, D., & Taner, Y. (2004). Reliability and validity of schedule for affective disorders and schizophrenia for school age children, present and lifetime version-Turkish version (K-SADS-PL-T). *Çocuk ve Gençlik Ruh Sagligi Dergisi*, 11, 109–116.

Gooding, H. C., Milliren, C. E., Austin, S. B., Sheridan, M. A., & McLaughlin, K. A. (2016). Child abuse, resting blood pressure, and blood pressure reactivity to psychosocial stress. *Journal of Pediatric Psychology*, 41, 5–14. http://dx.doi.org/10.1093/jpepsy/jsv040

Gordis, E. B., Feres, N., Olezeski, C. L., Rabkin, A. N., & Trickett, P. K. (2010). Skin conductance reactivity and respiratory sinus arrhythmia among

maltreated and comparison youth: Relations with aggressive behavior. *Journal of Pediatric Psychology*, 35, 547–558. https://doi.org/10.1093/jpepsy/jsp113

Gordis, E. B., Granger, D. A., Susman, E. J., & Trickett, P. K. (2008). Salivary alpha amylase-cortisol asymmetry in maltreated youth. *Hormones and Behavior*, 53, 96–103. https://doi.org/10.1016/j.yhbeh.2007.09.002

Grassi-Oliveira, R., Cogo-Moreira, H., Salum, G. A., Brietzke, E., Viola, T. W., Manfro, G. G., … Arteche, A. X. (2014). Childhood Trauma Questionnaire (CTQ) in Brazilian samples of different age groups: Findings from confirmatory factor analysis. *PloS one*, 9, e87118. https://doi.org/10.1371/journal.pone.0087118

Groh, E. M. G. (2010). *Die psychische Belastung bei Pflegekindern: Vorhersage ihrer posttraumatischen Symptomatik und Adaption eines neuen Instruments zur Erfassung ihrer allgemeinen psychischen Belastung* (Doctoral dissertation, LMU Munich).

Gunnar, M. R. (1992). Reactivity of the hypothalamic-pituitary-adrenocorticoid system to stressors in normal infants and children. *Pediatrics*, 90, 491–497.

Gunnar, M. R., Morison, S. J., Chisholm, K., & Schuder, M. (2001). Salivary cortisol levels in children adopted from Romanian orphanages. *Development and Psychopathology*, 13, 611–628. http://dx.doi.org/10.1017/S095457940100311X

Gunnar, M., & Quevedo, K. (2007). The Neurobiology of stress and development. *Annual Review of Psychology*, 58, 145–173. http://dx.doi.org/10.1146/annurev.psych.58.110405.085605

Harkness, K. L., Stewart, J. G., & Wynne-Edwards, K. E. (2011). Cortisol reactivity to social stress in adolescents: Role of depression severity and child maltreatment. *Psychoneuroendocrinology*, 36, 173–181. http://dx.doi.org/10.1016/j.psyneuen.2010.07.006

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

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

Heim, C., & Nemeroff, C. B. (2001). The role of childhood trauma in the neurobiology of mood and anxiety disorders: Preclinical and clinical studies. *Biological Psychiatry*, 49, 1023–39.

Hertzman, C. (1999). The biological embedding of early experience and its effects on health in adulthood. In N. E. Adler, M. Marmot, B. S. McEwen, J. Stewart, N. E. Adler, M. Marmot & J. Stewart (Eds.), *Socioeconomic status and health in industrial nations: Social, psychological, and biological pathways* (pp. 85–95). New York, NY: New York Academy of Sciences.

Hoffman, C., Crnic, K. A., & Baker, J. K. (2006). Maternal depression and parenting: Implications for children's emergent emotion regulation and behavioral functioning. *Parenting: Science and Practice*, 6, 271–295. https://doi.org/10.1207/s15327922par0604_1

Holochwost, S. J., Kolacz, J., & Mills-Koonce, W. R. (Under review). Towards an understanding of neurophysiological self-regulation in early childhood.

Jackson, J. H. (1958). Evolution and dissolution of the nervous system. In J. Taylor (Ed.), *Selected Writings of John Hughlings Jackson* (pp. 45–118). London: Staples Press.

