HHS Public Access

Author manuscript

Emotion. Author manuscript; available in PMC 2023 March 01.

Published in final edited form as:

Emotion. 2022 March ; 22(2): 318–330. doi:10.1037/emo0001016.

Autonomic reactivity to social rejection, peer difficulties, and the buffering effects of adolescent friendships following early psychosocial deprivation

Alva Tang[1], **Katie A. McLaughlin**[2], **Margaret A. Sheridan**[3], **Charles Nelson**[4,5], **Charles Zeanah**[6], **Nathan A. Fox**[1]

[1]Department of Human Development and Quantitative Methodology, University of Maryland, College Park, MD

[2]Department of Psychology, Harvard University, Cambridge, MA, USA

[3]Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

[4]Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

[5]Harvard Graduate School of Education, Cambridge, MA, USA

[6]Tulane University School of Medicine, New Orleans, LA, USA

Abstract

Autonomic nervous system reactivity has been posited to be a mechanism contributing to social and emotional problems among children exposed to early adversity. Leveraging data from the Bucharest Early Intervention Project, a longitudinal randomized controlled trial of foster care vs. institutional care of abandoned children in Romania, we assessed whether altered sympathetic reactivity to peer rejection feedback in early adolescence mediated the relation between early institutional rearing and peer problems in later adolescence. We also assessed whether adolescent friendship quality or randomized placement in foster care early in life moderated these associations. Participants include 68 institutionalized children randomized to care as usual, 68 institutionalized children randomized to foster care, and 135 never-institutionalized children. At age 12, participants reported friendship quality with respect to a best friend and completed a social rejection task while electrocardiogram and impedance cardiography were recorded. Sympathetic nervous system reactivity to rejection feedback was assessed using pre-ejection period (PEP). At ages 12 and 16, peer problems were reported by parents. Mediation analysis revealed that less PEP reactivity to social rejection at age 12 partially mediated the association between early institutionalization and greater peer problems at age 16. Further moderated mediation analysis revealed that this indirect effect was evidenced among previously institutionalized youths with low, but not high, quality friendships. We did not observe foster care intervention effects. These findings suggest that altered sympathetic reactivity to social rejection might be a mechanism linking early institutionalization to social difficulties into adolescence, however, positive adolescent friendships may buffer these effects.

Corresponding author: Alva Tang, Department of Human Development and Quantitative Methodology, University of Maryland, College Park, MD, USA. alvatang@umd.edu.

Keywords

deprivation; vagal regulation; social buffering; adolescence

Children reared in institutions experience severe psychosocial deprivation that places them at risk for peer problems, such as peer rejection and victimization (Almas et al., 2015; Pitula et al., 2014; Raaska et al., 2012), and psychopathology (Gunnar & Van Dulmen, 2007; Humphreys, Gleason, et al., 2015; Rutter et al., 2007). One developmental pathway through which chronic stress, resulting from early institutionalization, leads to the development of socioemotional problems is through its effects on maladaptive physiological stress-response systems (Gunnar & Vazquez, 2001; Lupien, McEwen, Gunnar, & Heim, 2009; McLaughlin et al., 2015). Indeed, few studies suggest that dysregulated stress-physiology indirectly explains the association between institutional rearing and socioemotional problems; however, nearly all of these studies are limited to the hypothalamic-pituitary-adrenocortical (HPA) system and early childhood (Koss, Mliner, Donzella, & Gunnar, 2016; Pitula, DePasquale, Mliner, & Gunnar, 2017). To provide further insight into this developmental pathway, this study examined whether sympathetic nervous system (SNS) reactivity acquired during a social rejection task in early adolescence explain changes in peer problems following early institutional rearing. We also examined whether supportive adolescent friendships can remediate these negative consequences linked to a lack of early parental care.

Maladaptive stress physiology following institutional rearing has been well-described for the HPA system, with blunted patterns of cortisol diurnal rhythm and reactivity widely reported in previously institutionalized children (Carlson & Earls, 1997; Gunnar, Frenn, Wewerka, & Van Ryzin, 2009; Koss, Hostinar, Donzella, & Gunnar, 2014; Koss et al., 2016; McLaughlin et al., 2015; Pitula et al., 2017). Compared to the HPA system's slower responses to stressors, the SNS involves relatively quicker responses, which is advantageous for capturing changes to different social evaluations. However, fewer studies have examined SNS reactivity to social evaluative feedback. The SNS is one branch of the autonomic nervous system that mediates responses to social challenges and maintains homeostasis (Porges, 2007). To meet demands of social challenges, the SNS activates, resulting in physiological changes (i.e., accelerated heart rate, increases in blood pressure, contractility of the heart), that mobilize metabolic and cognitive resources to enhance motor and cognitive performance (T. P. Beauchaine & Thayer, 2015; Porges, 2007). But not all individuals respond to social challenges the same way. Individual differences in SNS reactivity are thought to reflect differences in the ability to regulate emotions and motivational states that facilitate behavioral adaptation (T. Beauchaine, 2001). While several methods can capture SNS activity, the present study focuses on the cardiac pre-ejection period (PEP), reflecting the time elapsed between when the heart fills with blood and when blood is ejected from the heart (Berntson & Cacioppo, 2007), for several reasons. First, PEP is a relatively pure index of SNS activity (Berntson & Cacioppo, 2007) that can measure the degree of sympathetic activation. In situations involving social rejection that threaten a sense of social belonging, the degree of PEP reactivity provides insight into whether the individuals' SNS is engaged in adapting to these challenges. Second,

PEP reactivity is thought to underlie a motivational system (i.e., behavioral activation system) subserving approach-oriented behaviors (T. Beauchaine, 2001; Crowell et al., 2006; Ortiz & Raine, 2004; Richter & Gendolla, 2009) that carry implications for behavioral adaptations to social evaluative feedback. Third, maladaptive (i.e., blunted) PEP reactivity to laboratory tasks involving social stressors and incentives has been shown to be a useful physiological predictor of behavioral and social problems among children and adolescents (T. P. Beauchaine, Gatzke-Kopp, & Mead, 2007; Hinnant, Erath, Tu, & El-Sheikh, 2016; Obradović, Bush, & Boyce, 2011).

To date, only a small set of studies has examined PEP activity in relation to institutional rearing. The findings on resting PEP activity suggest that children with a history of institutionalization show higher resting SNS activity (Esposito, Koss, Donzella, & Gunnar, 2016; Gunnar et al., 2009; McLaughlin et al., 2015), which is in turn associated with later behavioral problems (Esposito et al., 2016). However, the two studies examining PEP reactivity to social stressors in previously institutionalized children between ages 10 to 12 report mixed findings of blunted (McLaughlin et al., 2015) and heightened (Gunnar et al., 2009) reactivity, which might be attributed to differences in the severity of early deprivation and later caregiving environments (i.e., foster and institutional care vs. international adoption) across the samples. While the scant research provides mixed findings on PEP reactivity, developmental models (Del Giudice, Ellis, & Shirtcliff, 2011; Lupien et al., 2009) and empirical evidence on the HPA system (Carlson & Earls, 1997; Gunnar et al., 2009; Koss et al., 2014; Koss et al., 2016; McLaughlin et al., 2015; Pitula et al., 2017) suggest that children exposed to severe and chronic forms of adversity are expected to show blunted stress physiology over time, which helps maintain allostasis. Given that the present sample of previously institutionalized children exhibited blunted PEP reactivity to peer evaluative feedback at age 12 (McLaughlin et al., 2015), we sought to extend this finding by examining its implications on later social problems in the present study.

One context in which blunted PEP reactivity could contribute to further social problems is peer rejection in adolescence. Peer rejection and victimization are common peer problems reported amongst previously institutionalized children (Humphreys, Gabard-Durnam, et al., 2018; Pitula et al., 2017), which can increase the risk of developing socioemotional problems in adolescence (Deater-Deckard, 2001; Guyer, Silk, & Nelson, 2016). However, existing studies on the effects of early institutionalization have only examined how HPA reactivity to strangers and unfamiliar contexts are linked to peer problems in early childhood (Koss et al., 2016; Pitula et al., 2017). In adolescence, adolescents' emotions and behaviors are motivated by peer acceptance. During this period, adolescents exhibit exaggerated emotional, neural and physiological responses when rejected during social evaluation and exclusion tasks compared to children and adults (Sebastian, Viding, Williams, & Blakemore, 2010; Stroud et al., 2009; Tang, Lahat, Crowley, Wu, & Schmidt, 2019; van den Bos, de Rooij, Miers, Bokhorst, & Westenberg, 2014). Contrasting with this normative pattern of hyper-reactivity to social rejection in adolescence, our prior study has found previously institutionalized adolescents to show blunted SNS reactivity to peer rejection feedback compared to never institutionalized adolescents (McLaughlin et al., 2015). Such deviation from the norm is consistent with the insensitive social behaviors reported in these children (Bruce, Tarullo, & Gunnar, 2009; Guyon-Harris, Humphreys, Fox, Nelson, & Zeanah, 2018;

Humphreys, McGoron, et al., 2015; Sonuga-Barke, Schlotz, & Kreppner, 2010) and might reflect a lack of reactivity or insensitivity to social punishment, that portend later social problems. In support of this idea, studies of typically developing adolescents suggest that variation in SNS reactivity to peer rejection and evaluation is related to prosocial behaviors. Compared to adolescents with less SNS reactivity to peer evaluation and rejection (i.e., greater skin conductance), those with greater SNS reactivity are more prosocial and accepted by peers (Erath & Tu, 2014), and express greater warmth toward their mothers (Diamond & Cribbet, 2013).

