Biological Psychology 120 (2016) 108–119

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Cardiovascular reactivity as a mechanism linking child trauma to adolescent psychopathology

Charlotte Heleniak[a,*], Katie A. McLaughlin[a], Johan Ormel[b], Harriette Riese[b]

[a] Department of Psychology, University of Washington, Seattle WA, USA
[b] Interdisciplinary Center Psychopathology and Emotion regulation, Department of Psychiatry, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

ARTICLE INFO

Article history:
Received 1 September 2015
Received in revised form 22 August 2016
Accepted 22 August 2016
Available online 24 August 2016

Keywords:
Cardiovascular system
Stress reactivity
Trauma
Child maltreatment
Adolescence
Internalizing
Externalizing

ABSTRACT

Alterations in physiological reactivity to stress are argued to be central mechanisms linking adverse childhood environmental experiences to internalizing and externalizing psychopathology. Childhood trauma exposure may influence physiological reactivity to stress in distinct ways from other forms of childhood adversity. This study applied a novel theoretical model to investigate the impact of childhood trauma on cardiovascular stress reactivity – the biopsychosocial model of challenge and threat. This model suggests that inefficient cardiovascular responses to stress – a *threat* as opposed to *challenge* profile – are characterized by blunted cardiac output (CO) reactivity and increased vascular resistance. We examined whether childhood trauma exposure predicted an indicator of the threat profile of cardiovascular reactivity and whether such a pattern was associated with adolescent psychopathology in a population-representative sample of 488 adolescents (M = 16.17 years old, 49.2% boys) in the TRacking Adolescents' Individual Lives Survey (TRAILS). Exposure to trauma was associated with both internalizing and externalizing symptoms and a pattern of cardiovascular reactivity consistent with the threat profile, including blunted CO reactivity during a social stress task. Blunted CO reactivity, in turn, was positively associated with externalizing, but not internalizing symptoms and mediated the link between trauma and externalizing psychopathology. None of these associations varied by gender. The biopsychosocial model of challenge and threat provides a novel theoretical framework for understanding disruptions in physiological reactivity to stress following childhood trauma exposure, revealing a potential pathway linking such exposure with externalizing problems in adolescents.

1. Introduction

Patterns of physiological reactivity to stress have frequently been shown to be disrupted following exposure to adverse childhood environments (Ellis, Essex, & Boyce, 2005; Gunnar, Morison, Chisholm, & Schuder, 2001; Gunnar, Sebanc, Tout, Donzella, & van Dulmen, 2003). These disruptions in stress response system functioning have been proposed as a predominant mechanism linking experiences of childhood adversity to risk for psychopathology (Ellis & Boyce, 2008; Tarullo & Gunnar, 2006). This work has led to the development of several influential theories regarding the role of adverse early environments in shaping the development of stress response systems and, ultimately, risk for psychopathology (Boyce & Ellis, 2005; Del Giudice, Ellis, & Shirtcliff, 2011; Ellis & Boyce, 2008; Tarullo & Gunnar, 2006). However, a central limitation in prior work on early adversity and stress reactivity has been a failure to distinguish between distinct forms of childhood adversity. Although support for existing theoretical models has been found in studies of children exposed to chronic stressors (e.g., family conflict, low socio-economic status) (Ellis et al., 2005; Evans & Kim, 2007; Gunnar, Frenn, Wewerka, & Van Ryzin, 2009), the predictions of these models are not consistent with patterns of stress reactivity observed in children exposed to traumatic events (e.g. child abuse, domestic violence), which we define as the unexpected experience of actual or threatened death, injury, sexual violation, or other harm to one's physical integrity, consistent with the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013). In the current paper we examine an alternative model – the biopsychosocial model of challenge and threat – for explaining patterns of physiological reactivity to stress among adolescents exposed to a diverse range of traumatic events.

* Corresponding author at: Department of Psychology, University of Washington, Box 351525, Seattle, WA 98195, USA.
E-mail address: heleniak@u.washington.edu (C. Heleniak).

http://dx.doi.org/10.1016/j.biopsycho.2016.08.007
0301-0511/

The prevailing model of the development of individual differences in stress reactivity – the biological sensitivity to context theory (Boyce & Ellis, 2005; Ellis et al., 2005) – posits that many children exposed to either high levels of stress or to very protected environments develop sensitivity to these environments characterized by heightened sympathetic nervous system (SNS) reactivity. This heightened SNS response is argued to be developmentally adaptive in that heightened reactivity may prepare children to be hyper-vigilant in dangerous environments, as well as to be most receptive to the benefits of adaptive environments (Ellis et al., 2005). Evidence from samples of children exposed to chronic family stressors (e.g., marital conflict, poverty, and parental mental illness) have generally supported this theory (Blair, Granger, & Razza, 2005; Ellis et al., 2005; Evans & Kim, 2007; Feldman et al., 2009; Obradović, Bush, Stamperdahl, Adler, & Boyce, 2010). However the predictions of biological sensitivity to context theory are inconsistent with a growing body of evidence that children exposed to traumatic stressors display a physiological stress response pattern characterized by blunted, not heightened, sympathetic nervous system reactivity (Cooley-Quille, Boyd, Frantz, & Walsh, 2001; Gump, Reihman, Stewart, Lonky, & Darvill, 2005; McLaughlin, Sheridan, Alves, & Mendes, 2014; Oosterman, De Schipper, Fisher, Dozier, & Schuengel, 2010).

The biological sensitivity to context theory has recently been extended to account for a more diverse range of physiological responses to stress in children exposed to adversity. The adaptive calibration model predicts that distinct stress-response profiles will emerge depending on the quality of early life experiences (Del Giudice, Benjamin, Ellis, & El-Sheikh, 2012; Del Giudice et al., 2011). Of these, the profile most relevant to this study posits that children reared in dangerous and unpredictable environments will develop stress reactivity patterns and their behavioral correlates that vary by gender, due to differences in stress response profiles that have evolved to enhance reproductive selection in severe environments. In particular, the adaptive calibration model argues that males will exhibit a pattern of blunted physiological reactivity and females will display heightened physiological reactivity following childhood exposure to traumatic stress. This theory is supported by several studies that have found that stress reactivity interacts with gender to predict psychopathology among children exposed to non-traumatic stressors such as marital conflict and harsh parenting (El-Sheikh, Keller, & Erath, 2007; Erath, El-Sheikh, & Mark Cummings, 2009). However, previous studies of children exposed to traumatic stress have not observed sex differences in patterns of physiological reactivity (Cooley-Quille et al., 2001; Gump et al., 2005; McLaughlin et al., 2014; Oosterman et al., 2010 Oosterman et al., 2010).

Both the biological sensitivity to context and adaptive calibration models predict cardiovascular reactivity profiles among children exposed to adversity (e.g. heightened reactivity, or reactivity that differs by gender) that have not been supported by research on youth exposed specifically to trauma. In the current study we apply an alternative theoretical model to better characterize physiological reactivity patterns in adolescents exposed to traumatic stress: the biopsychosocial model of challenge and threat. This model differentiates between adaptive and maladaptive patterns of response to acute stressors based on specific patterns of cardiovascular reactivity (Mendes, Blascovich, Major, & Seery, 2001; Mendes, Major, McCoy, & Blascovich, 2008). According to the theory (Blascovich, Mendes, Hunter, Lickel, & Kowai-Bell, 2001; Blascovich & Tomaka, 1996), appraisals that one's resources exceed situational demands are accompanied by an adaptive "challenge" response, in which increases in SNS activation are accompanied by increases in cardiac output (CO) and arterial vasodilation that facilitates the delivery of oxygen, glucose, and other nutrients to the brain and peripheral tissues. In contrast, appraisals that the demands of the situation exceed one's own resources to cope are paired with a maladaptive "threat" response consisting of SNS activation – although typically less SNS response than in challenge states (Mendes et al., 2008) – accompanied by static or blunted increases in CO and increased vascular resistance. This latter style of physiological responding has been associated with poor cognitive, affective, and behavioral responses to laboratory stressors, in both males and females (Drach-Zahavy & Erez, 2002; Jamieson, Nock, & Mendes, 2012; Tomaka, Blascovich, Kelsey, & Leitten, 1993).

We recently examined the utility of the biopsychosocial theory in characterizing patterns of cardiovascular reactivity in a sample of adolescents exposed to trauma related to physical and sexual abuse. Exposure to child maltreatment was associated with a pattern of cardiovascular reactivity consistent with threat; specifically, both male and female maltreated adolescents experienced similar, although slightly reduced, increases in SNS activation as those with no maltreatment history to a social-evaluative stressor but exhibited significantly blunted increases in CO and greater increases in peripheral vascular resistance (McLaughlin et al., 2014). This study provides preliminary evidence for the utility of the biopsychosocial model as a tool for differentiating adaptive and maladaptive patterns of physiological reactivity following traumatic stress; however, it represents the only existing test of the theory in youths exposed to trauma and was focused on a sample of youths exposed to physical and sexual abuse, a severe traumatic stressor. Given the high prevalence of exposure to trauma in adolescents (McLaughlin et al., 2013), we examined whether the biopsychosocial model explained patterns of cardiovascular reactivity in adolescents exposed to a wider range of more commonly occurring traumatic events. Specifically, we examined whether trauma exposure was associated with an indicator of the pattern of cardiovascular reactivity consistent with threat using data from a large population-based sample of adolescents with exposure to a wide range of traumatic events including natural disasters, accidents, inter-parental violence, and other forms of victimization.