Jackson, S. E., Kirschbaum, C., & Steptoe, A. (2017). Hair cortisol and adiposity in a population-based sample of 2,527 men and women aged 54 to 87 years. *Obesity*, 25, 539–544. https://doi.org/10.1002/oby.21733.

Jaffee, S. J., Ambler, A., Merrick, M., Goldman-Mellor, S., Odgers, C. L., Fisher, H. L., … Arseneault, L. (2018). Childhood maltreatment predicts poor economic and educational outcomes in the transition to adulthood. *American Journal of Public Health*, 108, 1142–1147. https://doi.org/10.2105/AJPH.2018.304587

Kaess, M., Parzer, P., Mattern, M., Resch, F., Bifulco, A., & Brunner, R. (2011). Childhood Experiences of Care and Abuse (CECA): Validation of the German version and results of investigation of correlations between adverse childhood experiences and suicidal behaviour. *Zeitschrift für Kinder-und Jugendpsychiatrie und Psychotherapie*, 39, 243–252. https://doi.org/10.1024/1422-4917/a000115

Kaess, M., Whittle, S., O'Brien-Simpson, L., Allen, N. B., & Simmons, J. G. (2018). Childhood maltreatment, pituitary volume and adolescent hypothalamic-pituitary-adrenal axis—Evidence for a maltreatment-related attenuation. *Psychoneuroendocrinology*, 98, 39–45. https://doi.org/10.1016/j.psyneuen.2018.08.004

Kaess, M., Whittle, S., Simmons, J. G., Jovev, M., Allen, N. B., & Chanen, A. M. (2017). The interaction of childhood maltreatment, sex, and borderline personality features in the prediction of the cortisol awakening response in adolescents. *Psychopathology*, 50, 188–194. https://doi.org/10.1159/000456549

Karanikas, E., Antoniadis, D., & Garyfallos, G. D. (2014). The role of cortisol in first episode of psychosis: A systematic review. *Current Psychiatry Reports*, 16, 503. doi:10.1007/s11920-014-0503-7.

Karlén, J., Ludvigsson, J., Frostell, A., Theodorsson, E., & Faresjö, T. (2011). Cortisol in hair measured in young adults - a biomarker of major life stressors? *BMC Clinical Pathology*, 11, 12. doi:10.1186/1472-6890-11-12

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

Keeshin, B. R., Strawn, J. R., Out, D., Granger, D. A., & Putnam, F. W. (2014). Cortisol awakening response in adolescents with acute sexual abuse related posttraumatic stress disorder. *Depression and Anxiety*, 31, 107–114. https://doi.org/10.1002/da.22154

Keeshin, B. R., Strawn, J. R., Out, D., Granger, D. A., & Putnam, F. W. (2015). Elevated salivary alpha amylase in adolescent sexual abuse survivors with posttraumatic stress disorder symptoms. *Journal of Child and Adolescent Psychopharmacology*, 25, 344–350. https://doi.org/10.1089/cap.2014.0034

Kemp, A. H., Quintana, D. S., Gray, M. A., Felmingham, K. L., Brown, K., & Gatt, J. M. (2010). Impact of depression and antidepressant treatment on heart rate variability: A review and meta-analysis. *Biological Psychiatry*, 67, 1067–1074. https://doi.org/10.1016/j.biopsych.2009.12.012

Kertes, D. A., Gunnar, M. R., Madsen, N. J., & Long, J. D. (2008). Early deprivation and home basal cortisol levels: A study of internationally adopted children. *Development and Psychopathology*, 20, 473–491. https://doi.org/10.1017/S0954579408000230

Kessler, R. C., Davis, C. G., & Kendler, K. S. (1997). Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. *Psychological Medicine*, 27, 1101–19.

King, J. A., Mandansky, D., King, S., Fletcher, K., & Brewer, J. (2001). Early sexual abuse and low cortisol. *Psychiatry and Clinical Neurosciences*, 55, 71–74.

Kirschbaum, C., Pirke, K. M., & Hellhammer, D. H. (1993). The 'Trier Social Stress Test' – A tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology*, 28, 76–81. http://dx.doi.org/10.1159/000119004

Klanecky, A., McChargue, D. E., & Bruggeman, L. (2012). Desire to dissociate: Implications for problematic drinking in college students with childhood or adolescent sexual abuse exposure. *The American Journal on Addictions*, 21, 250–256. doi:10.1111/j.1521-0391.2012.00228.x

Klika, B., Lee, S. J., & Lee, J. Y. (2018). Prevention of child maltreatment. In B. Klika & J. Conte (Eds.), *In American Professional Society on the Abuse of Children handbook on child maltreatment*. Thousand Oaks, CA: Sage.

