

UCSF

UC San Francisco Previously Published Works

Title

Evidence for discrete profiles of children's physiological activity across three neurobiological system and their transitions over time

Permalink

<https://escholarship.org/uc/item/35j8s2bh>

Journal

Developmental Science, 24(1)

ISSN

1363-755X

Authors

Roubinov, Danielle S
Boyce, William T
Lee, Matthew R
[et al.](#)

Publication Date

2021

DOI

10.1111/desc.12989

Peer reviewed



Published in final edited form as:

Dev Sci. 2021 January ; 24(1): e12989. doi:10.1111/desc.12989.

Evidence for discrete profiles of children's physiological activity across three neurobiological system and their transitions over time

Danielle S. Roubinov¹, William T. Boyce^{1,2}, Matthew R. Lee³, Nicole R. Bush^{1,2}

¹Department of Psychiatry, University of California, California, USA

²Department of Pediatrics, University of California, California, USA

³Center of Alcohol and Substance Use Studies (CAS), Graduate School of Applied and Professional Psychology, Rutgers, The State University of New Jersey, New Brunswick, New Jersey, USA

Abstract

The conceptualization of stress-responsive physiological systems as operating in an integrated manner is evident in several *theoretical* models of cross-system functioning. However, limited *empirical* research has modeled the complexity of multisystem activity. Moreover few studies have explored developmentally regulated changes in multisystem activity during early childhood when plasticity is particularly pronounced. The current study used latent profile analysis (LPA) to evaluate multisystem activity during fall and spring of children's transition to kindergarten in three biological systems: the parasympathetic nervous system (PNS), sympathetic nervous system (SNS), and hypothalamic pituitary adrenal (HPA) axis. Latent transition analysis (LTA) was then used to examine the stability of profile classification across time. Across both timepoints, three distinct profiles of multisystem activity emerged. One profile was characterized by heightened HPA axis activity (*HPA Axis Responders*), a second profile was characterized by moderate, typically adaptive patterns across the PNS, SNS, and HPA axis (*Active Copers/Mobilizers*), and a third profile was characterized by heightened baseline activity, particularly in the PNS and SNS (*Anticipatory Arousal/ANS Responders*). LTA of fall-to-spring profile classifications indicated higher probabilities that children remained in the same profile over time compared to probabilities of profile changes, suggesting stability in certain patterns of cross-system responsivity. Patterns of profile stability and change were associated with socioemotional outcomes at the end of the school year. Findings highlight the utility of LPA and LTA to detect meaningful patterns of complex multisystem physiological activity across three systems and their associations with early adjustment during an important developmental transition.

Correspondence: Danielle S. Roubinov, University of California, San Francisco, Department of Psychiatry, 3333 California Avenue, Suite 465, San Francisco, CA, 94118, USA. danielle.roubinov@ucsf.edu.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Dr. Roubinov upon reasonable request.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

Keywords

autonomic nervous system; developmental psychobiology; hypothalamic pituitary adrenal axis; latent profile analysis; latent transition analysis

1 | INTRODUCTION

Knowledge within the field of psychobiology has advanced at an astounding rate. Empirical findings to date have dually answered our most pressing questions regarding the relations between biological factors and mental states, while creating a strong foundation for investigations of increasingly complex phenomena. Such progress is particularly evident in our understanding of physiological responses to stress. First-generation research in this domain provided a comprehensive understanding of how single biological systems respond to stress. Next, theoretical frameworks delineated the potential importance of multisystem interactions. Recently, researchers have begun to empirically test these theoretical frameworks, addressing the ways in which multiple physiological systems may evidence patterns of coordination (or dis-coordination) in response to environmental challenge. The development of sophisticated statistical techniques has been integral to advancing multisystem research, providing a means by which to capture the nuances of physiological interactions. Understanding these relations is particularly important in childhood, as differences in physiological regulatory abilities may underlie susceptibility to stress-related physical and mental health problems across the lifespan. In the current paper, we leverage the power of latent profile analysis and a rare breadth of longitudinal data to understand the nuances of how multiple physiological systems – namely the parasympathetic nervous system (PNS), sympathetic nervous system (SNS), and hypothalamic pituitary adrenal (HPA) axis—work together in early childhood. We then use latent transition analysis (LTA) to explore the stability of multisystem response patterns over time.

1.1 | Overview of the physiological stress response system

Although a comprehensive review of stress response systems is beyond the scope of this paper, we provide a brief overview in the following section. The three main components are the PNS, SNS, and HPA axis, which are distinguished not only by anatomical differences, but in the timing, duration, and nature of their physiological response to stress (Del Giudice, Ellis, & Shirtcliff, 2011). When challenges are encountered, the fastest response is provided by PNS, followed by the SNS, and finally, the HPA axis (Gunnar & Quevedo, 2007).

The autonomic nervous system (ANS) is comprised of the PNS and SNS, which are conventionally conceptualized as acting in an opposing fashion on target organs (Berntson et al., 1997). The term ‘rest and digest’ is often used to characterize the PNS and describe its role in reducing physiological arousal and promoting restoration. Conversely, the SNS is frequently described in terms of its ‘flight or fight’ functioning, which prepares the body to respond defensively to challenge through a range of biological changes, including increased heart rate, respiration, blood supply, bloodstream glucose release, and suppressed vegetative functions (Goldstein & Kopin, 2008; Gunnar & Vazquez, 2006). Withdrawal or disengagement of the PNS in response to stress releases the ‘parasympathetic brake’ on the

SNS, increases arousal, and provides a rapid means by which to heighten awareness to the environment and mount an adaptive coping response (Porges, 2007). With regard to timing, activation of the sympathetic nervous systems is conceptualized as a ‘second layer of defense’ if PNS withdrawal is not sufficient to meet the demands of the challenge (Del Giudice et al., 2011). Respiratory sinus arrhythmia (RSA) and cardiac pre-ejection period (PEP) are among the most commonly measured indices of PNS and SNS functioning, respectively.

In contrast to the faster-acting functions of the ANS, the HPA axis mounts a more delayed, longer-term response to stress that begins with the secretion of corticotropin-releasing hormone (CRH) by the hypothalamus into the bloodstream. The release of CRH triggers a cascade of hormonal events that culminates in the release of cortisol by the adrenal cortex (Stratakis & Chrousos, 1995). Cortisol begins to rise approximately 5 min after stress exposure and reaches peak levels after 10 to 30 min (Sapolsky, Romero, & Munck, 2000). Cortisol is thought to facilitate adaptive responses to stress by increasing alertness, supporting information processing and memory consolidation, and suppressing nonessential biological functions (e.g., growth, reproduction; Barsegyan, Mackenzie, Kurose, McGaugh, & Roozendaal, 2010; Gold & Chrousos, 2002). Cortisol responsivity may also facilitate recovery from stress via its regulatory effects on SNS activity (Gunnar & Quevedo, 2007), described in more detail in the following section on multisystem functioning.

1.2 | Multisystem functioning: Theoretical perspectives

Although often studied in isolation of each other, components of the stress response system operate in an integrated manner that, under optimal conditions, facilitate coordinated physiological responses to maintain stability (McEwen, 1998). The brain is the ‘master regulator’ of responses across all stress response systems, and specific neural circuitry in the limbic forebrain, hypothalamus, and brainstem regulates the SNS, PNS, and HPA axis (Ulrich-Lai & Herman, 2009). *Allostasis*, a concept proposed by McEwen and Wingfield (2003), bears relevance to a discussion of multisystem theories because it postulates that in response to environmental demands, multiple physiological systems engage in an ongoing calibration in order to support homeostasis. In the context of chronic or repeated challenges, biomarkers across a range of bodily systems can become imbalanced (*allostatic state*), contributing to overall ‘wear and tear’ on the body (*allostatic load*) that reduces the capacity for adaptive physiological responses to future stressors and increases susceptibility to physical and mental health problems (McEwen & Wingfield, 2003). Importantly, accurate measures of allostatic load require a multisystem approach; as argued by Evans (2003), ‘seemingly small, modest alterations in functioning in one physiological system when considered jointly with other modest physiological changes may in fact markedly elevate risk, which is otherwise obscured or underestimated when the changes are viewed in isolation’ (p. 925). Alterations in the ANS and HPA axis may be the primary pathways through which allostatic load develops (Lupien et al., 2015).