Furthermore, adolescents increasingly rely on friends, rather than parents, as social support systems (Brown, 2004)— this natural shift in supportive social figures offers a salient window to examine friendship as a source of resilience. High-quality friendships provide youth with help and guidance, companionship, loyalty, and intimate exchange (Parker & Asher, 1993). The buffering effect of high-quality friendships in reducing maladjustment is evidenced in adolescents with adverse peer experiences (Asher & Paquette, 2003; Waldrip, Malcolm, & Jensen-Campbell, 2008), negative parenting styles (Gaertner, Fite, & Colder, 2010; Lansford, Criss, Pettit, Dodge, & Bates, 2003), and in children exposed to child maltreatment (Bolger, Patterson, & Kupersmidt, 1998) and family adversity (Criss, Pettit, Bates, Dodge, & Lapp, 2002). While difficulties in interacting with peers are widely reported in previously institutionalized youth (Almas et al., 2015; Bruce et al., 2009; Pitula et al., 2014; Raaska et al., 2012), few studies have examined their friendship quality. The small set of studies report mixed evidence of less supportive (Hodges & Tizard, 1989) and comparable friendship quality in post-institutionalized compared to never-institutionalized youth (Hawk & McCall, 2014; Vorria, Ntouma, & Rutter, 2014). Previously institutionalized youth also report having fewer friends than those in family care, but most have a best friend (Erol, Simsek, & Münir, 2010; Hawk & McCall, 2014; Tang et al., In press). These findings suggest that the ability to build a close friendship is not completely compromised. In fact, having one supportive close friendship can protect against maladjustment (Asher & Paquette, 2003; Bolger et al., 1998; Criss et al., 2002; Gaertner et al., 2010; Lansford et al., 2003; Waldrip et al., 2008). To identify how supportive friendships can alter maladpative pathways leading to peer problems in the present study, we tested a moderated mediation model.

The present study examined maladaptive SNS reactivity to peer rejection feedback as a mechanism that explains the link between early institutional rearing and peer problems, and the protective role of supportive friendships in changing this developmental pathway in the Bucharest Early Intervention Project (BEIP). The BEIP is the only randomized controlled trial of foster care as an alternative to institutional care (Zeanah et al., 2003). Participants include three groups: 1) adolescents who as infants were abandoned to institutions and randomized to the care as usual group (CAUG); 2) adolescents who were abandoned as infant and randomized to the foster care group (FCG) after 6–30 months of institutional care, and 3) adolescents who were never institutionalized (NIG). A prior report on this sample showed main effects of early institutionalization on blunted SNS response to peer rejection at age 12, such that both the care as usual and foster care groups showed less PEP reactivity to peer rejection compared to the never-institutionalized group (McLaughlin et al., 2015). Here, we extended that prior study by further examining: (1) whether SNS

reactivity to peer rejection in early adolescence at age 12 mediated changes in peer problems by late adolescence at age 16 in previously institutionalized adolescents using a mediation model; and (2) whether the strength of this indirect relation was moderated by high-quality friendships using a moderated mediation model.

We had two aims. First, we assessed the effect of institutionalization compared to never-institutionalized children (i.e., comparing the CAUG and FCG to the NIG). We hypothesized that less PEP reactivity to peer rejection at age 12 would mediate the association between early institutionalization and greater peer problems at age 16, accounting for prior peer problems. Furthermore, we expected supportive friendship to buffer against peer problems, such that the indirect effect of early institutionalization on peer problems via PEP reactivity would be diminished at high-quality friendship. Second, we tested the effect of foster care intervention, by comparing the FCG to the CAUG. Our prior work suggests that foster care intervention improves some aspects of peer interaction, such as social communication (Almas et al., 2015; Levin, Fox, Zeanah Jr, & Nelson, 2015), However, other aspects of peer interactions do not significantly improve (Almas et al., 2015), including PEP reactivity to peer rejection, though the pattern of PEP reactivity is slightly higher in the FCG compared to the CAUG (McLaughlin et al., 2015). Based on this prior knowledge, we explored whether the indirect effect via PEP reactivity would be diminished by higher quality friendships in adolescents assigned to the FCG relative to the CAUG.

Method

Participants

Trial design and participant selection have been previously described (Zeanah et al., 2003) and are shown in Figure 1. Physical examination was completed on 187 infants, ranging from 6–31 months, in six institutions in Bucharest, Romania; 51 children were excluded for serious medical conditions (e.g., fetal alcohol syndromes). Accordingly, 136 children (ages 6–30 months) were recruited. After the baseline assessment, half of the children were randomly assigned to care as usual (CAUG: n=68) or to foster care (FCG: n=68) (Zeanah et al., 2003). Within the FCG, the mean age of foster care placement was 22.63 months (SD=7.33, range= 6.81–33.01). At baseline, a group of age- and gender-matched never-institutionalized children (NIG: n= 72) was recruited from pediatric clinics in Bucharest; However, the NIG did not consistently return to the study, as such additional NIG were recruited in follow-up visits, at age 8 (n=61), and age 16 (n=2). At age 12 (M age= 12.64; SD= .53), participants completed a social rejection task, while electrocardiogram (ECG) and impedance cardiography (ICG) data were recorded (McLaughlin et al., 2015), and a friendship quality questionnaire. At both ages 12 and 16 (M age= 16.55; SD= .60), a primary caregiver of the participants completed questionnaires on peer problems.

Monte Carlo simulation-based power calculations performed in MPlus, version 8 (Muthén & Muthén, 2002) indicated that the secured sample size has sufficient power (.80) to detect unconditional and conditional (moderated) indirect effects of at least β=.11, even when participants with missing data are excluded.

Study procedures were approved by local commissions on child protection in Bucharest, the Romanian Ministry of Health, an ethics committee of Bucharest University, and institutional review boards of the institutions of the three principal investigators, including Boston Children's Hospital, Tulane University, and University of Maryland. Consent was obtained from children's legal guardian and assent was obtained from the children.

Physiological Baseline and Peer Evaluation Task at Age 12

Participants completed resting and task-based SNS activity assessments on the same day. Thirty minutes after arrival to the laboratory, participants sat quietly without moving while wearing ECG equipment for 5 min, during which baseline resting period was collected.

The peer evaluation task, adapted from a computerized social rejection task called the Chatroom (Guyer et al., 2008) designed for children and adolescents, took place over two sessions. The first session was completed on a prior day without physiological data collection. Participants were led to believe that they would play a game to learn how children choose friends and were presented with 30 photographs of children along with brief profiles of each child including information on their (1) favorite sport, (2) favorite food, and (3) favorite music/band/singer. Participants were told that they would have an opportunity to meet one of the other children in a subsequent visit and were asked to select 10 children that they were most interested in meeting. Then the participants had their own pictures taken and provided information about their favorite sport, food, and music/band/singer to create their own profile. Participants were told that the 30 other children would view the participants' picture and profile and decide whether they want to meet the participant.

In the session with physiological data recording on a subsequent day, participants were told that each of the 30 children had decided whether they wanted to meet the participant. Participants were then told that they would learn which of these children wanted to meet them. Trained experimenters delivered feedback about how the participants were ostensibly rated by other children in several phases. The photos of the 30 other children were arranged on two boards, one green and one red. The 10 photos of the children who the participants wanted to meet were placed on the green board; the 20 photos of children who the participant did not want to meet were placed on a red board. Children were told that each photo would be moved to another set of two new boards– photos moved to the green board were children who wanted to meet the participants, whereas photos moved to the red board were children who did not want to meet the participants.

First, the experimenter delivered feedback about 5 of the 10 children who the participant wanted to meet. Each of these photos were moved to the red board, indicating that these children did not want to meet the participant. Next, the experimenter delivered feedback about 10 of the 20 children who the participant did not want to meet. Half of the photos were moved to the green board, and half were moved to the red board. These two rounds of feedback were repeated for the remaining 5 children, who the participant wanted to meet, followed by the 10 children who the participant did not want to meet. The experimenters were trained to provide feedback every 20 seconds throughout the feedback phase and pretended to read responses off a piece of paper with responses of the 30 children about the participant. Physiological responses were recorded during the 2 min periods

when experimenters provided rejection feedback about the 10 children who the participant preferred and who did not want to meet the participant (i.e., 0 out of the 10 children wanted to meet the participants). After the task, participants reported their emotions using a visual-analog scale by circling a face that best described how they felt (*1*=more positive affect; *5*= more negative affect) (see Supplemental Figure S1). Research assistants then debriefed the participants about the true nature of the task and communicated that the other children had never provided evaluations of them and that the feedback that was given was not real.