Knorr, U., Vinberg, M., Kessing, L. V., & Wetterslev, J. (2010). Salivary cortisol in depressed patients versus control persons: A systematic review and meta-analysis. *Psychoneuroendocrinology*, 35, 1275–1286. doi:10.1016/j.psyneuen.2010.04.001

Kočovská, E., Wilson, P., Young, D., Wallace, A. M., Gorski, C., Follan, M., … Minnis, H. (2013). Cortisol secretion in children with symptoms of reactive attachment disorder. *Psychiatry Research*, 209, 74–77. https://doi.org/10.1016/j.psychres.2012.12.011

Koenig, J., Kemp, A. H., Beauchaine, T. P., Thayer, J. F., & Kaess, M. (2016). Depression and resting state heart rate variability in children and adolescents—a systematic review and meta-analysis. *Clinical Psychology Review*, 46, 136–150. https://doi.org/10.3389/fphys.2017.00582

Kolacz, J., Kovacic, K. K., & Porges, S. W. (2019). Traumatic stress and the autonomic brain-gut connection in development: Polyvagal Theory as an integrative framework for psychosocial and gastrointestinal pathology. *Developmental Psychobiology*, 61, 796–809. https://doi.org/10.1002/dev.21852

Kolacz, J., & Porges, S. W. (2018). Chronic diffuse pain and functional gastrointestinal disorders after traumatic stress: Pathophysiology through a

polyvagal perspective. *Frontiers in Medicine*, 5, 145. https://doi.org/10.3389/fmed.2018.00145.

Koopman, C., Carrion, V., Butler, L. D., Sudhakar, S., Palmer, L., & Steiner, H. (2004). Relationships of dissociation and childhood abuse and neglect with heart rate in delinquent adolescents. *Journal of Traumatic Stress*, 17, 47–54. https://doi.org/10.1023/B:JOTS.0000014676.83722.35

Kuhlman, K. R., Geiss, E. G., Vargas, I., & Lopez-Duran, N. L. (2015). Differential associations between childhood trauma subtypes and adolescent HPA axis functioning. *Psychoneuroendocrinology*, 54, 103–114. https://doi.org/10.1016/j.psyneuen.2015.01.020

Lang, C. M., & Sharma-Patel, K. (2011). The relation between childhood maltreatment and self-injury: A review of the literature on conceptualization and intervention. *Trauma, Violence, & Abuse*, 12, 23–27. doi:10.1177/1524838010386975

Larkin, C., Di Blasi, Z., & Arensman, E. (2014). Risk factors for repetition of self-harm: A systematic review of prospective hospital-based studies. *PLoS ONE*, 9, e84282. https://doi.org/10.1371/journal.pone.0084282

Laurent, H. K., Gilliam, K. S., Wright, D. B., & Fisher, P. A. (2015). Child anxiety symptoms related to longitudinal cortisol trajectories and acute stress responses: Evidence of developmental stress sensitization. *Journal of Abnormal Psychology*, 124, 68–79. https://doi.org/10.1037/abn0000009

Lee, B. K., Glass, T. A., McAtee, M. J., Wand, G. S., Bandeen-Roche, K., Bolla, K. I., & Schwartz, B. S. (2007). Associations of salivary cortisol with cognitive function in the Baltimore Memory Study. *Archives of General Psychiatry*, 64, 810–818. https://doi.org/10.1001/archpsyc.64.7.810

Leeb, R. T., Paulozzi, L., Melanson, C., Simon, T., & Arias, I. (2008). *Child maltreatment surveillance: Uniform definitions for public health and recommended data elements, version 1.0*. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control.