Several other theoretical frameworks propose more defined, a priori patterns of multisystem functioning. For example, the *doctrine of autonomic space* describes patterns of joint activity across the PNS and SNS (Berntson, Cacioppo, Quigley, & Fabro, 1994). In contrast to

previous theories that assumed the two branches of the ANS operated along a single dimension (i.e., heightened PNS activity necessitated decreased SNS activity and vice versa), Berntson et al. proposed a more complex two-dimension model in which the systems varied along dimensions of reciprocity (reciprocal to nonreciprocal) and coactivity (coactivation to coinhibition). In modes of reciprocal activation, the PNS and SNS operate together to either upregulate or downregulate target organs. In contrast, nonreciprocal activation modes capture instances in which PNS and SNS activity promote opposing functions that have an equivocal effect on regulation. Bauer, Quas, and Boyce (2002) proposed another model of joint functioning across two physiological systems, however in this theory, potential interactions across the SNS and HPA axis were addressed. Citing evidence that HPA axis activation may serve to restrain or suppress excessively high (and potentially damaging) levels of sympathetic arousal, those authors suggest that the most adaptive patterns of responsivity emerge when the systems are matched in their level of arousal (anywhere along the continuum of low to high). Conversely, dysregulation could result from any combination of asymmetry (e.g., high sympathetic activity and low HPA axis activity; low sympathetic activity and high HPA axis activity; Bauer et al., 2002).

The aforementioned theoretical frameworks are limited by their consideration of only two physiological systems. The more recently proposed Adaptive Calibration Model (ACM) distinguishes itself from prior frameworks by considering the SNS, PNS, and HPA axis and addressing how variability in *both* resting and reactivity levels may give rise to different patterns of joint activity (Del Giudice et al., 2011). The ACM proposes four physiological patterns: (a) *Sensitive* (high resting PNS and PNS reactivity, moderate resting SNS and moderate-to-high SNS reactivity, and moderate resting HPA axis and high HPA axis reactivity), (b) *Buffered* (moderate resting PNS and PNS reactivity, low-to-moderate resting SNS and SNS reactivity, and moderate resting HPA axis and HPA axis reactivity), (c) *Vigilant* (low resting PNS and low-to-moderate PNS reactivity, high resting SNS and SNS reactivity, and moderate-to-high resting HPA axis and high HPA axis reactivity), and (d) *Unemotional* (low resting and reactivity across all systems).

1.3 | Multisystem functioning: Empirical perspectives

Previous studies have approached examination of multisystem functioning in a variety of ways, including the use of cut-off points to create groups that reflect distinct profiles of multisystem functioning. For example, continuous respiratory sinus arrhythmia (RSA; a measure of PNS activity) and pre-ejection period (PEP; a measure of SNS activity) reactivity scores may be dichotomized on the basis reactors/nonreactors to create four possible combinations of parasympathetic/sympathetic activation and parasympathetic/sympathetic inhibition consistent with the doctrine of autonomic space. Using this approach, children and adolescents have been shown to primarily demonstrate sympathetic activation in combination with parasympathetic inhibition or joint sympathetic and parasympathetic inhibition (Alkon et al., 2003; Salomon, Matthews, & Allen, 2000). In one of the few studies to examine more than two physiological systems, Rash et al. (2016) dichotomized RSA, salivary alpha-amylase (sAA; a measure of SNS reactivity that is different from PEP), and HPA axis reactivity scores of 6-month-old infants and observed that most demonstrated asymmetrical patterns of activity across the ANS and HPA axis.

Although cross-tabulating patterns of physiological responsivity based on dichotomous reactive/nonreactive responses provides theoretically defensible multisystem groups, it is important to note that nuances are lost when this approach is used. For example, cross-tabulating groups diverse individuals with small to large physiological stress responses into a single category of ‘responders’, obscuring important information about variability in the magnitude of responsivity. Interaction terms derived from continuous variables provide a viable statistical alternative that preserves the degree of responsivity (Chen, Raine, & Granger, 2015), but are generally limited to studies of two physiological systems (e.g., El-Sheikh et al., 2009; Gordis, Granger, Susman, & Trickett, 2006). This is likely due to interpretive complications that ensue when attempting to model interactions between three or more variables (Rash et al., 2016) and the power required to conduct such analyses in a rigorous manner (Cohen, West, & Aiken, 2014). Interactive models, unless more complexly specified, also make assumptions about linearity when relations may be nonlinear.

Data driven or person-centered techniques address many of the aforementioned statistical limitations. Latent profile analysis (LPA) is one example of a person-centered approach that identifies discrete subgroups (‘profiles’) of individuals based on different patterns that emerge from the empirical data, rather than a priori hypotheses (Collins & Lanza, 2009). Latent profiles are derived from observed averages of continuous indicators (Tein, Coxe, & Cham, 2013) and thus when used to analyze physiological systems, are able to retain the rich variability of the data. There have been very few utilizations of LPA to analyze multisystem physiological activity. Latent profile analysis of PNS activity (as indicated by RSA) and SNS activity (as indicated by skin conductance level) in a sample of children derived four classes generally consistent with the ACM patterns of buffered, sensitive, vigilant, and unemotional (Del Giudice, Hinnant, Ellis, & El-Sheikh, 2012), though study conclusions are limited by the lack of HPA axis activity in the analyses. Subsequent studies have also found support for four profiles that ‘could be reasonably mapped on the four responsivity patterns described in the ACM’, with a number of important caveats (e.g., model fit indices were equally supportive of 3-profile and 4-profile solutions and the sample was comprised of adolescent males only; Ellis, Oldehinkel, & Nederhof, 2017, p. 1,016). Finally, in a previous examination of the current study’s sample of kindergarten children, Quas et al. (2014) used LPA to uncover six distinct physiological profiles across the PNS, SNS, and HPA axis, several of which bore similarity to ACM-hypothesized profiles.

1.4 | Longitudinal trajectories of multisystem functioning

Early childhood is understood to be a time of heightened plasticity during which the development of stress systems is particularly responsive to environmental influences (Bush & Boyce, 2016). Regulation of both the ANS and HPA axis is strongly influenced or “co-regulated” by primary caregivers during infancy and very early toddlerhood, while higher-order brain structures and circuitry that regulate physiological systems remain undeveloped. As children age, maturational shifts in neural regulation of these physiological systems provide for increasingly independent, organized responses to environmental challenges and decreasing dependence on primary caregivers (Atkinson, Jamieson, Khoury, Ludmer, & Gonzalez, 2016; Porges & Furman, 2011). This shift from ‘other regulation’ towards ‘self-regulation’ has been illustrated among children across early development such that maternal

emotional support was associated with RSA reactivity when children were age 3 and 4, but not 5 years old (Perry, Calkins, Nelson, Leerkes, & Marcovitch, 2012). The maturation of biological support systems during toddlerhood has also been hypothesized to underlie the use of increasingly sophisticated cognitive and behavioral regulatory strategies (Fox, 1994), which in turn, further facilitates adaptive physiological responses and creates positive feedback loops (Ursache, Blair, & Raver, 2012). Parents or other caregivers remain important during the transition to formal schooling, though dependence shifts. For example, prior research supports associations among qualities of the teacher-child relationship or classroom climate, children's physiological reactivity, and mental health outcomes during kindergarten (Essex, Armstrong, Burk, Goldsmith, & Boyce, 2011; Roubinov, Bush, Hagan, Thompson, & Boyce, 2019).