Physiological Data Analysis

ECG and ICG data were scored by blinded raters. Signals were averaged into 1 min epochs using Mindware Software (Mindware Technologies). PEP, a measure of sympathetic nervous system activation, representing the amount of time that elapses from the beginning of ventricular depolarization to the opening of the aortic valve (electrical systole), was calculated based on the ECG and ICG signals. The Q onset in the ECG and B onset in the ICG were placed using validated automated scoring algorithms (Berntson, Lozano, Chen, & Cacioppo, 2004; Lozano et al., 2007) that were visually inspected to ensure accurate placement and adjusted if needed. Stroke volume (SV), estimated from the *dz/dt* signal, provided an estimate of the amount of blood ejected from the heart on each cardiac cycle (Sherwood et al., 1990). There was high reliability across the two rejection feedback periods for PEP reactivity (r=. 97, p< .001). PEP reactivity scores were calculated by subtracting the mean value at baseline from the mean across the two social rejection periods. More negative values of PEP reactivity reflect greater sympathetic activation.

Adolescent Friendship Quality at Age 12

Participants completed the Friendship Quality Questionnaire (Parker & Asher, 1993), which measured multiple dimensions of relationship quality with reference to their best friend. The six dimensions of friendship quality include validation and caring, conflict resolution, conflict and betrayal, help and guidance, companionship and recreation, and intimate exchange. Examples of items include “would like me even if others didn’t” and “loan each other things all the time”. Items were rated on a 5-point scale (*0*= not at all true; *4*= really true). A total score of friendship quality was calculated by averaging the five dimensions measuring positive aspects of friendship quality which were correlated (r’s = .38 to .69, p’s < .001), excluding conflict and betrayal, which was uncorrelated or weakly correlated with the other five dimensions (r’s = −.03 to −.21) (Blair et al., 2014). This total scale showed strong internal consistency (α= .91).

Peer problems at Ages 12 and 16

Foster parents of the FCG and parents of the NIG completed the MacArthur Health and Behavior Questionnaire (Essex et al., 2002). For children living in institutions, a caregiver who knew the child best completed the questionnaire. The HBQ measures symptoms of mental and physical health problems, as well as social and school functioning of the child. Peer problems were measured using two subscales: (1) peer acceptance/rejection and (2) bullying. Example items include, “actively disliked by other kids, who reject him/her from their activities”, and “is teased or ridiculed by other kids”. Items were rated on a 4-point

scale (*1*= not at all like child; *4*= very much like child). In this sample, the subscales showed strong consistency (α = .87 to .93). Scores from the two subscales were combined to create a composite score of peer problems.

Data Analyses

Path analyses were performed in MPlus version 8 to test the study's hypotheses. To test whether PEP reactivity to peer rejection at age 12 indirectly explains the relation between study group and later peer problems, a simple mediation model was performed. To further test whether the indirect effects depended on levels of friendship quality, a moderated mediation model including an interactive pathway between PEP reactivity and friendship quality was performed. To assess the first aim examining the effect of institutionalization compared to never-institutionalized children, the models included two dummy-coded group variables with the NIG as the reference (CAUG vs. NIG and FCG vs. NIG) (Hayes & Preacher, 2014). To test the second aim assessing the effect of foster care compared to care as usual, the model was run again with CAUG coded as the reference (FCG vs. CAUG and NIG vs. CAUG). Statistical significance of indirect effects was determined with 10,000 bootstrapped 95% bias-corrected confidence intervals (CI; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002; Preacher & Hayes, 2008). Conditional effects of friendship quality on the indirect effect was assessed at high and low (±1 *SD*) levels of friendship quality. Moderators and mediators were mean-centered before creating the interaction terms.

In all models, we adjusted for sex differences and prior peer problems at age 12 (i.e., peer problems at age 16 was regressed on peer problems at age 12 and sex; PEP reactivity was regressed on sex). Residual covariances among predictors and the mediator were included, resulting in fully saturated models, thus we do not report model fit. Full information maximum likelihood estimation was used to reduce potential bias in parameter estimates due to missing data and to analyze all available data (i.e., *N*=271, 68 CAUG, 68 FCG, 135 NIG) (Enders & Bandalos, 2001). Individuals with missing data did not differ from those without missing data on key variables, including peer problems (p= .518), friendship quality (p= .839) and PEP reactivity (p= .776) at age 12, nor demographic variables, such as sex (p= .979). There were more missing data in the NIG compared to the CAUG and FCG (p< .001) since the NIG did not always return to the study. The percentage of participants with missing data in each group varied across variables of interest (PEP reactivity: 38% CAUG, 31% FCG, 65% FCG; friendship quality: 29% CAUG, 27% FCG, 63% NIG, peer problems at age 12: 19% CAUG, 24% FCG, 63% NIG; peer problems at age 16: 29% CAUG, 31% FCG, 66% NIG). However, we ensured that the recruited NIG always matched on sex and age to the CAUG and FCG.

In sensitivity analyses, the mediation and moderated mediation models were repeated using Bayesian path analyses in MPlus, version 8. Bayesian estimation performs better with smaller datasets and does not assume normality of distribution in the indirect effects compared to the maximum likelihood estimation and bootstrapping method in the main analysis (Van De Schoot, Broere, Perryck, Zondervan-Zwijnenburg, & Van Loey, 2015). Bayesian path analyses were estimated using Markov Chain Monte Carlo (MCMC) simulations and Gibb's algorithms. Samples were derived from 2 chains and 200,000

iterations, with the first 100,000 iterations as the "burn-in" phase which did not represent the posterior distribution. To derive indirect effects with two-tailed 95% credibility intervals and one-tailed p-values from posterior probability distributions, the input data were expressed as standardized values. Normally distributed informative priors for regression coefficients of the effect of group on PEP reactivity (CAUG vs NIG: β= .80, *SD*= .10; FCG vs NIG: β = .51, *SD*= .15; FCG vs CAUG: β= −.29, *SD*= .08), and the effect of PEP reactivity on social problems (β= .31, *SD*= .03) were expressed as standardized values and *SDs*. These priors were based on our previous report showing moderate to large effects of institutionalization and foster care intervention on PEP reactivity to various social stressors at age 12 (CAUG vs NIG: β=.65 to .95; FCG vs NIG: β= .44 to .58; FCG vs CAUG: β = −.21 to −.37) (McLaughlin et al., 2015), and a moderate association between PEP reactivity to social rejection and peer problems at age 12 (*r*=.31) (Table 2). A similar effect size for the relation between cardiac responses to social exclusion and peer problems (β= .30) also has been reported in another study (White et al., 2020). For the interaction effect between friendship quality and PEP reactivity, we used a medium effect size (β=.35, *SD*=.10). Convergence of the model was determined with a strict potential scale reduction (PSR) criterion value of 1.01 (Gelman et al., 2013). Model fit was determined with posterior predictive p-value between .05 to .50 (values close to .50 indicating excellent fit) and 95% confidence intervals for the chi-square difference between observed and simulated data, with the center of the interval being close to zero (Asparouhov & Muthén, 2020).

Results

Preliminary Analyses

Task effect.—Task effects have been previously reported (McLaughlin et al., 2015). In the full sample, peer rejection feedback elicited greater PEP (*M*=97.33; *SD*= 9.85) compared to baseline (*M*=98.90; *SD*=9.75), *t*(135)= − 5.14, *p*< .001. This indicated that peer rejection engaged SNS activation. Greater PEP reactivity to rejection feedback correlated with more negative affect reported after the task, (*r*= −.21, *p*= .015), indicating that changes in sympathetic reactivity was a correlate of negative affect linked to social rejection.

Descriptive statistics of measures across groups are reported in Table 1. Group contrasts using *t*-tests showed group differences in peer problems at ages 12 and 16, with the ever-institutionalized groups (both CAUG and FCG) showing more problems than the NIG. The FCG and CAUG showed comparable levels of peer problems at ages 12 and 16. For physiological and behavioral responses to the rejection task at age 12, the CAUG and FCG showed less PEP reactivity (i.e., less sympathetic activation) and more positive affect after the task compared to the NIG, as previously reported (McLaughlin et al., 2015). The CAUG and FCG did not differ in PEP reactivity and affective ratings after the task. There were no group differences in friendship quality at age 12.

Bivariate correlations among measures collapsed across groups are reported in Table 2. Less PEP reactivity to rejection feedback at age 12 correlated with more peer problems at ages 12 and 16 (*r's*= .29 to .31, *p's* <.001). Friendship quality at age 12 was not concurrently related to PEP reactivity or peer problems at age 12, but was related to fewer peer problems at age 16 (*r*= −.20, *p* <.05).