Leitzke, B. T., Hilt, L. M., & Pollak, S. D. (2015). Maltreated youth display a blunted blood pressure response to an acute interpersonal stressor. *Journal of Clinical Child and Adolescent Psychology*, 44, 305–313. https://doi.org/10.1080/15374416.2013.848774

Linares, L. O., Shrout, P. E., Nucci-Sack, A., & Diaz, A. (2013). Child maltreatment, dating perpetration of physical assault, and cortisol reactivity among disadvantaged female adolescents. *Neuroendocrinology*, 97, 252–259. https://doi.org/10.1159/000342958

Lukens, E., Puigantich, J., Behn, J., Goetz, R., Tabrizi, M., & Davies, M. (1983). Reliability of the psychosocial schedule for school age children. *Journal of the American Academy of Child Psychiatry*, 22, 29–39.

Lunkenheimer, E., Busuito, A., Brown, K. M., & Skowron, E. A. (2018). Mother-Child coregulation of parasympathetic processes differs by child maltreatment severity and subtype. *Child Maltreatment*, 23, 211–220. https://doi.org/10.1177/1077559517751672

Lupien, S. J., King, S., Meaney, M. J., & McEwen, B. S. (2001). Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. *Development and Psychopathology*, 13, 653–676. http://dx.doi.org/10.1017/S0954579401003133

MacMillan, H. L., Georgiades, K., Duku, E. K., Shea, A., Steiner, M., & Schmidt, L. A. (2009). Cortisol response to stress in female youths exposed to childhood maltreatment: Results of the Youth Mood Project. *Biological Psychiatry*, 66, 62–68. https://doi.org/10.1016/j.biopsych.2008.12.014

Madruga, C. S., Laranjeira, R., Caetano, R., Ribeiro, W., Zaleski, M., Pinsky, I., & Ferri, C. P. (2011). Early life exposure to violence and substance misuse in adulthood-the first Brazilian national survey. *Addictive Behaviors*, 36, 251–255. doi:10.1016/j.addbeh.2010.10.011

Majer, M., Nater, U. M., Lin, J. M., Capuron, L., & Reeves, W. C. (2010). Association of childhood trauma with cognitive function in healthy adults: A pilot study. *BMC Neurology*, 10, 61. doi:10.1186/1471-2377-10-61

Margolin, G., John, R. S., & Foo, L. (1998). Interactive and unique risk factors for husbands' emotional and physical abuse of their wives. *Journal of Family Violence*, 13, 315–344.

McEwen, B. S. (2005). Stressed or stressed-out: What is the difference? *Journal of Psychiatry & Neuroscience*, 30, 315–318.

McLaughlin, K. A., Sheridan, M. A., Alves, S., & Mendes, W. B. (2014a). Child maltreatment and autonomic nervous system reactivity: Identifying dysregulated stress reactivity patterns using the biopsychosocial model of challenge and threat. *Psychosomatic Medicine*, 76, 538–546. https://doi.org/10.1097/PSY.0000000000000098

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014b). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience and Biobehavioral Reviews*, 47, 578–591.

McLaughlin, K. A., Sheridan, M. A., Tibu, F., Fox, N. A., Zeanah, C. H., & Nelson, C. A., III. (2015). Causal effects of the early caregiving environment on development of stress response systems in children. *Proceedings of the National Academy of Sciences of the United States of America*, 112, 5637–5642. https://doi.org/10.1073/pnas.1423363112

Melby, J. N., & Conger, R. D. (2001). The Iowa Family Interaction Rating Scales: Instrument summary. In P. K. Kerig & K. M. Lindahl (Eds.), *Family observational coding systems: Resources for systemic research* (pp. 33–58). Philadelphia, PA: Brunner/Mazel.

Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a model of behavioral and biological mechanisms. *Psychological Bulletin*, 137, 959–997.

Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. *Psychological Bulletin*, 133, 25–45.

Miskovic, V., Schmidt, L. A., Georgiades, K., Boyle, M., & MacMillan, H. L. (2009). Stability of resting frontal electroencephalogram (EEG) asymmetry and cardiac vagal tone in adolescent females exposed to child maltreatment. *Developmental Psychobiology*, 51, 474–487. https://doi.org/10.1002/dev.20387

Morrison, A, Polisena, J, Husereau, D, Moulton, K, & Clark, M. (2012). The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *International Journal of Technology Assessment in Health Care*, 28, 138–144.

Munck, A., Guyre, P. M., & Hollbrook, N. J. (1984). Physiological functions of glucocorticoids in stress and their relation to pharmacological actions. *Endocrinology Review*, 5, 25–44.