In addition, we examined whether an indicator of the threat pattern of cardiovascular reactivity was associated with adolescent internalizing and externalizing psychopathology. Consistent evidence suggests that patterns of cardiovascular responding are associated with internalizing and externalizing psychopathology in youth (Beauchaine, Gatzke-Kopp, & Mead, 2007; Boyce, 2001; Crowell et al., 2006; El-Sheikh, 2005; Fowles, Kochanska, & Murray, 2000; Graziano & Derefinko, 2013; Shannon, Beauchaine, Brenner, Neuhaus, & Gatzke-Kopp, 2007; Weems, Zakem, Costa, Cannon, & Watts, 2005). Children and adolescents who report higher levels of internalizing problems, including symptoms of anxiety and depression, exhibit a distinctive pattern of heightened SNS and blunted parasympathetic nervous system (PNS) response to stress (Boyce, 2001; El-Sheikh, 2005; Fowles et al., 2000; Graziano & Derefinko, 2013; Obradović, Bush, & Boyce, 2011; Shannon et al., 2007; Weems et al., 2005). In contrast, a growing body of literature has identified blunted SNS reactivity – indicated by smaller reduction in the pre-ejection period (PEP) interval during a challenge task as compared to baseline – as a neurobiological marker of child and adolescent externalizing psychopathology including disruptive behavior disorders, conduct disorder, and attention deficit hyperactivity disorder (Beauchaine et al., 2007; Boyce, 2001; Crowell et al., 2006; Shannon et al., 2007). Interestingly, the same physiological pattern of blunted SNS responding has been identified in children and adolescents exposed to trauma (Cooley-Quille et al., 2001; Gump et al., 2005; Oosterman et al., 2010), suggesting that blunted SNS might be a mechanism linking trauma exposure with externalizing psychopathology. Indeed, in the one previous study examining trauma and CO reactivity in adolescents, blunted CO reactivity to a social stressor was associated with elevated symptoms of externalizing psychopathology (McLaughlin et al., 2014).

The present study examined whether exposure to traumatic stress in childhood is associated with blunted SNS and CO reactivity to stress using data from a large, population-representative cohort of adolescents from the Dutch TRacking Adolescents' Individual Lives Survey (TRAILS). We did not examine increased vascular resistance as a second indicator of the "threat" profile because it was not recorded during the task of interest in our study. Although the threat and challenge profiles are defined using measures of both cardiac output and vascular resistance, either measure can be conceptualized as an indicator of cardiovascular efficiency and used to distinguish the threat from the challenge profile (Blascovich, Seery, Mugridge, Norris, & Weisbuch, 2004; Mendes et al., 2008). Given growing evidence that slower cardiovascular recovery to baseline is associated with social stressors perceived as uncontrollable and may be an additional cardiac marker of a threat response (e.g., Dickerson & Kemeny, 2004), we also conducted an exploratory analysis examining the associations of CO recovery following stress with trauma exposure and with symptoms of psychopathology. We examined three hypotheses: (a) greater exposure to traumatic experiences would be associated with blunted SNS reactivity – measured using PEP reactivity – to a social evaluative stressor; (b) greater exposure to trauma would be associated with blunted CO reactivity and slower recovery characteristic of the "threat" response predicted by biopsychosocial theory; (c) that blunted CO reactivity and recovery would be associated with elevated symptoms of externalizing psychopathology among adolescents. Given sex differences in physiological reactivity during adolescence (Gunnar et al., 2009; Stroud et al., 2009) and the hypothesized sex differences in physiological reactivity among youths with traumatic stress exposure predicted by the adaptive calibration model, we tested whether these associations varied by gender. Finally, we examined whether blunted CO reactivity mediated the association between trauma and externalizing symptoms in a supplementary analysis.

2. Methods

2.1. Participants

Data were collected in a focus sample of TRAILS, a large prospective population study of Dutch adolescents with bi-or triennial measurements from age 11 years into adulthood. For a detailed description of this sample and how it was recruited please see Huisman et al. (2008). The first four assessment waves ran from March 2001 to July 2002 (T1), September 2003 to December 2004 (T2), September 2005 to December 2007 (T3), and October 2008 to September 2010 (T4). During T1, 2230 children were enrolled in the study (response rate 76.0%, de Winter et al., 2005), of whom 1816 (81.4% of the initial sample) participated in T3 and 1881 (84.3% of the initial sample) participated in T4. During T3, 744 adolescents were invited to perform a series of laboratory tasks (hereafter referred to as the experimental session) on top of the usual assessments, of whom 715 (96.1%) agreed to do so. The costly and labor-intensive nature of the laboratory tasks precluded assessing the whole sample.

Adolescents with an increased risk of mental health problems had a greater chance of being selected for the experimental session. Increased risk was defined based on temperament (high frustration and fearfulness, low effortful control), parental psychopathology (depression, anxiety, addiction, psychoses, or antisocial behavior), and environmental risk (living in a single-parent family) (Bouma, Riese, Ormel, Verhulst, & Oldehinkel, 2009). In total, 66.2% of the focus sample were randomly selected from the high-risk TRAILS participants and had at least one risk factor; the remaining 33.8% were randomly selected from the low-risk TRAILS participants. Exclusion criteria for selection included physical conditions that prohibit participation in the laboratory session and distance (>100 km from the laboratory). Although adolescents at elevated risk for psychopathology were oversampled, the sample included the total range of mental health problems present in a community population of adolescents, only in a different distribution. Almost all participants selected (n = 715, 96.1%) agreed to participate in the experimental session.

Participants who contributed valid electrocardiogram (ECG) and impedance cardiography (ICG) data were included in this study. Equipment malfunctions or poor quality data resulted in loss of cardiac autonomic nervous system data from 227 participants. As stress responses may be influenced by pubertal status (e.g. Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999), only females who had reached menarche prior to the experimental session were included. The final analytic sample included 488 participants (mean age 16.17, SD = 0.61, 49.2% boys). The ethnic composition of the study was largely of Dutch heritage (91.6%, n = 447), with the remaining 8.4% reporting ethnic minority status (n = 41). All procedures were approved by the Dutch Central Committee on Research Involving Human subjects (CCMO). Experiments were carried out with adequate understanding and written consent of all participants and one of their parents.

2.2. Procedure experimental session

During the experimental session, participants' electrocardiogram (ECG) and impedance cardiogram (ICG) data were acquired continuously while at rest and to a variety of challenging conditions, including orthostatic stress (from supine to standing), a spatial orienting task, a gambling task, a startle reflex task, and a social stress test. The test assistants, 16 in total, received extensive training in order to optimize standardization of the experimental session. The experimental sessions took place on weekdays, in soundproof rooms with blinded windows at selected locations in the towns where participants resided. The sessions lasted about 3 h and 15 min, and started between 08:00 and 09:30 a.m. (morning sessions, 49%), or between 01:00 and 02:30 p.m. (afternoon sessions, 51%). No differences were observed in cardiovascular reactivity based on the time of the session. Participants were asked to refrain from smoking and from using coffee, milk, chocolate, and other sugar containing foods in the 2 h before the session. At the start of the session, the test assistant explained the procedure and administered a short checklist on current medication use, quality of sleep, and physical activity in the last 24 h. Participants also filled out a number of questionnaires at the start and end of the session.

Participants were attached to the equipment for cardiovascular registrations, then asked to relax until 35 min after the start of the session. After this period of acclimation and rest, baseline physiological data were collected for five minutes during which participants were asked to sit quietly before completing the laboratory tasks in the aforementioned order. Although finger blood pressure data were acquired during the baseline, blood pressure was not recorded during the social stress task (described below) so that the participants could move their hands freely to express themselves during the task. Every task was followed by a short break. This social stress task was the last challenge of the experimental session. Thereafter, participants were debriefed about the experiment and could relax for about 35 min, after which cardiovascular measures were recorded once more for 5 min.

2.3. The Groningen social stress task (GSST)

The GSST (Bouma et al., 2009; Oldehinkel, Hartman, Nederhof, Riese, & Ormel, 2011) is inspired by the Trier Social Stress Task, a widely-used stress induction procedure that has been used with

children and adolescents (Buske-Kirschbaum et al., 1997; Stroud et al., 2009). Cardiovascular measures were recorded during multiple blocks: a 7-min speech preparation task, a 6-min speech task, a 3-min rest period, a 6-min arithmetic task and another final 3-min rest period. Participants were given seven minutes to prepare a speech about themselves and their lives and deliver this speech in front of a video camera. They were told that their videotaped performance would be judged on content of speech as well as on use of voice and posture, and rank-ordered by a panel of peers after the experiment. Next, participants were asked to speak continuously for the entire 6-min period. A research assistant watched the performance critically, without showing empathy or encouragement. After 6 min of speech, the participants were told that there was a problem with the computer and they had to sit still and be quiet for a 3-min period of rest. After the interlude, participants were instructed to subtract 17 repeatedly, starting with 13,278. Stress was further provoked by negative feedback by the research assistant, including remarks such as, "No, wrong again, begin at 13,278", "Stop wiggling your hands," or "You are too slow, be as quick as you can, we are running out of time." The GSST ended with another 3-min rest period.

For our primary reactivity analyses, we used cardiovascular data from the first minute of the rest condition and from the first minute of each portion of the task (preparation, speech, math), which is standard practice when examining speech and math tasks as reactivity is greatest during the first minute and habituates quickly (Blascovich, Vanman, Mendes, & Dickerson, 2011; Jamieson et al., 2012; Mendes et al., 2008). In exploratory recovery analyses, we used cardiovascular data from the first minute of the speech and math portions of the task and the third minute of their subsequent rest periods respectively.

