Developmental Psychology

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Online First Publication, August 31, 2015. http://dx.doi.org/10.1037/dev0000029

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0012-1649/15/$12.00 http://dx.doi.org/10.1037/dev0000029

Early Social Deprivation and the Social Buffering of Cortisol Stress Reponses in Late Childhood: An Experimental Study

Camelia E. Hostinar
Northwestern University and University of Minnesota

Anna E. Johnson and Megan R. Gunnar
University of Minnesota

The goal of the present study was to investigate the role of early social deprivation in shaping the effectiveness of parent support to alleviate hypothalamic–pituitary–adrenal (HPA)-axis-stress responses of children (ages 8.9–11, $M = 9.83$ years, $SD = .55$). The sample was equally divided between children who had been adopted internationally from orphanage care by age 5 ($n = 40$) and an age- and gender-matched group of nonadopted (NA) children ($n = 40$). On average, internationally adopted children were invited to the laboratory 7.6 years postadoption ($SD = 1.45$). We experimentally manipulated the provision of parent support during the 5-min speech preparation period before a modified Trier Social Stress Test (TSST) and examined its effect on levels of salivary cortisol secreted in response to this laboratory stressor. All participants were randomly assigned to receive support from their parent or a stranger. Analyses revealed a significant interaction of support condition and group such that parent support significantly dampened the cortisol-stress response in NA children compared with support from a stranger, whereas the cortisol response curves of postinstitutionalized (PI) children did not differ between the parent- and stranger-support conditions. Cortisol reactivity for PI children in both conditions was lower than that of NA children in the stranger-support condition. Social deprivation during the first few years of life may shape neurobehavioral development in ways that reduce selective responses to caregivers versus strangers.

Keywords: stress, parent support, postinstitutionalized children, cortisol, HPA axis

Developmental psychologists have had a long-standing interest in the enduring effects of early parental deprivation (Bowlby, 1951; Rutter, 1972). Children adopted internationally from orphanages provide a unique opportunity to study these effects, given that their social histories often include neglect and frequent caregiver turnover during what may be sensitive periods for the development of social bonds (Smyke, Dumitrescu, & Zeanah, 2002), followed by an opportunity to recover from these experiences as they transition into highly supportive families. Despite this marked improvement in their environment, some research suggests that the sequelae of early parental deprivation may still be notable later in development—for example, a lack of differentiation in hormonal and neural responses to parents versus strangers (Olsavsky et al., 2013; Wismer Fries, Shirtcliff, & Pollak, 2008; Wismer Fries, Ziegler, Kurian, Jacoris, & Pollak, 2005). However, an important question that remains unanswered is whether, many years after adoption, postinstitutionalized (PI) children can experience the same parental buffering of hormonal stress responses exhibited by their nonadopted (NA) peers. The present study aimed to address this question.

The Social Buffering of the Hypothalamic–Pituitary–Adrenal (HPA) Axis

Support from close relationships can be an important source of comfort during distress and can dampen the reactivity of the HPA stress system (Ditzen & Heinrichs, 2014; Hostinar, Sullivan, & Gunnar, 2014). This phenomenon has been named *social buffering*, which can be defined as a reduction in acute physiological stress responses with the presence or assistance of a conspecific during an otherwise stressful event. The buffering of HPA-axis stress responses by social partners has been well-documented in humans (Gunnar & Donzella, 2002; Hostinar, Sullivan, et al., 2014) and across diverse mammalian species (Hennessy, Kaiser, & Sachser, 2009; Kikusui, Winslow, & Mori, 2006). For typically developing children, parents are powerful regulators of HPA-axis

Camelia E. Hostinar, Cells to Society: The Center on Social Disparities and Health, Institute for Policy Research, Northwestern University and Institute of Child Development, University of Minnesota; Anna E. Johnson and Megan R. Gunnar, Institute of Child Development, University of Minnesota.

We thank the families from the Institute of Child Development Participant Pool for their participation. This work was supported by the Eva O. Miller Fellowship to Camelia E. Hostinar; a predoctoral U.S. Department of Health and Human Services, National Institutes of Health Interdisciplinary Training Program in Cognitive Science Fellowship (Grant NIH T32HD007151) to Anna E. Johnson; a seed grant from the NIH National Institute of Mental Health, Early Experience, Stress and Neurobehavioral Development Center (Grant P50 MH078105) to Megan R. Gunnar; a small grant award from the Institute of Child Development, University of Minnesota, and by travel awards from the Center of Neurobehavioral Development at the University of Minnesota.

Correspondence concerning this article should be addressed to Camelia E. Hostinar, Cells to Society: The Center on Social Disparities and Health, Institute for Policy Research, Northwestern University, 2040 Sheridan Road, Evanston, IL 60208. E-mail: camelia.caudill@northwestern.edu

reactivity during early development (for a review, see Hostinar & Gunnar, 2013). This has been studied by examining the effectiveness of the parent in secure attachment relationships to reduce or prevent cortisol increases to fear stimuli (Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996; Spangler, 1998) and to physically painful events (Gunnar, Brodersen, Nachmias, Buss, & Rigatuso, 1996) in samples of approximately 12–18-month-old children. Parental presence can reduce HPA reactivity even when infants continue to exhibit fear or distress behaviorally, suggesting possible dissociations between physiological, emotional, and behavioral stress reactions (Nachmias et al., 1996). More recent evidence from typically developing samples suggests that parental presence remains a potent buffer against HPA reactivity for older children, that is, between the ages of 7 and 12 years (Hostinar, Johnson, & Gunnar, 2014; Seltzer, Ziegler, & Pollak, 2010), but is no longer effective for adolescents aged 15–16 (Hostinar, Johnson, et al., 2014).

Despite this emerging evidence on normative developmental patterns, very little is known about the extent to which adverse early-life social experiences might shape the propensity to experience social buffering of stress by close social figures later in development. In 3-year-old rhesus monkeys (roughly corresponding to age 12 in human development), nursery-reared animals did not experience social buffering of their cortisol reactivity by a social companion in response to a novel cage when accompanied by a conspecific, whereas their mother-reared counterparts did show the expected blocking of cortisol elevations (Winslow, Noble, Lyons, Sterk, & Insel, 2003).

