Title

Externalizing and Internalizing Problems: Associations with Family Adversity and Young Children’s Adrenocortical and Autonomic Functioning

Journal

Research on Child and Adolescent Psychopathology, 49(5)

ISSN

2730-7166

Authors

Goulter, Natalie
Roubinov, Danielle S
McMahon, Robert J
et al.

Publication Date

2021-05-01

DOI

10.1007/s10802-020-00762-0

Peer reviewed

HHS Public Access

Author manuscript

Res Child Adolesc Psychopathol. Author manuscript; available in PMC 2022 November 15.

Published in final edited form as:

Res Child Adolesc Psychopathol. 2021 May ; 49(5): 629–642. doi:10.1007/s10802-020-00762-0.

EXTERNALIZING AND INTERNALIZING PROBLEMS: ASSOCIATIONS WITH FAMILY ADVERSITY AND YOUNG CHILDREN'S ADRENOCORTICAL AND AUTONOMIC FUNCTIONING

Natalie Goulter, Ph.D[1], **Danielle S. Roubinov, Ph.D**[2], **Robert J. McMahon, Ph.D**[1], **W. Thomas Boyce, Ph.D**[2], **Nicole R. Bush, Ph.D**[2]

[1]Simon Fraser University, Burnaby, BC, Canada; BC Children's Hospital Research Institute, Vancouver, BC, Canada

[2]University of California San Francisco, San Francisco, CA, USA

Abstract

The development of child mental health problems has been associated with experiences of adversity and dysregulation of stress response systems; however, past research has largely focused on externalizing *or* internalizing problems (rather than their co-occurrence) and single physiological systems in high-risk adolescent samples. The present study examined whether cumulative family adversity, functioning in the hypothalamic-pituitary-adrenal axis (i.e., cortisol) and the parasympathetic nervous system (i.e., respiratory sinus arrhythmia [RSA]), and their interactions, predicted trajectories of co-occurring externalizing and internalizing problems among young children. Participants included 338 socioeconomically and racially diverse children (*M* age=5.32 years, *SD*=.32; male=51.8%) from a community sample. Family adversity (assessed with six measures) and child daily cortisol output and resting RSA were assessed in kindergarten. Parents, teachers, and children reported on children's externalizing and internalizing psychopathology up to three times from kindergarten to grade 1. Latent class growth analyses identified stable trajectories of externalizing and internalizing psychopathology. Trajectories were combined to create groups: co-occurring externalizing and internalizing (13.1%), externalizing-only (14.0%), internalizing-only (11.3%), and low problems (61.3%). Family adversity and resting RSA significantly positively predicted co-occurring group membership. Tests for interactions showed adversity did not significantly interact with physiological indicators to predict group membership. However, the two physiological systems interacted, such that higher and lower daily cortisol predicted internalizing group membership for children with lower and higher resting

Corresponding Author Contact Details: Natalie Goulter, Simon Fraser University, Department of Psychology, 8888 University Drive, Burnaby, BC V5A 1S6, Canada, ngoulter@sfu.ca, P: +1 778 251 0665.

Conflicts of interest: None.

Ethics approval: This study was approved by the Committee for the Protection of Human Subjects of the University of California, Berkeley, and the Committee on Human Subjects of the University of California, San Francisco.

Consent to participate and for publication: Parents' and teachers' informed consent and children's assent to participate and for publication were obtained before data collection.

Availability of data and material: Upon request to Nicole R. Bush (nicole.bush@ucsf.edu).

Code availability: Upon request to Natalie Goulter (ngoulter@sfu.ca).

RSA, respectively. Findings support the importance of considering family context and multiple physiological systems to inform understanding of the development of mental health problems, and their co-occurrence, in early childhood.

Keywords

adversity; cortisol; respiratory sinus arrhythmia; externalizing; internalizing

Many studies have examined antecedents of externalizing (e.g., noncompliance, aggression) and internalizing (e.g., withdrawal, anxiety, depression) problems independently; however, recent recommendations advocate for a more integrated research approach for understanding psychopathology (Achenbach et al., 2016). Specifically, Achenbach and colleagues argue that research should recognize that externalizing and internalizing problems among young children are not mutually exclusive, that children may vary in scores across both dimensions, and that assessment should include a broad scope of problems comprising items for children and their informants. In line with suggestions that the term “co-occurring” reflects developmental problems, whereas “comorbid” should be reserved for two or more forms of psychopathology that are independent of each other (Kaplan et al., 2006), we focus on the concept of co-occurring problems in a community sample. Examining community samples in early childhood is needed for understanding distinct developmental trajectories of risk for psychopathology and sensitive periods for intervention. Within the field of developmental psychopathology, research on typical development among low-risk samples informs research on atypical development among high-risk samples and, reciprocally, both approaches advance understanding of adaptive and maladaptive development (Cicchetti & Rogosch, 1996).

Cumulative Family Adversity

Within the context of the home, several stressors have been associated with the development of child problem behavior including, but not limited to, parental stress, harsh or inconsistent parenting, maternal depression, marital conflict, and financial stress (Obradović et al., 2012). The extant literature on maladaptive outcomes in response to stress has tended to examine the impact of structural factors (e.g., socioeconomic status [SES]), severe adversity (e.g., abuse, maltreatment), or single indicators (Cicchetti, 2016; Roubinov et al., 2018), but adverse experiences often do not occur in isolation, especially in the home or family environment. The home environment is comprised of many dynamic direct and indirect indices of daily exposures, some of which may be adverse. Thus, examining the cumulative burden of environmental factors within a child’s rearing context may provide a more accurate representation of adversity within the home. Studies examining indices of cumulative contextual risk have found that it predicts a range of psychophysiological, psychopathological, and social functioning outcomes in childhood (Evans et al., 2007; Lengua et al., 2007, 2020). This methodology is also in line with research showing an association between cumulative counts of types of adverse experiences and poor mental health outcomes (Felitti et al., 1998; Hughes et al., 2017). Collectively, these findings point to the importance of examining the effect of cumulative exposure to stressors over single indicators, especially when considering their role in shaping mental health.

Adrenocortical Functioning

Research on biological mechanisms underpinning the development of psychopathological problems is important given that these systems are sensitive to the effects of environmental influence, including experiences of stress and adversity. The two principal stress responsive systems are the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS). In the HPA axis domain, there is a cascade of events from the hypothalamus to glucocorticoid hormone production that includes: a) the release of corticotropin releasing hormone (CRH) from the hypothalamus, b) which in turn triggers the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary, c) initiating the release of cortisol from the adrenal glands (McEwen, 1998). Basal cortisol levels display a diurnal rhythm characterized by a peak post-awakening followed by a decline throughout the course of the day (Kirschbaum & Hellhammer, 1994). Whereas this diurnal rhythm indexes healthy cortisol secretion, low morning or high evening cortisol levels may be an indicator of stress-induced system dysregulation (Koss & Gunnar, 2018). Although there is substantial research documenting diurnal variability in cortisol levels over the course of a day, assessments of cortisol throughout the day and across days more accurately capture trait vulnerability (Ross et al., 2014). However, this research has commonly relied on samples at high risk for psychopathology, and it is important to examine variations in daily cortisol in non-clinical samples, and the impact of family adversity on associations with daily cortisol and mental health outcomes. With the same sample as the present study, Bush and colleagues (2011b) found that a composite family adversity score was associated with greater HPA arousal for kindergartners, as indexed by higher daily cortisol levels. Variation in cortisol levels might be important in the prediction of mental health outcomes, particularly if it interacts with environmental stressors to predict child mental health.

Whereas some research has found that diurnal hypocortisolism (i.e., decreased cortisol production) is associated with externalizing problems (Popma et al., 2007) and diurnal hypercortisolism (i.e., increased cortisol production) is linked with internalizing problems (Cicchetti & Rogosch, 2001), other research has found no association or the opposite pattern (Fairchild et al., 2008; Klimes-Dougan et al., 2001). Equivocal findings may be because many studies examine either externalizing or internalizing problems; when both measures of externalizing and internalizing have been included, co-occurring problems have not been considered (e.g., Saridjan et al., 2014), or studies have not examined within-sample variation (e.g., Laurent et al., 2014; Ruttle et al., 2011; Zandstra et al., 2015). In addition, many studies use adolescent samples and, as emphasized in recent reviews, there is a need to consider developmental timing and early development is particularly sensitive to the effects of stress (Alink et al., 2008; Koss & Gunnar, 2018). Despite evidence of associations between adversity and cortisol and between cortisol and mental health (for a review, see Koss & Gunnar, 2018), prior research has failed to examine whether family adversity interacts with HPA activity to predict co-occurring, externalizing, and internalizing problems in young children. Furthermore, opposing externalizing versus internalizing adrenal profiles (i.e., hypocortisolism vs. hypercortisolism, respectively) and the developmental sensitivity of the HPA axis, support the need for further research examining physiology underpinning young children with co-occurring problems.