2.4. Measures

2.4.1. Exposure to traumatic events

At T4, information on trauma exposure that had occurred prior to the experimental session was collected using two self-report instruments. A 10-item self-report questionnaire assessed sexual abuse as well as a number of other traumatic experiences before the age of 16 years (described before in Van der Knaap et al., 2014). Questions about sexual abuse assessed whether an adult family member, friend of the family or stranger had forced the respondent to look at or touch his/her genitals or masturbated in front of them attempted to have intercourse, or forced the respondent to have intercourse with them. Other traumatic events included in the assessment were life-threatening accidents, natural disaster, witnessing severe injury or death of another person, and being the victim of physical violence or assault, threatened with a weapon, held captive or abducted. These items were originally scored on a 3-point Likert scale ranging from 1 (no/never) to 3 (yes, several times). Family violence and physical abuse of the participant by parents/caregivers were assessed using a modified 15-item self-report version of the Conflict Tactics Scales (CTS; Straus, 1979). These items were originally scored on a 5-point Likert scale ranging from 1 (no/never) to 5 (very often). Each scale was summed, yielding total scores for each. As is typical of trauma assessment in community samples, the total score of each scale was positively skewed and kurtotic. The composite of each scale was logarithmically transformed to ensure normal distribution, then standardized. The standardized composites of the sexual abuse and other traumatic events scale and the modified CTS scale were summed together to create a Total Trauma Index.

2.4.2. Psychopathology

Internalizing and externalizing psychopathology were assessed at T3 using the Youth Self Report (YSR) form and the parent-report Child Behavior Checklist (CBCL, Achenbach, 1991). The YSR and CBCL scales are among the most widely used measures of youth emotional and behavioral problems and use extensive normative data to generate age-standardized estimates of severity of internalizing and externalizing psychopathology. The broadband internalizing scale is comprised of withdrawn/depressed (e.g., "I would rather be alone than with others), somatic complaints (e.g., "I feel overtired without good reason") and anxious/depressed (e.g., "I am nervous or tense") subscales. The broadband externalizing scale is comprised of rule-breaking behavior (e.g., "I don't feel guilty after doing something I shouldn't") and aggressive behavior (e.g., "I destroy things belonging to other") subscales. The internalizing and externalizing scales have demonstrated validity in discriminating between youths with and without psychiatric disorders (Achenbach, 1991; Chen, Faraone, Biederman, & Tsuang, 1994; Seligman, Ollendick, Langley, & Baldacci, 2004).

2.4.3. Physiological measures

A three-lead ECG and a four-lead ICG were registered using 3 M/RedDot – Ag/AgCl electrodes (type 2255, 3 M Health Care, D-41453 Neuss, Germany). With a BIOPAC Amplifier-System (MP100), the signals were amplified and filtered before digitization at 250 Hz. Dedicated software (PreCARSPAN, previously used in, e.g., Dietrich et al., 2006) was used to check the ECG signal, correct for artifacts, detect R-peaks, and to calculate the interbeat interval (IBI) between heartbeats in ms. IBI is inversely related to HR by the equation HR = 60000/IBI. HR was defined as the number of beats per minute (bpm).

Thoracic impedance was assessed with a BIOPAC NICO100C Noninvasive Cardiac Output Module. Test assistants were instructed to check all signals prior to starting the recording, including checking whether the upstroke of the dZ/dt signal was clearly visible and whether the Z0 value was approximately 10 ohm for the VU-AMS spot electrode configuration used (www.vu-ams.nl). VU-AMS interactive software was used to graphically display the large-scale ensemble ICG averages over each measurement block (Riese et al., 2003). PEP (in ms) reflects the time interval between the onset of the electromechanical systole (Q-wave onset) in the ECG and the opening of the aortic valves co-occurring with the B-point in the ICG. The LVET (in ms) is defined by the interval between the B-point and the X-point, which signals the closure of the aortic valves. The dZ/dt(min) (in Ω/s) is the difference in amplitude of the dZ/dt waveform at its peak compared to the B-point. The upstroke (or B-point), dZ/dt(min) and the incisura (or X-point) were automatically detected and subsequently inspected by an extensively trained rater. The ICG scoring principles given in the VU-AMS manual (2013) were followed. This resulted in PEP data for 488 participants in each portion of the GSST.

Together, these signals were used to create measures of stroke volume (SV), and cardiac output (CO). Stroke volume (SV) estimated from the dZ/dt signal using the Kubicek formula (Kubicek, Patterson, & Witsoe, 1970) provides an estimate of the amount of blood ejected from the heart on each cardiac cycle (in mL/min). We calculated SV using the following equation:

$$SV = \mathrm{rho}\,(L/Z0)2 * LVET * dZ/dt(\mathrm{min})$$

ICG was measured with spot electrodes and the distance between the electrodes was measured and used in the formula for each individual participant (L). Z0, LVET, dZ/dt(min) values are standard output variables in our ICG scoring program. Rho is a(n assumed) constant value referring to resistivity of blood. CO for each minute was calculated as SVxHR/1000, and is expressed in L/min.

2.4.5. ECG data cleaning

ECG blocks were considered invalid if they contained artifacts with a duration of more than 5 s, if the total artifact duration was more than 10% of the registration, or if the block length was less than 100 s.

2.4.6. ICG data cleaning

The VU-AMS software assembles data into 1-min averages, which were visually inspected and scored by a rater independent of participant characteristics. When there was doubt about a scoring point, the scoring was discussed with a second rater. Outliers were checked and quality of the ratings was subjectively scored on a 0–10 scale. When one of the 1-min epochs was distorted, all individual raw ICG complexes used for the 1-min average were visually inspected and when considered invalid the whole 1-min average was rejected. Data were considered invalid if the quality of the signal was low (i.e. score < 6), the signal contained too many artifacts (including participants marked with arrhythmias or extrasystoles during the ECG data cleaning procedure), or if values of z0 were outside the range of acceptable values for this equipment (McGrath, O'Brien, Hassinger, & Shah, 2005).

Sherwood et al. (1990) noted that Z0 values, used in the Kubicek formula to calculate SV and subsequently CO, are typically lower when derived from spot rather than band electrodes due to the smaller distance between the two inner (receiving) electrodes in the spot electrode configuration. This results in values of SV and CO that are *higher* and also often outside the range of what is typically observed when using band electrodes. For this reason, and because it is widely accepted that absolute raw CO values derived from ICG instruments cannot be reliably interpreted (Sherwood et al., 1990), we standardized the values for CO prior to examining reactivity and recovery in all analyses. This procedure is consistent with the conclusion reached by Sherwood et al. (1990) in their Methodological Guidelines paper on CO; namely, that CO values are only meaningful when examined as within-person change rather than raw values derived from ICG instruments. Our analysis thus focuses only on within-person change and not raw values of CO.

2.5. Statistical analysis

We approached missing data (0.01%–21.16% of our primary variables of interest), by using full-information maximum likelihood (FIML) estimation for all analyses in Mplus software (Muthén & Muthén, 1998). FIML estimation is generally considered to be superior to other approaches for handling missing data, such as list-wise deletion and imputation because they can generate biased estimates in comparison to FIML. This is particularly noteworthy in large samples, when FIML is typically robust to missing data (Schafer & Graham, 2002). However, to ensure that this method did not influence the results, we re-ran all analyses using list-wise deletion to handle missing data, and found an identical pattern of results in terms of both effect sizes and statistical significance.

Before testing our hypotheses, we calculated descriptive statistics of demographic and baseline variables used in this study, as well as Pearson correlations between predictor and outcome variables of interest and used linear regression to confirm that experimental start time (morning or afternoon) did not influence our parameters of cardiovascular reactivity. Next, we examined changes in PEP across all participants to determine if participants experienced SNS activation (a requirement for examining the threat/challenge distinction; Mendes et al., 2008).

Our hypotheses were tested with a series of linear regression analyses. First, we used linear regression to examine the associations of trauma exposure with each parameter of cardiovascular reactivity (PEP and CO). We additionally added a quadratic term to these regression models to determine the functional form of the associations between trauma exposure and cardiovascular reactivity and examined the difference in model fit between the linear and quadratic model. The linear model was a better fit for these models. Second, we evaluated whether cardiovascular reactivity was associated with internalizing and externalizing psychopathology using linear regression and determined whether associations between cardiovascular reactivity and internalizing and externalizing psychopathology remained significant after controlling for exposure to trauma exposure. Finally, we conducted a mediation analysis in SPSS software, using a standard bootstrapping approach that provides confidence intervals for indirect effects in statistical mediation estimated from 1000 resamples of the data (Preacher & Hayes, 2008), to determine whether cardiovascular reactivity associated with the threat profile mediated the association of trauma exposure with internalizing and externalizing psychopathology.

We additionally conducted several supplementary analyses. First, we evaluated whether the associations of trauma with cardiovascular reactivity varied by gender by creating interaction terms between gender and trauma history, and whether the associations of cardiovascular reactivity with psychopathology varied by gender by creating interaction terms between gender and cardiovascular reactivity. We used linear regression to test whether the interaction terms predicted outcome measures (i.e., cardiovascular reactivity and psychopathology respectively) using standard methods (Hayes & Matthes, 2009). Second, we examined whether trauma exposure and psychopathology were associated with slower post-task CO recovery to baseline levels, another potential indicator of a threat response, using linear regression.

In all models, cardiovascular reactivity was analyzed by entering the first minute of each parameter of cardiovascular reactivity during each task (preparation, speech, math) as outcome variables, which is standard practice when examining speech and math tasks as reactivity is greatest during the first minute and habituates quickly (Blascovich et al., 2011; Jamieson et al., 2012; Mendes et al., 2008), and then entering the first minute of each parameter of cardiovascular reactivity during rest (taken after 35 min of rest and adjustment to lab, prior to GSST) as a covariate in order to analyze cardiovascular change while controlling for individual differences at baseline. Similarly, we entered each cardiovascular parameter during rest as a covariate before entering the corresponding parameter during the first minute of each task as the independent variable in models where we examined cardiovascular reactivity as the predictor. In recovery analyses, we followed the same procedure, but entered cardiovascular data from the first minute of the speech and math portions of the task as covariates and examined the third minute of their subsequent rest periods as the primary outcome or predictor variables respectively.

