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Stressor paradigms in developmental studies: What does and does not work to produce mean increases in salivary cortisol

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Summary

The stress response system is comprised of an intricate interconnected network that includes the hypothalamic–pituitary–adrenocortical (HPA) axis. The HPA axis maintains the organism's capacity to respond to acute and prolonged stressors and is a focus of research on the sequelae of stress. Human studies of the HPA system have been facilitated enormously by the development of salivary assays which measure cortisol, the steroid end-product of the HPA axis. The use of salivary cortisol is prevalent in child development stress research. However, in order to measure children's acute cortisol reactivity to circumscribed stressors, researchers must put children in stressful situations which produce elevated levels of cortisol. Unfortunately, many studies on the cortisol stress response in children use paradigms that fail to produce mean elevations in cortisol. This paper reviews stressor paradigms used with infants, children, and adolescents to guide researchers in selecting effective stressor tasks. A number of different types of stressor paradigms were examined, including: public speaking, negative emotion, relationship disruption/threatening, novelty, handling, and mild pain paradigms. With development, marked changes are evident in the effectiveness of the same stressor paradigm to provoke elevations in cortisol. Several factors appear to be critical in determining whether a stressor paradigm is successful, including the availability of coping resources and the extent to which, in older children, the task threatens the social self. A consideration of these issues is needed to promote the implementation of more effective stressor paradigms in human developmental psychoendocrine research.

Keywords

Salivary cortisol; Stressor paradigms; Human development

Human studies of the hypothalamic–pituitary–adrenocortical (HPA) system have been facilitated enormously by the development of salivary assays. In the study of child developmental psychoneuroendocrinology, the importance of these assays cannot be overstated. A review of the child literature on cortisol-behavior relations in 1986 revealed a mere handful of studies (Gunnar, 1986). Twenty years later, studies using salivary cortisol are plentiful both in work on typically developing children and in research on children at risk for physical and mental health disorders (see review, Gunnar and Vazquez, 2006). But while salivary assays of cortisol and other biomarkers (e.g., Granger et al., 1999; Goodyer et al., 2000; Gordis et al., 2006) are helping to explicate the role of neuroendocrine regulation in

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human neurobehavioral development, many child development studies rely on measures of hormone activity as children move about their everyday environments, rather than measures obtained in response to acute and well-circumscribed laboratory stressors.

Examining the everyday patterns of hormone production has been informative in studies of adults (Nicolson, 1992; van Eck et al., 1996) and in children (Adam, 2006). Studies measuring cortisol activity in children outside the laboratory have revealed, among other findings (1) rising rather than falling patterns of cortisol over the day among toddlers and preschoolers in child care, especially in settings characterized by poorer quality of care (see meta-analysis, Vermeer and van IJzendoorn, 2006), (2) reduced slope of the cortisol rhythm over the day among children experiencing neglectful care (see review, Gunnar and Fisher, 2006), and (3) evidence that maternal postnatal depression predicts elevated early morning cortisol levels among offspring, which mediates levels of depressive symptoms throughout adolescence (Halligan et al., 2007).

While we have gained traction by examining salivary cortisol activity under everyday conditions, we also need to be able to effectively assess cortisol reactivity to stressors under controlled laboratory conditions. There are numerous studies that have attempted to measure elevations in cortisol in response to acute stressors in children. But all too often, the stressor paradigms do not provoke increases in cortisol in all, or even most, of the children. Table 1 reveals how successful and unsuccessful developmental researchers have been in identifying effective stressor paradigms for children of different ages. Many studies have effectively utilized stressor tasks for infants three months or younger. For infants four through nine months of age, stressor paradigms are less successful in elevating cortisol levels. Success rates decrease even more for children twelve through twenty-four months of age. For children two through five years of age, hardly any stressor paradigm used has effectively elevated cortisol. Success rates begin to climb again for children between six and twelve years, and by adolescence, around half of the stressor studies published report significant increases in cortisol. Some of the variability associated with the effectiveness of stressor tasks may relate to neurodevelopmental changes affecting reactivity and regulation of the HPA system. For instance, until three months of age, infants do not exhibit the early morning peak characteristic of the typical diurnal pattern of cortisol secretion (Gunnar and White, 2001). Additionally, few stressors have successfully elevated cortisol levels during late infancy through early childhood. These findings have led some to believe that infancy through early childhood represents a period during development in which HPA responsivity is dampened. More recently, in studies of children during the transition to adolescence, both basal and response measures of cortisol have been found to be elevated (Gunnar et al., 2009;Stroud et al., 2009). The changing effectiveness of stressor tasks likely reflects changes in basal activity of the axis with development, descriptions of which are reviewed elsewhere (Gunnar and Vazquez, 2006). In addition, developmental changes in stressor paradigm effectiveness undoubtedly relates to our lack of understanding of the psychological processes critical to eliciting a stress response of the HPA axis in children of different ages; this is the focus of the present review and analysis.

As noted by Dickerson and Kemeny (2004) in their review of adult stressor paradigms, identifying paradigms that reliably provoke elevations in cortisol and understanding the psychological characteristics of these paradigms is critical to developing a coherent literature on the role of the HPA stress response in cognitive and emotional functioning. Their elegant quantitative review brought coherence to the adult field, which like the child field, suffered from many “stress” studies in which the stressor task failed to elevate cortisol (Biondi and Picardi, 1999). Dickerson and Kemeny (2004) identified three elements of psychological stressor paradigms that are critical to provoking cortisol elevations among adults: unpredictability, uncontrollability, and social-evaluative threat. Social evaluative threat “occurs when an important aspect of the self-identity is or could be negatively judged by

others" (p 358). Unpredictability and uncontrollability under conditions of social evaluation amplify the threat and hence, increase the HPA response.

The goal of the following review of child stressor paradigms is more modest and for good reason. If we presume that self-preservation underlies the potency of self-evaluative threat (as argued by Dickerson and Kemeny), then the developmental researcher faces the daunting task of identifying ethical stressors that threaten the integrity of the self across periods during which self processes are continuously changing (Gunnar and Sroufe, 1991). These changes include the emergence of a differentiated sense of self and self-referent emotions, the development of social-comparison processes, and shifts in sources of security from the parent–child attachment relationship in infancy to greater emphasis on self-reliance and relationships within the peer group by adolescence. From childhood to adolescence, we also see marked development in the attention and emotion regulatory competencies involved in the regulation of HPA responses to stress. Thus, our goal in this review is to describe the effectiveness of different types of stressor paradigms used in child and adolescent studies. Reasons for the effectiveness of some tasks and not others will be presented along with problems in the implementation of stressor tasks that may limit our ability to detect cortisol increases. Finally, we will suggest changes to our methods of choosing stressor tasks that might improve our ability to identify and employ tasks that are effective in activating the HPA system in stress research on children.