Munck, A., & Náray-Fejes-Tóth, A. (1995). Glucocorticoid action. Physiology. In L. J. DeGroot (Ed.), *Endocrinology* (pp. 1642–1656). Philadelphia: Saunders.

Nanni, V., Uher, R., & Danese, A. (2012). Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: A meta-analysis. *American Journal of Psychiatry*, 169, 141–51.

National Scientific Council on the Developing Child. (2005). *Excessive stress disrupts the architecture of the developing brain.* (Working paper #3). Retrieved from http://www.developingchild.net

Navalta, C. P., Polcari, A., Webster, D. M., Boghossian, A., & Teicher, M. H. (2006). Effects of childhood sexual abuse on neuropsychological and cognitive function in college women. *The Journal of Neuropsychiatry and Clinical Neurosciences*, 18, 45–53. doi:10.1176/ appi.neuropsych.18.1.45

Negriff, S., Saxbe, D. E., & Trickett, P. K. (2015). Childhood maltreatment, pubertal development, HPA axis functioning, and psychosocial outcomes: An integrative biopsychosocial model. *Developmental Psychobiology*, 57, 984–993. https://doi.org/10.1002/dev.21340

Nolin, P., & Ethier, L. (2007). Using neuropsychological profiles to classify neglected children with or without physical abuse. *Child Abuse & Neglect*, 31, 631–643. doi:10.1016/j.chiabu.2006.12.009

O'Connor, D. B., Ferguson, E., Green, J. A., O'Carroll, R. E., & O'Connor, R. C. (2016). Cortisol levels and suicidal behavior: A meta-analysis. *Psychoneuroendocrinology*, 63, 370–379. doi: 10.1016/j.psyneuen.2015.10.011

Oosterman, M., De Schipper, J. C., Fisher, P., Dozier, M., & Schuengel, C. (2010). Autonomic reactivity in relation to attachment and early adversity among foster children. *Development and Psychopathology*, 22, 109–118. https://doi.org/10.1017/S0954579409990290

Peckins, M. K., Susman, E. J., Negriff, S., Noll, J., & Trickett, P. K. (2015). Cortisol profiles: A test for adaptive calibration of the stress response system in maltreated and nonmaltreated youth. *Development and Psychopathology*, 27, 1461–1470. https://doi.org/10.1017/S0954579415000875

Perez, C. M., & Widom, C. S. (1994). Childhood victimization and long-term intellectual and academic outcomes. *Child Abuse & Neglect*, 18, 617–633.

Pollak, S. D., Nelson, C. A., Schlaak, M. F., Roeber, B. J., Wewerka, S. S., Wiik, K. L., … Gunnar, M. R. (2010). Neurodevelopmental effects of early deprivation in postinstitutionalized children. *Child Development*, 81, 224–236. doi:10.1111/j.1467-8624.2009.01391.x

Pollak, S. D., Vardi, S., Bechner, A. M. P., & Curtin, J. J. (2005). Physically abused children's regulation of attention in response to hostility. *Child Development*, 76, 968–977.

Porges, S. W. (1992). Vagal tone: A physiologic marker of stress vulnerability. *Pediatrics*, 90, 498–504.

Porter, C., Lawson, J. S., & Bigler, E. D. (2005). Neurobehavioral sequelae of child sexual abuse. *Child Neuropsychology*, 11, 203–220. doi:10.1080/092970490911379

Pruessner, J. C., Wolf, O., Hellhammer, D., Buske-Kirschbaum, A., von Auer, K., Jobst, S., … Kirschbaum, C. (1997). Free cortisol levels after awakening: A reliable marker for the assessment of adrenocortical activity. *Life Sciences*, 61, 2539–2549. https://doi.org/10.1016/s0024-3205(97)01008-4

Puetz, V. B., Zweerings, J., Dahmen, B., Ruf, C., Scharke, W., Herpertz-Dahlmann, B., & Konrad, K. (2016). Multidimensional assessment of neuroendocrine and psychopathological profiles in maltreated youth. *Journal of Neural Transmission*, 123, 1095–1106. https://doi.org/10.1007/s00702-016-1509-6