Due to continuing controversy surrounding the validity of reporting absolute CO values (Sherwood et al., 1990), we only report CO difference scores so that these values, reported for reactivity scores as change in standard deviation units calculated by subtracting the baseline rest standardized CO value from the standardized CO value during the first minute of each task and for recovery scores as change in standard deviation units calculated by subtracting the standardized CO value during the first minute of the speech and math tasks from the standardized CO value during the third minute of their subsequent rest periods, can be interpreted. Age, gender, and maternal education, an indication of socio-economic status, were included as covariates in all analyses. Significance was evaluated at $p \leq 0.05$ using 2-tailed tests. We report all measures analyzed.

3. Results

3.1. Descriptive statistics

Table 1 provides the means and standard deviations of all measures separately for males and females. Table 2 provides the zero-order correlations among all measures of trauma exposure, pre-ejection period, cardiac output, and internalizing and externalizing symptoms. For raw CO difference scores for the whole sample and for trauma-exposed and non-trauma exposed adolescents separately, please see Appendix Table A1 in Supplementary data.

3.2. Trauma and psychopathology

Trauma history was associated strongly with both internalizing and externalizing psychopathology (Table 3). Trauma-psychopathology associations accounting for reactivity are shown in Appendix Table A2 in Supplementary data.

3.3. Trauma and cardiovascular reactivity

Our primary hypothesis was that greater exposure to trauma would be associated with an indicator of the threat profile of cardiovascular reactivity. We first examined changes in PEP to determine if participants experienced SNS activation (because the challenge/threat distinction can only be evaluated in the context of acute stressors that result in SNS activation). Significant increases in SNS activation (i.e., lower PEP than baseline based on paired-samples *t*-tests) were observed in the entire sample during the preparation ($t = 12.96$, $p < 0.001$), speech ($t = 26.18$, $p < 0.001$), and math ($t = 13.63$, $p < 0.001$), periods.

We next examined the association between trauma history and PEP reactivity. Greater exposure to trauma was significantly associated with blunted decreases in PEP reactivity during the speech period ($\beta = 0.09$, $p = 0.002$), but not the preparation ($\beta = 0.06$, $p = 0.097$) and math ($\beta = 0.05$, $p = 0.12$) periods.

Next, we examined CO reactivity, one of the variables that consistently differentiates challenge and threat. Trauma history was associated with smaller increases in CO reactivity during all three periods of the GSST: preparation ($\beta = -0.10$, $p = 0.001$), speech ($\beta = -0.09$, $p = 0.009$) and math ($\beta = -0.08$, $p = 0.004$) periods (Table 4).

3.4. Cardiovascular reactivity and psychopathology

We examined whether CO reactivity was related to psychopathology (Table 5). CO reactivity was consistently associated with adolescent-reported externalizing, but not internalizing, symptoms. These patterns were observed for CO reactivity during the preparation and math periods of the GSST, but not the speech. The associations of CO reactivity and parent report of psychopathology produced a similar pattern of results, with CO reactivity during the math period of the GSST negatively associated with the externalizing scale. After adjusting for trauma exposure in our analyses, the associations of CO reactivity with youth- and parent- reported externalizing psychopathology remained significant, though at trend-level for parent-reported symptoms (Appendix Table A3 in Supplementary data).

We also examined whether PEP reactivity was related to psychopathology (Table 6). Lower PEP reactivity (as indicated by greater reactivity scores) during the speech and math periods of the GSST was associated with parent-reported externalizing symptoms. All analyses examining the associations between PEP reactivity and psychopathology remained significant after controlling for trauma exposure (Appendix Table A4 in Supplementary data).

3.5. Mediation model

We investigated whether blunted CO reactivity associated with trauma exposure may be responsible for elevated rates of externalizing symptoms using a bootstrapping test of statistical mediation that derives confidence intervals from indirect effects estimated across 1000 resamples of data (Preacher & Hayes, 2008). Blunted CO reactivity during the preparation portion of the GSST significantly mediated the association between trauma exposure and youth-reported externalizing symptoms, 95% CI: (0.0008–0.0079), and blunted CO reactivity during the math portion of the GSST significantly mediated the association between trauma exposure and parent-reported externalizing symptoms 95% CI: (0.0001–0.0012). Because our data was not longitudinal, caution is warranted in interpretation of these mediation results (Maxwell & Cole, 2007).

3.6. Variation by gender

Interactions between sex and trauma were added to regression models examining the associations between trauma and cardiovascular reactivity. None of these interactions were significant (Table 4). Interactions between sex and cardiovascular reactivity were added to each of the models examining cardiovascular reactivity and psychopathology to determine whether associations varied by gender. In no cases were these interactions were significant (Appendix Tables A5 and A6 in Supplementary data).

3.7. Cardiovascular recovery

Finally, we examined whether trauma exposure was associated with slower post-speech and math recovery and whether slower recovery periods were associated with psychopathology. CO recovery from the first minute of the math task to the third minute of the subsequent rest period was negatively correlated with parent-reported externalizing symptoms ($\beta = 0.23$, $p = 0.034$). Additionally, CO recovery from the first minute of the speech task to the third minute of the subsequent rest period was negatively associated with parent-reported internalizing symptoms ($\beta = -0.25$, $p = 0.006$). Although psychopathology was associated with recovery, we found no associations with trauma exposure.

4. Discussion

Exposure to a wide range of adverse early environments, including traumatic events and chronic stressors that are not traumatic, has been consistently linked to atypical patterns of stress reactivity (Cooley-Quille et al., 2001; De Bellis, MD et al., 1994; Elzinga et al., 2008; McLaughlin et al., 2014; Ornitz & Pynoos, 1989). Existing conceptual models are supported by evidence from samples of children exposed to a range of chronic stressors, including poverty, family psychopathology, and marital conflict (Blair et al., 2005; Ellis et al., 2005; Evans & Kim, 2007; Feldman et al., 2009; Obradović et al., 2010); however, these models do not sufficiently describe patterns of physiological reactivity among children who have experienced traumatic stressors that involve harm or threat of harm. The current study applied an alternative conceptual model for explaining patterns of stress reactivity in youths exposed to traumatic stressors using a large population-based sample of adolescents. We found that exposure to trauma was associated with a pattern of cardiovascular reactivity consistent with a threat profile, including blunted CO during a social stress task. Blunted CO, in turn, was positively associated with externalizing symptoms, which were elevated in adolescents with a history of trauma exposure. Taken together,

Table 1
Means and Standard Deviations of trauma exposure, pre-ejection period, standardized cardiac output difference scores, and internalizing and externalizing symptoms by gender.

Measure	Males		Females		Gender Difference
	Mean	(SD)	Mean	(SD)	t
1. Trauma	−0.09	(1.29)	−0.11	(1.35)	0.14
2. PEP bl	123.07	(20.44)	127.02	(17.66)	2.19*
3. PEP prep	115.20	(22.20)	115.88	(19.84)	0.34
4. PEP speech	103.92	(19.67)	102.22	(18.54)	0.94
5. PEP math	114.30	(21.47)	115.69	(18.50)	0.73
6. zCO dprep	−0.10	(0.47)	0.03	(0.52)	2.87**
7. zCO dspeech	−0.12	(0.73)	0.12	(0.76)	3.46*
8. zCO dmath	−0.08	(0.78)	0.07	(0.65)	2.27*
9. YSR int	0.23	(0.20)	0.38	(0.26)	6.33**
10. YSR ext	0.34	(0.24)	0.30	(0.21)	1.75
11. CBCL int	0.17	(0.16)	0.22	(0.23)	2.35*
12. CBCL ext	0.19	(0.21)	0.16	(0.18)	1.57

Note: Trauma = Total Trauma Index, calculated by summing the standardized composites of the sexual abuse and other traumatic events scale and the modified CTS scale; PEP bl, prep, speech, math = pre-ejection period at baseline rest and at the first minutes of speech preparation, speech, and math during GSST; zCO dprep, dspeech, dmath = change in cardiac output standard deviation units from baseline rest to the first minutes of speech preparation, speech, and math during GSST; YSR int = Youth Self Report internalizing scale; YSR ext = Youth Self Report externalizing scale; CBCL int = Child Behavior Checklist internalizing scale; CBCL ext = Child Behavior Checklist externalizing scale.
* $p < 0.05$
** $p < 0.01$.

Table 2
Correlations of trauma exposure, pre-ejection period, standardized cardiac output, and internalizing and externalizing symptoms.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Trauma	–												
2. PEP bl	−0.02	–											
3. PEP prep	0.06	0.64**	–										
4. PEP speech	0.10*	0.51**	0.78**	–									
5. PEP math	0.05	0.63**	0.87**	0.82**	–								
6. zCO dprep	−14**	−0.04	−0.24**	−0.19**	−0.18**	–							
7. zCO dspeech	−0.12*	−0.04	−0.21**	−0.30**	−0.21**	0.69**	–						
8. zCO dmath	−0.12*	−0.08	−0.24**	−0.23**	−0.31**	0.72**	0.79**	–					
9. YSR int	0.27**	0.08	0.02	<−0.01	0.05	−0.06	0.04	−0.01	–				
10. YSR ext	0.26**	0.02	0.05	0.08	0.06	−0.15**	−0.07	−0.09	0.35**	–			
11. CBCL int	0.16**	0.03	<−0.01	<−0.01	0.03	−0.07	−0.01	−0.05	0.45**	0.13**	–		
12. CBCL ext	0.22**	<0.01	0.04	0.11*	0.10*	0.05	−0.04	0.09	0.16**	0.37**	0.62**	–	

Note: Trauma = Total Trauma Index, calculated by summing the standardized composites of the sexual abuse and other traumatic events scale and the modified CTS scale; PEP bl, prep, speech, math = pre-ejection period at baseline rest and at the first minutes of speech preparation, speech, and math during GSST; zCO dprep, dspeech, dmath = change in cardiac output standard deviation units from baseline rest to the first minutes of speech preparation, speech, and math during GSST; YSR int = Youth Self Report internalizing scale; YSR ext = Youth Self Report externalizing scale; CBCL int = Child Behavior Checklist internalizing scale; CBCL ext = Child Behavior Checklist externalizing scale.
* $p < 0.05$.
** $p < 0.01$.