In preparing this review, both PubMed and PsycInfo were searched for studies using salivary cortisol measures in healthy, typically developing children. If the study involved a patient group and a comparison group of healthy children, information from the comparison children was abstracted. Until we have paradigms that are effective in normative samples of children, it will be difficult to develop a truly informative literature on alterations in cortisol stress reactivity and regulation in children with or at risk for disorders. Studies whose methodology examined pre- and post-test measures in response to tasks were selected. In many of the studies, the means and standard deviations for the cortisol data were not presented. This information occasionally appeared in graphs, and at times, only the significance and direction of the effect was noted, thus rendering the quantification of effect sizes near impossible. Therefore, in the tables and discussion, we only note whether the change in cortisol levels was statistically significant and the direction of change. The frequency and timing of the samples is also reported in the tables. Some of the studies obtained multiple samples of cortisol allowing examination of response and recovery. In each case, we judged whether the study produced an elevation by examining data obtained approximately 20–30 min after the onset or peak of the stressor. In some instances, samples were not taken at this time point, which might explain some of the null findings. Some studies examined subsamples of children who yielded evidence of a response. In these cases, the effectiveness of the stressor paradigms for the total group is reported; however, in the "comments" section of the table, the subgroup for which the stressor was effective is noted. Significant sex differences were noted and appear in the comments section. However, few of the studies reported significant main or interaction effects with the sex of the child.

This review was organized according to the different types of stressors used to elicit mean increases in cortisol. We have summarized the findings of these studies in a series of tables. We start with an examination of public speaking tasks of the type shown by Dickerson and Kemeny (2004) to be effective in research with adults (Table 2). We then follow with paradigms designed to provoke negative emotions, examining fear/wariness tasks and anger/frustration tasks separately (Table 3). We chose to examine these tasks next because Dickerson and Kemeny (2004) found that emotion provocation was not very effective in activating the HPA axis in adults and, as will be noted, this also appears to be true in children. Next, tasks designed to threaten or challenge social relations are reported (Tables 4-6). These tasks include maternal separation, parent–child conflict, and peer acceptance/rejection. Exposure to novelty, first-time

experience tasks, and handling stressors, are also reported (Table 7), as these are tasks which frequently activate the HPA axis in animals (e.g., Hennessy and Levine, 1979). Finally, tasks involving mild pain stressors including blood draws and inoculations are examined (Table 8). In order to present information by age and paradigm, often the data on the same children are presented in several places on the same or different tables. Thus, for longitudinal studies, data from the same children in response to the same stressor tasks will appear at different age points in the table. If the study involved presentation of different stressors to the same children, the same participants will appear in different tables. In the tables, a star next to the date of citation indicates that participants appear in the tables multiple times. Studies where children of different age groups are exposed to the same stressor task appear several times in the same table so that results can be presented within age groups. Presenting information by age allows the reader to discern changes with age in the effectiveness of different stressor paradigms.

1. Public speaking tasks

Table 2 presents the results for studies using various types of public speaking tasks. Seven-year-olds are the youngest age group with whom these paradigms have been published. In most instances, the public speaking task has either been the Trier Social Stress Test for Children (TSST-C; Buske-Kirschbaum et al., 1997) or a modification of this task. As in the adult TSST, the child TSST involves the elements that Dickerson and Kemeny (2004) identified as potent psychological triggers of the HPA axis: social-evaluation, uncontrollability, and unpredictability. In this task, children are required to prepare a speech and are told that the speech will be judged for its quality. Then, they give the speech to an audience while being videotaped, followed by a mental arithmetic task involving serial subtraction that is sufficiently difficult to result in errors in nearly all of the participants. When the children make a mistake, they are told to start over. Unlike in the adult TSST, the judges do not challenge the child's responses; however, they are more business-like than friendly in their feedback, and the children do not meet the judges until they are ushered into the room where they are to give their speech. Many researchers have used modifications of the TSST-C. These modifications include having the child give their speech to a one-way mirror behind which, they are told, the judges are seated (Jansen et al., 2000), not videotaping the speech (Klimes-Dougan et al., 2001;Gordis et al., 2006;Stroud et al., 2009), not telling the child that their speech will be judged for quality, and not including the serial subtraction task (Klimes-Dougan et al., 2001). Despite these variations, nearly all studies report significant increases in cortisol among children 13 years of age and older.

For children under 13 years of age, there are more failures to find significant increases in cortisol levels. For example, Schmidt et al. (1999) told the child they would be giving a speech about *their most embarrassing moment* which would seem a significant threat to the social self for this age, but did not require children to actually deliver their speech. This might account for the failure of their paradigm to elevate cortisol. If we examine studies using the actual TSST-C or only slight modifications of the TSST-C, three studies with 7 through 9-year-olds reported significant increases in cortisol (Jansen et al., 2000; Jones et al., 2006; Gunnar et al., 2009). Mixed results are found when investigating children 10–13 years of age. Some studies that included this age range reported significant increases (Buske-Kirschbaum et al., 1997, 2003; Klimes-Dougan et al., 2001; Gordis et al., 2006), while others did not (Dorn et al., 2003; Gunnar et al., 2009; Stroud et al., 2009). While we might suspect differences in methodology, two of these studies used the same methods and demonstrated significant increases at some ages but not others (Gunnar et al., 2009; Stroud et al., 2009). In both of these studies, the effectiveness of this stressor task was associated with pubertal development. Additionally, Gunnar et al. (2009) found elevations in cortisol for 13-year-old girls and for both sexes at 15 years. Only the 11-year-olds and 13-year-old boys failed to mount a significant cortisol response. Klimes-Dougan et al. (2001) also failed to find cortisol elevations among

11–13-year-old boys. While it is not clear how puberty may be interacting with this task's effectiveness in activating the HPA axis, its effects could be at either the cortico-limbic level, influencing how the social threat is processed, or at levels within the axis. Interestingly, Stroud et al. (2004) have noted sex differences, perhaps related to differences in pubertal status, in responsiveness to CRH challenge across this age period. And there is evidence of puberty-associated effects on cortico-limbic emotion processing systems (see Dahl and Gunnar, 2009). Notably, heart rate and self-report data showed that the children transitioning into adolescence experienced heightened self-perceptions of stress during the TSST-C, despite failures to produce elevations in cortisol (Gunnar et al., 2009; Stroud et al., 2009).

Thus, as in adults, the TSST-C and other closely related public speaking tasks appear to be effective in activating the HPA axis in children. However, there may be a period around the pubertal transition when elevations are more difficult to provoke. Why this is the case and the replicability of these findings needs to be examined further, as there is currently a paucity of studies explicitly designed to address this topic. In addition, to our knowledge, no one has attempted to use public performance tasks with children younger than seven years, although studies of behavioral inhibition have used tasks with preschoolers that require the child to stand up and tell a group of children about their last birthday party (Fox et al., 1995). From behavioral measures, these tasks appear to be quite anxiety provoking for some children and thus, might form the basis for an early childhood version of the TSST.