Although aimed at drawing conclusions about trajectories of physiological activity during the early years of life, longitudinal research has primarily focused upon single stress response systems. For example, baseline RSA appears to increase from infancy until it stabilizes in middle childhood (Alkon et al., 2003; Bornstein & Suess, 2000), while RSA reactivity remains more variable (Calkins & Keane, 2004). In a sample of children assessed repeatedly between the ages of 6 months to 5 years of age, measures of resting RSA and PEP were generally stable over time, while reactivity was not stable (Alkon, Boyce, Davis, & Eskenazi, 2011). Similarly, RSA reactivity was not stable among 5- to 6-year-old children who were measured on three occasions each separated by 2 weeks (Doussard-Roosevelt, Montgomery, & Porges, 2003). A longitudinal study of preschool children indicated that children's RSA reactivity did not change *on average* across a three-year period (Perry et al., 2012). However, this group-level summary score obscures significant variability: 46% of children showed increasing reactivity, 46% of children showed decreasing reactivity, and 8% of children showed stable reactivity (Perry et al., 2012). Little is known about PEP reactivity during the transition to formal schooling, likely in part due to the difficulty of collecting such cardiac measures from very young children. Scarce research of children under the age of 5 suggests increased baseline PEP (Alkon et al., 2011) and increased PEP reactivity with age (Alkon et al., 2003), though the latter study was cross-sectional only. Finally, although we are not aware of any repeated measures studies of HPA axis functioning among children age 3 to 6, a recent systematic review of children's cortisol response to kindergarten entry suggests cortisol rises in response to this transition, with recovery to baseline levels taking as long as 3 to 6 months (Parent et al., 2019).

In a sample of older children and adolescents, van den Bos and Westenberg (2015) observed low stability in anticipatory cortisol and cortisol reactivity across a two year period.

Much less is known about the stability of multisystem response tendencies over time, but limited evidence suggests a more nuanced perspective than simple increases or decreases in single system activity. Based on classifications prescribed by the doctrine of autonomic space, greater coordination across physiological systems appears to emerge with age, as evidenced by age-related increases in reciprocal sympathetic activation and reciprocal parasympathetic activation (Alkon et al., 2003, 2011). The aforementioned LPA conducted by Quas et al. included four samples of children ranging in age from 5 to 15 years old and found that children with more coordinated activity across systems were older than those

whose response tendencies were dominated by a single physiological system. Thus, it may be that the maturation of multisystem physiology is reflected in stronger patterns of cross-system reciprocity as children age, with increasingly integrated action to upregulate or downregulate biological arousal. However, not all children may follow identical developmental trajectories. Just as there are individual differences in the activity of single stress response systems, there may be heterogeneity in the type and timing of coordination across multiple stress response systems.

To address these significant gaps in the evidence, the current study examined cross-sectional and longitudinal multisystem physiological activity in a sample of children across the course of the kindergarten year. The transition to formal schooling is a crucial period in which to study multisystem physiological functioning, as it represents a significant developmental milestone during which children are exposed to new roles, responsibilities, and goals that challenge individual self-regulatory capacities (Rimm-Kaufman & Pianta, 2000). The emphasis on formal instructions, specific literacy objectives, and socialization with peers and teachers in kindergarten create an environment that is substantially different from the home environment and prior daycare settings, and one in which developmental changes are prolific (Schulting, Malone, & Dodge, 2005). The manner in which children navigate kindergarten entry is influenced by their core competencies (including physiological self-regulation) and, concomitantly, this transition initiates adaptive behavioral pathways that canalize across childhood (Blair & Raver, 2015; Ursache et al., 2012). The success of early school transitions also has implications for later socioemotional and academic outcomes (Duncan et al., 2007).

This study extends the prior Quas et al. study of this sample in several important ways. First, whereas Quas et al. conducted LPA with data collected in fall only, the present study conducted LPA using data collected in fall and spring of the kindergarten year and used latent transition analysis (LTA) to report on developmental patterns and potential shifts among profiles over time. Second, recent statistical advances have underscored the need to examine different latent profile covariance structures rather than accept the programmatic default constraints (Asparouhov & Muthén, 2014; Oberski, 2016; see our Statistical Analysis Plan and Supplementary Information for more details). Third, the prior LPA with this sample included baseline measures of HR, RSA, and PEP that were also used to calculate of physiological reactivity (i.e., baseline HR was used as a measure of baseline activity and was also subtracted from HR during challenge to calculate HR reactivity). To avoid the confounds of using the same physiological indicator to reflect baseline activity and to derive measures of reactivity, baseline measures of HR, RSA, and PEP used in the current LPA were collected at rest, prior to initiation of the challenge protocol (see Procedures for more information). Lastly, although the present study focused primarily on the modeling of multisystem profiles and developmental transitions, we also report on preliminary tests of profile differences in children's demographic characteristics and socioemotional outcomes to better contextualize the observed patterns of multisystem activity.

Guided by the ACM, but with an awareness that the complexities of 'real world' data may preclude exact replication of the theorized ACM classifications, we hypothesized that LPA would reveal three physiological profiles that broadly reflected the theorized patterns of

Sensitive, Buffered, and Vigilant in both fall and spring of the kindergarten year. We anticipated that we may not uncover an Unemotional profile given its generally low prevalence in the population and our use of a community sample of typically developing children. Following our separate models of fall and spring data, we used latent transition analysis (LTA) to evaluate patterns of stability and change in children's physiological profiles across the course of the school year. To the best of our knowledge, this is the first investigation in which transition analysis has been used to characterize longitudinal patterns of cross-system functioning and thus, we were wary of advancing detailed hypotheses. However, based on empirical research that has reported the relative stability of physiological response tendencies, we expected that children would be more likely to remain in the same profile over time than to shift profiles from fall to spring of the kindergarten year.

2 | METHOD

2.1 | Participants

Children ($n = 338$, $M_{\text{age}} = 5.32$ years, $SD = 0.32$) were drawn from a larger longitudinal study of social status, family adversity, physiology, and early physical and mental health (Obradovic, Bush, Stamperdahl, Adler, & Boyce, 2010). The sample included a balanced representation of sex ($n = 163$ girls, 48%) and reflected the significant ethnic/ racial diversity characteristic of the geographic region (19% African American, 11% Asian, 43% European or White, 4% Latino, 22% Multiethnic, and 2% Other). Parent/caregiver reported data were primarily collected from mothers (87%), with the remainder of data reported by biological fathers (9%), adoptive mothers (2.5%), biological grandmothers (0.6%), and individuals with other relationships with the child (0.9%). Average annual household income ranged from less than \$10,000 to over \$400,000, with the high sample mean/ median reflective of the area from which participants were drawn ($M = \$60,000$ - $\$79,000$, $Mdn = \$80,000$ - $\$99,000$).

2.2 | Procedures

Children and their parents were recruited in three cohorts during the fall of the kindergarten year from 29 classrooms in the San Francisco Bay Area (Oakland, Albany, and Piedmont Unified School Districts). All families who spoke English or Spanish and had a child in a participating classroom were invited to participate in the study. Parents' informed consent and children's assent were obtained prior to the start of data collection. This study was approved by the Committee for the Protection of Human Subjects of the University of California, Berkeley, and the Committee of Human Subjects of the University of California, San Francisco.

Data for the present study were collected at the beginning (fall) and end (spring) of the kindergarten year. In fall and spring, children completed a 20-min stress reactivity protocol that was administered in an identical manner at both time points and consisted of four developmentally-appropriate challenges across social, cognitive, sensory, and emotional domains. Given the fact that PNS functioning can be affected by activities unrelated to challenge or stress responsivity (e.g., speaking, attending in a focused manner, gesturing; Porges, 2007), a control condition that mirrored the motor and engagement demands of the

challenge condition preceded each challenge (stress) condition. Physiological scores gathered during the control condition yielded baseline values that, in conjunction with measures collected during challenge conditions, were used to derive measures of stress reactivity free from ancillary influences (Bush, Alkon, Obradovic, Stamperdahl, & Thomas Boyce, 2011). The protocol began with a two-minute baseline period during which children were read a calming story, after which the paired challenge-control tasks began. The protocol consisted of: (a) Social challenge (structured interview) and social control (naming common animals and colors), (b) Cognitive challenge (digit span) and cognitive control (one and two digit repetition), (c) Sensory challenge (taste identification of two drops of concentrated lemon juice) and sensory control (taste identification of two drops of water on the tongue), and (d) Emotional challenge (watching an emotionally evocative movie clip) and emotional control (watching an emotionally neutral movie clip). For a thorough description of the protocol and its development, we refer the reader to Alkon et al., 2003 and Bush et al., 2011. Children's socioemotional and behavioral outcomes were collected via parent and teacher proxy reports and children's self-report in spring of the kindergarten year.