In humans, research has primarily focused on associations between early adversity and later stress reactivity, largely ignoring the issue of how social experiences might influence the later effectiveness of social stimuli in regulating stress responses. For instance, some studies have reported associations between adverse experiences such as parental depression, low maternal care, or childhood maltreatment and later HPA reactivity (Bouma, Riese, Ormel, Verhulst, & Oldehinkel, 2011; Engert et al., 2010; Hackman et al., 2013; Seltzer, Ziegler, Connolly, Prososki, & Pollak, 2014). However, the evidence is very mixed. One study showed that PI children aged 10–12 did not differ from a NA comparison group in their pattern of cortisol responses to a social-evaluative task similar to the Trier Social Stress Test (TSST; Gunnar, Frenn, Wewerka, & Van Ryzin, 2009). Another report based on a longitudinally followed cohort that was internationally adopted into the Netherlands showed that adversity experienced during the ages of 0–5 years was not associated with cortisol reactivity, whereas stress during the pre- and immediately postnatal period or during middle childhood or adolescence was associated with altered cortisol responses in adolescents exposed to a social stress test similar to the TSST (Bosch et al., 2012). Reviewing the rich literature on the associations between childhood adversity and later stress reactivity is beyond the scope of this introduction, but it is noteworthy that there is a scarcity of studies examining the effects of early relationships on the later effectiveness of social support in regulating HPA responses.

One exception is a study of 4–5-year-olds who had been adopted internationally from orphanage care roughly 3 years prior. Results revealed that PI children had lower levels of basal arginine vasopressin and did not elevate urinary oxytocin output after a physical contact game with their mothers in the way that their NA counterparts did (Wismer Fries et al., 2005). Also, as expected, given the cortisol-dampening role of physical touch and oxytocin release (Carter, 1998), NA children showed reductions in cortisol after this interaction with the parent, when compared with both baseline and a condition involving interactions with a stranger. PI children did not show this cortisol reduction with the parent and exhibited no differences in cortisol output between the parent- and stranger-interaction conditions, both of which tended to show higher cortisol output compared with baseline (Wismer Fries et al., 2008). Even though this study had a small sample size (18 adopted, 21 NA children) and did not use a stress protocol to directly test the social buffering of HPA *reactivity* by parental stimuli, findings suggest the possibility that children who did not experience normative early-attachment relationships might not be able to derive the same stress relief from parent–child interactions as their NA counterparts, even after spending a few years in the new family. Some PI children also show other atypical patterns of social behavior (briefly reviewed next).

Patterns of Socioemotional Development in PI Children

Despite dramatic catch-up across developmental domains after adoption (van Ijzendoorn & Juffer, 2006), earlier research has also revealed some areas in which early institutional care remains associated with deficits or delays in socioemotional development. This is not surprising, given that PI children often experience neglect due to high child-to-caregiver ratios, frequent caregiver turnover, and minimal cognitive or social stimulation in such group-care situations, frequently starting at birth and continuing for the entire duration of their preadoptive lives (Zeanah, Smyke, & Dumitrescu, 2002).

One area of PI children's development that has garnered a lot of attention is their ability to form a secure attachment. For instance, internationally adopted children have been shown to exhibit less frequent secure attachments or more frequent disorganized attachment patterns with their adoptive parents within the first few years after adoption (for a meta-analysis, see van den Dries, Juffer, van IJzendoorn, & Bakermans-Kranenburg, 2009). When present, initial difficulties with forming attachments are fairly persistent several years later (Chisholm, 1998; O'Connor & Rutter, 2000). Despite these general patterns, some PI children develop secure and organized attachments to their parents and they can do so very quickly after adoption—within 7–9 months (Carlson, Hostinar, Mliner, & Gunnar, 2014). What remains unclear based on these studies of early attachment is whether parental support would be effective in lowering children's physiological stress responses many years after adoption.

In other socioemotional domains, some PI children exhibit atypical patterns of behavior such as a lack of appropriate reticence in interacting with strangers known as indiscriminate friendliness (Chisholm, 1998; Lawler, Hostinar, Mliner, & Gunnar, 2014; O'Connor, Bredenkamp, & Rutter, 1999; Roy, Rutter, & Pickles, 2004; Rutter et al., 2007; Zeanah et al., 2002), difficulties with emotion recognition and understanding (Wismer Fries & Pollak, 2004), and challenges in interacting with peers (Fisher, Ames, Chisholm, & Savoie, 1997; Vorria, Rutter, Pickles, Wolkind, & Hobsbaum, 1998). A recent report has also suggested that indiscriminate friendliness is associated with reduced differences in

neural activation patterns in response to parents versus strangers in the amygdala, an area that indexes affective salience (Olsavsky et al., 2013), suggesting a neural basis for some of the observed problem behaviors.

However, studies also show that high-quality parenting postadoption can mitigate the effects of early adversity on some child socioemotional outcomes such as emotion understanding and indiscriminate friendliness assessed around 3 years of age (Garvin, Tarullo, Van Ryzin, & Gunnar, 2012). Thus, substantial recovery in the socioemotional domain is possible, especially if parental support levels are high.

Despite the richness of information on the socioemotional development of PI children in early childhood, much less is known about the quality of their relationships with parents in late childhood and early adolescence, particularly about their ability to use parent support as a resource in times of stress.

Aims of the Present Study

For these reasons, the current study sought to examine the role of early life social deprivation in accounting for the effectiveness of parental social buffering of HPA reactivity to a laboratory stressor. Based on the previous evidence described above, we aimed to test the following: (a) whether parent support would be more effective than stranger support in lowering cortisol-stress responses for NA children, but not PI children, as a reflection of the enduring effects of severe early social deprivation; (b) whether PI and NA children differ in either observed or self-reported measures of parental support and negativity; (c) whether observed or perceived measures of parent–child relationship quality predict cortisol reactivity for children randomly assigned to receive support from their parents, and the extent to which differences in these relational quality measures may explain differences in cortisol reactivity or HPA social buffering between PI and NA children.