2. Tasks designed to elicit negative emotions

Beginning with infants as young as six months and extending to work with preadolescent children, researchers have made various attempts to activate the HPA axis by subjecting children to protocols designed to elicit negative emotions (see Table 3). Typically, in these studies the protocols are complex, involving multiple tasks. We have sorted the protocols into two groups: those whose predominant aim was to elicit wariness, fearfulness, or anxiety, and those whose principal goal was to provoke anger and frustration. Some protocols included both fear-eliciting and anger-eliciting tasks. In these cases, we sorted the study based on whether the timing of post-task cortisol assessment should have detected more of one versus the other type of provocation. In many cases, the emotion-eliciting tasks were drawn from the Laboratory Temperament Assessment Battery (Goldsmith and Rothbart, 1992;Goldsmith et al., 1999). Studies using tasks from this battery are indicated by a superscript in the table. The LabTAB includes brief tasks (3–5 min) designed to elicit specific emotions in young children. In nearly all of the studies with young children, fear- and anger-evocative tasks are preceded and followed by tasks designed either to be calming or to elicit positive emotionality. Furthermore, in all of the studies in this table, if intense negative responses were observed, the task was stopped and the child was comforted. Finally, for infants and toddlers, parents were typically in the room, although often seated behind the child during the provocation tasks.

Two primary approaches have been used to elicit shy or fearful behavior from young children in the laboratory setting: allowing the child to come in close contact with either strange, novel objects or events (e.g., scary gorilla mask) or an unfamiliar adult. Despite these varying approaches, in no instance were researchers successful in provoking a mean increase in cortisol (Table 3). Failure to elevate cortisol may be due to several factors, though two are of particular note. Many of the provocations used were mild and elicited significant individual differences in emotional reaction. For example, some children did display anxious, fearful behavior; however, some responded positively, with smiles and approach behaviors. Under such circumstances, we would not expect a main effect of the fear-evocative tasks, but rather cortisol responses that differed by whether the child responded with fear or not. In some instances, cortisol responses were noted that correlated with indices of fearfulness (e.g., freezing, Buss et al., 2004), but in other instances, even extremely fearful/anxious children did not show

evidence of elevations in cortisol, although their average cortisol levels across the session might be higher than for other children (Kagan et al., 1987).

The second issue of particular note in childhood fear/wariness paradigms is that failure to find "reactivity" differences among extremely fearful children may relate to the challenge of detecting such associations when the parent is present. One of the primary functions of the attachment relationship is to provide the infant and young child with a sense of security in the parent's presence (Bowlby, 1969). Thus, as noted in the study by Nachmias et al. (1996), elevations in cortisol to a series of threatening events (strange puppets, live clown, and loud mechanical toy) were seen only for a subsample of the children who were both fearful and accompanied by a parent with whom they had an insecure attachment relationship. Unfortunately, most of the studies of cortisol and fearfulness have not evaluated the security of the parent–child attachment relationship. Thus, we are left with the primary finding that fear-evocative stressor tasks are generally ineffective in elevating cortisol, even for the subset of children who appear to be clearly frightened by the task.

In summary, the failure of fear provocative tasks to produce significant increases in cortisol levels among children may be related to several key factors: (1) the termination of the task if the child evidences intense negative emotional reactivity, (2) the placement of threatening tasks between pleasant or calming tasks, (3) the poor timing of response samples, (4) the mildness of the provocation, and (5) the presence and availability of the parent. Changing some of these parameters may increase the evocative nature of the paradigm, but such changes are circumscribed by what is ethical with young children.

A variety of tasks designed to elicit anger and frustration have been used which attempt to elicit cortisol elevations (Table 3). With infants, the most common task is the still-face paradigm. In this task, mother and infant engage in en face interaction. Then for a period of several minutes, the mother is instructed to maintain a still, non-responsive, and neutral face. Following this, there is a recovery phase when the mother again interacts normally. The standard still-face paradigm involves one non-responsive period, while the extended still-face involves two such periods. Assuming that the infant's goal is to get the mother to respond, the still-face can be viewed as a goal-blocking task. Likewise, many of the anger/frustration tasks in the LabTAB restrict the child from reaching their goals, including tasks where the child is blocked from playing with attractive toys or tasks in which the child's movements are briefly restrained. Coding of facial expressions during all of these goal-blocking tasks indicates that anger is the predominant emotion, although other emotions (including sadness) are also evoked (Goldsmith and Rothbart, 1992;Goldsmith et al., 1999;Lewis and Ramsay, 2005). Several researchers have also used competitive challenges that include periods during which the child is losing to the competitor (Donzella et al., 2000). Notably, most of these paradigms fail to produce mean increases in cortisol in typically developing children.

The exception is a paradigm developed by van Goozen et al., (1998, 2000). This complex, 80 min protocol involves several periods during which the participant plays a difficult computer task under time pressure designed so that the participant will perform badly. During these periods, the video-opponent makes derogatory comments about the participant's performance, and mean increases in cortisol peak at 20–30 min after the mid-point of this frustration-provocation task. Why was this task effective in elevating cortisol when the other anger-frustration tasks were not? Certainly, the task developed by van Goozen and colleagues lasts longer than the tasks used in other studies and this might be an important factor. However, it is notable that the derogatory comments of the video-competitor meant that this was also a social-evaluative stressor (Dickerson and Kemeny, 2004). Thus, while the other tasks may have produced anger in response to goal-blocking, this task also involved shaming. The importance of negative self-evaluative emotions in eliciting cortisol responses was also

apparent in the study by Lewis and Ramsay (2002). In their study, four-year-old children solved a color matching task under time pressure. The task was rigged so that children solved the task on some trials but not on others. Facial expressions, body posture, and verbalizations were coded in response to failure trials. While anger was the predominant emotion, children also expressed shame and embarrassment. Those children who expressed high levels of these negative self-referent emotions exhibited increased cortisol in response to this task.

In summary, the literature suggests that stressor paradigms designed to evoke anger are ineffective in elevating cortisol unless the task also evokes negative self-referent emotions. If true, then the anger paradigms most effective in children will be ones that bear similarity to the public speaking paradigms reviewed earlier. Specifically, the child will need to be blocked from or fail at achieving goals in a way that is public or explicitly acknowledged. Additionally, Lewis et al. (1992) have shown that task difficulty may matter. Among three-year-old children, they found that expression of shame in response to failure was much more frequent for easy than difficult tasks. One of the hallmarks of childhood is that there are many things that you are unable to understand or do. However, children have a strong belief, and much confirmatory evidence, that they will be able to do these things when they get older. Thus, failing publicly on a task that even a younger child could do or losing a competition to an age-mate or younger child might be more likely to evoke feelings of shame and thus elevate cortisol, even more so than failing on a very difficult task or losing to an adult (e.g., Donzella et al., 2000). These types of tasks might be effective in elevating cortisol by the preschool years, once self-referent emotions have emerged (Lewis et al., 1989).