Effect of Early Institutionalization

Mediation.—The first question addressed whether PEP reactivity to social rejection mediates the effect of early institutionalization on peer problems. In the simple mediation model, both the CAUG and FCG showed less PEP reactivity (i.e., less sympathetic activation) to peer rejection at age 12; in turn, less PEP reactivity to peer rejection was related to greater in later peer problems at age 16 (Table 3). Follow-up analyses showed that the indirect effect via PEP reactivity to rejection in the associations between early institutionalization (i.e., both CAUG and FCG) and later peer problems were significantly different than zero relative to the NIG (Table 4A).

Moderated Mediation.—The second question addressed whether high quality friendship can attenuate the effect of early institutionalization on peer problems. Results from the moderated mediation (Figure 2A) showed that the indirect effect of study group on peer problems via PEP reactivity depended on friendship quality, $\beta = -.17$, $b = -.04$, $SE = .02$, $p < .05$ (Table 3). Simple slopes tests of this interaction indicated that at low (b=.05, SE=.02, p=.005), but not high (b=.00, SE=.01, p=.969), levels of friendship quality, less PEP reactivity at age 12 predicted more peer problems at age 16 (Figure 2B). Similarly, follow-up analyses revealed significant conditional indirect effects at low, but not high, levels of friendship quality (Table 4B): Among adolescents with a history of institutionalization (i.e., CAUG and FCG) with low quality friendships, less PEP reactivity predicted more peer problems, compared to the NIG. In contrast, the indirect effects were not statistically significant at high levels of friendship quality (Table 4B), indicating that high-quality friendships diminished this indirect effect.

Intervention Effect of Foster Care

To assess the intervention effect of foster care, we compared the FCG to the CAUG by repeating the prior models, whereby the reference group was changed to the CAUG. Results from the simple mediation model showed that the FCG and CAUG did not differ in the magnitude or direction of any path coefficients for direct effects on the outcome, mediator (Supplemental Table S1), nor indirect effect (Supplemental Table S2). Likewise, in the moderated-mediation model, none of the path coefficients (Supplemental Table S1) nor the conditional indirect effects (Supplemental Table S2) were statistically different.

Sensitivity Analysis

Results from the sensitivity analyses using Bayesian estimation revealed a similar pattern of results in the mediation model and moderated mediation models (Supplemental Table S3). In examining the effect of early institutionalization (i.e., CAUG and FCG) on peer problems, the unconditional indirect effect via less PEP reactivity was statistically significant at one-tailed p-values <. 05, though the two-tailed credibility intervals included zero. The conditional indirect effect through low friendship quality was also significant, as indicated by both one-tailed p-values < .05 and credibility intervals that did not include zero. In examining the effect of foster care intervention, we again found no statistically significant differences in the unconditional and conditional indirect effects between the FCG and CAUG (Supplemental Table S3).

Discussion

This study leverages data from the BEIP to examine sympathetic reactivity to social rejection feedback as a developmental pathway linking early institutional rearing with peer difficulties and the protective role of supportive friendships. Results showed that less PEP reactivity to social rejection feedback at age 12 partially explained the association between early institutionalization and greater peer problems at age 16, when previously institutionalized adolescents had low-quality friendships at age 12. In contrast, these indirect effects were not evidenced in previously institutionalized adolescents who had high-quality friendships at age 12. We found no effect of foster care intervention compared to care as usual in any direct or indirect effects. These findings suggest that blunted sympathetic responses to social rejection might play a role in contributing to greater peer problems following early institutionalization. However, the development of supportive friendships can diminish the effect of blunted sympathetic reactivity on further peer problems.

The mediating role of blunted sympathetic reactivity to social rejection feedback converge with studies of humans and animal models, which suggest that dysregulated stress physiology as a pathway through which early adverse caregiving experiences contribute to social and emotional difficulties (Gunnar, 2000; Lupien et al., 2009; McEwen, 2004). Our findings extend prior work reporting blunted HPA responses to strangers and novelty mediate the relations between early institutionalization and peer and externalizing problems in early childhood (Koss et al., 2016; Pitula et al., 2017). Less sympathetic reactivity in the context of social rejection observed among previously institutionalized adolescents might reflect fearlessness or unresponsiveness to being rejected. This interpretation aligns with their positive affective ratings after the task compared to the NIG who reported more negative affect, and aligns with studies showing associations between blunted sympathetic responses, callousness and poor social functioning (T. P. Beauchaine et al., 2007; Hinnant et al., 2016; Obradović et al., 2011; Ortiz & Raine, 2004). Under-responsiveness to social rejection can lead to inappropriate behavioral adaptation in social interactions, as hypo-arousal of the sympathetic adrenomedullary system influences individuals' attentional processes (Giuliano, Karns, Bell, et al., 2018; Giuliano, Karns, Roos, et al., 2018; Hajcak, McDonald, & Simons, 2003) and reaction to cues of punishment (van Honk, Schutter, Hermans, & Putman, 2003). Over time, bidirectional transactions among inappropriate interactions with peers, adverse peer experiences, including social withdrawal, a lack of peer relationships, and maladjustment are expected (Deater-Deckard, 2001; Rubin, Bukowski, & Parker, 2007). In fact, post-institutionalized youth are known to exhibit persistent insensitive social behaviors (Bruce et al., 2009; Guyon-Harris et al., 2018; Humphreys, McGoron, et al., 2015; Sonuga-Barke et al., 2010) and peer problems, including peer rejection which are associated with their inattentive and aggressive behaviors (Humphreys, Gabard-Durnam, et al., 2018; Pitula et al., 2017). Together, these findings suggest the ways in which blunted sympathetic reactivity to peer rejection might lead to further peer problems. However, we cannot establish discriminant predictive utility of peer rejection feedback beyond the social evaluative context of the task without data in other conditions. For example, blunted sympathetic reactivity to peer acceptance could also be related to inadequate behavioral and affective responses in peer interactions that contribute to social problems.

In addressing the role of friendships, we found that high-quality friendships diminished the effect of blunted SNS reactivity on peer problems in previously institutionalized youths in the main analysis and sensitivity analysis. This finding suggests that positive friendships, which provide adolescents with social support beyond parental figures, can remediate some harmful effects of early institutionalization. These results extend prior studies reporting that high-quality friendships help to reduce maladjustment in children and adolescents exposed to other forms of early adversity (Bolger et al., 1998; Criss et al., 2002; van Harmelen et al., 2016), or negative parenting (Gaertner et al., 2010; Lansford et al., 2003). Supportive friendships in adolescence may function in several ways to reduce peer problems such as peer victimization (Bollmer, Milich, Harris, & Maras, 2005; Kendrick, Jutengren, & Stattin, 2012). First, supportive friendships provide companionship and opportunities for socialization and developing social skills, including learning how to positively reciprocate with each other (i.e., talking, laughing), how to handle social conflicts, and what social norms to follow (Bukowski, Newcomb, & Hartup, 1998; Hartup & Stevens, 1997; Sullivan, 2013). Second, from a social capital perspective, supportive friendships are social resources that provide emotional support, self-esteem, and knowledge to help adolescents adjust to later challenges (Bukowski et al., 1998; Hartup & Stevens, 1997; Rubin et al., 2004; Sullivan, 2013). Third, from an attachment perspective, supportive friendships in previously institutionalized adolescents may compensate for missing close caregiving relationships (Nickerson & Nagle, 2005) to alter negative trajectories. These examples demonstrate the potential positive developmental significance of supportive friendships in previously institutionalized adolescents.

In assessing the effect of foster care intervention, we were unable to find statistically significant intervention effects in the main analysis and sensitivity analysis. This null effect might be due to statistical power limitations linked to our modest sample size, as such this result is interpreted with caution. Though, in line with this null effect, our prior studies in this sample suggest that foster care is effective in reversing negative outcomes in some, but not all, aspects of peer and social functioning. For example, in childhood, the FCG has better social communication skills (Levin et al., 2015) and is less verbally reticent during an interaction with an unfamiliar peer compared to the CAUG (Almas et al., 2015); however, the two groups show comparable displays of socially withdrawn (e.g., onlooking) and engaged (e.g., cooperative) behaviors during the peer interaction (Almas et al., 2015). Other negative social outcomes that are not eradicated by foster care intervention alone include peer rejection and victimization problems in adolescence (Table 1), which persist into adolescence. Furthermore, our previous study showed that while the foster care intervention remediated SNS reactivity to performance stressors, it did not improve SNS reactivity to peer evaluation measured in the current task (McLaughlin et al., 2015). The present findings and nuances in which specific outcomes the foster care intervention can improve do not invalidate prior beneficial effects of foster care documented in other development domains (Debnath, Tang, Zeanah, Nelson, & Fox, 2019; Humphreys, Miron, et al., 2018; Johnson et al., 2018; Nelson et al., 2007; Wade, Fox, Zeanah, & Nelson, 2018), nor the beneficial effects of supportive friendships.