Autonomic Functioning

An individual's nervous system activity within the sympathetic (SNS) and parasympathetic (PNS) branches reflects adaptation to environmental and physiological demands (Gross, 1998; Porges, 2001). In response to stress, the SNS readies the individual for fight, flight, or freeze by producing catecholamine-mediated responses inducing changes to target organs (Cacioppo et al., 1998). In contrast, PNS activation serves to restore homeostatic control of organ function and counteract excitation (Porges, 2007). Respiratory sinus arrhythmia (RSA), a measure of PNS regulation to the heart, occurs due to increases in inhibitory PNS influence during exhalation, and decreases during inhalation, thus decelerating and accelerating heart rate, respectively (Porges, 2001, 2007). Prefrontal activation is associated with changes in RSA activity, and meta-analytic studies have demonstrated a link between activation in specific prefrontal cortex regions (including dorsolateral, dorsomedial, and ventrolateral) and variability in emotion regulation (Buhle et al., 2014). Thus, it is suggested that lower resting RSA, a peripheral marker of prefrontal cortex dysfunction, is an indicator of emotion dysregulation and psychopathology (Thayer et al., 2012). Specifically, low resting RSA has been associated with symptoms of both externalizing and internalizing psychopathology, and can reflect longer-term adaptation to the environment (Beauchaine, 2012). Higher resting RSA is considered to index greater emotion regulation in response to stressors.

Whereas parasympathetic nervous system functioning has been viewed as an indicator of emotional functioning, less research has examined the interaction of family adversity and RSA fluctuations. Under conditions of stress, vagal tone increases heart rate by withdrawing the vagal nerve 'brake' and decreasing vagal output preparing the fight, flight, or freeze response (Porges, 2007). Polyvagal theory posits that when experiences of stress are severe or prolonged, the PNS may recalibrate resulting in persistent hyperactivity, which can confer risk for psychopathology (Porges, 2007). Research examining the relations between resting RSA and poor child outcomes is mixed, with findings suggesting that both higher and lower RSA activity contribute to greater risk for mental health problems (Dietrich et al., 2007; Hinnant & El-Sheikh, 2009). Inconsistencies between studies may be attributed to the absence of simultaneous consideration of an indicator of environmental stressors. For example, one study of adolescent boys found that lower resting RSA predicted higher externalizing and internalizing problems when social adversity (within the home) was also high, but was not associated with outcomes when adversity was low (Zhang et al., 2017). Similar to the aforementioned literature on adrenocortical functioning, research is yet to examine co-occurring psychopathological problems, and studies have focused on older samples. It is important to extend research on resting RSA with adolescent samples to earlier in childhood, given recent findings supporting developmental differences in system functioning, including greater within-individual stability and between-individual variability during childhood relative to adolescence (Dollar et al., 2020; Hinnant et al., 2018).

Adrenocortical and Autonomic Functioning

The HPA axis and the ANS do not act only orthogonally, however. Research has commonly examined associations between the HPA axis *or* the PNS and negative mental health outcomes, but these systems are highly interconnected. A multisystem examination is therefore necessary for a greater understanding of changes in physiological activity to stress and developmental outcomes. There are both anatomical and physiological substrates involved in the functional coordination of these two systems. For example, both systems are coordinated by a central autonomic network involving brainstem, subcortical, and cortical structures, which together indirectly regulate HPA axis activity via the amygdala and directly control PNS responsivity (Thayer & Sternberg, 2006). In addition, hypothalamic CRH and noradrenergic neurons have common inputs and are activated and inhibited by the same neurotransmitters; further, CRH and catecholaminergic neurons have reciprocal neural connections, allowing coordinated, counteracting patterns of activation between HPA and ANS (Stratakis & Chrousos, 1995). Thus, the HPA axis and ANS can become co-activated/ inhibited, and each system can modulate the activity of the other system (Bauer et al., 2002). Several theoretical models have been proposed to account for the relation between these systems. One prominent model, known as allostasis (McEwen & Wingfield, 2003), suggests that multiple physiological systems undergo calibration in order to maintain homeostasis in response to environmental stressors and demands. Under conditions of chronic stress, these physiological systems can become imbalanced resulting in allostatic load and reducing the capacity for future adaptive physiological responses. A consequence of this imbalance is an overall "weathering" of the body, increasing susceptibility to poor mental and physical health outcomes. It has been suggested that recalibration of the HPA axis and the ANS, specifically, may be the principal pathways through which the process of allostatic load unfolds (Lupien et al., 2015). Other theoretical models provide more directional nuance to multisystem patterning. For example, the PNS plays a modulating role on the HPA axis' response to stress (Porges, 2007) in that higher resting RSA is associated with lower resting cortisol levels, and vice versa, through a negative feedback mechanism.

Whereas some research has examined profiles of HPA and PNS activity among children (Quas et al., 2015; Roubinov et al., 2020), very little research has investigated the interaction of these stress systems at rest and their associations with mental health outcomes longitudinally. A cross-sectional study with two samples (*M* age = 8.81 years; *M* age = 9.31 years) found that the highest levels of anxiety and depression symptoms among children were predicted by lower resting RSA and higher basal cortisol, and the highest levels of depression symptoms were also predicted by higher resting RSA and lower basal cortisol (El-Sheikh et al., 2011). In addition, children with both higher resting RSA levels and higher basal cortisol exhibited the lowest anxiety symptoms. The authors suggested that higher RSA levels may be protective against the development of stress-related psychopathology when cortisol is also high, but not when cortisol is low. To our knowledge, no research has examined whether cumulative family adversity, multisystem functioning, and their interactions, predict developmental trajectories of externalizing and internalizing problems among young children in the community.

The Present Study

We observe five important methodological gaps in the literature that we aimed to address with the present study. First, most research has used adolescent samples at high risk for psychopathology. These sampling issues are critical limitations, as early development is a particularly sensitive period in which to examine the effects of stressful experiences and to advance understanding of developmental psychopathology. Second, it is important to discern whether cumulative indices of family adversity are associated with physiological dysregulation and poor mental health outcomes. Using a cumulative risk score captures more adversities that are likely relevant when testing associations with physiological functioning and externalizing and internalizing problems. Third, these relations are generally examined within clinical samples, rather than the community sample of young children displaying a full range of mental health symptoms employed in this study. Fourth, throughout both the autonomic and adrenocortical literatures, studies have tended to examine externalizing and internalizing problems separately. Where studies have included assessment of both, co-occurring problems have not been considered or studies have not examined within-sample variation. Fifth, inclusion of both the HPA axis and the ANS in models elucidating the development of maladaptive child outcomes is relatively recent, and an approach that considers multiple physiological systems is important given the high connectivity and biological interplay of these systems.

Thus, the present study aimed to examine associations between cumulative family adversity, HPA axis (i.e., daily cortisol) and PNS (i.e., resting RSA) functioning, and the development of externalizing and internalizing problems among young children. Based on prior literature, hypotheses regarding class membership were confirmatory, and hypotheses involving daily cortisol and resting RSA were more exploratory given inconsistencies in the literature. First, in line with recommendations (Achenbach et al., 2016), we examined potential within-sample variation in trajectories of externalizing and internalizing problems with multiple informants across three time points in kindergarten and grade 1. Kindergarten, and the kindergarten to grade 1 transition, are formative developmental periods characterized by important changes in social, emotional, behavioral, and biological functioning (Rimm-Kaufman & Pianta, 2000). We hypothesized that we would identify four classes reflecting a co-occurring group, an externalizing-only group, an internalizing-only group, and a low problems group. Second, we examined associations between cumulative family adversity, daily cortisol, and resting RSA, and identified externalizing and internalizing problem trajectory groups. Given conflicting research showing both externalizing and internalizing problems have been associated with higher daily cortisol and lower resting RSA, we had no a priori directional hypotheses for whether co-occurring, externalizing, or internalizing groups would be distinguished on daily cortisol and resting RSA levels. We sought to examine such associations in this well-characterized and diverse young child sample. Third, we assessed three two-way interactions (i.e., adversity × cortisol, adversity × RSA, cortisol × RSA) in the prediction of group membership. We hypothesized that we would identify a significant interaction between family adversity and daily cortisol or resting RSA and membership in co-occurring, externalizing, or internalizing groups, relative to the low problems group. Our expectation was that higher levels of adversity would predict group membership when cortisol was high and RSA was low. Based on prior empirical results (El-Sheikh et al., 2011), we hypothesized that the interaction between cortisol and RSA would predict internalizing group membership, such that high levels of cortisol would predict internalizing-only group membership when RSA was low.