Method

Participants

We recruited 81 children aged approximately 9–10 years (M = 9.85, SD = .55, range: 8.87–11.09), half of whom were internationally adopted PI children (N = 41, M age = 9.7 years, SD = .56, range 8.87–10.99; 51.2% girls) and half who were NA—that is, born and raised by their birth families in a large urban midwestern area (N = 40, M age = 9.97 years, SD = .52, range 9.09 −11.09; 50% girls). Results for the NA children were previously reported in Hostinar, Johnson et al. (2014) as part of a cross-sectional study of the effectiveness of parental social buffering in childhood versus adolescence. The NA and PI data, however, were concurrently collected. The sample size was calculated a priori based on the large effect sizes observed in adult social buffering studies for the difference between peak cortisol responses in the stranger support versus romantic partner support conditions (e.g., Cohen's d = .83 in Kirschbaum, Klauer, Filipp, & Hellhammer, 1995). The age range was chosen due to the fact that the TSST-C and TSST-M, which were the basis for the stress paradigm used here, were both validated on samples that were 9 years old or older (Buske-Kirschbaum et al., 1997; Yim, Quas, Cahill, & Hayakawa, 2010). This ensures sufficient cognitive maturity for the stressor to be effective. At the same time, participants older than 11 may begin entering puberty, and given that previous results indicated that typically developing pubertal adolescents aged 15–16 did not exhibit evidence of parental buffering of HPA responses (Hostinar, Johnson, et al., 2014), we wanted to examine PI–NA differences before the pubertal transition.

PI participants and their parents were recruited from the International Adoption Project registry at the University of Minnesota. The registry has been recruiting adopting families across the state for many years, drawing from a diverse set of adoption agencies. During recruitment, exclusion criteria were autism spectrum disorder, fetal alcohol syndrome, or any other major developmental disorder and use of steroid medications (due to their interference with cortisol assay results). During analyses, one PI participant had to be excluded due to a fetal alcohol syndrome diagnosis reported in the parent questionnaire and cortisol data for three other PI children (two boys, one girl) were excluded due to corticosteroid use reported at the time of testing or missing cortisol recovery data, respectively. However, their questionnaire data were complete and used (final sample size for cortisol analyses: n = 77; for questionnaire-based analyses: n = 80). NA participants were recruited from a participant recruiting pool maintained at the University of Minnesota.

Family income and parental education were comparably high for the two groups (PI median income: $100,000–$125,000; NA median income: $75,000–$100,000). Only three parents did not report their household income. Parental education ranged from less than a high school degree to doctorate level, with an average of 16 years of education for the parents attending the session as well as their spouses or partners in both the PI and NA groups. The majority of parents attending the session were mothers (88.8%), however there were no significant differences on any of the main study variables for children accompanied by their mothers versus their fathers (cortisol variables: ps $>$ .49; observed or perceived parental sensitivity and negativity variables: ps $>$ .13) and results did not change when excluding participants accompanied by fathers (n = 9), thus analyses are reported on the full sample.

PI participants had been adopted as children between the ages of 1 and 5.08 years, M age = 24.3 months., SD = 14.4 months. The vast majority of children (95% of them) had spent at least 50% of their pre-adoptive lives in an institution (e.g., orphanage or baby home), and 67.6% of all PIs had spent their entire pre-adoptive lives in an institution. They were adopted from diverse regions of the world: Russia and Eastern Europe (54.1%), East and Southeast Asia (35.1%), India/Nepal (8.1%), and Latin America (2.7%). PI children had higher rates of medication usage compared with NAs, but did not differ importantly on this variable by experimental condition (see Table 2). PIs were also more likely to use psychotropic medications (N = 7, with four in the parent condition and three in the stranger condition; vs. N = 0 for NAs), however medication use in general and psychotropic medication use in particular was not associated with cortisol reactivity in this sample. In the PI group, psychotropic medications were used to treat ADHD (N = 6), depression (N = 1, comorbid with ADHD) or anxiety (N = 1).

Procedure

Stress paradigm. The following research protocol was approved by the Institutional Review Board at the University of Minnesota. Participants completed an adapted version of the TSST using the story stem from the Modified Trier Social Stress Test (TSST-M, Yim et al., 2010; an adaptation of the TSST-C by Buske-Kirschbaum et al., 1997). This paradigm consisted of a public speaking task (introducing oneself to a hypothetical new classroom of students) and a mental arithmetic task (subtracting out loud by 3s from 307). The participant was alone in the room when giving the speech and performing the mental arithmetic in front of a two-way mirror and a conspicuously placed video camera. The participant was told that the experimenter and two other teachers (one man, one woman) would watch them from the other side of the mirror and rate their speech performance and their arithmetic accuracy. This was accomplished using an audio recording of two adults who sternly provided instructions for the speech as if they were present live behind the two-way mirror. Replacing an audience of three judges with a two-way mirror has been previously shown to be successful in elevating cortisol in 9-year-olds (Jansen et al., 2000). At the end of the session, all participants and parents were debriefed about the protocol and given positive feedback on their performance.

Session timeline. Participants were accompanied by one of their parents to two laboratory sessions spaced up to one week apart,[1] with all start times scheduled between 3:30–4:30 p.m. to control for the diurnal variation in cortisol levels. Session 1 included the following: consent process and reading leisurely in the welcome/waiting area (25 min.), participant moving to adjacent room with either the parent or a female experimenter (based on random assignment) and receiving TSST instructions (5 min.), speech preparation with parent or stranger (5 min.), moving to another room to complete the TSST alone (10 min.), returning to the waiting area and relaxing with the parent (10 min.), and completing questionnaires (approximately 1 hr). In the parent-support condition (88.8% mothers), the parents were instructed to help their children in any way they found useful. In the stranger-support condition, the female stranger[2] stated that she was ready to help in any way participants found useful. In this latter condition, the parent remained in the waiting room and did not accompany the participant into the testing area. Participants from both conditions could not see or contact their parents during the TSST. Salivary cortisol was collected four times during Session 1 (45, 65, 85, and 105 min after arrival), corresponding to 20 min after the end of the relaxation period and 20, 40, and 60 min after the end of the stress task.

Session 2 was conducted to collect two resting cortisol samples (45 and 65 min from arrival) and additional questionnaire measures. Prior work suggests that baseline cortisol samples are ideally collected in this fashion: in the same laboratory conditions, at the same time of day but on a different day, and during rest (Lovallo, Farag, & Vincent, 2010). This also eliminated the novelty of arriving to the laboratory and any anticipatory stress responses, because participants were told in advance that this session would only include "filling out paperwork," without any challenging tasks. These samples were important for examining whether PI and NA children differed in resting basal cortisol levels, in addition to differences in reactivity.