Puig-Antich, J., Lukens, E., Davies, M., Goetz, D., Brennan-Quattrock, J., & Todak, G. (1985a). Psychosocial functioning in prepubertal major depressive disorders: I. Interpersonal relationships during the depressive episode. *Archives of General Psychiatry*, 42, 500–507. https://doi.org/10.1001/archpsyc.1985.01790280082008

Puig-Antich, J., Lukens, E., Davies, M., Goetz, D., Brennan-Quattrock, J., & Todak, G. (1985b). Psychosocial functioning in prepubertal major depressive disorders: II. Interpersonal relationships during the depressive episode. *Archives of General Psychiatry*, 42, 500–507. https://doi.org/10.1001/archpsyc.1985.01790280093010

Putnam, F. W. (1993). Dissociative disorders in children: Behavioral profiles and problems. *Child Abuse and Neglect*, 17, 39–45. https://doi.org/10.1016/0145-2134(93)90006-q

Quevedo, K., Doty, J., Roos, L., & Anker, J. J. (2017). The cortisol awakening response and anterior cingulate cortex function in maltreated depressed versus non-maltreated depressed youth. *Psychoneuroendocrinology*, 86, 87–95. https://doi.org/10.1016/j.psyneuen.2017.09.001

Reese-Weber, M. (2008). A new experimental method assessing attitudes toward adolescent dating and sibling violence using observations of violent interactions. *Journal of Adolescence*, 31, 857–876.

Rinnewitz, L., Koenig, J., Parzer, P., Brunner, R., Resch, F., & Kaess, M. (2018). Childhood adversity and psychophysiological reactivity to pain in adolescent nonsuicidal self-injury. *Psychopathology*, 51, 346–354. https://doi.org/10.1159/000491702

Rogosch, F. A., Dackis, M. N., & Cicchetti, D. (2011). Child maltreatment and allostatic load: Consequences for physical and mental health in children from low-income families. *Development and Psychopathology*, 23, 1107–1124.

Rosmalen, J. G., Oldehinkel, A. J., Ormel, J., de Winter, A. F., Buitelaar, J. K., & Verhulst, F. C. (2005). Determinants of salivary cortisol levels in 10–12 year old children; a population-based study of individual differences. *Psychoneuroendocrinology*, 30, 483–495.

Sapolsky, R. M., Krey, L. C., & McEwen, B. S. (1986). The neuroendocrinology of stress and aging: The gluco-corticoid cascade hypothesis. *Endocrine Reviews*, 7, 284–301. https://doi.org/10.1210/edrv-7-3-284

Sapolsky, R. M., Romero, L. M., & Munck, A. U. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrine Reviews*, 21, 55–89. https://doi.org/10.1210/edrv.21.1.0389

Saxbe, D. E., Margolin, G., Spies Shapiro, L. A., & Baucom, B. R. (2012). Does dampened physiological reactivity protect youth in aggressive family environments? *Child Development*, 83, 821–830. https://doi.org/10.1111/j.1467-8624.2012.01752.x

Schulz, P, Kirschbaum, C, Pruessner, J, & Hellhammer, D. (1988). Increased free cortisol secretion after awakening in chronically stressed individuals due to work overload. *Stress Medicine*, 14, 91–97.

Schulz, P, Kirschbaum, C, Pruessner, J, & Hellhammer, D. (1998). Increased free cortisol secretion after awakening in chronically stressed individuals due to work overload. *Stress Medicine*, 14, 91–97.

Schwabe, L., Haddad, L., & Schachinger, H. (2008). HPA axis activation by a socially evaluated cold-pressor test. *Psychoneuroendocrinology*, 33, 890–895. https://doi.org/10.1016/j.psyneuen.2008.03.001

Seyle, H. (1950). *The Physiology and pathology of exposure to stress: A Treatise based on the concepts of the general-adaptation-syndrome and the diseases of adaptation*. Montreal: Acta.

Shalev, I., Moffitt, T. E., Sugden, K., Williams, B., Houts, R. M., Danaese, A., … Caspi, A. (2012). Exposure to violence during childhood is associated with telomere erosion from 5 to 10 years of age: A longitudinal study. *Molecular Psychiatry*, 18, 576–581. doi: 10.1038/mp.2012;.32.