Method

Participants

The Peers and Wellness Study (PAWS; Bush et al., 2011a) comprised 338 kindergarten children (*M* age = 5.32 years, *SD* = .32; male = 51.8%) who participated in a longitudinal study of social status, biological responses to adversity, and child mental and physical health. Participants were recruited in three waves from 29 kindergarten classrooms within six public schools in the San Francisco Bay Area (Oakland, Albany, and Piedmont Unified school districts) during the falls of 2003-2005. The sample was ethnically diverse including 19% African American or Black, 11% Asian, 43% European or White, 4% Latino, 22% Multi-ethnic, and 2% identified as 'other' by their caregiver. Primary caregivers were 87% biological mothers, 9% biological fathers 2.5% adoptive mothers, 0.6% biological grandmothers, and 0.9% 'other' relations to the child. Average annual household income ranged from <$10,000 to >$400,000 (*M* = $60–79,999, *Mdn* = $80–99,999). The highest level of educational attainment ranged from less than a high school diploma (2.4%) to advanced degrees (42.9%), with 75% of households having a member with at least a college degree. When data were collected, income and education were representative from the geographic area from which participants were recruited. This study was approved by the institutional review boards of the University of California at Berkeley and San Francisco campuses.

Measures

Covariates.—Covariates were assessed in fall of kindergarten and included: child age, sex (0 = male; 1 = female), race/ethnicity (0 = European or White; 1 = racial or ethnic minorities), and family SES; composite of standardized income and highest education, *M* = −.01; *SD* = .89).

Psychopathology.—Externalizing and internalizing psychopathology were assessed with parent and teacher report on the MacArthur Health and Behavior Questionnaire (HBQ; Armstrong et al., 2003) and child report on the Berkeley Puppet Interview (BPI; Ablow et al., 2003). For fall and spring of kindergarten time points, principal component analyses were used to derive a multi-reporter (i.e., parent, teacher, and child report) index of externalizing or internalizing problems (Kraemer et al., 2003). Three components were extracted: trait, reporter/perspective, and context dimensions (see Obradović et al., 2011). The trait dimension represented the common variance across informants that was mostly free of informant and contextual effects, and thus, the present study utilized this dimension. In spring of grade 1, a mean composite (allowing one to be missing) was created with parent and teacher report on the HBQ (the BPI was not administered at this time point). For further details, see Supplementary Information.

Cumulative family adversity.—Children's exposure to current or recent (e.g., in the past week or two) adversity within the home was assessed with parent reports across six indices in fall of kindergarten, including *financial stress* (Essex et al., 2002), *parenting challenges* (Essex et al., 2002), *marital conflict* (Johnson & O'Leary, 1987; Porter & O'Leary, 1980), *negative and anger expressiveness* (Halberstadt, 1986; Spielberger, 1988), *maternal depression* (Radloff, 1977), and *harsh and restrictive parenting* (Block, 1965; Deković et al., 1991; Rickel & Biasatti, 1982). The six indices were standardized and averaged to create one adversity composite. For further details, see Supplementary Information.

Diurnal salivary cortisol.—Salivary cortisol collection was sampled from participants during the first and last 20 minutes of the school day on 3 consecutive school days in fall of kindergarten (missingness = 7.1%). Children did not ingest solids or liquids in the 30 minutes prior to sampling. Children were then provided with cotton rolls to chew for 20-30 seconds until they became saturated. The cotton rolls were deposited in Salivette tubes (Sarstedt, Nümberg, Germany) and frozen at −7°C until they were shipped to the University of Dresden for assay using a commercial immunoassay with chemiluminescence detection (Cortisol Luminescence Immunoassay; IBL-Hamburg, Hamburg, Germany). The detection limit of the assay was 0.41 nmol/l with mean inter- and intra-assay variations of 8.5% and 6.1%, respectively. Values greater than 55 nmol/l were considered unreliable and were discarded (<1% of sample met this criteria). Ten children were excluded from the model because of the use of prescription medications with known effects on salivary cortisol levels (e.g., human growth hormone, exogenous glucocorticoids). Cortisol values were skewed and $\log_{10}$ transformed. Average cortisol values and times of collection were computed using the well-established, standardized trapezoid formula (Pruessner et al., 2003). We calculated an area under the curve with respect to ground (AUCg) for each school day using both the morning and afternoon samples. We then averaged the AUCg values across the 3 days to create a single AUCg score. Multiple days of measurement are recommended in order to ascertain a more reliable measure of daily cortisol (Adam & Kumari, 2009). This approach has been previously used in studies with this cohort (Bush et al., 2011b; Roubinov et al., 2017, 2018). Cortisol AUCg reflects total cortisol output and provides a measure of children's HPA axis arousal.

Respiratory sinus arrhythmia.—During an adaptation period, children spent several minutes being familiarized with the equipment to acclimate to the environment and were allowed to rest quietly for several minutes after hook-up to achieve a resting state. Children were instructed to remain seated and still, and to keep their hands placed on hand outlines on the table. Following the adaptation period, children's resting PNS activity was assessed using RSA assessed over the course of 2 minutes while a trained experimenter read the child a non-emotional, neutral story in a standardized manner during the fall of kindergarten (missingness = 3.6%). RSA was estimated as the natural logarithm of the variance of the heart period within the frequency bandpass associated with respiration at this age (i.e., 0.15 to 0.80 Hz; Bar-Haim et al., 2000). Four spot electrodes (two current, two impedance) were placed in the standard tetrapolar configuration on the child's neck and chest, and electrocardiograph (ECG) electrodes were placed on the right clavicle and lower left rib. A 4 mA AC current at 100 kHz was passed through the two current electrodes. Data were acquired using the Biopac MP150 (Biopac Systems, Santa Barbara, CA) interfaced to a PC-based computer. Analog data were continuously monitored on the computer for signal and noise, and digitized data were stored for offline analysis. The sampling frequency was 1 kHz. Prior to analyses, each waveform was verified, interbeat intervals were visually checked, and artifacts were identified using the MindWare software program (Berntson et al., 1990). AcqKnowledge files from the Biopac program were scored by task, in 60-second task intervals. A minimum of 30 seconds of continuous data collection was required for scoring in most cases; however, a few incidents with two blocks of 20-29 seconds interrupted by a brief burst of “noise” were scored at the discretion of the advanced scorer in consultation with the expert faculty member when such choices appeared to result in representative results.

Data Analyses

Descriptive statistics were conducted using SPSS version 24 (IBM Corp., 2016); all other analyses were conducted using Mplus 8 (Muthén & Muthén, 2017). Little’s test of Missing Completely at Random (MCAR) was not significant ($\chi^2(94) = 110.77$, $p = .114$) indicating the data were missing completely at random. With MCAR data, we were able to estimate models using full-information maximum likelihood (FIML), which allows participants with at least one outcome measure available to be included in analyses (Rubin & Little, 2002). First, we conducted separate latent class growth analyses (LCGA) for standardized externalizing and internalizing problems across three time points to identify the appropriate number of trajectories. The optimal number of latent trajectories was determined by comparing model fit across four models. Fit statistics included the sample-adjusted Bayesian information criterion (aBIC), Bayesian information criterion (BIC), Akaike information criterion (AIC), Lo-Mendel-Rubin likelihood ratio test (LMR-LRT), Vuong-Lo-Mendell-Rubin likelihood ratio test (VLRT-LRT) (Nylund et al., 2007). The model with the lowest BIC, aBIC, and AIC values is preferred; a non-significant χ^2 value ($p > .05$) for the LMR-LRT and VLMR-LRT statistics suggests that a model with one fewer class may be preferred (i.e., k-1); and higher entropy values closer to 1.00 indicate clearer classification and greater power to predict class membership. Multiple random starting values were used to avoid a local minimum. In addition, classification, accuracy, parsimony, and interpretability were also considered to ensure models fit with theory and previous research. Second, these trajectories were used to create groups of interest.[1] Third, the logistic regression model with covariates (i.e., age, sex, SES, race/ethnicity), cumulative family adversity, physiological variables (i.e., daily cortisol, resting RSA), their interactions (i.e., adversity × cortisol, adversity × RSA, cortisol × RSA), and dichotomous externalizing/internalizing grouping variables was estimated with Monte Carlo integration and logit link function (Atkins et al., 2013). Finally, significant interactions were probed with the Johnson-Neyman technique (Preacher et al., 2006). The region of significance was defined by the 95% confidence

[1]We also conducted parallel process LCGA to attempt to account for covariation between externalizing and internalizing problems. These analyses indicated an optimal three-class solution for both externalizing and internalizing problems resulting in nine classes once combined; however, the prevalence rates of four of these classes were very small ($n = 7$, 2.1%; $n = 8$, 2.4%; $n = 9$, 2.8%; $n = 12$, 3.7%). These findings suggest that parallel process LCGA may be too inclusive for our sample size. We discuss this further in our limitations section noting the importance of future research for addressing this issue.

interval and, similarly, was considered significant if the confidence intervals did not include the 0 value.