The protective effects of supportive friendships have implications for interventions. Establishing and maintaining high-quality friendships require the ability to appropriately

reciprocate during peer interactions, which can be difficult tasks for previously institutionalized children. Interventions that improve social communication skills, such as listening to their peers to understand others' perspectives and responding empathically, and interpersonal problem-solving skills, such as controlling negative emotions and behaviors while resolving peer-conflicts, might be beneficial. As these adolescents age into adulthood, it would be important to examine other significant sources of social support, such as romantic partners, as buffers against maladjustment in adulthood.

Our findings are considered based on several strengths and limitations. Strengths include a longitudinal randomized design and theoretically grounded mediation models with variables and covariates in appropriate temporal sequences to support causal inferences about biological mechanisms. We also used a laboratory-based task to examine autonomic responses to peer rejection feedback at salient social development stages. However, there were several limitations. First, autonomic data were not collected during acceptance conditions. As such we cannot provide discriminant validity or draw definitive conclusions about task manipulation based on differences between acceptance compared to rejection conditions, beyond the peer evaluative component of the task. Second, even though the passive receipt of rejection feedback reduces artifacts in the autonomic data, this design did not allow for participant interactions. Third, friendship quality was self-reported, which reflect the participants' subjective perception, and peer problems were reported by parents which may not provide a holistic perspective of peer problems in school settings. As such, it would be important for future studies to obtain more objective peer-nominations. Fourth, due to small sample sizes, we were unable to examine interactions with sex. To our knowledge, no prior studies have examined sex interactions in the relations between the SNS and peer problems among previously institutionalized adolescents, though studies of typically developing adolescents suggest sex differences in some forms of peer victimization (i.e., physical bullying) (Hong & Espelage, 2012) and some aspects of friendships (i.e., expression of intimacy) (Hussong, 2000; Rose & Rudolph, 2006). Future studies should use larger sample sizes to examine potential sex differences in this developmental pathway. Finally, while our goal was to identify how friendship might exert its protective effect on peer outcomes, we cannot establish causal relations between friendship and peer problems. Even though friendship quality with a best friend and peer likability and victimization by peers (measured by our peer problems composite) are distinct constructs theoretically and empirically (Table 2), it is possible that these relations are driven by a third unmeasured construct. For example, children with certain personalities (e.g., sociable) or children who were already more socially competent, would be able to attract supportive friendships and might be more resilient to peer rejection and victimization.

In conclusion, blunted sympathetic reactivity to social rejection is one pathway that links early institutionalization with peer difficulties in adolescence, though this pathway depends on friendship quality. These findings have implications for targeting stress-regulation early in life and/or building social skills and peer support systems of institutionalized children to alter adverse developmental pathway

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

We thank the participants and families for supporting this research. This research was supported by the John D. and Catherine T. MacArthur Foundation, the Binder Family Foundation, the Jacobs Foundation, and the National Institute of Mental Health (R01MH091363) to CA Nelson and the Palix Foundation to CH Zeanah.

References

Almas AN, Degnan KA, Walker OL, Radulescu A, Nelson CA, Zeanah CH, & Fox NA (2015). The effects of early institutionalization and foster care intervention on children's social behaviors at the age of eight. Social Development, 24(2), 225–239. [PubMed: 26294847]

Asher SR, & Paquette JA (2003). Loneliness and peer relations in childhood. Current Directions in Psychological Science, 12(3), 75–78.

Asparouhov T, & Muthén B (2020). Advances in Bayesian model fit evaluation for structural equation models. Structural equation modeling: a multidisciplinary journal, 1–14.

Beauchaine T (2001). Vagal tone, development, and Gray's motivational theory: Toward an integrated model of autonomic nervous system functioning in psychopathology. Development and psychopathology, 13(2), 183–214. [PubMed: 11393643]

Beauchaine TP, Gatzke-Kopp L, & Mead HK (2007). Polyvagal theory and developmental psychopathology: Emotion dysregulation and conduct problems from preschool to adolescence. Biological psychology, 74(2), 174–184. [PubMed: 17045726]

Beauchaine TP, & Thayer JF (2015). Heart rate variability as a transdiagnostic biomarker of psychopathology. International Journal of Psychophysiology, 98(2), 338–350. [PubMed: 26272488]

Berntson GG, & Cacioppo JT (2007). Integrative physiology: Homeostasis, allostasis and the orchestration of systemic physiology. Handbook of psychophysiology, 3, 433–452.

Berntson GG, Lozano DL, Chen YJ, & Cacioppo JT (2004). Where to Q in PEP. Psychophysiology, 41(2), 333–337. [PubMed: 15032999]

Blair BL, Perry NB, O'Brien M, Calkins SD, Keane SP, & Shanahan L (2014). The indirect effects of maternal emotion socialization on friendship quality in middle childhood. Developmental Psychology, 50(2), 566. [PubMed: 23795555]

Bolger KE, Patterson CJ, & Kupersmidt JB (1998). Peer relationships and self-esteem among children who have been maltreated. Child development, 69(4), 1171–1197. [PubMed: 9768492]

Bollmer JM, Milich R, Harris MJ, & Maras MA (2005). A friend in need: The role of friendship quality as a protective factor in peer victimization and bullying. Journal of interpersonal violence, 20(6), 701–712. [PubMed: 15851537]

Brown BB (2004). Adolescents' relationships with peers. Handbook of adolescent psychology, 363–394.

Bruce J, Tarullo AR, & Gunnar MR (2009). Disinhibited social behavior among internationally adopted children. Development and psychopathology, 21(1), 157–171. [PubMed: 19144228]

Bukowski WM, Newcomb AF, & Hartup WW (1998). The company they keep: Friendships in childhood and adolescence: Cambridge University Press.

Carlson M, & Earls F (1997). Psychological and neuroendocrinological sequelae of early social deprivation in institutionalized children in Romania. Annals of the New York Academy of Sciences, 807(1), 419–428. [PubMed: 9071367]

Criss MM, Pettit GS, Bates JE, Dodge KA, & Lapp AL (2002). Family adversity, positive peer relationships, and children's externalizing behavior: A longitudinal perspective on risk and resilience. Child development, 73(4), 1220–1237. [PubMed: 12146744]

Crowell SE, Beauchaine TP, Gatzke-Kopp L, Sylvers P, Mead H, & Chipman-Chacon J (2006). Autonomic correlates of attention-deficit/hyperactivity disorder and oppositional defiant disorder in preschool children. Journal of abnormal psychology, 115(1), 174. [PubMed: 16492108]

Deater-Deckard K (2001). Annotation: Recent research examining the role of peer relationships in the development of psychopathology. The Journal of Child Psychology and Psychiatry and Allied Disciplines, 42(5), 565–579. [PubMed: 11464962]

Debnath R, Tang A, Zeanah CH, Nelson CA, & Fox NA (2019). The Long-term effects of institutional rearing, foster care intervention and disruptions in care on brain electrical activity in adolescence. Developmental science, e12872. [PubMed: 31148302]

Del Giudice M, Ellis BJ, & Shirtcliff EA (2011). The adaptive calibration model of stress responsivity. Neuroscience & Biobehavioral Reviews, 35(7), 1562–1592. [PubMed: 21145350]

Diamond LM, & Cribbet MR (2013). Links between adolescent sympathetic and parasympathetic nervous system functioning and interpersonal behavior over time. International Journal of Psychophysiology, 88(3), 339–348. [PubMed: 22940642]

Enders CK, & Bandalos DL (2001). The relative performance of full information maximum likelihood estimation for missing data in structural equation models. Structural equation modeling, 8(3), 430–457.

Erath SA, & Tu KM (2014). Peer stress in preadolescence: Linking physiological and coping responses with social competence. Journal of Research on Adolescence, 24(4), 757–771.

Erol N, Simsek Z, & Münir K (2010). Mental health of adolescents reared in institutional care in Turkey: challenges and hope in the twenty-first century. European child & adolescent psychiatry, 19(2), 113–124. [PubMed: 19644732]

Esposito EA, Koss KJ, Donzella B, & Gunnar MR (2016). Early deprivation and autonomic nervous system functioning in post-institutionalized children. Developmental psychobiology, 58(3), 328–340. [PubMed: 26497289]

Essex MJ, Boyce WT, Goldstein LH, Armstrong JM, Kraemer HC, Kupfer DJ, & Group MABW (2002). The confluence of mental, physical, social, and academic difficulties in middle childhood. II: Developing the MacArthur Health and Behavior Questionnaire. Journal of the American Academy of Child & Adolescent Psychiatry, 41(5), 588–603. [PubMed: 12014792]

Gaertner AE, Fite PJ, & Colder CR (2010). Parenting and friendship quality as predictors of internalizing and externalizing symptoms in early adolescence. Journal of Child and Family Studies, 19(1), 101–108.