Shamseer, L., Moher, D., Clarke, M., Ghersi, D., Liberati, A., Petticre, M., … Stewart, L. A. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: Elaboration and explanation. *Research Methods & Reporting*, 349, g7647. http://dx.doi.org/10.1136/bmj.g.7647.

Shenk, C. E., Noll, J. G., Putnam, F. W., & Trickett, P. K. (2010). A prospective examination of the role of childhood sexual abuse and physiological asymmetry in the development of psychopathology. *Child Abuse & Neglect*, 34, 752–761. https://doi.org/10.1016/j.chiabu.2010.02.010

Shenk, C. E., Putnam, F. W., & Noll, J. G. (2012). Experiential avoidance and the relationship between child maltreatment and PTSD symptoms: Preliminary evidence. *Child Abuse & Neglect*, 36, 118–126. https://doi.org/10.1016/j.chiabu.2011.09.012

Siddaway, A. P., Wood, A. M., & Hedges, L. V. (2019). How to do a systematic review: A best practice guide for conducting and reporting narrative reviews, meta-analyses, and meta-syntheses. *Annual Review of Psychology*, 70, 747–770. https://doi.org/10.1146/annurev-psych-010418-102803

Şimşek, Ş, Yüksel, T., Kaplan, İ, Uysal, C., & Alaca, R. (2015). Examining the levels of BDNF and cortisol in children and adolescent victims of sexual abuse – A preliminary study. *Comprehensive Psychiatry*, 61, 23–27. https://doi.org/10.1016/j.comppsych.2015.04.013

Sinha, R. (2008). Chronic stress, drug use, and vulnerability to addiction. *Annals of the New York Academy of Sciences*, 1141, 105–130. doi:10.1196/annals.1441.030

Skowron, E. A., Cipriano-Essel, E., Gatzke-Kopp, L. M., Teti, D. M., & Ammerman, R. T. (2014). Early adversity, RSA, and inhibitory control: Evidence of children's neurobiological sensitivity to social context. *Developmental Psychobiology*, 56, 964–978. https://doi.org/10.1002/dev.21175

Skowron, E. A., Loken, E., Gatzke-Kopp, L. M., Cipriano-Essel, E. A., Woehrle, P. L., Van Epps, J. J., … Ammerman, R. T. (2011). Mapping cardiac physiology and parenting processes in maltreating mother–child dyads. *Journal of Family Psychology*, 25, 663–674. https://doi.org/10.1037/a0024528

Slopen, N., McLaughlin, K. A., & Shonkoff, J. P. (2014). Interventions to improve cortisol regulation in children: A systematic review. *Pediatrics*, 133, 312–326. https://doi.org/10.1542/peds.2013-1632

Straus, M. A. (1979). Measuring intrafamily conflict and violence: The Conflict Tactics Scale. *Journal of Marriage and Family*, 41, 75–88. https://doi.org/10.2307/351733

Straus, M. A., Hamby, S. L., Finkelhor, D., Moore, D. W., & Runyan, D. (1998). Identification of child maltreatment with the Parent-Child Conflict Tactics Scales: Development and psychometric data for a national sample of American parents. *Child Abuse & Neglect*, 22, 249–270. https://doi.org/10.1016/s0145-2134(97)00174-9

Sturge-Apple, M. L., Davies, P. T., Cicchetti, D., & Manning, L. G. (2012). Interparental violence, maternal emotional unavailability and children's cortisol functioning in family contexts. *Developmental Psychology*, 48, 237–249. https://doi.org/10.1037/a0025419

Sullivan, M. W., Bennett, D. S., & Lewis, M. (2013). Individual differences in the cortisol responses of neglected and comparison children. *Child Maltreatment*, 18, 8–16. https://doi.org/10.1177/1077559512449378

Sumner, J. A., McLaughlin, K. A., Walsh, K., Sheridan, M. A., & Koenen, K. C. (2014). CRHR1 genotype and history of maltreatment predict cortisol reactivity to stress in adolescents. *Psychoneuroendocrinology*, 43, 71–80. https://doi.org/10.1016/j.psyneuen.2014.02.002

Suor, J. H., Sturge-Apple, M. L., Davies, P. T., Cicchetti, D., & Manning, L. G. (2015). Tracing differential pathways of risk: Associations among family adversity, cortisol, and cognitive functioning in childhood. *Child Development*, 86, 1142–1158. https://doi.org/10.1111/cdev.12376