Results

Descriptive Statistics

Descriptive statistics, missingness, and correlations of main study variables are described in Supplementary Information and presented in Supplementary Table 1.

Externalizing and Internalizing Trajectories

Two LCGA were conducted to identify groups of individuals based on externalizing and internalizing problems across three time points. Across both analyses of externalizing and internalizing problems, the aBIC, BIC, and AIC decreased from the one-class model through to the four-class model, the entropy value was greater than .70 in classes two through four, and the LMR-LRT and the VLRT-LRT became non-significant in the three-class model for externalizing problems and the four-class model for internalizing problems (see Table 1). While we note that the likelihood ratio tests may indicate three-classes for internalizing problems, the third class in this model was comprised of only 13 participants and so taking into account other fit indices the two-class model was identified as the optimal fit for both externalizing and internalizing problems. For externalizing problems, analyses identified high (n = 89, 27.2%; intercept = 1.30, p < .001; slope = −.05, p = .385) and low (n = 238, 72.8%; intercept = −.47, p < .001; slope = .03, p = .068) trajectories from fall of kindergarten to grade 1 (see Figure 1). For internalizing problems, analyses identified high (n = 80, 24.4%; intercept = 1.19, p < .001; slope = −.08, p = .213) and low (n = 247, 75.5%; intercept = −.39, p < .001; slope = .03, p = .221) trajectories from fall of kindergarten to grade 1 (see Figure 1).

Next, four possible combinations of assignment to either high or low externalizing and internalizing trajectories were used to create groups of interest (see Figure 2): a co-occurring group (high externalizing/high internalizing; n = 43, 13.1%); an externalizing-only group (high externalizing/low internalizing; n = 46, 14.0%); an internalizing-only group (low externalizing/high internalizing; n = 37, 11.3%); and a low problems group (low externalizing/low internalizing; n = 201, 61.3%). Groups were then dummy coded, with the low group as the reference group, to be included in the structural model.

Structural Model

With regard to covariate associations with adversity and physiological variables, SES (B(SE) = −.20(.08), p = .015) and being male (B(SE) = −.28(.11), p = .013) were negatively associated with adversity; and SES (B(SE) = −.26(.08), p = .001) and being an ethnic minority (B(SE) = .44(.12), p < .001) were negatively associated with daily cortisol.

Table 2 reports findings among main study variables. With regard to covariates, SES negatively predicted co-occurring group membership (odds ratio [OR] = .53), and being male predicted externalizing-only group membership (OR = .22). Experiences of family adversity and resting RSA significantly positively predicted co-occurring group membership (*OR* = 1.81; 2.95, respectively). Finally, the interaction of cortisol-by-RSA negatively predicted internalizing-only group membership (*OR* = .34). The Johnson-Neyman technique revealed that daily cortisol was positively associated with internalizing-only group membership when resting RSA was at or below −1.57 and at or above 1.00 (see Figure 3).

Discussion

Studies examining the physiological basis of risk have produced mixed findings, which may occur, in part, due to the lack of integrated data from more than one system, particularly in the simultaneous examination of trajectories of both externalizing and internalizing problems. Thus, the present study aimed to extend current understanding of interrelated patterns of adrenocortical and autonomic activity associated with cumulative family adversity and child psychopathology among a community sample of young children with a range of developmental risk. We identified stable trajectories across three time points of multi-reporter-derived externalizing and internalizing problems, and their co-occurrence, among a socioeconomically and racially/ethnically diverse community sample of children, adding to the developmental psychopathology literature examining clinical samples.

Cumulative Family Adversity

Children exhibiting co-occurring externalizing and internalizing problems were more likely to reside in homes with lower SES and higher cumulative family adversity, compared with the low problems group. Conversely, neither lower SES nor higher family adversity elevated risk for the externalizing-only or internalizing-only problems relative to the low problem group, suggesting that lower SES and higher cumulative burden within the home may contribute specifically to the development of co-occurring externalizing and internalizing problems. Our measure of family adversity was comprised of several indices of stress within the home. While some of the constructs reflected direct stressful experiences toward the child (e.g., negative and anger expressiveness, harsh and restrictive parenting), other constructs captured stressors with potential direct and indirect effects on child behavior. For example, one index assessing parenting challenges included items regarding parents' feelings of being overwhelmed and a lack of time to do things they wanted to do. Although these types of stressors may not directly affect child wellbeing, they can create a more negative home environment. Parents lacking time for themselves and feeling overwhelmed by their lives may result in greater negative emotions and parenting, poorer health behaviors, and less time and capacity for positive engagement with their child. In the present study, we conceptualized cumulative family adversity as an index of both direct and indirect stress exposures within the home, to provide a rich representation of the multifaceted home social environment. Notably, the children with co-occurring problems did not show higher daily cortisol levels associated with experiences of adversity, and this may be perhaps due to their simultaneous presentation of externalizing and internalizing problems.

Adrenocortical Functioning

The extant research examining associations between daily cortisol concentrations and psychopathology has been contradictory (Koss & Gunnar, 2018), and the narrow focus on one dimension may be limiting current understanding, given that externalizing and internalizing problems commonly co-occur. Our findings suggest that aggregate experiences of stress have a particularly deleterious effect on young child behavior problems, but this association may not be underpinned by HPA dysregulation. Other reasons for these findings may be because our measure of cumulative family adversity did not directly assess some major types of severe adverse experiences (e.g., maltreatment), and meta-analytic findings support severity and chronicity as a factor in changes in HPA activity (Miller et al., 2007). A final consideration is the timing of the stressor, such that hormonal activity may be elevated at or during the stressor and returns to baseline or lower with passing time (Miller et al., 2007). Our measure of cumulative family adversity was reflective of current and recent events, and not a historical account of stressful experiences. It would be important for further research to examine HPA activity and co-occurring problems at distinct developmental stages given the aforementioned inconsistencies in the literature.

Autonomic Functioning

The higher resting RSA scores among children with co-occurring externalizing and internalizing problems was unexpected. Past research has tended to suggest that higher resting RSA is associated with emotion regulation and that lower resting RSA is a biomarker of emotion dysregulation and associated with symptoms of psychopathology (Porges, 2007). However, prior studies have not adjusted for HPA axis activity or examined co-occurring problems, particularly over time, and thus, discrepant findings may be due to whether HPA activity is simultaneously modelled and the examination of both externalizing and internalizing problems. In addition, past research has predominantly been comprised of clinical samples (our sample was comprised of low-risk community children), and very low resting RSA may be more commonly observed in individuals with greater adverse experiences and higher levels of psychopathology. Alternatively, there may be a methodological explanation for this finding. While lower resting RSA is often observed in individuals with mental health problems, such as externalizing and internalizing psychopathology, research findings on RSA reactivity are more equivocal (Beauchaine et al., 2019). In the present study, we aimed to measure general, trait-like vulnerability through resting RSA; however, other researchers have examined RSA reactivity to assess state stress reactivity. Although participants were allowed to acclimate to the environment, and baseline activity was ascertained while the child was relaxed and participating in a neutral activity (i.e., listening to a non-emotional story, a standard procedure with young children [Bush et al., 2011b] due to difficulty obtaining true rest in young children), a parasympathetic response may be evoked when attending to the resting task even if it is ‘neutral’ in context (Dollar et al., 2020). While our methodology adhered to best practice, the unexpected finding linking higher resting RSA and co-occurring group membership, and the equivocal state of the broader field, point to the importance of considering moderators in research examining the role of physiology in mental health. Developmental stage may be particularly important in this regard.

Adrenocortical and Autonomic Functioning

We did not find evidence of an interaction between cumulative family adversity and daily cortisol or resting RSA and group membership. The present sample has previously been used to illustrate biological sensitivity to context (BSC; Boyce & Ellis, 2005), using low adversity as a close (although insufficient) proxy for positive environments; thus, we had intended to consider the range of family adversity in that context. We acknowledge the limitations of lacking a true "optimal positive environment" variable to ideally test this theory. Our findings suggest physiology-externalizing/internalizing group associations do not vary on the basis of family-level environmental stress composite levels. The relation between adversity, physiology, and mental health in early childhood may be better modeled as a mediating process. Prominent theories in both the adrenocortical and autonomic literatures posit that these biological systems may be the primary pathways through which experiences of adversity shape child outcomes (Lupien et al., 2015), yet empirical findings continue to be inconsistent (such that lower and higher levels of daily cortisol and resting RSA have each been associated with poor child outcomes), and this may largely be due to examination of cross-sectional data. Returning to the model of allostasis, physiological systems respond to environmental demands, but in the face of chronic experiences of stress, this response can result in a recalibration of the HPA and ANS processes, suggesting a developmental mechanism of change over time (McEwen & Wingfield, 2003). Although our family adversity measure was comprised of measures assessing current or recent stressors (i.e., in the past week or two) that may be persistent, both family adversity and child physiology were assessed at the same time point (i.e., fall of kindergarten); thus, study design precluded optimal testing for mediation. This constitutes an important future direction for other studies. Further research is needed with longer durations between measures and employing longitudinal designs to empirically test a developmental mediation model of cumulative family adversity, HPA and ANS system activity, and child mental health outcomes.