3. Threats to social relationships

Presumably, social evaluative situations activate the HPA axis because they threaten one's social status which is critical to self-preservation. However, as Taylor et al. (2000) have argued, threats to close and supportive relationships may also activate the stress response system, especially in women. While their tend-and-befriend hypothesis was formulated to explain sex differences in patterns of stress and coping among adults, various iterations of this hypothesis are likely to be important in understanding stress and coping in children and adolescents. We will consider three types of tasks that threaten social relationships: (1) separation tasks that directly challenge the infant and young child's needs for the presence and availability of the attachment figure, (2) conflict–discussion tasks that threaten to disrupt or disturb important emotional relationships, and (3) peer rejection tasks that activate fears of being socially undesirable.

3.1. Maternal separation

The results of maternal separation studies are shown in Table 4. Before discussing these studies, it is important to note that although maternal separation is a potent stimulus of the HPA axis in non-human primate infants (Coe et al., 1993), separation paradigms in human studies differ markedly from those used in monkey research. Human separation paradigms do not always involve *maternal* separation, although they typically involve separation from a primary attachment figure. Unless the separation is very brief (i.e., <3 min), the infant or young child is never left alone. Additionally, if the child cries at any point, an adult provides comfort, and if that does not suffice, the child is reunited with their parent. Even separations with a substitute caregiver present are typically brief. The Strange Situation paradigm is most often used and involves a total of 9 min of separation, one 3-min period and one 6-min period. The longest separation period used in any of the studies described in Table 4 was 30 min. Thus, the laboratory separation paradigms that have been used involve relatively short periods of separation under conditions where the child is comforted by an adult or reunited with the parent if he/she becomes distressed. Human laboratory separation paradigms, therefore, would appear to be very mild stressor tasks in their current form.

Nonetheless, as shown in Table 4, separation paradigms do evoke elevations in cortisol, at least for children of certain ages and under certain conditions of separation. Human children begin to resist separation from attachment figures at about six months of age. Four of the five studies of children between six and nine months in Table 4 noted significant increases in cortisol. One of these studies (Gunnar et al., 1992) obtained a significant elevation in cortisol only for the condition in which the baby was given a low responsive rather than high responsive substitute caregiver. Thus, during the latter part of the first year, separation paradigms evoke elevations in cortisol that appear to be moderated by the sensitivity and responsiveness of the person caring for the child in the parent's absence.

Strikingly, by about a year of age, infants do not produce elevations in cortisol to separation even when the substitute caregiver is low responsive (Gunnar and Nelson, 1994). By a year of age, infants are mobile and have developed social-initiation skills. Gunnar and Nelson (1994) noted that when faced with a low responsive caregiver, some 13-month-olds took the book the caregiver was reading out of her hands, placed their toys in her lap, and insisted on being picked up. Thus, toddlers compared to babies, are less helpless in the parent's absence. This may explain why only two of the eight separation studies with children between 12 and 18 months of age (Table 4) reported significant mean increases in cortisol. Several of the studies did note increases in cortisol for insecurely attached children who were also highly fearful (Spangler and Gorssman, 1993; Gunnar et al., 1996b; Nachmias et al., 1996). Insecurely attached infants have histories of less parental responsiveness, and thus might have lower expectations of being able to get a substitute caregiver to respond to them. However, only one study in this table found that insecure attachment alone predicted larger elevations in cortisol to separation (Spangler and Grossman, 1993). In the others studies, the insecurely attached child also had to be highly fearful. The potential importance of child fearfulness is worth comment. On the one hand, this might reflect a greater vulnerability of the HPA axis in children with more reactive fear systems (Kagan et al., 1987). On the other hand, toddlers who are shy or fearful may find it more difficult to use a stranger as a temporary source of comfort (Gunnar and Nelson, 1994). The fact that fearful, insecurely attached toddlers continue to exhibit elevations in cortisol to brief separations at an age when most toddlers do not, conforms to the hypothesis that the HPA axis responds under conditions in which the individual lacks the resources to cope with threat (Levine, 1989).

By the second year of life, most infants appear to be able to tolerate a few minutes of separation without producing increases in cortisol. However, this does not mean that they can do so during longer separations. Indeed, Ahnert et al. (2004) noted elevations in cortisol for both securely and insecurely attached toddlers following entry into child care. As reviewed by Vermeer and van IJzendoorn (2006), there are now a number of reports that, on average, cortisol levels rise over the day at child care for children under four years of age.

In summary, separation may continue to be a potent stressor for children well beyond the first birthday, but perhaps the very mild forms of separation used in laboratory experiments cease to provoke mean increases in most typically developing children by the second year of life. The child care studies suggest that laboratory paradigms can mimic conditions of placement in a new child care environment. Additionally, researchers can exert experimental control over naturally occurring conditions of starting a new child care, such that we might effectively use separation as a stressor paradigm in children beyond a year of age.

3.2. Conflict–discussion and parent–infant interaction tasks

Conflict–discussion tasks have been used in studies of both adult couples (Kiecolt-Glaser et al., 1996; Roisman, 2007) and parent–child dyads (Granger et al., 1994) to examine differences in the ways dyads manage arguments. Many of these studies have focused on autonomic reactivity (Jacobson et al., 1994); however, a handful have also included measures of HPA axis

reactivity. Among adults, those assessing cortisol have failed to show that simply arguing with one's spouse activates the HPA axis. Elevations depend both on the target and the partner's behavior during conflict (Kiecolt-Glaser et al., 1996). In developmental research, conflict–discussion paradigms have been used to reveal patterns in the parent–child relationship associated with child adjustment (Granic and Lamey, 2002). In studies of maltreated children, simulated parent–parent conflicts have also been used to examine emotion regulation and stress reactivity in children (Atkins et al., 1993; Davies et al., 2007).

Remarkably, of the six studies that examined changes in salivary cortisol levels over the course of either parent–child or simulated parent–parent conflict, none produced significant elevations in cortisol (Table 5). In fact, three of these studies noted significant decreases in cortisol over the conflict period. Consistent with the data on separation paradigms, although many children showed either no change or decreasing patterns of cortisol production, arguments with parents provoked increases in cortisol among a subset of children, particularly those who were socially anxious and attributed their successes and failures to factors out of their control (Granger et al., 1994). It seems likely that, as in the adult work, cortisol increases are evident when the characteristics of the child and the behavior of the partner heighten the child's expectation that they cannot win the argument *and* that the parent or others will judge them badly in the process. This hypothesis is supported by the study of Smeekens et al. (2007). This study with five-year-olds did not involve a parent–child conflict–discussion, but simply involved the parent getting the child to label emotional expressions and then remember a time when he or she had experienced that emotion. Both child characteristics (low ego resilience as rated by a teacher) and maternal behavior during the task (negativity to the child) were needed to provoke a cortisol response.