Gelman A, Carlin JB, Stern HS, Dunson DB, Vehtari A, & Rubin DB (2013). Bayesian data analysis: CRC press.

Giuliano RJ, Karns CM, Bell TA, Petersen S, Skowron EA, Neville HJ, & Pakulak E (2018). Parasympathetic and sympathetic activity are associated with individual differences in neural indices of selective attention in adults. Psychophysiology, 55(8), e13079. [PubMed: 29624675]

Giuliano RJ, Karns CM, Roos LE, Bell TA, Petersen S, Skowron EA, . . . Pakulak E (2018). Effects of early adversity on neural mechanisms of distractor suppression are mediated by sympathetic nervous system activity in preschool-aged children. Developmental Psychology, 54(9), 1674. [PubMed: 30148395]

Gunnar MR (2000). Early adversity and the development of stress reactivity and regulation. The effects of early adversity on neurobehavioral development, 31, 163–200.

Gunnar MR, Frenn K, Wewerka SS, & Van Ryzin MJ (2009). Moderate versus severe early life stress: Associations with stress reactivity and regulation in 10–12-year-old children. Psychoneuroendocrinology, 34(1), 62–75. [PubMed: 18835102]

Gunnar MR, & Van Dulmen MH (2007). Behavior problems in postinstitutionalized internationally adopted children. Development and psychopathology, 19(1), 129–148. [PubMed: 17241487]

Gunnar MR, & Vazquez DM (2001). Low cortisol and a flattening of expected daytime rhythm: Potential indices of risk in human development. Development and psychopathology, 13(3), 515–538. [PubMed: 11523846]

Guyer AE, Lau JY, McClure-Tone EB, Parrish J, Shiffrin ND, Reynolds RC, . . . Fox NA (2008). Amygdala and ventrolateral prefrontal cortex function during anticipated peer evaluation in pediatric social anxiety. Archives of general psychiatry, 65(11), 1303–1312. [PubMed: 18981342]

Guyer AE, Silk JS, & Nelson EE (2016). The neurobiology of the emotional adolescent: From the inside out. Neuroscience & Biobehavioral Reviews, 70, 74–85. [PubMed: 27506384]

Guyon-Harris KL, Humphreys KL, Fox NA, Nelson CA, & Zeanah CH (2018). Course of disinhibited social engagement disorder from early childhood to early adolescence. Journal of the American Academy of Child & Adolescent Psychiatry, 57(5), 329–335. e322. [PubMed: 29706162]

Hajcak G, McDonald N, & Simons RF (2003). To err is autonomic: Error-related brain potentials, ANS activity, and post-error compensatory behavior. Psychophysiology, 40(6), 895–903. [PubMed: 14986842]

Hartup WW, & Stevens N (1997). Friendships and adaptation in the life course. Psychological bulletin, 121(3), 355.

Hawk BN, & McCall RB (2014). Perceived relationship quality in adolescents following early social-emotional deprivation. Clinical child psychology and psychiatry, 19(3), 439–459. [PubMed: 23785051]

Hayes AF, & Preacher KJ (2014). Statistical mediation analysis with a multicategorical independent variable. British Journal of Mathematical and Statistical Psychology, 67(3), 451–470. [PubMed: 24188158]

Hinnant JB, Erath SA, Tu KM, & El-Sheikh M (2016). Permissive parenting, deviant peer affiliations, and delinquent behavior in adolescence: The moderating role of sympathetic nervous system reactivity. Journal of abnormal child psychology, 44(6), 1071–1081. [PubMed: 26667026]

Hodges J, & Tizard B (1989). Social and family relationships of ex-institutional adolescents. Journal of Child Psychology and Psychiatry, 30(1), 77–97. [PubMed: 2925822]

Hong JS, & Espelage DL (2012). A review of research on bullying and peer victimization in school: An ecological system analysis. Aggression and violent behavior, 17(4), 311–322.

Humphreys KL, Gabard-Durnam L, Goff B, Telzer EH, Flannery J, Gee DG, . . . Tottenham N (2018). Friendship and social functioning following early institutional rearing: The role of ADHD symptoms. Development and psychopathology, 1–11.

Humphreys KL, Gleason MM, Drury SS, Miron D, Nelson CA 3rd, Fox NA, & Zeanah CH (2015). Effects of institutional rearing and foster care on psychopathology at age 12 years in Romania: follow-up of an open, randomised controlled trial. The Lancet Psychiatry, 2(7), 625–634. [PubMed: 26303560]

Humphreys KL, McGoron L, Sheridan MA, McLaughlin KA, Fox NA, Nelson CA III, & Zeanah CH (2015). High-quality foster care mitigates callous-unemotional traits following early deprivation in boys: a randomized controlled trial. Journal of the American Academy of Child & Adolescent Psychiatry, 54(12), 977–983. [PubMed: 26598472]

Humphreys KL, Miron D, McLaughlin KA, Sheridan MA, Nelson CA, Fox NA, & Zeanah CH (2018). Foster care promotes adaptive functioning in early adolescence among children who experienced severe, early deprivation. Journal of Child Psychology and Psychiatry, 59(7), 811–821. [PubMed: 29389015]

Hussong AM (2000). Distinguishing mean and structural sex differences in adolescent friendship quality. Journal of Social and Personal Relationships, 17(2), 223–243.

Johnson DE, Tang A, Almas AN, Degnan KA, McLaughlin KA, Nelson CA, . . . Drury SS (2018). Caregiving disruptions affect growth and pubertal development in early adolescence in institutionalized and fostered Romanian children: A randomized clinical trial. The Journal of pediatrics, 203, 345–353. e343. [PubMed: 30172435]

Kendrick K, Jutengren G, & Stattin H (2012). The protective role of supportive friends against bullying perpetration and victimization. Journal of adolescence, 35(4), 1069–1080. [PubMed: 22464910]

Koss KJ, Hostinar CE, Donzella B, & Gunnar MR (2014). Social deprivation and the HPA axis in early development. Psychoneuroendocrinology, 50, 1–13. [PubMed: 25150507]

Koss KJ, Mliner SB, Donzella B, & Gunnar MR (2016). Early adversity, hypocortisolism, and behavior problems at school entry: A study of internationally adopted children. Psychoneuroendocrinology, 66, 31–38. [PubMed: 26773398]

Lansford JE, Criss MM, Pettit GS, Dodge KA, & Bates JE (2003). Friendship quality, peer group affiliation, and peer antisocial behavior as moderators of the link between negative parenting and adolescent externalizing behavior. Journal of Research on Adolescence, 13(2), 161–184. [PubMed: 20209019]

Levin AR, Fox NA, Zeanah CH Jr, & Nelson CA (2015). Social communication difficulties and autism in previously institutionalized children. Journal of the American Academy of Child & Adolescent Psychiatry, 54(2), 108–115. e101. [PubMed: 25617251]

Lozano DL, Norman G, Knox D, Wood BL, Miller BD, Emery CF, & Berntson GG (2007). Where to B in dZ/dt. Psychophysiology, 44(1), 113–119. [PubMed: 17241147]

Lupien SJ, McEwen BS, Gunnar MR, & Heim C (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nature reviews neuroscience, 10(6), 434. [PubMed: 19401723]

McEwen BS (2004). Protection and damage from acute and chronic stress: allostasis and allostatic overload and relevance to the pathophysiology of psychiatric disorders. Annals of the New York Academy of Sciences, 1032(1), 1–7. [PubMed: 15677391]

McLaughlin KA, Sheridan MA, Tibu F, Fox NA, Zeanah CH, & Nelson CA (2015). Causal effects of the early caregiving environment on development of stress response systems in children. Proceedings of the National Academy of Sciences, 201423363.

Muthén LK, & Muthén BO (2002). How to use a Monte Carlo study to decide on sample size and determine power. Structural equation modeling, 9(4), 599–620.

Nelson CA, Zeanah CH, Fox NA, Marshall PJ, Smyke AT, & Guthrie D (2007). Cognitive recovery in socially deprived young children: The Bucharest Early Intervention Project. Science, 318(5858), 1937–1940. [PubMed: 18096809]

Nickerson AB, & Nagle RJ (2005). Parent and peer attachment in late childhood and early adolescence. The Journal of Early Adolescence, 25(2), 223–249.

Obradović J, Bush NR, & Boyce WT (2011). The interactive effect of marital conflict and stress reactivity on externalizing and internalizing symptoms: The role of laboratory stressors. Development and psychopathology, 23(1), 101–114. [PubMed: 21262042]

Ortiz J, & Raine A (2004). Heart rate level and antisocial behavior in children and adolescents: A meta-analysis. Journal of the American Academy of Child & Adolescent Psychiatry, 43(2), 154–162. [PubMed: 14726721]

Parker JG, & Asher SR (1993). Friendship and friendship quality in middle childhood: Links with peer group acceptance and feelings of loneliness and social dissatisfaction. Developmental Psychology, 29(4), 611.