2.3 | Measures

2.3.1 | Autonomic nervous system (ANS) measures—Measures of resting respiratory sinus arrhythmia (RSA), pre-ejection period (PEP), and heart rate (HR) were collected throughout the protocol using the Biopac MP150 (Biopac Systems, Santa Barbara, CA) that was interfaced to a PC-based computer. After familiarizing children with the equipment, four disposable spot electrodes were affixed in the standard tetrapolar configuration on the child's neck and chest and ECG electrodes were placed on the right clavicle and lower left rib to collect impedance, ECG, and respiratory measures. Analog data were monitored on the computer for signal and noise and digitized data were stored offline for later analysis. Data cleaning and scoring were completed with Mindware software (www.mindwaretech.com), which was used to verify each waveform, perform visual checks of I Bis, and identify artifacts. Outliers were defined as >3 standard deviations from the group mean and were checked minute-by-minute. All resting ANS measures reflect measures collected during the two-minute resting period that preceded the start of the four paired control-challenge tasks. All ANS reactivity measures reflect task-specific reactivity, described in more detail below.

2.3.2 | Resting RSA and RSA reactivity—RSA is the periodic oscillation in sinus rhythm occurring at the frequency of respiration and was estimated as the natural logarithm of the variance of heart period within the high-frequency bandpass associated with respiration at this age (i.e., 0.15–0.80 Hz; Bar-Haim, Marshall, and Fox (2000); Rudolph, Rudolph, Hostetter, Lister, & Siegel, 2003). Measures of resting RSA and RSA reactivity were derived using the guidelines of the Society for Psychophysiological Research Committee on heart rate variability (Berntson et al., 1997). The sampling frequency was 1 kHz. Mean RSA magnitude was calculated for each one minute interval during the resting period, then averaged to create a measure of resting RSA. Mean RSA magnitude was also calculated for each one-minute interval within each of the control and challenge tasks and then averaged to create overall means within the four *control tasks* and four *challenge task conditions* (across social, cognitive, sensory, and emotional domains).¹ To control for

baseline arousal and other incidental influences on RSA, four standardized residual scores were created by regressing RSA values during the challenge tasks on RSA values during the parallel control tasks. Finally, the four standardized residual scores were averaged to create a single index of RSA reactivity. Negative residual scores are indicative of greater RSA reactivity (a decrease in RSA; parasympathetic withdrawal) while positive residual scores are indicative of lower RSA reactivity (an increase in RSA; parasympathetic activation).

2.3.3 | Resting PEP and PEP reactivity—PEP is the time interval (measured in milliseconds) from the onset of ventricular depolarization to the onset of ventricular. Average PEP was calculated in one-minute intervals and measures of resting PEP and PEP reactivity were calculated in the manner described above for RSA. Negative residual PEP scores are indicative of greater PEP reactivity (a decrease in PEP; PEP shortening or sympathetic activation) while positive residual scores are indicative of lower PEP reactivity (an increase in PEP; PEP lengthening or sympathetic deactivation).

2.3.4 | Resting HR and HR reactivity—HR was calculated as the number of R-waves per unit of time (i.e., each one-minute interval). Measures of resting HR and HR reactivity were derived in the manner described above for RSA and PEP. Positive HR residual scores are indicative of HR acceleration (i.e., a stress reactivity response) to the challenge protocol. HR is influenced by dynamic interactions among the PNS, SNS, and other cardiovascular reflexes (Porges & Furman, 2011), and thus is not a ‘pure’ measure of PNS or SNS activity. Its utility for pediatric research is large, due to the ease with which it can be measured and comprehended as an indicator of physiological responsiveness (Zisner & Beauchaine, 2016). Moreover although HR is parasympathetically influenced, individuals can demonstrate increased HR without concomitant suppression of vagal tone (Moore & Calkins, 2004), suggesting that useful information can be gleaned from HR in and of itself. HR was also included in prior work by Quas et al. (2014), the study on which the present research broadens and builds.

2.3.5 | Hypothalamic pituitary adrenal (HPA) axis measures—Prior to the initiation of the protocol (i.e., prior to the application of the electrodes and any of the challenge or control tasks), children provided a saliva sample by chewing on cotton roll for 20–30 s and depositing it into a salivette tube. This process was repeated at the culmination of the protocol to collect a post-protocol sample. The average length of the protocol was 27 min ($SD = 3$ min, $Range = 19–38$ min). Thus, samples collected after the conclusion of the protocol captured HPA axis reactivity to mildly stressful, novel challenges (e.g., strange experimenter, application of electrodes, varied challenge tasks) that were accumulated by the midpoint of the protocol. All samples were stored at -7°C until assayed 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 and the mean interassay and intra-assay variations were 8.5% and 6.1%, respectively. Cortisol

¹The ANS and the HPA axis may be differentially activated by specific stressor types. For example, the HPA axis is particularly engaged by perceptions of threat (Dickerson & Kemeny, 2004). The systems also differ in the type/extent of information provided about the environment (e.g., the HPA axis response is ‘information rich’ while the parasympathetic response is more ‘non-specific’ (Del Giudice, Ellis, Shirtcliff, 2011). Thus, aggregating across varied challenge types is an optimal approach for analyses that simultaneously examine functioning across multiple, differentially activated physiological systems.

outliers were excluded. This includes cortisol values that exceeded 55 nmol/L (less than 1% of samples). Samples were also excluded for children taking medication with known effects on salivary cortisol samples (e.g., human growth hormone, exogenous glucocorticoids; less than 3% of samples). The pre-protocol sample was used as a measure of resting cortisol in all analyses. To measure cortisol reactivity, a standardized residual score was calculated by regressing the post-protocol cortisol value on the pre-protocol value, adjusting for time of day at the first sample. Positive residual scores indicate heightened cortisol reactivity (i.e., a stress response) during the challenge protocol. In fall of the kindergarten year, 37.3% of the sample evidenced a cortisol response to the challenge protocol and in spring of the kindergarten year, 37.1% of the sample evidenced a cortisol response to the challenge protocol.

2.3.6 | Children’s socioemotional outcomes—At the end of the kindergarten year, child, parent, and teachers reported on children’s internalizing symptoms, externalizing symptoms, prosocial behavior, and school engagement. Children’s self-reported symptoms in each of the aforementioned domains were assessed using the Berkeley Puppet Interview (Ablow & Measelle, 1993). During administration of the BPI, children are provided with contrasting statements from two puppets that represent the positive or negative dimensions of different behaviors and attributes, after which they are asked with which puppet they most identify. Responses were videotaped and coded on a 7-point scale based on the specific statement that was endorsed and the degree to which the child endorsed it. Interrater reliability was high (ICC = 0.92). Parents and teachers completed parallel subscales on the Health and Behavior Questionnaire (Essex et al., 2002). Given the advantages of multi-informant versus single-reporter methods in the assessment of children’s adjustment, a composite of parent-, teacher, and child-report measures was created using methods outlined by Kraemer et al. (2003). Briefly, each reporter’s data were entered into principal components analysis and three components were extracted: a trait component, reflecting individual differences in externalizing symptoms; an informant component that captured differences due to parent, teacher, and child perspectives of symptoms; and a context component that reflected differences due to the context or environment in which symptoms are expressed (for more information, see Obradovic et al., 2010). This approach has been extensively used in prior studies (Boyce et al., 2006; Obradovic, Bush, & Boyce, 2011; Roubinov, Boyce, & Bush, 2018; Roubinov et al., 2019). Analyses for the present study used internalizing, externalizing, prosocial behavior, and school engagement scores based on the trait (first) component of the principal components analysis.

2.4 | Statistical analysis plan and results

2.4.1 | Initial model building with latent profile analysis (LPA)—All latent profile and latent transition analyses were conducted in Mplus Version 8 (Muthén & Muthén, 1998–2017). As is standard practice, our model-building procedures contrasted LPA models that specified different numbers of latent statuses (i.e., profiles or groups), ranging from two to six. Contrasts among competing models were made primarily on the basis of the BIC relative fit index, as this strategy provides a relatively general approach allowing contrasts among both nested and non-nested models (West, Taylor, & Wu, 2012). In both fall and spring, our model building contrasts generally revealed better fit (e.g., lower BIC) for

models specifying either three or four latent profiles when compared to models specifying two, five, or six latent profiles (see Tables S1A,B). Although there were some exceptions where a lower BIC was obtained in models with five or six latent profiles, very small numbers of participants across one or more profiles in these models (i.e., between 2 and 5 children) precluded further consideration of these models (Adams et al., 2011).