Daily cortisol was not independently associated with internalizing-only group membership; however, when considered in conjunction with resting RSA, it was predictive. Both higher cortisol and lower RSA (PNS withdrawal), as well as lower cortisol with higher RSA (PNS activation) positively predicted internalizing group membership. The activation of the HPA axis and deactivation of the PNS among individuals with internalizing problems was in line with predictions and supports theoretical models suggesting dual-system hyperarousal as a risk factor (Bauer et al., 2002; Del Giudice et al., 2011). Illustratively, El-Sheikh and colleagues (2011) also found that higher cortisol and lower resting RSA were associated with the highest levels of anxiety and depression symptoms in children. As indicated by the authors, this patterning of physiological hyperarousal is commonly reflected in internalizing psychopathology, and particularly, anxiety symptoms. We also found that the inverse pattern—deactivation of the HPA axis and activation of the PNS—was associated with internalizing-only group membership. While El-Sheikh and colleagues (2011) identified a similar pattern, it only predicted depression and not anxiety symptoms in their sample. In contrast to anxiety, depression symptoms are more commonly characterized as blunted affect and underarousal. In young children, anxious and depressive symptoms commonly covary and are thus assessed as "internalizing problems"; it may be the case that our interaction is capturing those individuals scoring highly on depression rather than anxiety internalizing problems.

It may be important for further research to examine the interaction of daily cortisol and resting RSA in the prediction of anxiety and depression problems separately. Further, it may be illuminating to examine whether higher cortisol and lower RSA (i.e., hyperarousal) and lower cortisol and higher RSA (i.e., hypoarousal) may be associated with anxiety and depression, respectively. There is burgeoning evidence demonstrating great heterogeneity not only within the broader internalizing spectrum, but even within narrower components of anxiety and depression (Conway et al., 2019). These findings suggest that research examining associations between physiological systems and child mental health may benefit from a more nuanced subfactor or symptoms approach. Further, whereas El-Sheikh and colleagues' sample was approaching adolescence (*M* age = 9.31 years), our sample was much younger (*M* age = 5.32 years). Biological systems during this earlier developmental period are associated with greater sensitivity and distinct patterning (Alink et al., 2008; Koss & Gunnar, 2018). Because of the developmental sensitivity of stress-responsive systems, and potential canalization of individuals' biological stress response across development, future longitudinal research is needed examining the coupling of adrenocortical and autonomic processes over time to understand both developmental shifts and stability within individuals due to experience. Our findings inform and extend current understanding of adrenocortical and autonomic operation in early childhood—a time of heightened plasticity and sensitivity to environmental influences.

Strengths and Limitations

The present study had several methodological strengths, including our longitudinal assessment of both externalizing and internalizing problems among young community children. We also used a statistical approach to capture the development of both psychopathological dimensions. Further, our measure of psychopathology included both child and adult (parent and teacher) informant reports, extending research that has tended to focus solely on adult informant report with younger samples. The present study also examined the interaction of the adrenocortical and autonomic systems, when most research has focused on outcomes associated with only one of these systems. Methodological strengths notwithstanding, the present study also had limitations. First, although our sample was sufficient, once divided into classes our main comparison groups were only moderate in size (i.e., *n*s = 37-45); thus, findings should be replicated with larger samples. Related to this, our analytic approach included two LCGA to identify trajectories of externalizing and internalizing problems, which we used to then create groups. While we acknowledge that this approach does not simultaneously take into account the covariation of externalizing and internalizing problems, we identified a distinct subgroup of children scoring highly across both types of psychopathology. As outlined in the Footnotes, we also examined a parallel process approach; however, these analyses appeared to be overly inclusive resulting in several groups not large enough for accurate comparisons and not in line with current theory and research. It is important for future research to include larger sample sizes to examine whether current findings are replicated with parallel modelling of externalizing and internalizing problems and models that capture the dimensional nature of trajectories. Second, although our measure of psychopathology included both child and adult informant report, child report was limited to the two kindergarten time points. Finally, as indicated earlier, our measures of family adversity and HPA and ANS activity were assessed at a similar single time point (i.e., fall of kindergarten). Future research should also include multiple time point assessments of physiological activity, given recent research findings of within-individual stability and between-individual variability during the child developmental period relative to adolescence (Dollar et al., 2020; Hinnant et al., 2018). Recent recommendations advocate for both within- and between-person analytic approaches in longitudinal research (Curran & Bauer, 2011; Curran et al., 2014). Whereas theoretical perspectives commonly describe within-person change, most analytic methods are designed to examine between-person effects, which do not account for time-specific relationships between processes. This research could yield important developmental understanding of stress-responsive systems and child health outcomes.

Implications and Conclusion

Examining endocrine and physiological correlates of co-occurring, externalizing, and internalizing patterns of psychopathology has important theoretical and clinical implications. Many studies attempting to identify biomarkers underpinning adjustment problems have relied on high-risk adolescent samples. Our research adds to the field by informing theoretical models on developmental consequences of milder adverse experiences on physiology and behavior among preschool children. Our findings also have implications for interventionists. Although less commonly considered in attempts to understand the effectiveness of treatments and preventive interventions, a surge of recent research supports the utility of biological indices for predicting treatment response (Glenn, 2019). In the context of our study, individuals with internalizing problems and hyperarousal (i.e., higher cortisol and lower RSA) may benefit from treatment targeting emotion dysregulation. In contrast, treatment with a focus on depression symptoms may be more beneficial for those individuals with internalizing problems and hyporarousal (i.e., lower cortisol and higher RSA).

To conclude, there are inconsistencies in the literature with regards to physiological functioning and these may be due, in part, to cross-sectional designs, the examination of different developmental periods, and utilization of only one biological system. Thus, there have been recent recommendations from the scientific community for a multiple systems biological approach for understanding the developmental consequences of stress and risk (Buss et al., 2018). To address this call for research, the present study adopted a longitudinal, multi-informant, multisystem methodology for examining associations between cumulative family adversity, physiology, and psychopathology problems among young children. Using this integrated approach, we identified patterns of HPA and ANS co-activity associated with risk of experiencing co-occurring and internalizing-only problems in early childhood, providing potential guidance for differential intervention strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This study was supported by grants awarded to W. Thomas Boyce from the National Institute of Mental Health (R01 MH62320), the MacArthur Foundation Research Network on Psychopathology and Development, and the Canadian Institute for Advanced Research. Dr. Boyce and Dr. Bush received support for this work from The Lisa and John Pritzker Family Foundation.

References

Ablow JC, & Measelle JR, & The MacArthur Working Group on Outcome Assessment (2003). Manual for the Berkeley Puppet Interview: Symptomatology, Social, and Academic Modules (BPI 1.0). University of Pittsburgh Press, MacArthur Foundation Research Network on Psychopathology and Development.

Achenbach TM, Ivanova MY, Rescorla LA, Turner LV, & Althoff RR (2016). Internalizing/externalizing problems: Review and recommendations for clinical and research applications. Journal of the American Academy of Child & Adolescent Psychiatry, 55(8), 647–656. [PubMed: 27453078]

Adam EK, & Kumari M (2009). Assessing salivary cortisol in large-scale, epidemiological research. Psychoneuroendocrinology, 34(10), 1423–1436. [PubMed: 19647372]

Alink LRA, van IJzendoorn MH, Bakermans-Kranenburg MJ, Mesman J, Juffer F, & Koot HM (2008). Cortisol and externalizing behavior in children and adolescents: Mixed meta-analytic evidence for the inverse relation of basal cortisol and cortisol reactivity with externalizing behavior. Developmental Psychobiology, 50(5), 427–450. [PubMed: 18551461]

Armstrong JM, Goldstein LH, & The MacArthur Working Group on Outcome Assessment. (2003). Manual for the MacArthur Health and Behavior Questionnaire (HBQ 1.0). University of Pittsburgh Press, MacArthur Foundation Research Network on Psychopathology and Development.