Pitula CE, DePasquale CE, Mliner SB, & Gunnar MR (2017). Peer problems among postinstitutionalized, internationally adopted children: Relations to hypocortisolism, parenting quality, and ADHD symptoms. Child development.

Pitula CE, Thomas KM, Armstrong JM, Essex MJ, Crick NR, & Gunnar MR (2014). Peer victimization and internalizing symptoms among post-institutionalized, internationally adopted youth. Journal of abnormal child psychology, 42(7), 1069–1076. [PubMed: 24619483]

Porges SW (2007). The polyvagal perspective. Biological psychology, 74(2), 116–143. [PubMed: 17049418]

Raaska H, Lapinleimu H, Sinkkonen J, Salmivalli C, Matomäki J, Mäkipää S, & Elovainio M (2012). Experiences of school bullying among internationally adopted children: results from the Finnish Adoption (FINADO) study. Child Psychiatry & Human Development, 43(4), 592–611. [PubMed: 22362203]

Richter M, & Gendolla GH (2009). The heart contracts to reward: Monetary incentives and preejection period. Psychophysiology, 46(3), 451–457. [PubMed: 19226305]

Rose AJ, & Rudolph KD (2006). A review of sex differences in peer relationship processes: potential trade-offs for the emotional and behavioral development of girls and boys. Psychological bulletin, 132(1), 98. [PubMed: 16435959]

Rubin KH, Bukowski WM, & Parker JG (2007). Peer interactions, relationships, and groups. Handbook of child psychology, 3.

Rubin KH, Dwyer KM, Booth-LaForce C, Kim AH, Burgess KB, & Rose-Krasnor L (2004). Attachment, friendship, and psychosocial functioning in early adolescence. The Journal of Early Adolescence, 24(4), 326–356. [PubMed: 16703116]

Rutter M, Beckett C, Castle J, Colvert E, Kreppner J, Mehta M, . . . Sonuga-Barke E (2007). Effects of profound early institutional deprivation: An overview of findings from a UK longitudinal study of Romanian adoptees. European Journal of Developmental Psychology, 4(3), 332–350.

Sebastian C, Viding E, Williams KD, & Blakemore S-J (2010). Social brain development and the affective consequences of ostracism in adolescence. Brain and cognition, 72(1), 134–145. [PubMed: 19628323]

Sherwood A, Allen MT, Fahrenberg J, Kelsey RM, Lovallo WR, & Van Doornen LJ (1990). Methodological guidelines for impedance cardiography. Psychophysiology, 27(1), 1–23. [PubMed: 2187214]

Sonuga-Barke EJ, Schlotz W, & Kreppner J (2010). V. Differentiating developmental trajectories for conduct, emotion, and peer problems following early deprivation. Monographs of the Society for Research in Child Development, 75(1), 102–124. [PubMed: 20500635]

Stroud LR, Foster E, Papandonatos GD, Handwerger K, Granger DA, Kivlighan KT, & Niaura R (2009). Stress response and the adolescent transition: Performance versus peer rejection stressors. Development and psychopathology, 21(1), 47–68. [PubMed: 19144222]

Sullivan HS (2013). The interpersonal theory of psychiatry: Routledge.

Tang A, Almas AN, Zeytinoglu S, Zeanah CH, Nelson CA, & Fox NA (In press). Long-term effects of institutional rearing and enhanced attachment relationships on adolescent friendships. Child development.

Tang A, Lahat A, Crowley MJ, Wu J, & Schmidt LA (2019). Neurodevelopmental differences to social exclusion: An event-related neural oscillation study of children, adolescents, and adults. Emotion, 19(3), 520. [PubMed: 29781644]

Van De Schoot R, Broere JJ, Perryck KH, Zondervan-Zwijnenburg M, & Van Loey NE (2015). Analyzing small data sets using Bayesian estimation: The case of posttraumatic stress symptoms following mechanical ventilation in burn survivors. European Journal of Psychotraumatology, 6(1), 25216. [PubMed: 25765534]

van den Bos E, de Rooij M, Miers AC, Bokhorst CL, & Westenberg PM (2014). Adolescents' increasing stress response to social evaluation: Pubertal effects on cortisol and alpha-amylase during public speaking. Child development, 85(1), 220–236. [PubMed: 23638912]

van Harmelen A-L, Gibson JL, St Clair MC, Owens M, Brodbeck J, Dunn V, . . . Kievit RA (2016). Friendships and family support reduce subsequent depressive symptoms in at-risk adolescents. PLoS One.

van Honk J, Schutter DJ, Hermans EJ, & Putman P (2003). Low cortisol levels and the balance between punishment sensitivity and reward dependency. Neuroreport, 14(15), 1993–1996. [PubMed: 14561936]

Vorria P, Ntouma M, & Rutter M (2014). The behaviour of adopted adolescents who spent their infancy in residential group care: the Greek Metera study. Adoption & Fostering, 38(3), 271–283.

Wade M, Fox NA, Zeanah CH, & Nelson CA (2018). Effect of foster care intervention on trajectories of general and specific psychopathology among children with histories of institutional rearing: a randomized clinical trial. JAMA psychiatry, 75(11), 1137–1145. [PubMed: 30267045]

Waldrip AM, Malcolm KT, & Jensen-Campbell LA (2008). With a little help from your friends: The importance of high-quality friendships on early adolescent adjustment. Social Development, 17(4), 832–852.

White LO, Bornemann B, Crowley MJ, Sticca F, Vrtička P, Stadelmann S, . . . von Klitzing K (2020). Exclusion Expected? Cardiac Slowing Upon Peer Exclusion Links Preschool Parent Representations to School-Age Peer Relationships. Child development.

Zeanah CH, Nelson CA, Fox NA, Smyke AT, Marshall P, Parker SW, & Koga S (2003). Designing research to study the effects of institutionalization on brain and behavioral development: The Bucharest Early Intervention Project. Development and psychopathology, 15(4), 885–907. [PubMed: 14984131]

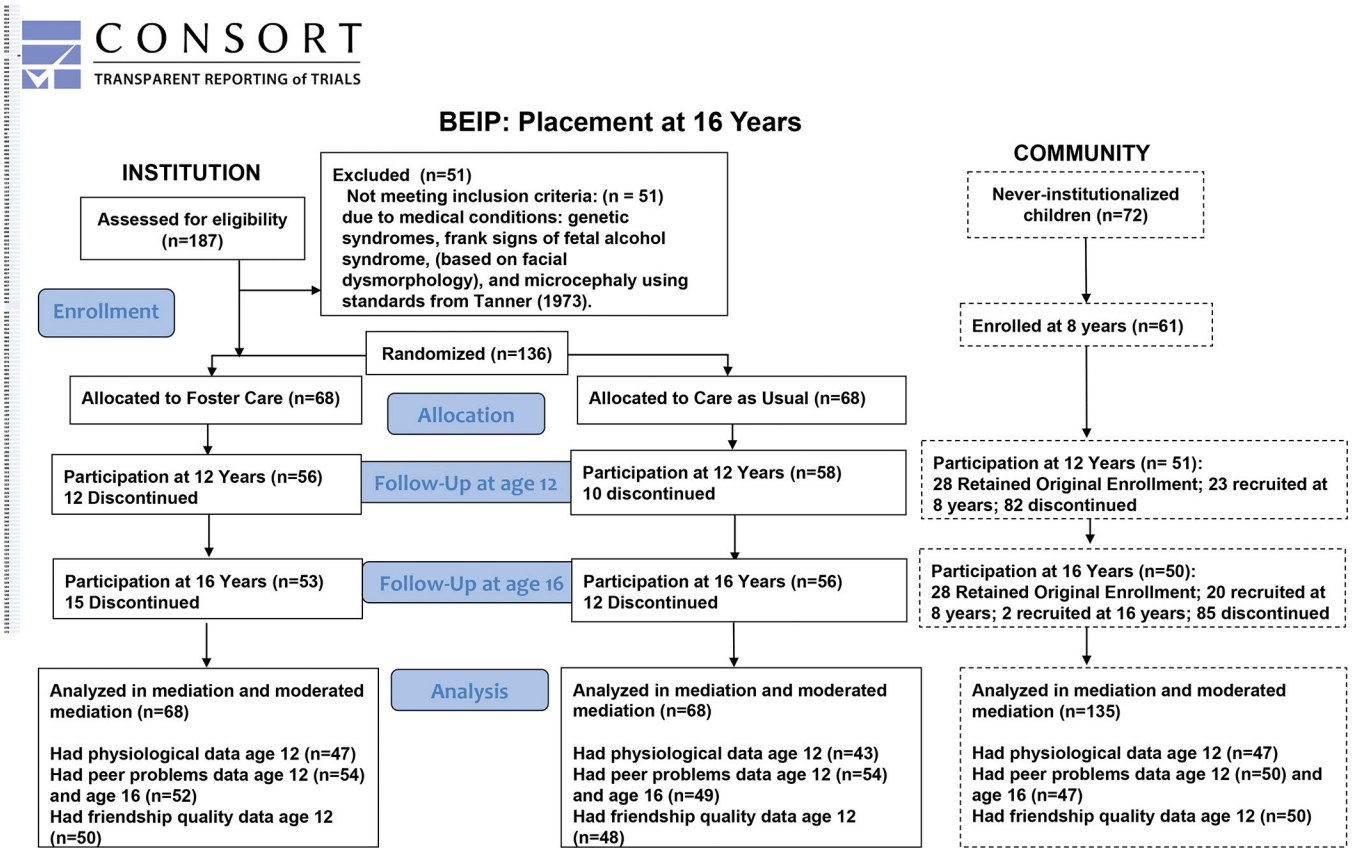

Figure 1.
CONSORT diagram.