Finally, Table 5 includes parent–infant interaction tasks. There is no particular reason to expect that such tasks would produce increases in cortisol. In fact, to the extent that playing with the parent is enjoyable, decreases in cortisol might be expected. We included these studies in Table 5, because, as in conflict–discussion paradigms, when infants play with their parent, the parent and child need to negotiate the flow of the interaction. There are often periods of mild conflict when the parent's and child's goals for play collide. Such "free play" paradigms are used in developmental research to obtain measures of parent sensitivity and responsiveness to the infant (e.g., Biringen et al., 1998). Interacting with an insensitive parent might be stressful to infants and young children, and indeed, there is evidence in Table 5 that this is the case for very young babies. At three months of age, simply playing with an insensitive parent for 15 min elevated the baby's cortisol levels. For the same infants, this was not the case at six and nine months (Spangler and Schieche, 1994). By these ages, playing with the mother lowered cortisol levels for the infants of high responsive mothers, but had no such effect for infants of low responsive mothers. The importance of adult sensitivity and responsiveness in regulating activity of the HPA axis has already been noted in studies of maternal separation, and it will appear again when we discuss infant cortisol responses to handling and blood draw/inoculation stressors.

In summary, conflict–discussion and parent–child interaction tasks do not appear to be successful in elevating cortisol for most children. However, these tasks appear to be useful in identifying the psychosocial processes in parent–child dyads, possibly resulting in the parent–child relationship providing either a less effective buffer of the HPA axis or being the source of evocation of HPA responses.

4. Peer social stress

We found only three studies using either peer entry or social rejection tasks to elevate cortisol, which are summarized in Table 6. Stansbury and Harris (2000) found that 4-year-old but not

3-year-old children showed an increase in cortisol to a 5 min peer entry stressor. This peer entry task was designed to make it difficult for the child to enter the group. The peers, all children from the same laboratory preschool, were seated together working on a project when the target child was shown into the room. The adult did not introduce the target child to the children and there was nothing else in the room for the target child to do. Interestingly, Brotman et al. (2007) did not find similar elevations in cortisol in the same age group. The peer entry task used by Brotman et al. (2007) simply required the target child to play in a preschool classroom of same-aged, unfamiliar peers during the class's free play period. While there were many children with whom the target child could try to play, there were also many activities available that did not require peer interaction. Thus, it is likely that the latter task involved fewer peer rejection cues than did the former one, as well as greater opportunities for the implementation of various coping strategies. The differences between these studies suggest that peer-rejection tasks may be effective even for young children as long as the cues of rejection are made highly salient to the child and the child interprets the cues as indicative of rejection.

The Yale Interpersonal Stressor task for Children (YIPS-C), designed by Stroud et al. (2009) is the only social rejection paradigm so far used to elevate cortisol in children and adolescents. The YIPS-C involves having the participant interact with two unfamiliar, similar-age, same-sex confederates. Using both verbal and nonverbal techniques, the confederates gradually exclude the participant from a conversation by bonding with each other. This task is based on a paradigm previously used with adults (YIPS; Stroud et al., 2002). In the adult study, women showed a stronger cortisol response to the peer rejection task than did men. In the child study, adolescents (13+ years) showed more marked sympathetic responses to the rejection paradigm than did children (7–13 years) and, overall, cortisol levels were higher among the adolescents (Table 6; Stroud et al., 2009). However, in neither age group did the paradigm produce increases in cortisol. One reason may be that, unlike in the adult study, the adolescent's cortisol levels were high in anticipation of the peer task, potentially masking any elevations associated with the paradigm. This was true even though the participants were given time to adapt after entering the laboratory and had, in fact, come to the laboratory on a separate day in order to reduce potential cortisol responses to novelty. Eliminating anticipatory cortisol responses is a significant challenge in developmental research, as will be discussed below.

5. Exposure to novel stimulation and handling

In animals, being placed in a novel chamber or even having the bedding changed in the home cage can produce significant activation of the HPA axis (Hennessy and Levine, 1978). It is also well known that handling can elevate corticoids (Gunnar et al., 1981; Levine and Wiener, 1988). The top section of Table 7 describes cortisol responses to handling stressors in infants between birth and six months, the age period during which this has been examined. Notably, for infants three months of age and younger, handling is an effective stressor. This appears to be true whether the handling involves a brief physical examination, developmental assessments (e.g., Neonatal Behavioral Assessment Scale, NBAS), or events common in the experience of babies such as being taken from the bath or having a diaper changed. After three months, these types of handling experiences cease to produce mean increases in cortisol. Thus, there appears to be a marked developmental change in the reactivity and regulation of the HPA axis to handling around 3–4 months of age, a point we have made previously (Gunnar et al., 1996a; Larson et al., 1998).

The bottom half of Table 7 describes studies involving novel stimulation for most young children, including being taken swimming for the first time, going in an MRI machine, and an ERP/EEG assessment. Strikingly, none of these experiences elevated cortisol, even among children as young as one year of age. In fact, pre-test to post-test decreases in cortisol were

noted in several of the studies. Researchers argued that cortisol decreased over the assessment because it was elevated in anticipation of the task. While this might be reasonable for studies involving older children, this explanation seems less likely for the studies involving infants, including the study involving infants being taken swimming for the first time. These babies experienced a multitude of novel stimulation in the swim class environment (e.g., the smell of chlorine, the sight of the swimming pool). There is no evidence that their pre-swim cortisol levels were elevated as they were comparable to pre-test levels of a comparison group who merely came to the laboratory and played with toys in their mother's presence. Thus, in the infant swim study, true decreases in cortisol to the assessment paradigm were observed. In addition to novelty activating the HPA axis in animals, there is evidence that first exposures to emotionally challenging situations provoke elevations in cortisol among human adults as well (Rose, 1980); thus, it is not clear why children did not respond to these novel, first-time experiences. One possibility is that in all instances the adults present, including the children's parents, were attempting to make the experience pleasant and safe. As we saw for separation paradigms, the supportiveness of adults provides a potent stress buffer for children.