Atkins DC, Baldwin SA, Zheng C, Gallop RJ, & Neighbors C (2013). A tutorial on count regression and zero-altered count models for longitudinal substance use data. Psychology of Addictive Behaviors, 27(1), 166–177. [PubMed: 22905895]

Bar-Haim Y, Marshall PJ, & Fox NA (2000). Developmental changes in heart period and high-frequency heart period variability from 4 months to 4 years of age. Developmental Psychobiology, 37(1), 44–56. [PubMed: 10937660]

Bauer AM, Quas JA, & Boyce WT (2002). Associations between physiological reactivity and children's behavior: Advantages of a multisystem approach. Journal of Developmental & Behavioral Pediatrics, 23(2), 102–113. [PubMed: 11943973]

Beauchaine TP (2012). Physiological markers of emotion and behavior dysregulation in externalizing psychopathology. Monographs of the Society for Research in Child Development, 77(2), 79–86. [PubMed: 25242827]

Beauchaine TP, Bell Z, Knapton E, McDonough-Caplan H, Shader T, & Zisner A (2019). Respiratory sinus arrhythmia reactivity across empirically based structural dimensions of psychopathology: A meta-analysis. Psychophysiology, 56(5), e13329. [PubMed: 30672603]

Berntson GG, Quigley KS, Jang JF, & Boysen ST (1990). An approach to artifact identification: Application to heart period data. Psychophysiology, 27(5), 586–598. [PubMed: 2274622]

Block JH (1965). The Child-Rearing Practices Report. Unpublished manuscript, University of California, Berkeley.

Boyce WT, & Ellis BJ (2005). Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. Development and Psychopathology, 17(2), 271–301. [PubMed: 16761546]

Buhle JT, Silvers JA, Wager TD, Lopez R, Onyemekwu C, Kober H, Weber J, & Ochsner KN (2014). Cognitive reappraisal of emotion: A meta-analysis of human neuroimaging studies. Cerebral Cortex, 24(11), 2981–2990. [PubMed: 23765157]

Bush NR, Alkon A, Stamperdahl J, Obradović J, & Boyce WT (2011a). Differentiating challenge reactivity from psychomotor activity in studies of children's psychophysiology: Considerations for theory and measurement. Journal of Experimental Child Psychology, 110(1), 62–79. [PubMed: 21524757]

Bush NR, Obradović J, Adler N, & Boyce WT (2011b). Kindergarten stressors and cumulative adrenocortical activation: The "first straws" of allostatic load? Development and Psychopathology, 23(4), 1089–1106. [PubMed: 22018083]

Buss KA, Jaffee S, Wadsworth ME, & Kliewer W (2018). Impact of psychophysiological stress-response systems on psychological development: Moving beyond the single biomarker approach. Developmental Psychology, 54(9), 1601–1605. [PubMed: 30148389]

Cacioppo JT, Berntson GG, Malarkey WB, Kiecolt-Glaser JK, Sheridan JF, Poehlmann KM, Burleson MJ, Ernst JM, Hawkley LC, & Glaser R (1998). Autonomic, neuroendocrine, and immune responses to psychological stress: The reactivity hypothesis. Annals of the New York Academy of Sciences, 840(1), 664–673. [PubMed: 9629293]

Cicchetti D (2016). Socioemotional, personality, and biological development: Illustrations from a multilevel developmental psychopathology perspective on child maltreatment. Annual Review of Psychology, 67, 187–211.

Cicchetti D, & Rogosch FA (1996). Equifinality and multifinality in developmental psychopathology. Development and Psychopathology, 8(4), 597–600.

Cicchetti D, & Rogosch FA (2001). The impact of child maltreatment and psychopathology on neuroendocrine functioning. Development and Psychopathology, 13(4), 783–804. [PubMed: 11771908]

Conway CC, Forbes MK, Forbush KT, Fried EI, Hallquist MN, Kotov R, … & Sunderland M (2019). A hierarchical taxonomy of psychopathology can transform mental health research. Perspectives on Psychological Science, 14(3), 419–436. [PubMed: 30844330]

Curran PJ, & Bauer DJ (2011). The disaggregation of within-person and between-person effects in longitudinal models of change. Annual Review of Psychology, 62, 583–619.

Curran PJ, Howard AL, Bainter SA, Lane ST, McGinley JS (2014). The separation of between-person and within-person components of individual change over time: A latent curve model with structured residuals. Journal of Clinical and Consulting Psychology, 82(5), 879–894.

Deković M, Janssens JMAM, & Gerris JRM (1991). Factor structure and construct validity of the Block Child Rearing Practice Report (CRPR). Psychological Assessment, 3(2), 182–187.

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

Dietrich A, Riese H, Sondeijker FE, Greaves-Lord K, Ormel J, Neeleman J, & Rosmalen JG (2007). Externalizing and internalizing problems in relation to autonomic function: A population-based study in preadolescents. Journal of the American Academy of Child & Adolescent Psychiatry, 46(3), 378–386. [PubMed: 17314724]

Dollar JM, Calkins SD, Berry NT, Perry NB, Keane SP, Shanahan L, & Wideman L (2020). Developmental patterns of respiratory sinus arrhythmia from toddlerhood to adolescence. Developmental Psychology, 56(4), 783–794. [PubMed: 31999180]

El-Sheikh M, Arsiwalla DD, Hinnant JB, & Erath SA (2011). Children's internalizing symptoms: The role of interactions between cortisol and respiratory sinus arrhythmia. Physiology & Behavior, 103(2), 225–232. [PubMed: 21315098]

Essex MJ, Klein MH, Cho E, & Kalin NH (2002). Maternal stress beginning in infancy may sensitize children to later stress exposure: Effects on cortisol and behavior. Biological Psychiatry, 52(8), 776–784. [PubMed: 12372649]

Evans GW, Kim P, Ting AH, Tesher HB, & Shannis D (2007). Cumulative risk, maternal responsiveness, and allostatic load among young adolescents. Developmental Psychology, 43(2), 341–351. [PubMed: 17352543]

Fairchild G, van Goozen SH, Stollery SJ, Brown J, Gardiner J, Herbert J, & Goodyer IM (2008). Cortisol diurnal rhythm and stress reactivity in male adolescents with early-onset or adolescence-onset conduct disorder. Biological Psychiatry, 64(7), 599–606. [PubMed: 18620338]

Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, & Marks JS (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. American Journal of Preventive Medicine, 14(4), 245–258. [PubMed: 9635069]

Glenn AL (2019). Using biological factors to individualize interventions for youth with conduct problems: Current state and ethical issues. International Journal of Law and Psychiatry, 65, 1–8.

Gross JJ (1998). The emerging field of emotion regulation: An integrative review. Review of General Psychology, 2(3), 271–299.

Halberstadt AG (1986). Family socialization of emotional expression and nonverbal communication styles and skills. Journal of Personality and Social Psychology, 51(4), 827–836.

Hinnant JB, & El-Sheikh M (2009). Children's externalizing and internalizing symptoms over time: The role of individual differences in patterns of RSA responding. Journal of Abnormal Child Psychology, 37(8), 1049–1061. [PubMed: 19711181]

Hinnant JB, Philbrook LE, Erath SA, & El-Sheikh M (2018). Approaches to modeling the development of physiological stress responsivity. Psychophysiology, 55(5), e13027. [PubMed: 29086432]

Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, Jones L, & Dunne MP (2017). The effect of multiple adverse childhood experiences on health: A systematic review and meta-analysis. The Lancet Public Health, 2(8), e356–e366. [PubMed: 29253477]

Corp IBM. (2016). IBM SPSS Statistics for Windows, Version 24.0. Author.

Johnson PL, & O'Leary KD (1987). Parental behavior patterns and conduct problems in girls. Journal of Abnormal Child Psychology, 15(4), 573–581. [PubMed: 3437092]

Kaplan B, Crawford S, Cantell M, Kooistra L, & Dewey D (2006). Comorbidity, co-occurrence, continuum: What's in a name? Child: Care, Health and Development, 32(6), 723–731. [PubMed: 17018047]

Kirschbaum C, & Hellhammer DH (1994). Salivary cortisol in psychoneuroendocrine research: Recent developments and applications. Psychoneuroendocrinology, 19(4), 313–333. [PubMed: 8047637]

Klimes-Dougan B, Hastings PD, Granger DA, Usher BA, & Zahn-Waxler C (2001). Adrenocortical activity in at-risk and normally developing adolescents: Individual differences in salivary cortisol basal levels, diurnal variation, and responses to social challenges. Development and Psychopathology, 13(3), 695–719. [PubMed: 11523855]

Koss KJ, & Gunnar MR (2018). Annual research review: Early adversity, the hypothalamic–pituitary–adrenocortical axis, and child psychopathology. Journal of Child Psychology and Psychiatry, 59(4), 327–346. [PubMed: 28714126]

Kraemer HC, Measelle JR, Ablow JC, Essex MJ, Boyce WT, & Kupfer DJ (2003). A new approach to integrating data from multiple informants in psychiatric assessment and research: Mixing and matching contexts and perspectives. American Journal of Psychiatry, 160(9), 1566–1577. [PubMed: 12944328]