Measures

Salivary cortisol. Participants expelled saliva through a straw into prelabeled vials. They were instructed to refrain from eating large, protein-filled meals and consuming caffeine or energy drinks 2 hr before arriving to the laboratory. The samples were stored in a laboratory freezer at −20 °C until being shipped to the University of Trier, Germany to be assayed using a time-resolved fluorescence immunoassay (dissociation-enhanced lanthanide fluorescent immunoassay [DELFIA]; intra-assay coefficient of variation <7%, interassay coefficient of variation < 10%). All of the samples from each participant were included in the same assay batch, and the assay batches were balanced by group and condition. Samples were assayed in duplicate and averaged. All sample collections were timed and prompted by experimenters, thus, missing data rates were low (.006% of samples).

Daily diaries. The parent and the child each completed a daily diary on session days, for which they reported information about the participant relevant to cortisol collection: time of wake-up, medication usage, caffeine consumption, distressing events experienced that day (e.g., arguments with siblings or parents), and number of hours of sleep during the previous night. Child reports were the primary source of information. However, for type of medication used by the offspring, the parents' report on this variable was used instead when the child's information was missing, too vague, or incomplete. All other child-reported variables were either complete or missing less than 5% of data so imputation was not necessary.

Child Life Events Scale. This is a widely used and ecologically valid measure of life stressors for children (Boyce et al., 1995). The scale asked parents to select any major life events that occurred in their children's life in the 3 months prior to testing (from a list of 40 possible events—e.g., serious illness of parent, death of a grandparent, change in schools, problems with teachers, moving to a new home, etc.). One of the items is an open category allowing the parent to add any life events not previously listed. A total score was created by adding 1 for each event experienced by children and adolescents during this period ($M = 1.27$, $SD = 1.77$, range = 0–10).

Observational ratings of parent support. Speech preparation with the parent (for participants randomized to this condition) was rated in real time by the experimenter using 5-point Likert-type items yielding two subscales: Parent Support (four items: parental sensitivity, positive affect toward the child, effective communication, and validation of the child's perspective; Cronbach's $\alpha = .88$) and parent negativity (three items measuring intrusiveness, criticism, and authoritarianism; scale Cronbach's $\alpha = .77$). For each item, the experimenter rated how often (1 = *never* to 5 = *the entire time*) the parent engaged in a type of behavior (e.g., being intrusive). Parent behavior from the same segment was also later double-coded from videotapes by two other

[1] Number of days between sessions was not significantly associated with Session-2 cortisol intercept ($p = .33$) or slope ($p = .24$).

[2] Across the duration of the study, the stranger role was played by one of two Caucasian women researchers in their late 20s. Thus, the parent and stranger were gender-matched in 88.8% of situations. Future research should examine the role of age, ethnicity, and gender mismatches between parent and stranger, child and stranger, and parent and child to test these more complex contributions to stress reactivity and social buffering.

independent coders (average agreement between these two coders was .65 intraclass correlation). Coders completed 5-point Likert-type scales to yield a measure of parent support (5 items: encouragement, validation, coping assistance, positivity, and helpfulness; Cronbach's $\alpha = .72$) and a measure of parent negativity (2 items: criticism and intrusiveness; Cronbach's $\alpha = .83$). Experimenter ratings and the average of the two coders' ratings were standardized and the z-scores averaged to create one measure of observed parent support and one of parent negativity.

Network of Relationships Inventory: Social Provisions Version (NRI-SPV). The NRI-SPV (Furman & Buhrmester, 1985, 2009) is a well-validated questionnaire that was designed to be used with children and adolescents. It assesses 10 relationship qualities using three questions for each and including seven facets of support (companionship, instrumental aid, intimate disclosure, nurturance, affection, reassurance of worth, and reliable alliance), two negative relationship features (conflict, antagonism) and a measure of relative power. We used participants' ratings of these qualities for the parent attending the session with them. For instance, participants completed Likert-type items rating "how much does this person like or love you?" or "how much do you and this person get upset with or mad at each other?" using scales from 1 (*little or none*) to 5 (*the most*). Principal components analysis with a varimax rotation indicated that, as expected, the seven facets of support loaded highly on a single factor (loadings between .67 and .83), whereas conflict and antagonism loaded highly on a second factor (loadings of .95 and .96). The relative power scale loaded on a third factor by itself and was not analyzed further, given that it was only composed of three questions. We therefore created summary measures of Support and Negative Interactions with the parent attending the session. Given that these global self-report ratings were not significantly correlated with observational measures of behavior during speech preparation (see Table 1), we examined them separately because they captured different aspects of relationships.

Data-Analysis Plan

Data preparation. Preliminary analyses were conducted to identify outliers in cortisol concentrations and values more than 3 *SD* from the mean were Winsorized (seven values for Day 1 and three values for Day 2) and replaced with the value at the 99.9th percentile. Because cortisol measures displayed high skewness and kurtosis, a $\log_{10}$ transformation was applied to these concentrations after Winsorizing to normalize their distributions and meet assumptions for statistical analyses.

Statistical analyses. Hierarchical linear modeling (HLM, Raudenbush & Bryk, 2002) was used to analyze the cortisol data because it is ideal for auto-correlated samples collected from the same individual and it allows for greater statistical power than traditional repeated-measures ANOVA models (Raudenbush & Bryk, 2002). Analyses were implemented using the PROC MIXED procedure for linear mixed modeling in the SAS 9.2 software (SAS Institute, Inc., 2009). The Level-1 model represented individual change in levels of cortisol as a function of time. We anticipated based on previous research (Lam, Dickerson, Zoccola, & Zaldivar, 2009; Smith, Loving, Crockett, & Campbell, 2009) and the sampling times in this design that both a linear and quadratic term for time would be necessary to model cortisol reactivity (i.e., sample time and time-squared were entered as predictors). Indeed, the quadratic time term included in the model was significant: $F(1, 151) = 9.13$, $p = .003$, suggesting the expected significant peaked cortisol response with the TSST. Time was coded as 0, 1, 2, and 3 given that the samples were equally spaced at 20-min intervals. The linear time term represented the instantaneous rate of change in cortisol and the quadratic time term represented the curvature of the cortisol trajectory. We also added a peak term to the intercept (a dummy code indicating whether the value was Sample 2 or not) to superimpose upon the quadratic model (similar to methodology for modeling the cortisol awakening response as a peak elevation above the diurnal rhythm curve; Adam, Hawkley, Kudielka, & Cacioppo, 2006). The Level-2 model explained between-subjects differences based on several independent variables: two dummy variables coding for group (PI vs. NA), and condition (stranger vs. parent support), as well as their interaction, and other person-level covariates (described in more detail in the next section). Type-3 *F* tests of fixed effects were reported for each main or interaction effect and specific β parameters were used to follow up on significant interactions and interpret directionality of effects through