Table 3
Trauma and psychopathology.[a,b]

	Youth Self Report									
	Internalizing					Externalizing				
	β	b	t	df	p-value	β	b	t	df	p-value
Trauma	0.27**	0.05	5.33	419	<0.001	0.29**	0.05	5.37	425	<0.001
	Child Behavior Checklist									
	Internalizing					Externalizing				
	β	b	t	df	p-value	β	b	t	df	p-value
Trauma	0.16**	0.03	3.10	412	0.002	0.20**	0.03	3.60	413	<0.001

* $p < 0.05$. ** $p < 0.01$.
[a] Linear regressions controlling for age, gender, maternal education.
[b] t-values are calculated using the Mplus Est/S.E. output for the linear regression models reported (Prescott, 2004).

these findings suggest that the biopsychosocial model of challenge and threat may be a useful framework for conceptualizing patterns of stress reactivity following trauma exposure and understanding their role in the onset of adolescent externalizing psychopathology.

Established models of the development of individual differences in stress reactivity posit that adversity predisposes children to become acutely responsive to environmental stressors, and to develop a variety of biological and behavioral stress responses consistent with heightened arousal (Boyce & Ellis, 2005; Del Giudice et al., 2011). However, multiple studies have observed that children exposed to specific kinds of trauma such as abuse, terrorist attacks, and community violence, display patterns of blunted SNS reactivity (Cooley-Quille et al., 2001; Gump et al., 2005; Oosterman et al., 2010). This pattern of physiological reactivity is not well explained

Table 4
Trauma history and standardized cardiovascular reactivity.[a,b,c]

	Trauma					Trauma × Sex				
	β	b	t	df	p-value	β	b	t	df	p-value
Pre-ejection period (ms)										
Preparation	0.06	0.92	1.66	433	0.097	0.01	0.25	0.23	433	0.818
Speech	0.09*	1.32	2.33	433	0.020	−0.02	−0.52	0.47	433	0.642
Math	0.05	0.83	1.57	433	0.117	0.01	0.17	0.16	433	0.871
Cardiac Output (z-score L/min)										
Preparation	−0.10**	−0.05	3.27	386	0.001	0.04	0.03	0.92	386	0.357
Speech	−0.09**	−0.06	2.60	391	0.009	0.05	0.05	1.06	391	0.290
Math	−0.08**	−0.06	2.92	392	0.004	0.01	0.01	0.16	392	0.876

* $p < 0.05$. ** $p < 0.01$.
[a] Linear regressions controlling for age, gender, maternal education.
[b] Values represent reactivity scores calculated by entering the first minute of each task as the dependent variable and entering the first minute of the baseline period as a covariate. All CO values have been z-scored.
[c] t-values are calculated using the Mplus Est/S.E. output for the linear regression models reported (Prescott, 2004).

Table 5
Cardiovascular reactivity and psychopathology.[a,b,c]

	Youth Self Report									
	Internalizing					Externalizing				
	β	b	t	df	p-value	β	b	t	df	p-value
CO Reactivity (z-score L/min)										
Preparation	−0.12	−0.04	1.73	427	0.083	**−0.22****	**−0.08**	**3.12**	**427**	**0.002**
Speech	0.03	0.01	0.46	433	0.645	−0.07	−0.02	0.96	433	0.336
Math	−0.04	−0.01	0.47	432	0.642	**−0.18***	**−0.05**	**2.33**	**432**	**0.020**
	Child Behavior Checklist									
	Internalizing					Externalizing				
	β	b	t	df	p-value	β	b	t	df	p-value
CO Reactivity (z-score L/min)										
Preparation	−0.12	−0.04	1.54	427	0.083	−0.11	−0.03	1.49	427	0.136
Speech	−0.03	0.01	0.38	433	0.703	−0.05	−0.01	0.71	433	0.475
Math	−0.07	−0.02	0.83	432	0.407	**−0.21***	**−0.05**	**2.51**	**432**	**0.012**

Bold values are the statistically significant results.
* $p < 0.05$.
** $p < 0.01$.
[a] Linear regressions controlling for age, gender, maternal education.
[b] Values represent reactivity scores calculated by entering the first minute of each task as the dependent variable and entering the first minute of the baseline period as a covariate. All CO values have been z-scored.
[c] t-values are calculated using the Mplus Est/S.E. output for the linear regression models reported (Prescott, 2004).

Table 6
PEP reactivity and psychopathology.[a,b,c]

	Youth Self Report									
	Internalizing					Externalizing				
	β	b	t	df	p-value	β	b	t	df	p-value
PEP Reactivity (ms)										
Preparation	−0.05	<0.01	0.83	461	0.407	0.03	<0.01	0.48	468	0.630
Speech	<−0.01	<0.01	0.19	461	0.853	0.07	<0.01	1.25	468	0.213
Math	<−0.01	<0.01	0.07	461	0.943	<0.01	<0.01	1.08	468	0.281
	Child Behavior Checklist									
	Internalizing					Externalizing				
	β	b	t	df	p-value	β	b	t	df	p-value
PEP Reactivity (ms)										
Preparation	−0.01	<0.01	0.58	446	0.890	0.06	<0.01	1.08	447	0.282
Speech	0.01	<0.01	0.17	446	0.863	**0.15****	**<0.01**	**2.95**	**447**	**0.003**
Math	0.04	<0.01	0.58	446	0.564	**0.16****	**<0.01**	**2.78**	**447**	**0.006**

Bold values are the statistically significant results.
* $p < 0.05$.
** $p < 0.01$.
[a] Linear regressions controlling for age, gender, maternal education.
[b] Values represent reactivity scores calculated by entering the first minute of each task as the dependent variable and entering the first minute of the baseline period as a covariate.
[c] t-values are calculated using the Mplus Est/S.E. output for the linear regression models reported (Prescott, 2004).

by the preeminent models of how environmental stressors influence the development of stress response systems. In the current study, adolescents exposed to higher levels of trauma displayed blunted SNS reactivity to a social stressor. We also extend previous findings on cardiovascular reactivity by documenting a pattern of blunted CO reactivity among adolescents with greater exposure to trauma, consistent with a recent study we conducted examining a small sample of severely maltreated adolescents (McLaughlin et al., 2014). These findings suggest that traumatic events may be unique in the way they influence the development of stress response systems and ultimately influence reactivity to the environment.

Traumatic events may be associated with a distinctive pattern of stress reactivity because, unlike other types of environmental stressors, these events involve significant threats to survival. The traumatic events assessed in this study – exposure to physical assault, sexual assault, domestic violence, death, life-threatening accidents and natural disasters – are both unpredictable and uncontrollable. As a result, children exposed to traumatic stress may develop a pattern of cardiovascular responses adapted for survival in an environment of inescapable threat. Conserving metabolic resources to facilitate survival by freezing is an adaptive response when an individual is unable to reduce the immediate environmental threat level by fleeing or fighting (Keay & Bandler, 2001; Mendes, Gray, Mendoza-Denton, Major, & Epel, 2007; Porges, 2007); indeed, while we did not include direct vagal measures of freezing in this study, blunted CO reactivity in response to acute stressors has been conceptualized as a freezing response to threat in prior studies (Blascovich & Mendes, 2000; Blascovich & Tomaka, 1996). In contrast, stressors such as poverty, parental mental illness and institutionalization are chronic stressors that, although equally uncontrollable, may be more *predictable*. Children reared in these environments may develop heightened cardiovascular reactivity (Blair et al., 2005; El-Sheikh, 2005; Ellis et al., 2005; Evans & Kim, 2007; Feldman et al., 2009; Obradović et al., 2010; Oosterman et al., 2010) because sensitivity to cues of danger within these environments is adaptive and is therefore reinforced over time. Indeed, this latter pattern of stress exposure and heightened cardiovascular reactivity is supported by the biological sensitivity to context and adaptive calibration theories (Boyce & Ellis, 2005; Del Giudice et al., 2011).

The biopsychosocial model of challenge and threat may provide a more useful framework for characterizing cardiovascular reactivity specifically among trauma-exposed youth. In a prior study, we applied this model to the study of stress reactivity in a sample exposed to child maltreatment, a severe form of child trauma. We found that adolescents exposed to physical or sexual abuse exhibited a pattern of blunted CO reactivity and heightened peripheral resistance, consistent with a threat profile (McLaughlin et al., 2014). This pattern of results mirrors the results in our current study, with two minor exceptions. First, in the earlier study, the associations between trauma exposure and blunted PEP reactivity during all stress tasks were stronger, and reached significance during the math task rather than the speech task. The relatively stronger association between trauma and blunted PEP reactivity is likely attributable to the greater severity and chronicity of trauma exposure in the sample of the previous study, consistent with prior research indicating that children exposed to severe trauma are more likely to demonstrate blunted sympathetic responses to stress (Cooley-Quille et al., 2001; Gump et al., 2005; Oosterman et al., 2010). Second, the previous study found that the association between maltreatment and blunted CO reactivity was marginally significant on the speech portion of the Trier task, in addition to the significant associations between trauma and blunted CO reactivity in other portions of the task. This variation in findings across the two studies may stem from minor differences in how the stress tasks were administered. Participants in our earlier study were instructed to deliver their speech in front of two peers who had been trained to appear neutral or slightly negative without providing any positive feedback. In the current study, participants delivered their speeches to a video camera with only one test assistant in the room who was trained to watch the performance without empathy or encouragement, and were told that the videotape of their speech would be judged at a later time. It is possible that performing a speech for a video camera that will be rank-ordered by peers later in time more closely resembles the social media context in which adolescents are evaluated by peers, heightening the in-vivo social-evaluative nature of the task in our study and producing the stronger association with diminished cardiovascular reactivity during the speech task. Finally, in the current study we included an exploratory analysis of CO recovery following social stress, though did not find an association with trauma, suggesting recovery may be less sensitive to environmental experience than initial stress reactivity. Despite these minor variations in findings, results from the current study extend our previous work by demonstrating that adolescents drawn from a population-representative sample and exposed to a much wider range of commonly occurring traumatic events display the same blunted profile of CO reactivity characteristic of threat responses in the biopsychosocial model. Taken together, these studies indicate that a specific pattern of cardiovascular reactivity may emerge following childhood trauma exposure.