6. Blood draws and inoculations

Blood draws and inoculations are the last type of stressor task we examined (Table 8). These mild pain stressors have been used extensively to examine reactivity of the HPA axis in infants and for good reason. Up through six months of age, blood draws (typically heel lances) and inoculations provoke significant mean elevations in cortisol. Blood draws and inoculations become less reliable stressors by the second year of life. Indeed, only one of the seven studies of children between 13 months and 17 years reported mean increases in cortisol to blood draws or inoculations, and a study by Felt et al. (2000) may shed light as to why this is the case. Their study involved two groups of parents: those who were given brief written instructions on how they could support their infants during the inoculation procedures and those who were given no instructions. The instructions described ways of touching, holding and comforting the infants while they were being given their shots. The study showed that the 2–24-month-old infants of parents given these instructions showed no increases in cortisol to the inoculation procedures. Studies of the impact of inoculations and blood draws on HPA axis activity differ in the instructions given to parents. In some, parents are allowed to comfort the child throughout (Gunnar et al., 1996a,b), while in other studies, parents are told to withhold comforting for 30 s following inoculations in order to obtain measures of child distress that are not confounded with parental behavior (Lewis and Ramsay, 1995a). It is possible that this is why at 18 months, Lewis and Ramsay (1995b) observed an elevation in cortisol when others studying infants of comparable ages did not. Regardless, by about one year of age, there is little evidence that either blood draws or inoculations activate the HPA axis in children and adolescents. As with the separation paradigms, it seems likely that by this age children have the social skills needed to elicit the comforting and support they need from their attachment figure, unless the parent is specifically instructed to withhold that support.

7. Issues, conclusions and future directions

7.1. Achieving baseline pre-test levels

In stressor studies with adults, it is common to have the participants in the laboratory engaging in non-stressful activities for a fairly long period before beginning the stressor task (Kirschbaum et al., 1993). These periods are important in achieving low pre-test cortisol levels and clear evidence of response to the stressor task. Many of the studies of older children and adolescents have included these periods of relaxation prior to the onset of the stressor task (Buske-Kirschbaum et al., 1997; van Goozen et al., 2000); however, this is not always the case. Indeed, in a number of studies, researchers have ended up using the first cortisol sample as the index of a stress response as it is the highest level assessed (Ellis et al., 2005). While initial

values do often correlate as expected with measures of personality, temperament, or behavior problems, it would be better to add relaxation or adaptation periods to stressor paradigms in order to ensure that the stressor task is imposed after the HPA axis has recovered from anticipatory elevations. When activity of the HPA axis is only one of many foci of investigation, it is difficult to impose such stringent criteria. Furthermore, when researchers are studying very young children who cannot tolerate long laboratory sessions, using the first 45 min to an hour to allow the child's HPA system to adapt to the laboratory may push the limits of both the experimenter's and child's tolerance. Nonetheless, we need to be much more careful about adaptation periods if we are to effectively study cortisol stress responses under controlled laboratory conditions in children.

7.2. Intensity of fear evocative events

For ethical reasons, when researchers study fear-eliciting events in infants and young children, tasks are designed to produce fear or wariness for only a few moments and are terminated if they provoke an intense fear response. Parents are typically present and, even when not, ethical standards require the experimenters to be responsive to the child's bids for support. While such mild evocation may activate the HPA axis among very young infants, with development, it is likely that most children develop the coping skills needed to manage such situations without mounting an HPA stress response. Given the ethical constraints of laboratory studies of fearfulness in young children, it seems very likely that we will never be able to develop laboratory fear-evocative paradigms which will produce mean increases in cortisol. These paradigms may still be very useful in psychoneuroendocrine studies as they may reveal individual differences in reactivity of the HPA axis or identify subgroups of children more vulnerable to heightened or prolonged HPA activation. However, if tasks are to be used successfully, we need assess not only individual differences in fearful behavior, but also differences in the child's access to personal, social, and situational resources that impact the child's ability to cope with the fear-evocative event.

7.3. Supportive care from parents and other adults

One message from this review of stressor paradigms is that the supportiveness of adults is a very critical factor in determining cortisol responses to a range of stressors in infants and children. These effects are apparent as early as they have been examined, as indexed by Spangler et al. (1994) study of parent–infant play interactions. The history of support, as reflected in the security of the parent–child attachment relationship, plays a critical role in determining whether fearful infants exhibit cortisol increases by the second year of life. One reason why it may become more difficult to provoke elevations in cortisol to many stressors with development is that children become increasingly capable of eliciting the adult support they need from the child-friendly researchers who populate research laboratories. When that support is threatened, particularly in children who may hold low expectations of their own social potency, even innocuous situations such as talking about past emotion-eliciting experiences, can produce elevations in cortisol (Smeekens et al., 2007).

The power of social support in buffering the HPA axis in young children leads to the hypothesis that the most critical element of stress-evocative situations for young children will involve threats to their adult support systems. While we have focused most of our attention on developing stressor paradigms that threaten the child, perhaps with young children we should refocus our attention on developing paradigms that threaten their main sources of security: specifically, their primary attachment figure(s). Figuring out how to do this in a way that is ethical is challenging to consider; however, there are developmental studies in which the child observes the parent being verbally attacked by an experimenter, and these have been used effectively to study emotions and coping in maltreated children (Cummings et al., 1994). Thus,

there may be ways to create ethical “threaten the child’s primary source of security” paradigms to study HPA stress reactivity in children.

7.4. Individual differences

Although the current review has evaluated existing stress paradigms and their ability to elicit mean increases in salivary cortisol in samples of children of varying ages, this analysis has also revealed sources of individual differences that might relate to varying patterns of HPA responsivity, including pubertal status, sex, age, behavioral approach vs. inhibition, utilization of available coping resources, and the quality of the parent–child relationship. These differences may be important in identifying subgroups of children who might display sensitivity to cortisol elevations relative to their peers, which may perhaps map onto differing patterns of risk or resilience with respect to (e.g.) the development of psychopathology.

8. Conclusions

What this review should make very clear is that just because a paradigm appears stressful, it might not effectively produce mean increases in cortisol in children. With the exception of tasks that clearly threaten the social self, there is little evidence that researchers have carefully crafted and tested their paradigms to be sure that they are effective in activating the HPA axis. Additionally, it is rare to find that the paradigm has been examined against conditions in which the same or other children experience conditions that are comparable, but do not involve the stressor tasks. Thus, in many, but certainly not all, of the work on stress reactivity with children, we are trying to move forward without doing the basic studies to show that the stressor paradigms we employ actually produce a stress response. This review should make it clear that we very much need this basic work, especially in research on stress reactivity in children between about one and seven years. In lieu of some concerted effort to develop reliable stressor tasks for this age range, we may be left with a broad span of development during which we cannot really assess reactivity of the axis in typically developing children. Thus, it may be challenging to understand how reactivity is altered either by early adverse experiences or by a mental disorder. As it is likely that the neural systems regulating the development of HPA reactions to stressors are being shaped by an interaction of genes and experience over these early years, lack of ethical, appropriate, and effective stressor paradigms for use in this age group is particularly troubling.