Trickett, P. K., Gordis, E., Peckins, M. K., & Susman, E. J. (2014). Stress reactivity in maltreated and comparison male and female young adolescents. *Child Maltreatment*, 19, 27–37. https://doi.org/10.1177/1077559513520466

Trickett, P. K., Noll, J. G., Susman, E. J., Shenk, C. E., & Putnam, F. W. (2010). Attenuation of cortisol across development for victims of sexual abuse. *Development and Psychopathology*, *22*, 165–175. https://doi.org/10.1017/S0954579409990332

Tyrka, A. R., Price, L. H., Kao, H. T., Porton, B., Marsella, S. A., & Carpenter, L. L. (2010). Childhood maltreatment and telomere shortening: Preliminary support for an effect of early stress on cellular aging. *Biological Psychiatry*, *67*, 531–534.

US Department of Health & Human Services, Administration for Children and Families, Administration on Children, Youth and Families, Children's Bureau. (2017). *Child Maltreatment 2015.* Available from http://www.acf.hhs.gov/programs/cb/research-data-technology/statistics-research/child-maltreatment

Usta, M. B., Tuncel, O. K., Akbas, S., Aydin, B., & Say, G. N. (2016). Decreased dehydroepiandrosterone sulphate levels in adolescents with post-traumatic stress disorder after single sexual trauma. *Nordic Journal of Psychiatry*, *70*, 116–120. https://doi.org/10.3109/08039488.2015.1056752

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., … Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: A meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin*, *38*, 661–671.

Veldhorst, M. A. B., Noppe, G., Jongejan, M. H. T. M., Kok, C. B. M., Mekic, S., Koper, J. W., … van den Akker, E. L. T. (2014). Increased scalp hair cortisol concentrations in obese children. *The Journal of Clinical Endocrinology & Metabolism*, *99*, 285–290. https://doi.org/10.1210/jc.2013-2924

Vreeburg, S. A., Hoogendijk, W. J., van Pelt, J., DeRijk, R. H., Verhagen, J. C., van Dyck, R., … Penninx, B. W. (2009). Major depressive disorder and hypothalamic-pituitary-adrenal axis activity: Results from a large cohort study. *Archives of General Psychiatry*, *66*, 617–626. doi: 10.1001/archgenpsychiatry.2009.50

Wagner, S. L., Cepeda, I., Krieger, D., Maggi, S., D'Angiulli, A., Weinberg, J., & Grunau, R. E. (2016). Higher cortisol is associated with poorer executive functioning in preschool children: The role of parenting stress, parent coping and quality of daycare. *Child Neuropsychology*, *22*, 853–869. https://doi.org/10.1080/09297049.2015.1080232

Watson, S., Gallagher, P., Ritchie, J. C., Ferrier, I. N., & Young, A. H. (2004). Hypothalamic-pituitary-adrenal axis function in patients with bipolar disorder. *British Journal of Psychiatry*, *184*, 496–502. https://doi.org/10.1192/bjp.184.6.496

White, L. O., Ising, M., Klitzing, K., Sierau, S., Michel, A., Klein, A. M., … Stalder, T. (2017). Reduced hair cortisol after maltreatment mediates externalizing symptoms in middle childhood and adolescence. *Journal of Child Psychology and Psychiatry*, *58*, 998–1007. https://doi.org/10.1111/jcpp.12700

Widom, C. S. (1999). Posttraumatic stress disorder in abused and neglected children grown up. *American Journal of Psychiatry*, *156*, 1223–1229.

Wiegers, G. J., & Reul, J. M. H. M. (1998). Induction of cytokine receptors by glucocorticoids: Functional and pathological significance. *Trends in the Pharmacological Sciences*, *19*, 317–321. https://doi.org/10.1016/s0165-6147(98)01229-2

Wismer Fries, A. B., Shirtcliff, E. A., & Pollak, S. D. (2008). Neuroendocrine dysregulation following early social deprivation in children. *Developmental Psychobiology*, *50*, 588–599. https://doi.org/10.1002/dev.20319

World Health Organization. (2017). *Child Maltreatment Fact Sheet.* Available from http://www.who.int/mediacentre/factsheets/fs150/en/