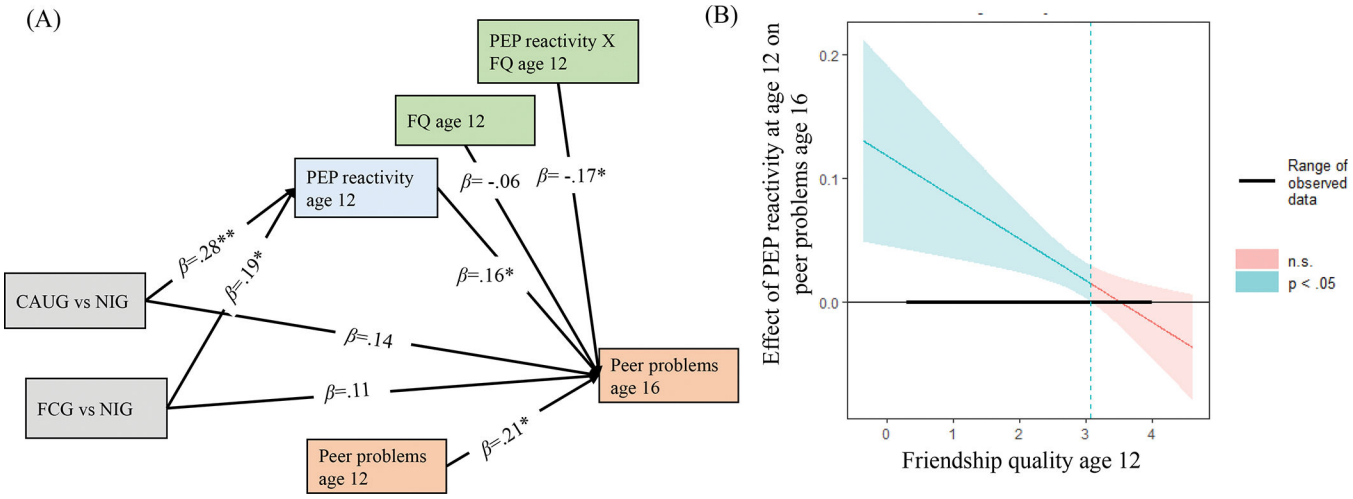

Figure 2.

Results from the moderated mediation model and (B) interaction between PEP reactivity to peer rejection feedback and friendship quality on peer problems.

Note. **p< .001. *p< .05. FQ= friendship quality. PEP= pre-ejection period. Standardized estimates are shown in path diagram. Group was dummy coded with NIG as the reference. To test the intervention effect, the analyses were run again with CAUG as the reference group. Paths accounting for sex are not shown for simplicity but are in Table 3.

Table 1.

Descriptive statistics

	NIG	CAUG	FCG	p values from group contrasts		
	***M* ±*SD* (Range)**			**CAUG vs NIG**	**FCG vs NIG**	**CAUG vs FCG**
PEP reactivity to peer rejection age 12	−2.85 ± 4.61 (−16.55, 3.30)	−.50 ± 2.41 (−5.61, 7.10)	−1.25 ± 2.84 (−9.85, 3.40)	.004	.046	.183
Affect after peer rejection age 12[a]	2.26 ± .68 (1.00, 3.00)	1.63 ± .79 (1.00, 5.00)	1.87 ± .65 (1.00, 3.00)	<.001	.006	.110
Friendship quality age 12	3.06 ± .66 (.31, 4.00) IQR= .78	2.84 ± .64 (1.41, 3.89) IQR= 1.02	2.88 ± .62 (1.66, 3.96) IQR= .85	.102	.168	.760
Peer problems age 12	1.29 ± .39 (1.00, 2.55)	1.80 ± .66 (1.00, 3.81)	1.67± .58 (1.00, 3.25)	<.001	<.001	.277
Peer problems age 16	1.19 ± .31 (1.00, 2.29)	1.60 ± .55 (1.00, 3.39)	1.52 ± .65 (1.00, 3.41)	<.001	.002	.534
Sex (*n* female, %)	71 (52.6%)	35 (51.5%)	34 (50.0%)			
Ethnicity (%)						
Romanian	91.90%	50.00%	61.00%			
Roma	7.10%	37.50%	25.50%			
Other or unknown	1.00%	12.50%	13.50%			
Age at foster care placement (months)	--	--	22.63 (6.81, 33.01)			

Note. NIG= Never-institutionalized group. CAUG= Care as usual group. FCG= Foster care group. PEP= pre-ejection period. PEP and affective ratings (n=137), friendship quality (*n*=148), peer problems at age 12 (*n*= 158) and age 16 (*n*= 148). Age at foster care placement (*n*=65).

[a]Higher values indicate negative affect.

Table 2.

Bivariate correlations among variables

	1	2	3	4	5	6
1. PEP reactivity to peer rejection age 12	--					
2. Affect after peer rejection age 12[a]	−.21*	--				
3. Friendship quality age 12	−.06	−.13	--			
4. Peer problems age 12	.31**	−.05	−.02	--		
5. Peer problems age 16	.29**	−.14	−.20*	.37**	--	
6. Sex (male)	.08	.20*	−.34**	.09	.30*	--
Age at foster care placement	−.05	−.02	−.19	.10	.19	.26

Note.

** $p < .001$.

* $p < .05$.

PEP= pre-ejection period. PEP and affective ratings (n=137), friendship quality (n=148), problems at age 12 (n= 158) and age 16 (n= 148). Age at foster care placement (n=65).

[a] Higher values indicate negative affect.

Table 3.

Results from mediation and moderated mediation models comparing institutionalized groups (i.e., CAUG and FCG) to the never institutionalized group (NIG).

	Simple mediation		Moderated mediation	
	β	***b (95% CI)***	***β***	***b (95% CI)***
Effect on mediator: PEP age 12				
CAUG vs NIG	.28**	2.31 (.90, 3.88)	.28**	2.32 (.89, 3.91)
FCG vs NIG	.19*	1.56 (.08, 3.15)	.19*	1.57 (.08, 3.17)
Sex (male)	0.05	.37 (−.80, 1.48)	0.05	.37 (−.80, 1.48)
Effect on outcome: peer problems age 16				
PEP age 12	.13*	.02 (.01, .04)	.16*	.02 (.01, .05)
CAUG vs NIG	.17*	.21 (.01, .42)	0.14	.17 (−.04, .39)
FCG vs NIG	0.13	.17 (−.00, .36)	0.11	.14 (−.03, .33)
Peer problems age 12	.24**	.22 (.07, .38)	.24**	.21 (.07, .38)
Sex (male)	.23**	.25 (.09, .42)	.21*	.23 (.05, .42)
FQ age 12			−0.07	−.06 (−.20,.09)
FQ X PEP			−.17*	−.04 (−.09, −.01)
R^2 PEP	.08		.08	
R^2 Peer problems age 16	.24		.27	

Note. N in analyses=271. Reference group was NIG= Never-institutionalized group. CAUG= Care as usual group. FCG= Foster care group. PEP= Pre-ejection period. FQ= Friendship quality.

** $p \leq .01$.

* $p \leq .05$.

Table 4.

Unstandardized indirect effects from the mediation model (A) and conditional indirect effects at low and high levels of friendship quality from the moderated mediation model (B).

	b **(95% CI)**	
(A) Indirect effects		
CAUG vs NIG	.045 (.005, .116)*	
FCG vs NIG	.030 (.001, .092)*	
(B) Conditional indirect effects	at low FO (−1 *SD*)	at high FO (+1 *SD*)
CAUG vs NIG	.112 (.031, .249)*	−.001 (−.079, .054)
FCG vs NIG	.076 (.007, .202)*	−.001 (−.056, .039)

Note. N in analyses=271. NIG= Never-institutionalized group. CAUG= Care as usual group. FCG= Foster care group. FQ= Friendship quality. CI=confidence intervals.

* $p<.05$.