Laurent HK, Neiderhiser JM, Natsuaki MN, Shaw DS, Fisher PA, Reiss D, & Leve LD (2014). Stress system development from age 4.5 to 6: Family environment predictors and adjustment implications of HPA activity stability versus change. Developmental Psychobiology, 56(3), 340–354. [PubMed: 23400689]

Lengua LJ, Thompson SF, Moran LR, Zalewski M, Ruberry EJ, Klein MR, & Kiff CJ (2020). Pathways from early adversity to later adjustment: Tests of the additive and bidirectional effects of executive control and diurnal cortisol in early childhood. Development and Psychopathology, 32(2), 545–558. [PubMed: 31072416]

Lengua LJ, Honorado E, & Bush NR (2007). Contextual risk and parenting as predictors of effortful control and social competence in preschool children. Journal of Applied Developmental Psychology, 28(1), 40–55. [PubMed: 21687825]

Lupien SJ, Ouellet-Morin I, Hupbach A, Tu MT, Buss C, Walker D, Mcewen BS (2015). Beyond the stress concept: Allostatic load—A developmental biological and cognitive perspective. In Cicchetti D, & Cohen DJ (Eds.), Developmental psychopathology: Volume two: Developmental neuroscience (pp. 578–628). Wiley.

McEwen BS (1998). Stress, adaptation, and disease: Allostasis and allostatic load. Annals of the New York Academy of Sciences, 840, 33–44. [PubMed: 9629234]

McEwen BS, & Wingfield JC (2003). The concept of allostasis in biology and biomedicine. Hormones and Behavior, 43(1), 2–15. [PubMed: 12614627]

Miller GE, Chen E, & Zhou ES (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychological Bulletin, 133(1), 25–45. [PubMed: 17201569]

Muthén BO, & Muthén LK (2017). Mplus Version 8: User's guide. Authors.

Nylund KL, Asparouhov T, & Muthén BO (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. Structural Equation Modeling, 14(4), 535–569.

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]

Obradović J, Shaffer A, & Masten AS (2012). Risk and adversity in developmental psychopathology: Progress and future directions. In Mayes LC & Lewis M (Eds.), A developmental environment measurement handbook (pp. 35–57). Cambridge University Press.

Popma A, Doreleijers TA, Jansen LM, Van Goozen SH, Van Engeland H, & Vermeiren R (2007). The diurnal cortisol cycle in delinquent male adolescents and normal controls. Neuropsychopharmacology, 32(7), 1622–1628. [PubMed: 17228341]

Porges SW (2001). The polyvagal theory: Phylogenetic substrates of a social nervous system. International Journal of Psychophysiology, 42(2), 123–146. [PubMed: 11587772]

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

Porter B, & O'Leary KD (1980). Marital discord and childhood behavior problems. Journal of Abnormal Child Psychology, 8(3), 287–295. [PubMed: 7410730]

Preacher KJ, Curran PJ, & Bauer DJ (2006). Computational tools for probing interactions in multiple linear regression, multilevel modeling, and latent curve analysis. Journal of Educational and Behavioral Statistics, 31(4), 437–448.

Pruessner JC, Kirschbaum C, Meinlschmid G, & Hellhammer DH (2003). Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology, 28(7), 916–931. [PubMed: 12892658]

Quas JA, Yim IS, Oberlander TF, Nordstokke D, Essex MJ, Armstrong JM, Bush N, Obradović J, & Boyce WT (2014). The symphonic structure of childhood stress reactivity: Patterns of sympathetic, parasympathetic, and adrenocortical responses to psychological challenge. Development and Psychopathology, 26(401), 963–982. [PubMed: 24909883]

Radloff LS (1977). The CES-D scale: A self-report depression scale for research in the general population. Applied Psychological Measurement, 1(3), 385–401.

Rickel AU, & Biasatti LL (1982). Modification of the Block Child Rearing Practices Report. Journal of Clinical Psychology, 38(1), 129–133.

Rimm-Kaufman SE, & Pianta RC (2000). An ecological perspective on the transition to kindergarten: A theoretical framework to guide empirical research. Journal of Applied Developmental Psychology, 21(5), 491–511.

Ross KM, Murphy ML, Adam EK, Chen E, & Miller GE (2014). How stable are diurnal cortisol activity indices in healthy individuals? Evidence from three multi-wave studies. Psychoneuroendocrinology, 39, 184–193. [PubMed: 24119668]

Roubinov DS, Boyce WT, Lee MR, & Bush NR (2020). Evidence for discrete profiles of children's physiological activity across three neurobiological system and their transitions over time. Developmental Science, e12989. [PubMed: 32416021]

Roubinov DS, Hagan MJ, Boyce WT, Adler NE, & Bush NR (2018). Family socioeconomic status, cortisol, and physical health in early childhood: The role of advantageous neighborhood characteristics. Psychosomatic Medicine, 80(5), 492–501. [PubMed: 29742755]

Roubinov DS, Hagan MJ, Boyce WT, Essex MJ, & Bush NR (2017). Child temperament and teacher relationship interactively predict cortisol expression: The prism of classroom climate. Development and Psychopathology, 29(5), 1763–1775. [PubMed: 29162182]

Rubin DB, & Little RJ (2002). Statistical analysis with missing data. Wiley.

Ruttle PL, Shirtcliff EA, Serbin LA, Fisher DBD, Stack DM, & Schwartzman AE (2011). Disentangling psychobiological mechanisms underlying internalizing and externalizing behaviors in youth: Longitudinal and concurrent associations with cortisol. Hormones and Behavior, 59(1), 123–132. [PubMed: 21056565]

Saridjan NS, Velders FP, Jaddoe VW, Hofman A, Verhulst FC, & Tiemeier H (2014). The longitudinal association of the diurnal cortisol rhythm with internalizing and externalizing problems in pre-schoolers. The Generation R Study. Psychoneuroendocrinology, 50, 118–129. [PubMed: 25202831]

Spielberger CD (1988). Manual for the State-Trait Anger Expression Inventory (STAXI). Psychological Assessment Resources.

Stratakis CA, & Chrousos GP (1995). Neuroendocrinology and pathophysiology of the stress system. Annals of the New York Academy of Sciences, 771(1), 1–18. [PubMed: 8597390]

Thayer JF, Åhs F, Fredrikson M, Sollers JJ, & Wager TD (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. Neuroscience & Biobehavioral Reviews, 36(2), 747–756. [PubMed: 22178086]

Thayer JF, & Sternberg E (2006). Beyond heart rate variability: Vagal regulation of allostatic systems. Annals of the New York Academy of Sciences, 1088(1), 361–372. [PubMed: 17192580]

Zandstra ARE, Hartman CA, Nederhof E, van den Heuvel ER, Dietrich A, Hoekstra PJ, & Ormel J (2015). Chronic stress and adolescents' mental health: Modifying effects of basal cortisol and parental psychiatric history. The TRAILS study. Journal of Abnormal Child Psychology, 43(6), 1119–1130. [PubMed: 25617009]

Zhang W, Fagan SE, & Gao Y (2017). Respiratory sinus arrhythmia activity predicts internalizing and externalizing behaviors in non-referred boys. Frontiers in Psychology, 8, 1–13. [PubMed: 28197108]

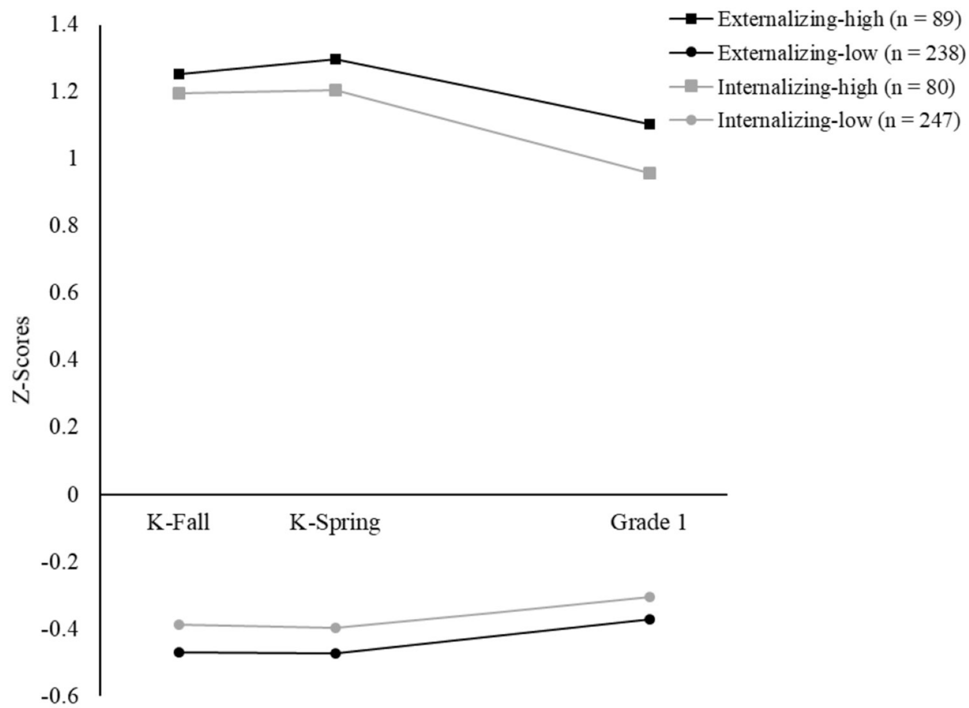

Figure 1.