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Table 1

Successful cortisol reactivity studies by age group.

Age group	Number of studies/tests	Percentage showing mean increase in cortisol
≤3 months	23	91
4–9 months	20	55
12–24 months	15	20
2–5 years	11	9
6–11 years	18	28
12–18 years	14	42

Table 2

Public speaking tasks.

First author	Date	Stressor	Age (years)	Sex	*N*	Sampling times	ΔCortisol
Schmidt	1999	Anticipation of self disclosure	7	Both	36	0, +20, +36	ns
Jones	2006	TSST-C	7–9	Both	140	7×	Increase
Jansen	2000	TSST-C modified	9	Both	12	7×	Increase
Gunnar	2009[a]	TSST-C	9	Both	22	6×	Increase
Gunnar	2009[a]	TSST-C	11	Both	18	6×	Decrease
Stroud	2009[a]	TSST-C modified	7–12	Both	24	6×	ns
Buske-Kirschbaum	2003	TSST-C	7–12	Both	18	10×	Increase
Buske-Kirschbaum	1997	TSST-C	8–14	Both	16	10×	Increase
Dorn	2003	TSST-C	8–16	Both	14	6×	ns
Gordis	2006	TSST-C modified	10–14	Both	32	6×	Increase
Klimes-Dougan	2001	TSST-C modified	11–17	Both	71	0, +20, +40	Increase[b]
Gunnar	2009[a]	TSST-C	13	Both	22	6×	Increase[c]
Gunnar	2009[a]	TSST-C	15	Both	21	6×	Increase
Martel	1999	TSST-C modified	15	Girls	18	0, +10	Decrease[d]
Popma	2006	TSST-C modified	12–17	Boys	30	7×	Increase
Stroud	2009[a]	TSST-C modified	13–17	Both	27	6×	Increase
Zonnevylle-Bender	2005	TSST-C modified	14–18	Girls	22	8×	Increase

[a] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[b] No increase for 11–13-year-old boys.

[c] No increase for 13-year-old boys.

[d] Pretest (time 0) elevated over home baseline.

Table 3

Paradigms designed to elicit negative emotions.

First author	Date	Stressor	Age	Sex	*N*	Sampling times	ΔCortisol
Fear/behavioral inhibition paradigms							
Buss	2003	Stranger approach[a]	6 m	Both	41	0, +20	ns
Nachmias	1996[b]	Strange events/people	18 m	Both	77	0, +30	ns[c]
Goldberg	2003[b]	Strange events/people	18 m	Both	27	0, +20, +40	ns
Ouellet-Morin	2008	Strange events/people	19 m	Both	418	0, +20	ns
Buss	2004	Risk room/stranger approach[a]	2 y	Both	58	Pre/Pst visit	ns
Sethre-Hofstad	2002	High balance beam	2–4 y	Both	64	0, +30	ns
Zimmerman	2004	Stranger approach[a]	3 y	Both	53	0, +20, +35	ns
Kagan	1987	Strange events/people	5.5 y	Both	48	0, +90	ns
Quas	2004	Strange events, intense sensations	4–6 y	Both	63	0, +50	ns
Battaglia	1997	Scary movie clips	4–8 y	Both	16	0, +15	ns
Ashman	2002	Air-blast startle	7–8 y	Both	29	0, +20–30	ns
Kagan	1988	Strange events/people	7.5 y	Both	41	Pre, mid, end	ns
Boyce	2006	Strange events/intense sensations	7 y	Both	120	4×	Decrease
Anger/frustration paradigms							
Lewis	2005	Extinction of reinforcing action	4 m	Both	56	0, +20	ns
Azar	2007	Arm restraint	4 m	Both	218	0, +20	ns
Lewis	2005	Standard still face paradigm	6 m	Both	84	0, +20	ns
Hayley	2003	Repeated still face paradigm	6 m	Both	43	0, +30	Increase
Blair	2006	Frustration tasks[a]	6 m	Both	988	0, +20, +40	Increase
Luby	2003	Frustration tasks[a]	3–5.6 y	Both	57	0, +30	ns
Lewis	2002	Rigged failure tasks	4 y	Both	53	0, +20	ns[d]
Donzella	2000	Rigged competition	3–5 y	Both	61	0, +40	ns[e]
van Goozen	1998	Competition + insults	8–11 y	Both	31	6×	Increase
van Goozen	2000	Competition + insults	8–12 y	Both	38	9×	Increase

[a] Tasks from the Laboratory Temperament Assessment Battery (LabTAB).

[b] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[c] Elevations for fearful + insecurely attached.

[d] Increases correlated with shame, embarrassment.

[e] Increases correlated with tense/angry behavior.

Table 4

Maternal separation with child in the care of unfamiliar adult[a].

First author	Date	Stressor	Age	Sex	*N*	Sampling times	ΔCortisol
Gunnar	1989[b]	Separation, reunion, separation[c]	9 m	Both	66	0, +60	Increase
Larson	1991	30 min separation	9 m	Both	37	0, +30	Increase
Gunnar	1992	Exp 1: 30 min separation	9 m	Both	38	0, +30, +45	Increase[d]
Gunnar	1992	Exp 2: 30 min separation	9 m	Both	64	0, +30	ns[e]
Spangler	1993	Ainsworth strange situation	12 m	Both	32	0, +15, +30	ns[f]
Spangler	1998	Ainsworth strange situation	12 m	Both	106	0, +15, +30	ns[g]
Goldberg	2003[b]	Ainsworth strange situation	12 m	Both	27	0, +20, +40	Increase
Gunnar	1994[b]	30 min separation	13 m	Both	49	0, +30	ns
Gunnar	1989[b]	Ainsworth strange situation	13 m	Both	66	0, +30	ns
van Bakel	2004	Modified strange situation	15 m	Both	85	0, +55	Increase
Nachmias	1996[b]	Ainsworth strange situation	18 m	Both	77	0, +45	ns[g]
Gunnar	1996b	Ainsworth strange situation	18 m	Both	73	0, +45	ns[g]
Luby	2003[b]	Separation	3–5.6 y	Both	57	0, +30	Decrease

[a] Adult with child is low responsive unless otherwise indicated.

[b] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[c] Total separation was 49 min.

[d] Only for low responsive care condition.

[e] High responsive care.

[f] Ainsworth strange situation: 9 min separation total, 3 min with children alone. Increase only for insecurely attached children.

[g] Only for insecurely attached and highly fearful children.

Table 5

Parent–child interaction and conflict–discussions.