Based on the above considerations, we conducted an in-depth inspection of promising results from the three- and four-profile models. From a conceptual/substantive standpoint, the three-profile models provided a much more sensible solution than the four-profile model when considering how within-profile means differentiated the groups on the physiological measures of interest (see Tables S2A,B). Furthermore, in the three-profile models, the patterning of indicator means and class sizes was more robust across different parameter constraint scenarios and across the fall and spring time points (see Table 1 and Figure 1), which provided an important foundation for subsequent latent transition analysis. Conversely, the four-profile models often yielded solutions that were more highly variable across different parameter constraint scenarios, as well as at least one very small and substantively uninterpretable profile group. Finally, we evaluated alternative parameter constraint scenarios, which are described in Supporting Information.

Based on the above considerations and those described in Supporting Information, we ultimately retained the following model specifications in both fall and spring of the kindergarten year: (a) three latent profiles, (b) within-profile covariances constrained to zero except for four covariances between resting and reactivity assessments of the same physiological measure that were estimated but constrained to be equal across profiles (e.g., resting RSA with RSA reactivity indicative of a type of ‘method effect’ to be expected with such data; Qu, Tan, & Kutner, 1996), and (c) all within-profile variances estimated and freed to vary across profiles (see Table 1 and Figure 1). As described below, we then combined these retained fall and spring models to construct a latent transition analysis. Finally, in order to provide initial support for the meaning and conceptualization of the profiles, we exported profile membership (based on participants’ most likely latent class membership; Muthén & Muthén, 1998–2017) to SPSS and used one-way ANOVAs to compare the profiles on demographic characteristics (child sex, racial/ ethnic minority status, and family socioeconomic status) and socioemotional outcomes at the end of the school year (internalizing symptoms, externalizing symptoms, prosocial behavior, and school engagement).

2.4.2 | Model building with latent transition analysis (LTA)—Latent transition analysis (LTA) characterized longitudinal transitions among the three latent profiles from fall to spring of the kindergarten year. To improve interpretability, the LTA constrained indicator means and indicator variances to be equal between the two waves (i.e., measurement invariance over time). The lower BIC values suggest the constrained model offered a better fit to the data as compared to the unconstrained model (unconstrained BIC = 16,899.594, constrained BIC = 16,706.955). Finally, model-fitting procedures evaluated additional constraints between the two waves on the four “method effect” resting-reactivity covariances. These constraints were rejected (Wald $\chi^2(4) = 21.997, p < .01$), indicating a decrement in model fit when the resting-reactivity covariances were constrained to be equal

over time. The BIC was also further improved in the model in which the resting-reactivity covariances were not constrained overtime (BIC = 16,691.365), supporting a final model in which these covariances were left free to vary over time.

The profile-specific indicator means and confidence interval from the final retained longitudinal transition model are presented in Table 1 and displayed graphically in Figure 2. A lack of overlap in the confidence intervals for a given indicator among profiles suggests the profiles differ significantly on that indicator. Of note, results of this LTA model that included both fall and spring found latent profiles that were highly similar in structure, patterning of results, and sizes of profiles when compared to results of the cross-sectional fall and spring LPA models (see Figure 1 in comparison to Figure 2). This additional evidence provides further support for the specifications that were retained through our LPA model-building procedures and suggests that the three LTA profiles reflect substantively distinct and meaningful groups.

2.4.3 | Key results: Characteristics of the three latent profiles—The first profile included children whose physiological stress response was dominated by higher than average levels of HPA axis activity (fall profile $n = 42$, spring profile $n = 54$), including elevated resting cortisol (M (nmol/L) = 0.85, CI = 0.81,0.89) and elevated cortisol reactivity ($M = 3.28$, CI = 2.52,4.04). Children in this profile also exhibited low-to-moderate levels of activity within the PNS, including values of resting RSA that fell between the other two retained profiles ($M = 6.94$, CI = 6.80, 7.07) and no pronounced RSA change in response to the stressor ($M = 0$, CI = -0.09–0.09). Thus the term, *HPA Axis Responders* was used to describe children in this profile. Children in the next profile (fall $n = 136$, spring $n = 133$) exhibited the highest resting RSA across all profiles ($M = 7.64$, CI = 7.53–7.75), mounted a moderate PEP response to stress ($M = -0.10$, CI = -0.14, -0.05), and had levels of resting cortisol ($M = 0.60$, CI = 0.59, 0.62) and cortisol reactivity ($M = -0.59$, CI = -0.72, -0.46) that were neither excessively high or low. Children exhibiting this pattern of activity across systems were thus termed *Active Copers/Mobilizers*.

Finally, the third profile (fall $n = 159$, spring $n = 150$) was characterized by the lowest levels of resting PEP ($M = 77.63$, CI = 77.06, 78.21) and resting RSA ($M = 6.05$, CI = 5.94, 6.17) across all profiles, which reflects heightened sympathetic activation and greater parasympathetic withdrawal prior to the initiation of stress protocol, respectively. Resting cortisol levels among children in this profile were similar to children in the Active Copers/Mobilizers profile, however, children in the former exhibited lower cortisol reactivity levels in response to the task ($M = -0.87$, CI = -0.99, -0.75). Interestingly, children in this profile also exhibited higher levels of RSA reactivity ($M = -0.12$, CI = -0.18, -0.07) than children in the HPA Axis Responders or the Active Copers/Mobilizers profiles. Although greater RSA withdrawal is often observed among those with higher resting RSA (i.e., law of initial values), this was not the case for the more RSA-reactive children in this third profile who also had lower resting RSA. Of note, the law of initial values has not received universal support across the literature and several previous studies of children have observed relations between resting RSA and RSA reactivity similar to those found in this profile (Calkins & Keane, 2004; Suess, Porges, & Plude, 1994). To capture the relative dominance of the ANS

and the heightened levels of arousal at rest, this final profile was termed *Anticipatory Arousal/ANS Responders*.

2.4.4 | Key results: Transitions among profiles between fall and spring of the kindergarten year—Table 2 presents the transitional probabilities from the LTA model, which quantifies the likelihood of transitions among the aforementioned three multisystem profiles from fall to spring of the kindergarten year. Rates of profile stability ranged from 0.569 to 0.680 and exceeded rates of profile transitions, the highest of which was 0.272. The probabilities of remaining in the Active Copers/Mobilizers profile and Anticipatory Arousal/ANS Responders profile from fall to spring were similar (0.68 and 0.67, respectively), and noticeably higher than the probability of remaining in the HPA Axis Responders profile (0.57). We subsequently examined if stability rates were significantly different across profiles using Wald χ^2 tests of equality constraints (i.e., constraints that imposed equality among (a) the likelihood of staying in the HPA Axis Responders profile, (b) the likelihood of staying in the Active Copers/Mobilizers profile, and (c) the likelihood of staying in the Anticipatory Arousal/ANS Responders profile from fall to spring). The omnibus test did not reject these constraints (Wald $\chi^2(2) = 0.541, p = .76$), suggesting that the likelihood of stability from fall to spring of the kindergarten year did not differ across the profiles. Without clear evidence of differences among stability probabilities from the omnibus test, we did not conduct any follow-up tests of specific transition contrasts.

Using equality constraints, we also examined if rates of shifting were significantly different across profiles (i.e., constraints that imposed equality among: (a) the likelihood of shifting from the HPA Axis Responders profiles to another profile, (b) the likelihood of shifting from the Active Copers/Mobilizers profile to another profile, and (c) the likelihood of shifting from the Anticipatory Arousal/ANS Responders profile to another profile). The omnibus test rejected these constraints (Wald $\chi^2(9) = 9.89, p = .02$). Follow-up tests indicated that children in the HPA Axis Responders profile shifted into a different profile about as often as they stayed in the same profile from fall to spring (Wald $\chi^2(1) = 0.23, p = .63$). However, children in the Active Copers/Mobilizers profile (Wald $\chi^2(1) = 7.68, p = .01$) and in the Anticipatory Arousal/ANS Responders profile (Wald $\chi^2(1) = 5.31, p = .02$) were more likely to stay in the same profile over time than they were to shift into a different profile.