If childhood traumatic stress does indeed shape stress reactivity, the specific pattern predicted by the biopsychosocial model is a plausible pathway linking child trauma with the onset of mental illness. Indeed, our results indicate that blunted SNS and CO reactivity during social stress as well as blunted CO recovery following stress is a pattern of cardiovascular responding associated with externalizing symptoms in adolescents. These findings are consistent with a growing body of literature that has identified blunted SNS arousal in response to environmental stress as a biological marker of externalizing, not internalizing, psychopathology (Beauchaine et al., 2007; Boyce, 2001; Crowell et al., 2006; Shannon et al., 2007; Sijtsema, Van Roon, Groot, & Riese, 2015). They also replicate findings from our earlier study, in which reduced CO was associated with externalizing and not internalizing problems in a sample of maltreated children (McLaughlin et al., 2014). These findings, together with our mediation results, suggest that blunted CO reactivity during stress might represent a physiological marker of threat perception sensitivity and a mechanism linking trauma exposure and aggression in children, a pattern supported by our mediation analysis. Although mounting a cardiovascular response that supports early identification of uncontrollable and inescapable threat may be adaptive for surviving a traumatic event, mounting the same cardiovascular response to social evaluation, a stressor commonly and frequently encountered throughout adolescence, may promote aggressive behavior that is inappropriate in most social situations. Indeed, prior evidence indicates that the tendency to interpret neutral interactions as hostile (Dodge, Bates, & Pettit, 1990), and to have a bias towards angry faces (Pollak & Kistler, 2002; Pollak, Klorman, Thatcher, & Cicchetti, 2001) constitute behavioral links between violence exposure and perpetration. Our findings suggest that a threat profile marked by both blunted SNS and CO reactivity is a potential neurobiological marker of sensitivity to threat that increases risk specifically for aggressive behavior and other externalizing problems among adolescents.

At first glance, the lack of association between the blunted CO and internalizing symptoms may be surprising, as prior literature has identified disruptions in SNS responses to stress among children with internalizing symptoms (e.g. Boyce, 2001). However, evidence suggests that children with internalizing symptoms exhibit *elevated* SNS reactivity (Hastings, Zahn-Waxler, & Usher, 2007; Vasey & Lonigan, 2000; Zahn-Waxler, Klimes-Dougan, &

Slattery, 2000), a pattern that contrasts with the threat profile examined here, which is characterized by a blunted pattern of SNS responding and blunted vascular reactivity (McLaughlin et al., 2014; Mendes et al., 2008 Mendes et al., 2008). It is possible that adolescents with internalizing symptoms are more likely to mount a classic fight or flight response to threatening stimuli characterized by elevated reactivity in the sympathetic nervous system, whereas adolescents with externalizing symptoms are likely to exhibit a *freezing* response, which may be indicated by blunted SNS reactivity. Our finding that children with internalizing problems demonstrated a slower cardiovascular recovery from social stress suggests that while these adolescents may be quick to engage with a stressor, they experience difficulty *dis*engaging from stressful content. These results are consistent with prior work that has identified a pattern of greater emotional reactivity yet slower physiological recovery among adolescents with internalizing problems (Shapero, Abramson, & Alloy, 2015) and may be explained by their perseverative thinking style that rehashes rather than distances stressful events (Michl, McLaughlin, Shepherd, & Nolen-Hoeksema, 2013; Rood, Roelofs, Bögels, Nolen-Hoeksema, & Schouten, 2009).

Study findings should be interpreted with caution given the following limitations. First, cardiovascular and psychopathology data for this study were collected at a single timepoint, precluding us from examining whether stress reactivity predicts changes in internalizing and externalizing symptoms over time. For this reason, we interpret results of our mediation model with caution (Maxwell & Cole, 2007). Replication of these findings in future longitudinal studies is an important goal for future research. Second, we did not assess adolescent appraisals of their perceptions of threat vs. challenge using the measures typically used to assess these types of appraisals in studies of the BPS model, or (finger) blood pressure during the laboratory stress task. As a result, we were unable to examine appraisals of threat perception or to calculate total peripheral resistance, other variables indicating threat or challenge profiles according to the biopsychosocial model (Blascovich & Mendes, 2000). We also did not assess quality of performance during the GSST, precluding us from ascertaining other processes that may have influenced our pattern of results, such as learned helplessness or disengagement from the task. Third, adolescents were assessed for trauma history prior to T3 at the T4 assessment, precluding us from establishing with certainty that the trauma exposure occurred before adolescents completed our physiological assessments and measurements of psychopathology and limiting our any causal interpretation of our mediation results. Finally, we relied upon parent and youth-reported measures of symptomatology rather than administering structured diagnostic interviews of psychopathology. Although administration of a structured interview to establish diagnoses would represent a methodological improvement, the validity of the parent and youth report measures used in this study are well-established (Achenbach & Edelbrock, 1981; Achenbach, 1991) and the inclusion of both parent and youth reports is advantageous (Hope et al., 1999).

We extend the developmental psychopathology literature by demonstrating the utility of the biopsychosocial model of threat and challenge as a conceptual framework for understanding pattern of stress reactivity in adolescents exposed to trauma. Adolescents exposed to a variety of traumatic experiences exhibited blunted CO reactivity to a social stressor, an indicator of the cardiovascular threat profile proposed by the biopsychosocial model. Blunted SNS and blunted CO response to social stress were, in turn, associated with externalizing problems in adolescence. These findings provide novel evidence for one potential neurodevelopmental mechanism linking trauma exposure to externalizing problems. Future research is needed to determine whether interventions targeting amplified threat perception in trauma-exposed children ameliorate these atypical patterns of stress reactivity and their behavioral consequences.

Acknowledgments

This research is part of the TRacking Adolescents' Individual Lives Survey (TRAILS). Participating centers of TRAILS include various departments of the University Medical Center and University of Groningen, the Erasmus University Medical Center Rotterdam, the University of Utrecht, the Radboud Medical Center Nijmegen, and the Parnassia Bavo group, all in the Netherlands. TRAILS has been financially supported by various grants from the Netherlands Organization for Scientific Research NWO (Medical Research Council program grant GB-MW 940-38-011; ZonMW Brainpower grant 100-001-004; ZonMw Risk Behavior and Dependence grants 60-60600-97-118; ZonMw Culture and Health grant 261-98-710; Social Sciences Council medium-sized investment grants GB-MaGW 480-01-006 and GB-MaGW 480-07-001; Social Sciences Council project grants GB-MaGW 452-04-314 and GB-MaGW 452-06-004; NWO large-sized investment grant 175.010.2003.005; NWO Longitudinal Survey and Panel Funding 481-08-013), the Dutch Ministry of Justice (WODC), the European Science Foundation (EuroSTRESS project FP-006), Biobanking and Biomolecular Resources Research Infrastructure BBMRI-NL (CP 32), the Participating Universities, and Accare Center for Child and Adolescent Psychiatry. This research was additionally supported by the Doris Duke Fellowship for the Promotion of Child Wellbeing and a grant from the National Institute of Mental Health to Charlotte Heleniak (F31-MH108245), as well as by the Jacobs Foundation Early Career Fellowship and grants from the National Institute of Mental Health to Katie McLaughlin (R01-MH103291, R01-MH106482). We are grateful to all adolescents, their parents and teachers who participated in this research and to everyone who worked on this project and made it possible.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.biopsycho.2016.08.007.

References

Achenbach, T. M., & Edelbrock, C. S. (1981). *Behavioral problems and competencies reported by parents of normal and disturbed children aged four through sixteen*. Chicago, III: Published by the University of Chicago Press for the Society for Research in Child Development.

Achenbach, T. M. (1991). *Integrative guide for the 1991 CBCL/4-18, YSR, and TRF profiles*. Department of Psychiatry: University of Vermont Burlington.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (DSM-5®)*. American Psychiatric Pub.

Beauchaine, T. P., Gatzke-Kopp, L., & Mead, H. K. (2007). Polyvagal theory and developmental psychopathology: Emotion dysregulation and conduct problems from preschool to adolescence. *Biological Psychology*, *74*(2), 174–184. http://dx.doi.org/10.1016/j.biopsycho.2005.08.008

Blair, C., Granger, D., & Razza, R. P. (2005). Cortisol reactivity is positively related to executive function in preschool children attending head start. *Child Development*, *76*(3), 554–567.

Blascovich, J., & Mendes, W. B. (2000). Challenge and threat appraisals: The role of affective cues. In *Feeling and thinking: the role of affect in social cognition*. pp. 59–82. New York, NY, US: Cambridge University Press.