Table 1
Descriptive Statistics and Bivariate Correlations Among Main Study Variables

Variables	1	2	3	4	5	6	7	8	9	10
1. Log cortisol 1	—	.64**	.67**	.52**	−.13	.19	−.26	.05	.11	−.03
2. Log cortisol 2		—	.86**	.69**	−.19	.31**	−.15	−.05	−.02	−.08
3. Log cortisol 3			—	.86**	−.23*	.23*	−.35*	.15	.003	−.09
4. Log cortisol 4				—	−.24*	.20	−.38*	.14	.06	−.09
5. Time since wake-up					—	−.13	.39*	−.40*	.04	.07
6. Sex (female = 1)						—	.18	−.06	.06	−.15
7. Observed parent support							—	−.45**	.04	−.10
8. Observed parent negativity								—	−.04	.10
9. Perceived parent support									—	.02
10. Perceived parent negative interactions										—
Mean	.45	.47	.37	.30	8.80	.51	0	0	3.86	1.81
SD	.27	.32	.28	.28	1.18	.50	1	1	.64	.79

Note. Observed parent support and negativity measures were *z* scores and were derived only for participants randomly assigned to the parent support condition using their speech preparation episode.
* $p < .05$. ** $p < .01$.

Table 2
Exploring Evidence of Successful Randomization: Differences Between the Two Conditions Within the Nonadopted (NA) and Postinstitutionalized (PI) Groups

Variable	NA Group			PI Group		
	Stranger	Parent	*p*	Stranger	Parent	*p*
Age (years)	9.97 (.50)	9.96 (.54)	.94	9.50 (.44)	9.92 (.61)	.02*
Sex (% female)	50%	50%	1.0	52.6%	44.4%	.86
Family income (1–11 scale)	6.65 (2.41)	5.95 (1.93)	.32	8.06 (1.89)	6.94 (2.48)	.14
Time since wake-up (hours)	9.07 (1.09)	8.56 (1.53)	.23	8.73 (.91)	8.88 (1.15)	.66
Sleep hours (night before experiment)	9.37 (1.79)	9.64 (1.30)	.58	10.38 (.94)	10.08 (.95)	.35
Distressing events (day of experiment)	.55 (60)	.80 (89)	.31	.61 (.70)	.37 (.60)	.26
Number of life events (previous 3 months)	1.45 (2.74)	1.55 (1.47)	.89	.89 (1.08)	1.15 (1.31)	.51
Consumed caffeine (day of experiment)	25%	5%	.08	16.7%	22.2%	.67
Using medication (day of experiment)	0%	5%	.31	26.3%	22.2%	.77
Length of time in orphanage care (months)	N/A	N/A		20.78 (12.2)	17.7 (5.7)	.35

Note. Means (*SD*s) are presented for continuous variables and percentages for frequency data.

simple slope analysis (Aiken & West, 1991). All continuous variables were mean-centered. Kenward-Roger adjusted degrees of freedom were used (Kenward & Roger, 1997).

Cortisol covariates. Cortisol is sensitive to numerous sleep, diet, medication, experiential, and demographic factors (Cohen, Doyle, & Baum, 2006; Kudielka, Hellhammer, & Wüst, 2009). Of the Daily Diary and demographic factors relevant for cortisol measures (age, sex, family income, time since wake-up, number of hours slept the previous night, number of distressing events experienced the day of testing, number of major life events in the previous 3 months, caffeine consumption, and medication usage coded according to Granger, Hibel, Fortunato, & Kapelewski, 2009), the only variables that were significantly or marginally associated with any cortisol measures on the experimental day were time since wake-up and sex (see Table 1 for bivariate correlations). Thus, these two measures were included as covariates for intercepts, linear and quadratic terms in every model. Results did not change when models were run without these covariates. Participants did not differ by condition on any of these demographic or daily diary measures ($p > .10$), suggesting that randomization was successful. Furthermore, when examining these factors by condition within each of the two groups, there were no significant differences (see Table 2) with the exception of a small mean age difference between PIs in the stranger ($M = 9.50$ years, $SD = .44$) versus parent condition ($M = 9.92$ years, $SD = .61$). This is not likely to affect our interpretation of results concerning parental buffering given that PIs in the parent condition had a nearly identical mean age as NAs in the parent condition ($M = 9.96$ years, $SD = .54$). Nevertheless, we verified that results did not change when controlling for child age and, within our narrow recruitment range, age was not associated with cortisol reactivity (as already described), thus it was dropped from our statistical models.

Models tested. We began by testing the first prediction (stronger stress-buffering effects with parents vs. strangers for NA but not PI children) in a model including condition, group, and their interaction as predictors of cortisol trajectories, with sex and time since wake-up entered as covariates at every level of the model. Preliminary analyses indicated that there were no significant interactions with sex (Group × Sex, Condition × Sex, or Group × Condition × Sex, ps $>.08$), thus we proceeded to control solely for the main effect of sex in all analyses. We then tested group differences in basal cortisol levels from Day 2 to rule out the possibility that cortisol reactivity differences would be due to differences in basal HPA activity. For our second aim—examining group differences in the quality of parent–child relationships—we used *t* tests to compare PI and NA children on observational and self-reported measures of parent support and parental negativity for participants randomized to the parent-support condition, as well as on perceived support and negative interactions with the parent derived from the Network of Relationships Inventory (NRI). Third, to examine whether parent–child relationship qualities explained differences between PI and NA children, we tested the association between four parent–child relational measures (observed or self-reported parent support and negativity) and cortisol reactivity within the parent support experimental condition, modeled in HLM as described above.