2.4.5 | Children's demographics and socioemotional outcomes in spring of the kindergarten year in relation to profile membership—Profile membership in fall of the kindergarten year did not differ on the basis of sex ($p = .51$), ethnic minority versus nonminority status ($p = .36$), or family SES ($p = .52$). Analysis of the spring profiles indicated a greater proportion of boys relative to girls in the HPA Axis Responders and the Anticipatory Arousal/ANS Responders profiles and a greater proportion of girls relative to boys in the Active Copers/Mobilizers profile ($\chi^2(2) = 8.76, p = .01$). No spring profile differences were found for ethnicity ($p = .63$) or SES ($p = .75$).

In testing differences in spring of kindergarten socioemotional outcomes across the three patterns of stable profile membership, there was a significant association with children's externalizing symptoms ($F(2,228) = 3.53, p = .03$) and a marginally significant association with children's school engagement ($F(2,228) = 2.52, p = .08$), but associations with

internalizing symptoms ($p = .21$) and prosocial behavior ($p = .20$) were not significant. Follow-up pairwise comparisons showed that children who remained in the HPA Axis Responders profile over the course of the kindergarten year exhibited significantly greater externalizing symptoms ($M = 0.46$, $SD = 1.30$) than children who remained in the Active Copers/Mobilizers Profile ($M = -0.06$, $SD = 0.90$) and children who remained in the Anticipatory Arousal/ ANS Responders profile ($M = -0.08$, $SD = 0.91$). In contrast, children who remained in the latter two profiles did not differ from each other on externalizing symptoms. Follow-up pairwise comparisons also showed higher school engagement among children who were stable in the Active Copers/Mobilizers Profile ($M = 0.13$, $SD = 0.89$) and Anticipatory Arousal/ANS Responders profile ($M = -0.01$, $SD = 0.93$) compared to those who remained in the HPA Axis Responders profile ($M = -0.37$, $SD = 1.52$), whereas children in the former two profiles did not differ from each other on school engagement.

Given that *stability* in the HPA Axis Responders profile may indicate heightened risk, we examined whether a *shift* from the HPA Axis Responders profile in the fall to either of the other profiles in the spring was associated with outcomes. Children who shifted out of the HPA Axis Responders profile had lower internalizing ($M = -0.42$, $SD = 0.62$; $t(40) = 2.53$, $p = .02$) and lower externalizing ($M = -0.39$, $SD = 0.76$, $t(40) = 2.37$, $p = .02$) compared to those who remained stable in that profile across the school year (internalizing: $M = 0.35$, $SD = 1.12$; externalizing: $M = 0.46$, $SD = 1.30$). Similarly, children who shifted out had marginally higher levels of school engagement ($M = 0.39$, $SD = 0.95$; $t(40) = -1.99$, $p = .05$) than those who remained stable ($M = -0.37$, $SD = 1.52$). There were no differences in prosocial behavior between those who remained stable in the HPA Axis Responders profile and those who did not ($p = .28$).

3 | DISCUSSION

The current study addresses several critical gaps in current literature on developmental psychobiology by advancing knowledge of individual differences in children's multisystem physiological activity and examining patterns of stability and change over time. Using latent profile analyses of data collected in fall of the kindergarten year, we uncovered three profiles of multisystem activity across the sympathetic and parasympathetic nervous systems (SNS and PNS) and hypothalamic–pituitary–adrenal (HPA) axis. Repeated LPA of data collected in spring of the kindergarten year revealed three profiles that looked remarkably similar in number and structure to the fall profiles. Latent transition analyses (LTA) of the profiles from fall to spring of the school year indicated that within certain patterns of multisystem activity, children were more likely to remain in the same multisystem profile over time than shift to a different profile.

Across both timepoints, findings suggested that three profiles of baseline physiological activity and reactivity best captured the multisystem patterns of children in kindergarten. In both fall and spring of the kindergarten year, the largest number of children was classified in the Active Copers/Mobilizers profile in which children exhibited the highest levels of resting parasympathetic activity and a moderate sympathetic response to challenge. Elevated resting parasympathetic activity is associated with relaxation, sustained attention, and engagement with the environment (Porges, 2007; Zisner & Beauchaine, 2016) and moderate sympathetic

activation may be conceptualized as mobilizing the resources needed to cope effectively with stressors (Bauer et al., 2002; Beauchaine, 2001; Del Giudice et al., 2011; Porges, 1997). To draw parallels with the doctrine of autonomic space (Berntson et al., 1994), only consideration of SNS and PNS reactivity is needed. Within this profile, the dual activation of both branches may suggest some similarity with the *coactivation* pattern. However, the patterns posited by the doctrine of autonomic space do not account for indicators of HPA axis functioning, which play a key role in the overall organization of the physiological stress response. In fact, a more comprehensive conceptualization of this profile is derived by also considering HPA axis functioning: Children in the Active Copers/Mobilizers profile did not demonstrate a pronounced cortisol response to the challenges and such modest levels of cortisol may facilitate adaptive neurobiological and behavioral responses to stress (Gunnar & Vazquez, 2001; Sapolsky et al., 2000). Thus, the combination of PNS, SNS, and HPA axis activity in this profile may reflect children with integrated regulatory capacities who tend to cope successfully with perceived controllable challenges. Complementary to this interpretation is the fact that the pattern of cross-system functioning observed among Active Copers/Mobilizers is most consistent with the ACM profile of *Buffered*, which has been suggested to reflect ‘optimal’ or ‘protective’ physiological response tendencies (Del Giudice et al., 2011). As was observed in the present study, other empirical research has found the *Buffered* profile to be most common in community, non-clinical samples (Del Giudice et al., 2012; Ellis et al., 2017).

A substantial number of children were also classified in the Anticipatory Arousal/ANS Responders profile, which was characterized by lower levels of resting PEP and resting RSA, alongside heightened resting HR. Children in this profile also had resting cortisol levels that were in the moderate range, falling between the levels observed among HPA Axis Responders (described below) and Active Copers/Mobilizers, and they did not mount a strong cortisol response to the stressful protocol. Such patterns of heightened baseline activity may capture individual tendencies of anticipatory arousal and as suggested by Quas et al. (2014), activation prior to the initiation of the stressor could be maladaptive or may represent a preparatory response learned over time that promotes successful handling of challenges (Gunnar & Quevedo, 2007). Notably, children in the Anticipatory Arousal/ANS Responders profile also exhibited the highest levels of parasympathetic reactivity, which also typically reflects an appropriate response to environmental challenges and has been associated with greater social and emotional regulatory capacities (Porges, 2007). The moderate parasympathetic withdrawal and minimal to moderate decrease in sympathetic activation are somewhat suggestive of the patterns of *uncoupled parasympathetic withdrawal* or *coinhibition* set forth within the doctrine of autonomic space (Berntson et al., 1994), however, it is important to note that baseline physiological levels (which are not central to the doctrine of autonomic space) appear particularly important to the derivation of this profile. When interpreted within the theoretical framework proposed by Bauer et al. (2002), the generally symmetrical levels of activity across the SNS and HPA axis among children in this profile (i.e., moderate to high resting PEP and moderate to high resting cortisol, low PEP reactivity, and low cortisol reactivity) are also aligned with patterns theorized to be an adaptive response to stress. In regards to the ACM, the high levels of parasympathetic activation and moderate HPA activity at baseline render Anticipatory Arousal/ANS

Responders most similar the proposed *Sensitive* profile, though there are also clear divergences of this empirically-derived profile from that which was theorized by the ACM. For example, HPA axis responsivity is low among individuals in the Anticipatory Arousal/ANS Responders profile, but proposed to be high in the original formulation of *Sensitive* individuals. Thus, the ACM-proposed moderate to high basal and reactivity levels across all systems in the *Sensitive* profile was not observed in the present study. Rather, our results suggest this profile may be characterized by greater differentiation in the physiological activity levels across the SNS, PNS, and HPA axis.