Blascovich, J., & Tomaka, J. (1996). The biopsychosocial model of arousal regulation. In M. P. Zanna (Ed.), *Advances in experimental social psychology* (Vol. 28) (pp. 1–51). Academic Press. Retrieved from http://www.sciencedirect.com/science/article/pii/S006526010860235X

Blascovich, J., Mendes, W. B., Hunter, S. B., Lickel, B., & Kowai-Bell, N. (2001). Perceiver threat in social interactions with stigmatized others. *Journal of Personality and Social Psychology*, *80*(2), 253–267. http://dx.doi.org/10.1037/0022-3514.80.2.253

Blascovich, J., Seery, M. D., Mugridge, C. A., Norris, R. K., & Weisbuch, M. (2004). Predicting athletic performance from cardiovascular indexes of challenge and threat. *Journal of Experimental Social Psychology*, *40*(5), 683–688. http://dx.doi.org/10.1016/j.jesp.2003.10.007

Blascovich, J. J., Vanman, E., Mendes, W. B., & Dickerson, S. (2011). *Social psychophysiology for social and personality psychology*. SAGE Publications Ltd.
Bouma, E. M. C., Riese, H., Ormel, J., Verhulst, F. C., & Oldehinkel, A. J. (2009). Adolescents' cortisol responses to awakening and social stress; Effects of gender, menstrual phase and oral contraceptives. The TRAILS study. *Psychoneuroendocrinology*, *34*(6), 884–893. http://dx.doi.org/10.1016/j.psyneuen.2009.01.003
Boyce, W. T., & Ellis, B. J. (2005). Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. *Development and Psychopathology*, *17*(02), 271–301.
Boyce, W. T. (2001). Autonomic reactivity and psychopathology in middle childhood. *The British Journal of Psychiatry*, *179*(2), 144–150. http://dx.doi.org/10.1192/bjp.179.2.144
Buske-Kirschbaum, A., Jobst, S., Wustmans, A., Kirschbaum, C., Rauh, W., & Hellhammer, D. (1997). Attenuated free cortisol response to psychosocial stress in children with atopic dermatitis. *Psychosomatic Medicine Psychosomatic Medicine*, *59*(4), 419–426.
Chen, W. J., Faraone, S. V., Biederman, J., & Tsuang, M. T. (1994). Diagnostic accuracy of the child behavior checklist scales for attention-deficit hyperactivity disorder: A receiver-operating characteristic analysis. *Journal of Consulting and Clinical Psychology*, *62*(5), 1017.
Cooley-Quille, M., Boyd, R. C., Frantz, E., & Walsh, J. (2001). Emotional and behavioral impact of exposure to community violence in inner-city adolescents. *Journal of Clinical Child & Adolescent Psychology*, *30*(2) http://dx.doi.org/10.1207/s15374424jccp3002_7
Crowell, S. E., Beauchaine, T. P., 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), 174–178. http://dx.doi.org/10.1037/0021-843X.115.1.174
De Bellis, M. D., Chrousos, G. P., Dorn, L. D., Burke, L., Helmers, K., Kling, M. A., & Putnam, F. W. (1994). Hypothalamic–pituitary–adrenal axis dysregulation in sexually abused girls. *The Journal of Clinical Endocrinology & Metabolism*, *78*(2), 249–255. http://dx.doi.org/10.1210/jcem.78.2.8106608
Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). The adaptive calibration model of stress responsivity. *Neuroscience & Biobehavioral Reviews*, *35*(7), 1562–1592. http://dx.doi.org/10.1016/j.neubiorev.2010.11.007
Del Giudice, M., Benjamin, J., Ellis, B. J., & El-Sheikh, M. (2012). Adaptive patterns of stress responsivity: A preliminary investigation. *Developmental Psychology*, *48*(3), 775–790. http://dx.doi.org/10.1037/a0026519
Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, *130*(3), 355–391. http://dx.doi.org/10.1037/0033-2909.130.3.355
Dietrich, A., Riese, H., van Roon, A. M., van Engelen, K., Ormel, J., Neeleman, J., & Rosmalen, J. G. (2006). Spontaneous baroreflex sensitivity in (pre) adolescents. *Journal of Hypertension*, *24*(2), 345–352.
Dodge, K. A., Bates, J. E., & Pettit, G. S. (1990). Mechanisms in the cycle of violence. *Science*, *250*(4988), 1678–1683.
Drach-Zahavy, A., & Erez, M. (2002). Challenge versus threat effects on the goal-performance relationship. *Organizational Behavior and Human Decision Processes*, *88*(2), 667–682. http://dx.doi.org/10.1016/s0749-5978(02)00004-3
El-Sheikh, M., Keller, P. S., & Erath, S. A. (2007). Marital conflict and risk for child maladjustment over time: Skin conductance level reactivity as a vulnerability factor. *Journal of Abnormal Child Psychology*, *35*(5), 715–727. http://dx.doi.org/10.1007/s10802-007-9127-2
El-Sheikh, M. (2005). The role of emotional responses and physiological reactivity in the marital conflict-child functioning link. *Journal of Child Psychology and Psychiatry*, *46*(11), 1191–1199. http://dx.doi.org/10.1111/j.1469-7610.2005.00418.x
Ellis, B. J., & Boyce, W. T. (2008). Biological sensitivity to context. *Current Directions in Psychological Science*, *17*(3), 183–187.
Ellis, B. J., Essex, M. J., & Boyce, W. T. (2005). Biological sensitivity to context: II. Empirical explorations of an evolutionary–developmental theory. *Development and Psychopathology*, *17*(02), 303–328.
Elzinga, B. M., Roelofs, K., Tollenaar, M. S., Bakvis, P., van Pelt, J., & Spinhoven, P. (2008). Diminished cortisol responses to psychosocial stress associated with lifetime adverse events. *Psychoneuroendocrinology*, *33*(2), 227–237. http://dx.doi.org/10.1016/j.psyneuen.2007.11.004
Erath, S. A., El-Sheikh, M., & Mark Cummings, E. (2009). Harsh parenting and child externalizing behavior: Skin conductance level reactivity as a moderator. *Child Development*, *80*(2), 578–592. http://dx.doi.org/10.1111/j.1467-8624.2009.01280.x
Evans, G. W., & Kim, P. (2007). Childhood poverty and health: Cumulative risk exposure and stress dysregulation. *Psychological Science*, *18*(11), 953–957.
Feldman, R., Granat, A., Pariente, C., Kanety, H., Kuint, J., & Gilboa-Schechtman, E. (2009). Maternal depression and anxiety across the postpartum year and infant social engagement, fear regulation, and stress reactivity. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*(9), 919–927. http://dx.doi.org/10.1097/CHI.0b013e3181b21651
Fowles, D. C., Kochanska, G., & Murray, K. (2000). Electrodermal activity and temperament in preschool children. *Psychophysiology*, *37*(06), 777–787. http://doi.org/null
Graziano, P., & Derefinko, K. (2013). Cardiac vagal control and children's adaptive functioning: A meta-analysis. *Biological Psychology*, *94*(1), 22–37. http://dx.doi.org/10.1016/j.biopsycho.2013.04.011
Gump, B. B., Reihman, J., Stewart, P., Lonky, E., & Darvill, T. (2005). Terrorism and cardiovascular responses to acute stress in children. *Health Psychology*, *24*(6), 594–600. http://dx.doi.org/10.1037/0278-6133.24.6.594
Gunnar, M. R., Morison, S. J., Chisholm, K., & Schuder, M. (2001). Salivary cortisol levels in children adopted from Romanian orphanages. *Development and Psychopathology*, *13*(03), 611–628.
Gunnar, M. R., Sebanc, A. M., Tout, K., Donzella, B., & van Dulmen, M. M. H. (2003). Peer rejection, temperament, and cortisol activity in preschoolers. *Developmental Psychobiology*, *43*(4), 346–368. http://dx.doi.org/10.1002/dev.10144
Gunnar, M. R., Frenn, K., Wewerka, S. S., & Van Ryzin, M. J. (2009). Moderate versus severe early life stress: Associations with stress reactivity and regulation in 10–12-year-old children. *Psychoneuroendocrinology*, *34*(1), 62–75. http://dx.doi.org/10.1016/j.psyneuen.2008.08.013
Hastings, P. D., Zahn-Waxler, C., & Usher, B. A. (2007). Cardiovascular and affective responses to social stress in adolescents with internalizing and externalizing problems. *International Journal of Behavioral Development*, *31*(1), 77–87. http://dx.doi.org/10.1177/0165025407073575
Hayes, A. F., & Matthes, J. (2009). Computational procedures for probing interactions in OLS and logistic regression: SPSS and SAS implementations. *Behavior Research Methods*, *41*(3), 924–936. http://dx.doi.org/10.3758/BRM.41.3.924
Hope, T. L., Adams, C., Reynolds, L., Powers, D., Perez, R. A., & Kelley, M. L. (1999). Parent vs. self-report: Contributions toward diagnosis of adolescent psychopathology. *Journal of Psychopathology and Behavioral Assessment*, *21*(4), 349–363. http://dx.doi.org/10.1023/A:1022124900328
Huisman, M., Oldehinkel, A. J., de Winter, A., Minderaa, R. B., de Bildt, A., Huizink, A. C., . . . & Ormel, J. (2008). Cohort profile: The dutch TRacking adolescents individual lives' survey'; TRAILS. *International Journal of Epidemiology*, *37*(6), 1227–1235. http://dx.doi.org/10.1093/ije/dym273
Jamieson, J. P., Nock, M. K., & Mendes, W. B. (2012). Mind over matter: Reappraising arousal improves cardiovascular and cognitive responses to stress. *Journal of Experimental Psychology: General*, *141*(3), 417–422. http://dx.doi.org/10.1037/a0025719
Keay, K. A., & Bandler, R. (2001). Parallel circuits mediating distinct emotional coping reactions to different types of stress. *Neuroscience & Biobehavioral Reviews*, *25*(7–8), 669–678. http://dx.doi.org/10.1016/S0149-7634(01)00049-5
Kirschbaum, C., Kudielka, B. M., Gaab, J., Schommer, N. C., & Hellhammer, D. H. (1999). Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus–pituitary–adrenal axis. *Psychosomatic Medicine*, *61*(2), 154–162.
Kubicek, W. G., Patterson, R. P., & Witsoe, D. A. (1970). Impedance cardiography as a noninvasive method of monitoring cardiac function and other parameters of the cardiovascular system. *Annals of the New York Academy of Sciences*, *170*(2), 724–732. http://dx.doi.org/10.1111/j.1749-6632.1970.tb17735.x
Maxwell, S. E., & Cole, D. A. (2007). Bias in cross-sectional analyses of longitudinal mediation. *Psychological Methods*, *12*(1), 23–44. http://dx.doi.org/10.1037/1082-989X.12.1.23
McGrath, J. J., O'Brien, W. H., Hassinger, H. J., & Shah, P. (2005). Comparability of spot versus band electrodes for impedance cardiography. *Journal of Psychophysiology*, *19*(3), 195–203.
McLaughlin, K. A., Koenen, K. C., Hill, E. D., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2013). Trauma exposure and posttraumatic stress disorder in a national sample of adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry*, *52*(8), 815–830.e14. http://dx.doi.org/10.1016/j.jaac.2013.05.011
McLaughlin, K. A., Sheridan, M. A., Alves, S., & Mendes, W. B. (2014). Child maltreatment and autonomic nervous system reactivity: Identifying dysregulated stress reactivity patterns by using the biopsychosocial model of challenge and threat. *Psychosomatic Medicine*, *76*(7), 538–546.
Mendes, W. B., Blascovich, J., Major, B., & Seery, M. (2001). Challenge and threat responses during downward and upward social comparisons. *European Journal of Social Psychology*, *31*(5), 477–497. http://dx.doi.org/10.1002/ejsp.80
Mendes, W. B., Gray, H. M., Mendoza-Denton, R., Major, B., & Epel, E. S. (2007). Why egalitarianism might Be good for your health. *Psychological Science*, *18*(11), 991–998. http://dx.doi.org/10.1111/j.1467-9280.2007.02014.x
Mendes, W. B., Major, B., McCoy, S., & Blascovich, J. (2008). How attributional ambiguity shapes physiological and emotional responses to social rejection and acceptance. *Journal of Personality and Social Psychology*, *94*(2), 278–291. http://dx.doi.org/10.1037/0022-3514.94.2.278
Michl, L. C., McLaughlin, K. A., Shepherd, K., & Nolen-Hoeksema, S. (2013). Rumination as a mechanism linking stressful life events to symptoms of depression and anxiety: Longitudinal evidence in early adolescents and adults. *Journal of Abnormal Psychology*, *122*(2), 339–352. http://dx.doi.org/10.1037/a0031994
Muthén, L. K., & Muthén, B. O. (1998). *Mplus: The comprehensive modeling program for applied researchers: user's guide*. Los Angeles, CA: Muthén & Muthén.
Obradović, J., Bush, N. R., Stamperdahl, J., Adler, N. E., & Boyce, W. T. (2010). Biological sensitivity to context: The interactive effects of stress reactivity and family adversity on socioemotional behavior and school readiness. *Child Development*, *81*(1), 270–289. http://dx.doi.org/10.1111/j.1467-8624.2009.01394.x
Obradović, J., Bush, N. R., & Boyce, W. T. (2011). The interactive effect of marital conflict and stress reactivity on externalizing and internalizing symptoms: The role of laboratory stressors. *Development and Psychopathology*, *23*(01), 101–114. http://dx.doi.org/10.1017/S0954579410000672