First author	Date	Stressor	Age	Sex	*N*	Sampling times	ΔCortisol
Spangler	1994[a]	15 min play with mother	3 m	Both	41	0, +25	ns[b]
Spangler	1994[a]	15 min play with mother	6 m	Both	41	0, +25	ns[c]
Spangler	1994[a]	15 min play with mother	9 m	Both	41	0, +25	ns[c]
Larson	1991[a]	30 min play with mother	9 m	Both	24	0, +30	ns
Davies	2007	Simulated parent argument	4–5 y	Both	178	0, +25, +36	Decrease
Smeekens	2007	10 min emotion discussion task	5 y	Both	129	0, +20	ns[d]
Granger	1998	Conflict–discussion task	5–11 y	Both	62	0, +20	ns
Granger	1994	Conflict–discussion task	7–17 y	Both	102	0, +20	Decrease[e]
Kliewer	2006	Discussion of violent video clip	8–14 y	Both	101	0, +20, +40	ns
Granger	1996	Conflict–discussion task	9–16 y	Both	64	0, +20	ns[e]
Klimes-Dougan	2001	Conflict–discussion task	11–17 y	Both	71	0, +20, +40	Decrease

[a] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[b] Increase if mother is insensitive.

[c] Decrease if mother is sensitive.

[d] Increase if child low ego resilient and parent high negativity.

[e] Clinic-referred youth.

Table 6

Peer entry and peer rejection paradigms.

First author	Date	Stressor	Age	Sex	*N*	Sampling times	ΔCortisol
Stansbury	2000[a]	Peer entry	3 y	Both	38	0, +25	ns
Stansbury	2000[a]	Peer entry	4 y	Both	25	0, +25	Increase
Brotman	2007	Peer entry	2.8–5 y	Both	92	0, +30	ns
Stroud	2009[a]	Peer rejection/social exclusion	7–12 y	Both	39	6×	ns
Stroud	2009[a]	Peer rejection/social exclusion	13–17 y	Both	43	6×	Increase[b]

[a] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[b] Elevated over baseline taken on another day in anticipation of the peer interaction task, prior to exclusion/rejection.

Table 7

Handling and strange/novel stimulation.

First author	Date	Stressor	Age	Sex	*N*	Sampling times	ΔCortisol
Handling stressors							
Gunnar	1989	Physical examination	Newborn	Both	49	0, +25	Increase[a]
Gunnar	1992	Physical examination	Newborn	Both	22	0, +25	Increase[a]
Spangler	1993	NBAS[b]	Newborn	Both	51	0, +15	increase[c]
Keenan	2002[d]	Physical examination	Newborn	Both	62	0, +20, +45	Increase
Gunnar	1996a[d]	Physical examination	2 m	Both	18	0, +25	Increase
Lewis	1995a[d]	Physical examination	2 m	Both	64	0, +30	Increase
Larson	1998	Physical and dev'l examination	2–3.8 m	Both	86	0, +60	Increase[e]
Morelius	2007	Diaper change	<3 m	Both	15	0, +30	Increase
Albers	2008	Removal from bath	3 m	Both	64	0, +25, +40	Increase[f]
Lewis	1995a[d]	Physical examination	4 m	Both	64	0, +30	ns
Gunnar	1996a[d]	Physical examination	4 m	Both	18	0, +25	ns
Lewis	1995a[d]	Physical examination	6 m	Both	64	0, +30	ns
Gunnar	1996a[d]	Physical examination	6 m	Both	18	0, +25	ns
Novel event stressors							
Hertsgaard	1992	1st infant swim class	8–12 m	Both	41	0, +35	Decrease
Gunnar	1994[d]	Event-related potential testing	12 m	Both	49	0, +30	ns
Schmidt	1997	EEG assessment and startle task	4 y	Both	61	0, +35	ns
Corbett	2006	Mock MRI scanner	6–11 y	Boys	10	4×	Decrease
Moss	1999	Event-related potential testing	10–12 y	Boys	178	0, +35	Decrease
Hardie	2002	Event-related potential testing	10–12 y	Both	189	0, +35	Decrease[g]

[a] No response to same stressor 24 h later.

[b] Brazelton Neonatal Behavioral Assessment Scale.

[c] Only for subset where electrodes were placed for heart rate prior to NBAS.

[d] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[e] Increase only for infants 11 weeks old and younger.

[f] Returned to baseline by +40 and more rapidly for infants of sensitive mothers.

[g] Sample overlaps with Moss et al. (1999).

Table 8

Blood draws and inoculations.

First author	Date	Stressor	Age	Sex	*N*	Sampling times	ΔCortisol
Gunnar	1992	Heel lance	Newborn	Both	18	0, +25	Increase
Gunnar	1995	Heel lance	Newborn	Both	48	0, +25	Increase
Keenan	2002[a]	Heel lance	Newborn	Both	64	0, +20, +45	Increase
Buske-Kirschbaum	2004	Heel lance	Newborn	Both	20	0, +10, +20	Increase
Mantagos	1991	Venipuncture	1–6 m	Both	33	0, +30, +60	Increase
Lewis	1994	Inoculation	2–6 m	Both	62	0, +20	Increase
Ramsay	1994	Inoculation	2 m	Both	40	0, +20	Increase
Lewis	1995a[a]	Inoculation	2 m	Both	64	0, +20	Increase
Gunnar	1996a[a]	Inoculation	2 m	Both	67	0, +25	Increase
Ramsay	1996[a]	Inoculation	2 m	Both	9	0, +20	Increase
Braarud	2006	Inoculation	3 m	Both	37	0, +20	Increase[b]
Ramsay	1994	Inoculation	4 m	Both	40	0, +20	Increase
Lewis	1995a[a]	Inoculation	4 m	Both	64	0, +20	Increase
Gunnar	1996a[a]	Inoculation	4 m	Both	67	0, +25	Increase
Ramsay	1996[a]	Inoculation	6 m	Both	5	0, +20	ns
Lewis	1995a[a]	Inoculation	6 m	Both	64	0, +20	Increase
Gunnar	1996a[a]	Inoculation	6 m	Both	67	0, +25	Increase
Felt	2000	Inoculation	2–24 m	Both	102	4×	Increase[b]
Jacobson	1999	Finger stick	13 m	Both	64	0, +30	ns
Gunnar	1996a[a]	Inoculation	15 m	Both	67	0, +25	ns
Lewis	1995b[a]	Inoculation	18 m	Both	34	0, +20	Increase[c]
Gutteling	2004	Inoculation	4–6 yr	Both	24	5×	ns
Lee	2006	Venipuncture	6–15 yr	Both	30	0, +1, +60	ns
Susman	1997	Venipuncture	10–15 yr	Both	36	0, +20, +40	ns
Conte	2003	Venipuncture	7–17 yr	Both	16	0, +20–30	ns

[a] Age groups appear separately in this table or children were also exposed to other stressor tasks described in other tables.

[b] Only if mother less supportive.

[c] Data from 2, 4 and 6 months in Lewis and Ramsay (1995b): 18 month response less than at 6 mo.