The final profile comprised the fewest children in fall and spring of the kindergarten year. Within this HPA Axis Responders profile, children exhibited the highest levels of resting cortisol and mounted a particularly pronounced cortisol response relative to the other two profiles. Parasympathetic and sympathetic reactivity levels were minimal among children in this profile, which may reflect the role of the HPA axis in regulating ANS activity, particularly within the SNS (Bauer et al., 2002; Sapolsky et al., 2000). According to the doctrine of autonomic space, the lack of ANS responsivity would classify children in this profile in the *baseline* pattern (Berntson et al., 1994). It is well-established that the HPA axis is activated by socially evaluative stressors and challenges that are deemed unpredictable or uncontrollable (Dickerson & Kemeny, 2004); thus, this profile may reflect particular physiological sensitivity to social/interpersonal judgment and/or stressors where the coping response that is needed to achieve the desired outcome is unclear. When evaluating this profile in relation to the ACM, the elevated levels of HPA axis activity at baseline and in response to stress, particularly in the absence of strong parasympathetic reactivity, suggest that HPA Responders may reflect the *Vigilant* profile (Del Giudice et al., 2011). However, children in the HPA Axis Responders profile did not exhibit the elevated SNS activity originally postulated to be part of the ACM *Vigilant* profile, consistent with previously observed discrepancies between the empirically-derived *Vigilant* profiles and the patterns originally hypothesized in the ACM. For example, Ellis et al. (2017) observed a *Vigilant* profile characterized by high levels of parasympathetic activity (rather than the originally postulated low levels) without the expected elevations in SNS or HPA axis activity, though the generalizability of such results may be limited by their adolescent, male-only sample. It has been hypothesized that as peer relationships increase in importance and competition for social status/dominance intensifies, select children who initially demonstrate *Vigilant*-like patterns of high responsivity may transition to patterns of lower responsivity, which reduces sensitivity to (potentially aversive) social feedback and promotes (potentially beneficial in the short-term) risk-taking behaviors (Del Giudice et al., 2011). Children in the present study were assessed during the transition to formal schooling, a developmental milestone in which interpersonal relationships with peers and adults outside the immediate family are strengthened. As children in the HPA Axis Responders profile displayed lower levels of SNS activity than theorized by the *Vigilant* profile, it may be the case that the social exposures accompanying the transition to kindergarten prompted a downregulation of activity, at least within some physiological systems.

Notably, two of the three profiles appeared to exhibit a multisystem pattern characterized by the relative dominance of one physiological system. It has been suggested that earlier in life, there is higher physiological ‘complexity’ as evidenced by greater variability in the nature

and strength of responsivity across different biological systems (Lipsitz & Goldberger, 1992). In other words, physiological reactivity to challenge may be exhibited by a robust response in one system without a parallel robust response in another system. The fact that the Anticipatory Arousal/ANS Responders profile appears predominantly driven by ANS activity without concomitant HPA axis (and the converse was observed in the HPA Axis Responders profile) may reflect the greater differentiation that tends to characterize physiological functioning earlier in life. Illustratively, in a study of children ranging in age from 4 to 14 years old, those that exhibited high reactivity across multiple physiological systems were older than those whose physiologic profiles were characterized by the disproportionate involvement of one system (Quas et al., 2014). Complexity is proposed to decline in older adulthood and may be one reason for increasing impairment in the ability to adapt to stress later in life (Goldberger et al., 2002), however less is known about the adaptive or maladaptive implications of this in childhood. Simultaneous activation of multiple systems may benefit individuals by promoting relatively fast attainment of ‘target’ arousal levels or it may be detrimental by contributing to overarousal (Gatzke-Kopp & Ram, 2018).

The evidence of consistency in the profiles of multisystem activity from fall to spring of the kindergarten year supported our latent transition analysis to examine patterns of stability and change. It is notable that the probabilities of stability (i.e., the probabilities that reflected the likelihood that children remained in the same profile from fall to spring of the kindergarten year) were larger than the probabilities of change (i.e., the probabilities that reflected a shift in profile membership from fall to spring of the kindergarten year). Early childhood is well-known to be a period of pronounced plasticity in the development of neurobiological systems, though environmentally-induced ‘calibration’ may occur predominantly during the first 3 to 5 years of life (Boyce & Ellis, 2005). Children in the present study were approximately 5–6 years old and at the cusp of the culmination of this period of heightened plasticity; thus, they may have exhibited more stability than change in multisystem physiological activity. The generally moderate levels of stability that were observed in the present study are also at least somewhat consistent with prior research. For example, moderate correlations over time were recorded in measures of baseline RSA and RSA reactivity among children from 9 months to 3 years of age (Porges, Doussard-Roosevelt, Lourdes Portales, & Suess, 1994). Moderate stability in resting RSA and PEP has also been observed among children assessed repeatedly from infancy through 5 years, though reactivity measures over time were weakly correlated (Alkon et al., 2011).

Although the overall likelihood of longitudinal stability did not significantly differ across profiles, there appeared to be cross-profile differences in the likelihood of longitudinal shifts. More specifically, children in the HPA Axis Responders profile were generally as likely to stay in the HPA Axis Responders profile from fall to spring of the kindergarten year as they were to shift to either the Anticipatory Arousal/ANS Responders profile or the Active Copers/Mobilizers profile. However, children in the other two profiles were *more likely* to remain in the same profile over time rather than to shift to another profile. The developmental progression of stress response systems may be such that the HPA axis stabilizes later and remains more variable in early childhood compared to other systems, though additional research is needed to draw more definitive conclusions. Of note, the

current results should not be interpreted to suggest that such profiles will remain stable across the remainder of children's development. Transitions between life stages are thought to be characterized by heightened plasticity (Del Giudice et al., 2011) and this may include the shifts from early childhood (3 to 6 years) to middle childhood (7 to 11 years) and adolescence (12–17 years). In particular, research suggests the onset of puberty is accompanied by substantial changes in biological stress responses (Dahl & Gunnar, 2009).

Initial evidence of associations with children's socioemotional outcomes in spring of the kindergarten year is valuable in further conceptualizing the nature of the profiles. HPA axis dysregulation has well-established associations with poor physical and mental health (McEwen & Wingfield, 2003). Illustratively, children whose fall and spring multisystem profiles were dominated by heightened resting cortisol and cortisol reactivity exhibited higher externalizing symptoms and lower school engagement than children in either of the other two profiles. The detrimental effects of heightened cortisol may be particularly pronounced if sustained over time (Miller, Chen, & Zhou, 2007). In the present analyses, children with stable membership in the HPA Axis Responders profile demonstrated higher internalizing/externalizing and lower school engagement than those who were only classified within the HPA Axis Responders profile at the beginning of the school year, suggesting the potential that shifts to more adaptive physiological regulatory functioning exert protective effects. Importantly, such analyses must be considered a preliminary foundation on which to conduct more complex modeling. As suggested by the theory of differential neurobiological susceptibility, contexts do not affect children in a universal manner, nor does children's physiological functioning typically exert direct effects on mental and physical health (Bush & Boyce, 2016). Rather, specific patterns of physiological activity may render children particularly susceptible to the positive and negative features of their early rearing conditions (Belsky & Pluess, 2009; Boyce & Ellis, 2005). Future research is well-poised to explore dynamic interactions between early environmental conditions and multisystem physiology to predict early developmental outcomes.

The results of the present study must be interpreted in light of several limitations. We relied upon LPA to derive distinct, meaningful profiles of physiological activity from our sample of kindergarten children. This data-driven analytic approach is ideally suited to capture the rich variability of children's physiological response patterns, but final conclusions about the number of different profiles are based upon a foundation of (objective) statistical parameters and (subjective) substantive interpretation as this is the standard, recommended practice (Masyn, 2013). In the present study, we pursued a three-profile rather than four-profile solution based on the body of statistical, theoretical, and empirical evidence, though model fit indices were somewhat varied in their support for three versus four subgroups. It is possible that our three-profile solution merged two separable subgroups that could have been retained in a four-profile solution. However, the fact that three latent statuses were replicated across two timepoints and performed well in latent transition analyses (which did not occur when four profiles were analyzed) renders this a less likely possibility. Nonetheless, further research is needed to test the replicability of such multisystem physiological parameters in other samples.