Results

Descriptive statistics and bivariate correlations involving the main study variables are presented in Table 1.

Condition and Group Differences in Cortisol Trajectories

The fixed-effects of group, condition, and their interaction were tested as predictors of cortisol trajectories, including relevant cortisol covariates (see Data Analysis Plan section). Results (see Table 3) indicated a significant interaction of Group × Condition on cortisol reactivity, linear term: $F(1, 194) = 5.08$, $p = .025$; quadratic term: $F(1, 147) = 3.76$, $p = .055$, with no main effects of group or condition on reactivity (ps $> .09$). There were also no significant effects of group, condition, or Group × Condition on intercepts, which reflected initial cortisol levels (ps $> .33$). To follow-up on the Group × Condition interaction, simple slope analyses revealed a significant effect of condition for NA children such that, as previously reported (Hostinar, Johnson et al., 2014), cortisol reactivity was significantly reduced in the parent- compared with the stranger-support condition, linear term: $\beta = -.16$, $SE = .07$, $t(194) = -2.22$, $p = .028$; quadratic term: $\beta = .04$, $SE = .02$, $t(147) = 1.94$, $p = .054$). However, this was not the case

Table 3
Type 3 F Tests for the Primary Model (Results Depicted in Figure 1)

Fixed effect	Numerator *df*	Denominator *df*	*F*	*p*
Linear	1	182	.48	.489
Quadratic	1	147	1.16	.284
Peak (effect of being Sample 2)	1	147	5.07	.026*
Time since wake-up	1	79.6	1	.321
Time since wake-up × Linear	1	194	1.42	.235
Time since wake-up × Quadratic	1	147	.64	.426
Sex	1	79.6	2.63	.109
Sex × Linear	1	194	2.39	.124
Sex × Quadratic	1	147	3.38	.068
Group	1	79.6	.97	.329
Group × Linear	1	194	2.94	.088
Group × Quadratic	1	147	2.11	.149
Condition	1	79.6	.45	.506
Condition × Linear	1	194	.69	.406
Condition × Quadratic	1	147	.58	.446
Group × Condition	1	79.6	.1	.752
Group × Condition × Linear	1	194	5.08	.025*
Group × Condition × Quadratic	1	147	3.76	.055

* $p < .05$.

for the PI children. For PI children, no effect of Condition was observed, linear term: $\beta = -.07$, $SE = .07$, $t(194) = -0.99$, $p = .32$; quadratic term: $\beta = .02$, $SE = .02$, $t(147) = 0.82$, $p = .41$. Figure 1 displays predicted cortisol trajectories by Group and Condition based on model estimates. When comparing the two groups within condition, PI children exhibited significantly lower cortisol reactivity than NA children in the Stranger condition, linear term: $\beta = -.20$, $SE = .07$, $t(194) = -2.78$, $p = .006$; quadratic term: $\beta = .05$, $SE = .02$, $t(147) = 2.38$, $p = .02$, but did not differ significantly from NAs in the parent condition ($ps > .64$).

To rule out the possibility that cortisol reactivity differences were due to differences in basal HPA activity, resting cortisol levels (i.e., Day-2 samples) were examined next in a separate HLM controlling for the same covariates as in Day-1 analyses (time-since-wake-up and sex). There were no group differences in initial cortisol levels, $F(1, 69) = .51$, $p = 48$ or slopes, $F(1, 69) = .10$, $p = 75$. Estimated cortisol trajectories for Day 2 are also shown in Figure 1.

Examining Group Differences in Parent–Child Relationship Quality

We first sought to test whether PI and NA participants randomly assigned to the Parent-support condition differed in observed or perceived Support and Negative Interactions with their parent. Independent samples *t* tests revealed that PIs and NAs in the Parent-support condition did not differ in observed support received, $t(37) = .16$, $p = .87$ or observed negativity with their parent during the speech preparation period, $t(37) = -.07$, $p = .94$. Furthermore, they also did not differ in self-reported perceived global Support or Negative Interactions with the same parent derived from NRI ratings, $t(38) = 1.20$, $p = .24$ and $t(38 = 1.46$, $p = .15$, respectively). Figure 2 displays means and standard errors for each of these measures by group.

Relationship Quality as an Explanatory Factor?

Our final goal was to examine whether the Group × Condition differences noted with cortisol reactivity were due to the observed or perceived quality of the relationship with the parent. As noted above, this is unlikely given that PIs and NAs did not differ significantly on any of the relational quality measures. The four relational predictors were tested separately to maximize degrees of freedom, in models controlling for the same covariates used previously (time since wake-up and sex). We first retested our final model but controlling for each of the two self-reported relational quality predictors available in the entire sample, and found that the significant Group × Condition interaction and all other results were identical after parsing out cortisol variance due to self-reported parental support or negativity. Second, within the parent-support condition none of the measures of observed or perceived parent support or negativity moderated cortisol reactivity ($ps > .19$ for both linear and quadratic terms).

Discussion

Early-life adversity predicts approximately 45% of childhood-onset and 30% of adult-onset psychopathology (Green et al., 2010). Furthermore, individuals who experience early-life adversity often also have a history of disrupted relationships, making it difficult to access and benefit from social support, an important protective factor against mental and physical illness across the life span (Cohen, 2004; Taylor, 2011). The study of children adopted from orphanages overseas provides a unique natural experiment in which adversity is circumscribed to the first few years of life and children subsequently have access to welcoming families and parent support moving forward. One question that remains mostly unanswered in this natural experiment is whether children retain the ability to use their caregivers as a buffer against stress, despite their early history of social deprivation. We aimed to answer this question in the present study, which would have the potential to