Identified trajectories of externalizing (black) and internalizing (grey) scores from the LCGA for kindergarten (K) - fall, K - spring, and grade 1.

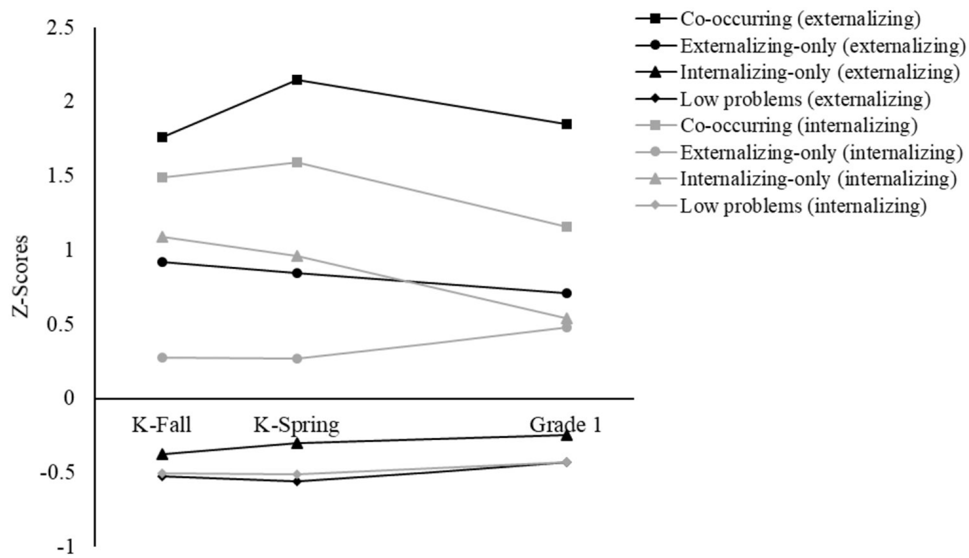

Figure 2.

Trajectories of externalizing (black) and internalizing (grey) scores for each symptoms trajectory group (co-occurring, *n* = 43; externalizing-only, *n* = 45; internalizing-only, *n* = 37; low problems, *n* = 212) for kindergarten (K) - fall, K - spring, and grade 1.

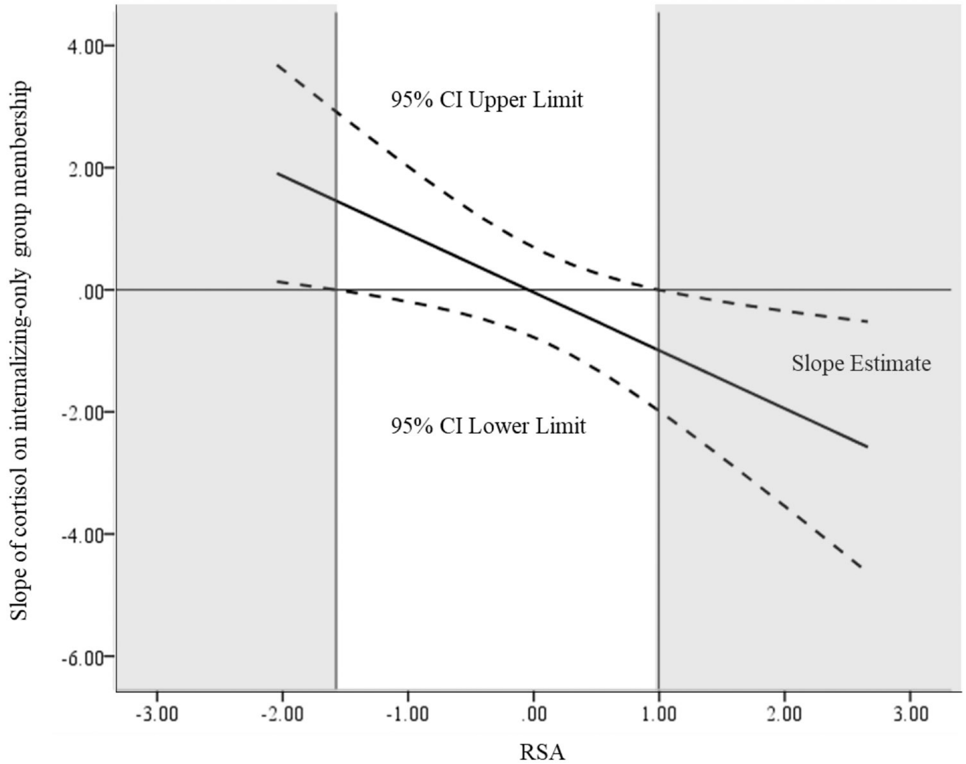

Figure 3.
Prediction (*B* with 95% confidence intervals [CI]) of internalizing-only group membership by daily cortisol output along resting respiratory sinus arrhythmia (RSA) levels, such that daily cortisol predicted internalizing-only group membership when resting RSA was at group-standardized levels of at or below −1.57 and at or above 1.00.

Table 1

Model Fit Statistics from two Latent Class Growth Analyses for Externalizing and Internalizing Trajectories

Classes	aBIC	BIC	AIC	Entropy	LMR-LRT	VLRT-LRT
Externalizing						
1	2672.01	2687.87	2668.92	NA	NA	NA
2	**2294.51**	**2319.88**	**2289.56**	**.90**	**<.001**	**<.001**
3	2228.77	2263.67	2221.98	.88	.294	.281
4	2182.24	2226.64	2173.58	.88	.241	.230
Internalizing						
1	2672.01	2687.87	2668.92	NA	NA	NA
2	**2489.22**	**2514.59**	**2484.27**	**0.79**	**<.001**	**<.001**
3	2451.04	2485.93	2444.24	0.79	.029	.024
4	2432.53	2476.94	2423.88	0.79	.286	.271

Note. Bolded text indicates the best-fitting model. aBIC = sample-adjusted Bayesian information criterion, BIC = Bayesian information criterion, AIC = Akaike information criterion, LMR-LRT = Lo-Mendel-Rubin likelihood ratio test, VLRT-LRT = Vuong-Lo-Mendell-Rubin likelihood ratio test.

Table 2

Estimates of Covariates, Adversity, and Biological Variables Regressed on Each Group

Group	***B*(*SE*)**	***OR***	***p***
Co-occurring			
Age	.67(.65)	1.96	.299
Sex	−.44(.41)	.65	.285
Race	−.12(.48)	.89	.806
SES	−.64(.26)	.53	.015
Adversity	.59(.19)	1.81	.001
Cortisol	.41(.30)	1.51	.170
RSA	1.08(.42)	2.95	.010
Adversity × Cortisol	−.25(.18)	.78	.180
Adversity × RSA	.01(.31)	1.01	.981
Cortisol × RSA	−.38(.42)	.69	.373
Externalizing-only			
Age	.12(.55)	1.12	.833
Sex	−1.50(.41)	.22	<.001
Race	−.31(.39)	.74	.425
SES	−.25(.21)	.78	.277
Adversity	.27(.19)	1.31	.144
Cortisol	.03(.21)	1.03	.874
RSA	−.14(.28)	.87	.620
Adversity × Cortisol	−.02(.17)	.98	.915
Adversity × RSA	−.41(.22)	.66	.064
Cortisol × RSA	.09(.34)	1.09	.801
Internalizing-only			
Age	−1.17(.67)	.31	.078
Sex	.18(.39)	1.19	.648
Race	−.32(.44)	.73	.462
SES	.06(.23)	1.06	.804
Adversity	.02(.21)	1.02	.920
Cortisol	.23(.20)	1.26	.234
RSA	−.19(.35)	.83	.587
Adversity × Cortisol	.15(.17)	1.16	.373
Adversity × RSA	.24(.34)	1.27	.482
Cortisol × RSA	−1.09(.48)	.34	.023

Note. SES = socioeconomic status; RSA = respiratory sinus arrhythmia.