Oldehinkel, A. J., Hartman, C. A., Nederhof, E., Riese, H., & Ormel, J. (2011). Effortful control as predictor of adolescents' psychological and physiological responses to a social stress test: The Tracking Adolescents' Individual Lives Survey. *Development and Psychopathology*, *23*(02), 679–688. http://dx.doi.org/10.1017/S0954579411000095

Oosterman, M., De Schipper, J. C., Fisher, P., Dozier, M., & Schuengel, C. (2010). Autonomic reactivity in relation to attachment and early adversity among foster children. *Development and Psychopathology*, *22*(01), 109–118. http://dx.doi.org/10.1017/S0954579409990290

Ornitz, E. M., & Pynoos, R. S. (1989). Startle modulation in children with posttraumatic stress disorder. *The American Journal of Psychiatry*, *146*(7), 866–870.

Pollak, S. D., & Kistler, D. J. (2002). Early experience is associated with the development of categorical representations for facial expressions of emotion. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(13), 9072–9076. http://dx.doi.org/10.1073/pnas.142165999

Pollak, S. D., Klorman, R., Thatcher, J. E., & Cicchetti, D. (2001). P3b reflects maltreated children's reactions to facial displays of emotion. *Psychophysiology*, *38*(02), 267–274.

Porges, S. W. (2007). The polyvagal perspective. *Biological Psychology*, *74*(2), 116–143. http://dx.doi.org/10.1016/j.biopsycho.2006.06.009

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods*, *40*(3), 879–891.

Prescott, C. A. (2004). Using the Mplus computer program to estimate models for continuous and categorical data from twins. *Behavior Genetics*, *34*(1), 17–40.

Riese, H., Groot, P. F., van den Berg, M., Kupper, N. H., Magnee, E. H., Rohaan, E. J., . . . & de Geus, E. J. (2003). Large-scale ensemble averaging of ambulatory impedance cardiograms. *Behavior Research Methods, Instruments, & Computers*, *35*(3), 467–477.

Rood, L., Roelofs, J., Bögels, S. M., Nolen-Hoeksema, S., & Schouten, E. (2009). The influence of emotion-focused rumination and distraction on depressive symptoms in non-clinical youth: A meta-analytic review. *Clinical Psychology Review*, *29*(7), 607–616. http://dx.doi.org/10.1016/j.cpr.2009.07.001

Schafer, J. L., & Graham, J. W. (2002). Missing data: Our view of the state of the art. *Psychological Methods*, *7*(2), 147–177. http://dx.doi.org/10.1037/1082-989X.7.2.147

Seligman, L. D., Ollendick, T. H., Langley, A. K., & Baldacci, H. B. (2004). The utility of measures of child and adolescent anxiety: A meta-analytic review of the revised children's manifest anxiety scale, the state-trait anxiety inventory for children, and the child behavior checklist. *Journal of Clinical Child and Adolescent Psychology*, *33*(3), 557–565.

Shannon, K. E., Beauchaine, T. P., Brenner, S. L., Neuhaus, E., & Gatzke-Kopp, L. (2007). Familial and temperamental predictors of resilience in children at risk for conduct disorder and depression. *Development and Psychopathology*, *19*(03), 701–727. http://dx.doi.org/10.1017/S0954579407000351

Shapero, B. G., Abramson, L. Y., & Alloy, L. B. (2015). Emotional reactivity and internalizing symptoms: Moderating role of emotion regulation. *Cognitive Therapy and Research*, *40*(3), 328–340. http://dx.doi.org/10.1007/s10608-015-9722-4

Sherwood, A., Allen, M. T., Fahrenberg, J., Kelsey, R. M., Lovallo, W. R., & van Doornen, L. J. (1990). Methodological guidelines for impedance cardiography. *Psychophysiology*, *27*(1), 1–23.

Sijtsema, J. J., Van Roon, A. M., Groot, P. F. C., & Riese, H. (2015). Early life adversities and adolescent antisocial behavior: The role of cardiac autonomic nervous system reactivity in the TRAILS study. *Biological Psychology*, *110*, 24–33. http://dx.doi.org/10.1016/j.biopsycho.2015.06.012

Straus, M. A. (1979). Measuring intrafamily conflict and violence: The conflict tactics (CT) scales. *Journal of Marriage and the Family Journal of Marriage and the Family*, *41*(1), 75.

Stroud, L. R., Foster, E., Papandonatos, G. D., Handwerger, K., Granger, D. A., Kivlighan, K. T., & Niaura, R. (2009). Stress response and the adolescent transition: Performance versus peer rejection stressors. *Development and Psychopathology*, *21*(01), 47. http://dx.doi.org/10.1017/s0954579409000042

Tarullo, A. R., & Gunnar, M. R. (2006). Child maltreatment and the developing HPA axis. *Hormones and Behavior*, *50*(4), 632–639. http://dx.doi.org/10.1016/j.yhbeh.2006.06.010

Tomaka, J., Blascovich, J., Kelsey, R. M., & Leitten, C. L. (1993). Subjective, physiological, and behavioral effects of threat and challenge appraisal. *Journal of Personality and Social Psychology*, *65*(2), 248–260. http://dx.doi.org/10.1037/0022-3514.65.2.248

Van der Knaap, L. J., Riese, H., Hudziak, J. J., Verbiest, M. M. P. J., Verhulst, F. C., Oldehinkel, A. J., & van Oort, F. V. A. (2014). Glucocorticoid receptor gene (NR3C1) methylation following stressful events between birth and adolescence. The TRAILS study. *Translational Psychiatry*, *4*(4), e381. http://dx.doi.org/10.1038/tp.2014.22

Vasey, M. W., & Lonigan, C. J. (2000). Considering the clinical utility of performance-based measures of childhood anxiety. *Journal of Clinical Child Psychology*, *29*(4), 493–508. http://dx.doi.org/10.1207/S15374424JCCP2904_4

Weems, C. F., Zakem, A. H., Costa, N. M., Cannon, M. F., & Watts, S. E. (2005). Physiological response and childhood anxiety: Association with symptoms of anxiety disorders and cognitive bias. *Journal of Clinical Child & Adolescent Psychology*, *34*(4), 712–723. http://dx.doi.org/10.1207/s15374424jccp3404_13

de Winter, A., Oldehinkel, A. J., Veenstra, R., Brunnekreef, J. A., Verhulst, F. C., & Ormel, J. (2005). Evaluation of non-response bias in mental health determinants and outcomes in a large sample of pre-adolescents. *European Journal of Epidemiology*, *20*, 173–181.

Zahn-Waxler, C., Klimes-Dougan, B., & Slattery, M. J. (2000). Internalizing problems of childhood and adolescence: Prospects, pitfalls, and progress in understanding the development of anxiety and depression. *Development and Psychopathology*, *12*(3), 443–466.