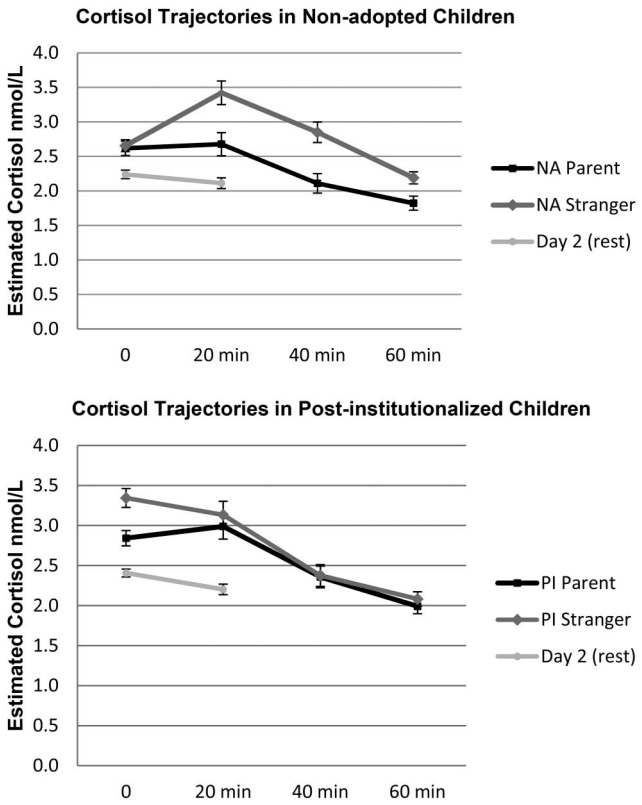

Figure 1. Estimated cortisol curves based on hierarchical linear modeling results by group and condition (stranger support or parent support). The stress task lasted 10 min and ended at the 0-min mark on this graph. Analyses were conducted with log-transformed cortisol and estimated values were exponentiated to present nmol/L concentrations. Error bars are standard errors of estimated values. Day-2 samples were estimated in a separate linear model controlling for the same covariates and include children from both conditions. NA = nonadopted; PI = postinstitutionalized.

inform interventions with pediatric populations experiencing a wide range of adverse early-life experiences.

Previous research has shown that parental support is a potent regulator of stress responses and can dampen the HPA reactivity of typically developing children, whereas support from strangers encountered in the laboratory does not have these effects (Hostinar, Johnson, et al., 2014; Hostinar, Sullivan, et al., 2014; Seltzer et al., 2010). To our knowledge, this is the first experimental study to show that children who spent the first few years of their life in orphanages did not show significantly different cortisol curves in response to a controlled laboratory stressor when receiving support from parents versus strangers. In contrast, as reported previously (Hostinar, Johnson et al., 2014), NA children showed a significant reduction in cortisol production in the parent-support condition compared with the stranger condition.

The lack of selective responses to parents versus strangers in PI children may be due to the absence of a stable and discriminate attachment relationship with a caregiver early in development, given the typically high caregiver turnover and the high child-to-caregiver ratio often encountered in institutions (Zeanah et al., 2002). Previous research on socioemotional difficulties in PI children has also shown that indiscriminate friendliness, or excessive familiarity with and lack of appropriate reticence around strangers, is a prominent feature in samples experiencing early institutional deprivation (Chisholm, 1998; Lawler et al., 2014; O'Connor et al., 1999; Roy et al., 2004; Rutter et al., 2007; Zeanah et al., 2002) and may contribute to the pattern of results observed here. The fact that, on average, PI children exhibited lower cortisol reactivity in the stranger condition compared with NA children suggests the possibility that strangers might be able to buffer their stress responses. Overall, our results are consistent with a study by Olsavsky et al. (2013) reporting that PI children (mean age 10) showed reduced differentiation in their amygdala activation in response to mothers' versus strangers' faces compared with their NA counterparts, who exhibited increased neural activity to maternal compared with stranger faces (Olsavsky et al., 2013); this is the expected result given that the amygdala responds preferentially to affectively salient stimuli (Olsavsky et al., 2013). Our results are also consistent with those of a study with younger PI children (ages 4–5), which reported that PI's did not show increases in urinary oxytocin and reductions in cortisol after a close interaction with their parent in the same way that NA children did (Wismer Fries et al., 2005, 2008). Importantly, PI children in this study showed comparable cortisol output when interacting with their parent or with a stranger, suggesting the same lack of selective responses to one's caregiver observed in our study.

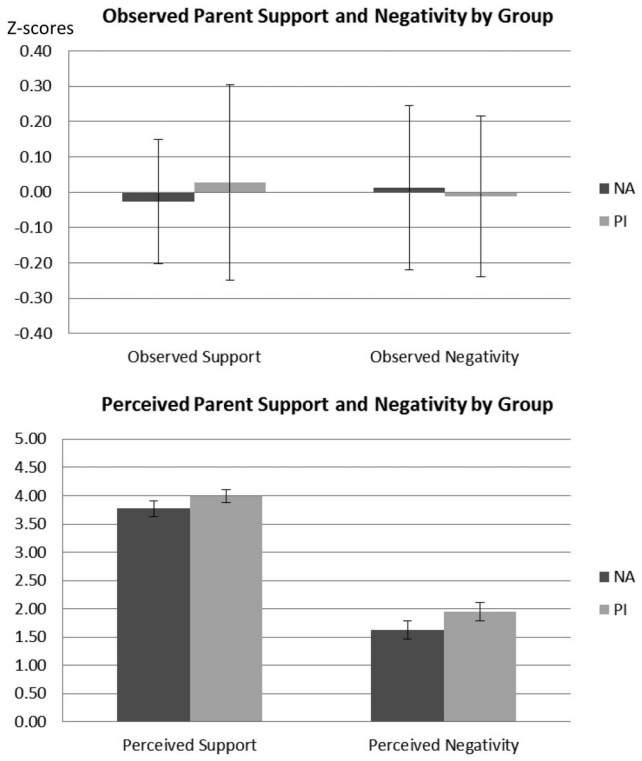

Figure 2. Mean support and negativity from the parent for participants randomly assigned to the parent-support condition ($n = 40$). Error bars are standard errors of the mean. Observational measures are z scores and based on session ratings, whereas perceived measures are global relationship ratings derived from the Network of Relationships Inventory and measured on a scale from 1 (*little or none*) to 5 (*the most*). NA = nonadopted; PI = postinstitutionalized.

Both groups showed the expected declining cortisol slope at rest (on Day 2), and there were no group differences in absolute cortisol levels or slopes, suggesting that the Group × Condition effects on cortisol trajectories during the experimental day cannot be explained by differing initial levels.

An alternative explanation for our findings is that adoptive parents could provide less support than parents in the control group, making differences between parent and stranger support difficult to emerge. Our analyses argue against this interpretation, as objective observational ratings of parent support and parent negativity during speech preparation did not differ between PI versus NA children. Children's self-reported levels of global support and negative interactions with the parent confirmed this pattern, showing no group differences. Furthermore, neither observed nor perceived measures of parent support or negativity were associated with cortisol reactivity in the Parent-support condition, reinforcing the idea that the results we obtained are not likely to be due to qualitative differences in family relationships and current social environments between NA and PI children. The lack of association between support or negativity and cortisol reactivity may be due to the low-risk nature of the sample and the high levels of parental support observed in both groups (e.g., mean perceived ratings of parent support were near 4 out of a maximum possible of 5, with little variation around the mean). Other studies have indeed suggested that both parental responsiveness and conflict/disagreement can shape children's HPA reactivity (Hackman et al., 2013; Spies, Margolin, Susman, & Gordis, 2011; Sturge-Apple, Davies, Cicchetti, & Manning, 2012), thus future research should expand the current investigation to higher-risk samples, examining broader variation in parenting.

In sum, our results suggest that PI children may exhibit reduced differentiation between their HPA responses to parents and strangers. These findings are consistent with those from other studies reporting PI's reduced discrimination between mothers and strangers as indexed by neural activity patterns (Olsavsky et al., 2013) or oxytocin levels (Wismer Fries et al., 2005). More research is needed to understand the potential mental and physical health consequences of not exhibiting preferential responses to parents versus strangers. It could be that these behaviors hinder children's social adjustment, and make it difficult to establish close, intimate relationships with friends or romantic partners. However, the possibility of beneficial effects such that children experience stress-buffering equally with strangers and parents cannot be ruled out. Longitudinal research with larger samples and more in-depth adjustment measures will be necessary to tease apart these competing possibilities.

The neurobiological mechanisms through which parents buffer children's HPA axis are also not well characterized even in normative samples. Recent models propose a role for hypothalamic oxytocin or HPA-inhibitory pathways by prefrontal cortical regions which relay safety signals triggered by stimuli associated with attachment figures (Hostinar, Sullivan, et al., 2014). It seems that a certain level of emotional intimacy with a social partner is necessary to elicit these HPA-buffering effects—for example, parents and romantic partners have been shown to be more effective stress buffers than strangers (Hostinar, Johnson, et al., 2014; Kirschbaum et al., 1995), but the neural underpinnings for how these relational figures affect HPA reactivity are unknown. More research is also needed to understand how early social deprivation might shape this circuitry and neurobehavioral development to produce a lack of selective hormonal and neural responses to caregivers versus strangers. It will be especially important to examine the potential downstream consequences of this lack of selectivity for children's coping with stress and for their overall well-being. Furthermore, developmental changes in the potency of parent support to dampen HPA responses beyond age 11 need further scrutiny in normative samples as well as in youth exposed to early-life adversity. A recent report suggested that parent support was not effective in buffering cortisol reactivity for typically developing 15–16-year olds (Hostinar, Johnson, et al., 2014), and we are currently examining whether changes in parental buffering across the ages of 11–13.5 are linked to pubertal stage or chronological age—we expect both to play a role.

The present study had a number of strengths and several limitations. The study of internationally adopted children has the advantage of shedding light on the effects of circumscribed periods of early adversity, while at the same time examining the possibility of recovery with positive social interventions. The use of an experimental stressor and a laboratory paradigm for eliciting parent support allowed us to show a more complex pattern of results than if we had used a questionnaire measure of parent support alone, as was evident here. The study also had several limitations that are typical of work with this population. First, orphanage rearing deprives children of more than just a consistent caregiver, and often includes nutritional deficits and lower levels of cognitive stimulation. Thus, it is difficult to know whether these results are precisely due to the lack of a consistent, sensitive, and responsive caregiver, or due to broader developmental impairments or delays associated with this atypical rearing scenario. Nevertheless, co-occurrence of risk factors is common for many children experiencing adversity (e.g., in poverty contexts: Evans, Li, & Whipple, 2013), thus this research may generalize to a broad range of high-risk samples. Second, the sample size may have limited statistical power to detect more subtle differences in HPA reactivity or to draw conclusions regarding the roles of age at adoption, country of origin, or time spent with a family before institutionalization. However, given the difficulties reaching this population many years after adoption and the fact that the only prior study collecting cortisol measures to answer a similar question was conducted with a different age group (4–5-year-olds) and a smaller sample size (18 PI and 21 NA children; Wismer Fries et al., 2005, 2008), this study makes a significant step toward better understanding the important question at hand. A third limitation was that the saliva sampling schedule used here did not allow a detailed assessment of anticipatory stress responses. Given the possibility of atypical HPA-reactivity profiles in this population, it will be important for future work to sample saliva at a higher frequency during the early portion of the laboratory session. In addition, the present study used a between-subjects design to compare responses to parent versus stranger support. It would be ideal to replicate these results using a within-subjects design; however, repeating the Trier Social Stress Test causes some habituation of HPA-axis reactions (Schommer, Hellhammer, & Kirschbaum, 2003). Thus, both study designs have their limitations and should be used jointly to inform conclusions. Lastly, adding a no-support condition whereby children prepared their speech alone would have allowed a clearer interpretation of the Stranger condition for both groups—that is, does the stranger have any effect on reactiv-

ity compared with preparing alone, and to what extent is this moderated by group? Second, this would have allowed us to examine group differences in cortisol reactivity in the absence of any additional experimental manipulations. Future work will have to address these questions that could not be tested with the present design.

Despite these limitations, this study raises new questions about the mechanisms through which early-life social relationships might shape brain and behavioral development in ways that promote resilience or vulnerability to stress during later development. Given that early-life adversity often acts as a "double whammy," simultaneously exposing children to higher levels of adverse events and depriving them of a blueprint for soothing social interactions, we need to better understand how early adversity shapes individual differences in the social regulation of stress responses. This will allow us to design the most effective stress-reducing interventions for the most vulnerable populations.

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Received July 16, 2014
Revision received March 4, 2015
Accepted May 19, 2015 ■