We also made several other theoretically- and methodologically informed decisions regarding children's physiology that necessitate continued study and replication in future research. For example, HPA and ANS responses were aggregated across stressor types given the differentially activated nature of physiological systems; future research should consider the potential for unique profiles to emerge across varied and non-aggregated stressor types. Subsequent studies may also benefit from considering individual differences in the timing of peak physiological reactivity (e.g., landmark registration). We were afforded a large sample size for the examination of multiple physiological systems and all children were drawn from the community. Given distinct (but less common) patterns of stress responsivity that may emerge in the context of clinical psychopathology and exposure to severe trauma, we may have been limited in our ability to uncover the full range of stress response profiles that exist in early childhood. Although this work with community samples is critical to establish 'typical' forms of development, an important next step in research of multisystem physiological activity will be exploration of these profiles in other samples that have greater exposure to adversity/trauma and/or are enriched for mental health diagnoses.

This study is the first to evaluate latent transitions of multisystem physiology, although the time duration of our analyses (fall to spring of the kindergarten year; approximately 7–8 months) may have been relatively limited in its capacity to capture change. The existence of significant developmentally induced and hormonally regulated physiological shifts will likely require longitudinal studies that span periods of expected change. Repetition of the same protocol may have also influenced responses in spring; however, the benefits for interpretation likely outweigh the costs. Protocol differences between the two timepoints would likely create observed differences in patterns of multisystem functioning that were due to changes in the stress reactivity protocol itself, rather than individual and/or developmental differences. Our hypotheses regarding different multisystem profiles were heavily guided by those proposed within the ACM (Del Giudice et al., 2011), yet our analyses do not consider genetic inputs in the determination of responsivity patterns, which is an important component of the ACM framework. Finally, Shader et al. (2018) recently recommended a revision to the respiratory frequency band that was the prior prevailing standard when RSA for the present study was computed. Although it is not feasible to re-score RSA for the present study, we acknowledge that the analyses may overestimate baseline RSA and underestimate RSA reactivity. Future research of multisystem physiology may benefit from considering the evolution in recommendations for respiratory frequency bands.

In summary, we conducted a novel, methodologically and statistically rigorous examination of multisystem stress responsivity across two timepoints in a sample of kindergarten children. LPA of the SNS, PNS, and HPA axis yielded three distinct patterns of multisystem activity that were strikingly similar from fall to spring of the school year, increasing our confidence in the patterns of findings and their potential utility. LTA revealed that within certain profiles, children were more likely to remain in the same profile over time than shift to a different profile, suggesting that certain multisystem response styles may be relatively stable during the important developmental transition to formal schooling. While individual differences in the physiological profiles uncovered by the present study were consistent with extant theoretical frameworks of cross-system response patterns, there were also notable

discrepancies that provide important directions for future research. Notwithstanding the need for replication studies across different samples, identifying a means by which to model multisystem physiological activity in a robust manner provides a foundation for continuing to ask key interdisciplinary empirical questions about children's development: *What are the contextual and environmental factors that influence children's multisystem profile membership (e.g., prenatal stress, parent mental health, early attachment)? Are these profiles a product of genetic variation, environmental variation, developmental timing, or epigenetic processes reflecting gene by environment interactions? Are there certain patterns of multisystem activity that render children more sensitive to the effects of their environment?* The answers to these questions have the potential to help us understand those children who are at greatest risk for poor outcomes and those who have the greatest capacity for flourishing. Our ultimate goal should be to diminish the chasm that separates these groups so all children can thrive.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding information

National Institute of Mental Health, Grant/Award Number: K23MH113701 and R01MH62320; MacArthur Foundation Research Network on Psychopathology and Development; Canadian Institute for Advanced Research

CONFLICTS OF INTEREST AND SOURCE OF FUNDING

The authors have no conflicts of interest to report. This study was supported by grants from the National Institute of Mental Health (R01 MH62320 to Boyce and K23MH113701 to Roubinov), the MacArthur Foundation Research Network on Psychopathology and Development (Boyce), and the Canadian Institute for Advanced Research (Boyce).

REFERENCES

- Ablow J, & Measelle J (1993). Berkeley Puppet Interview: Administration and scoring system manuals. Berkeley, CA: University of California.
- Adams MA, Sallis JF, Kerr J, Conway TL, Saelens BE, Frank LD, ... Cain KL (2011). Neighborhood environment profiles related to physical activity and weight status: A latent profile analysis. *Preventive Medicine*, 52(5), 326–331. 10.1016/j.ypmed.2011.02.020 [PubMed: 21382400]
- Alkon A, Boyce WT, Davis NV, & Eskenazi B (2011). Developmental changes in autonomic nervous system resting and reactivity measures in Latino children from 6 to 60 months of age. *Journal of Developmental and Behavioral Pediatrics*, 32(9), 668–677. 10.1097/DBP.0b013e3182331fa6 [PubMed: 22008788]
- Alkon A, Goldstein LH, Smider N, Essex MJ, Kupfer DJ, & Boyce WT (2003). Developmental and contextual influences on autonomic reactivity in young children. *Developmental Psychobiology*, 42(1), 64–78. 10.1002/dev.10082 [PubMed: 12471637]
- Asparouhov T, & Muthén B (2014). Auxiliary variables in mixture modeling: Three-step approaches using Mplus. *Structural Equation Modeling*, 21(3), 329–341.
- Atkinson L, Jamieson B, Khoury J, Ludmer J, & Gonzalez A (2016). Stress physiology in infancy and early childhood: cortisol flexibility, attunement and coordination. *Journal of Neuroendocrinology*, 28(8). 10.1111/jne.12408

- 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. 10.1002/1098-2302(200007)37:1<44:AID-DEV6>3.0.CO;2-7 [PubMed: 10937660]
- Barsegyan A, Mackenzie SM, Kurose BD, McGaugh JL, & Roozendaal B (2010). Glucocorticoids in the prefrontal cortex enhance memory consolidation and impair working memory by a common neural mechanism. *Proceedings of the National Academy of Sciences*, 107(38), 16655–16660. 10.1073/pnas.1011975107
- Bauer AM, Quas JA, & Boyce WT (2002). Associations between physiological reactivity and children's behavior: Advantages of a multisystem approach. *Journal of Developmental and Behavioral Pediatrics*, 23(2), 102–113. 10.1097/00004703-200204000-00007 [PubMed: 11943973]
- Beauchaine T (2001). Vagal tone, development, and Gray's motivational theory: Toward an integrated model of autonomic nervous system functioning in psychopathology. *Development and Psychopathology*, 13(2), 183–214. [PubMed: 11393643]
- Belsky J, & Pluess M (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, 135(6), 885. 10.1037/a0017376 [PubMed: 19883141]
- Berntson GG, Cacioppo JT, Quigley KS, & Fabro VT (1994). Autonomic space and psychophysiological response. *Psychophysiology*, 31(1), 44–61. 10.1111/j.1469-8986.1994.tb01024.x [PubMed: 8146254]
- Berntson GG, Thomas bigger J, Eckberg DL, Grossman P, Kaufmann PG, Malik M, ... Van der molen MW (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, 34(6), 623–648. 10.1111/j.1469-8986.1997.tb02140.x [PubMed: 9401419]
- Blair C, & Raver CC (2015). School readiness and self-regulation: A developmental psychobiological approach. *Annual Review of Psychology*, 66, 711–731. 10.1146/annurev-psych-010814-015221
- Bornstein MH, & Suess PE (2000). Child and mother cardiac vagal tone: Continuity, stability, and concordance across the first 5 years. *Developmental Psychology*, 36(1), 54–65. 10.1037/0012-1649.36.1.54 [PubMed: 10645744]
- 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]
- Boyce WT, Essex MJ, Alkon A, Goldsmith HH, Kraemer HC, & Kupfer DJ (2006). Early father involvement moderates biobehavioral susceptibility to mental health problems in middle childhood. *Journal of the American Academy of Child & Adolescent Psychiatry*, 45(12), 1510–1520. 10.1097/01.chi.0000237706.50884.8b [PubMed: 17135997]
- Bush NR, Alkon A, Obradovi J, Stamperdahl J, & Thomas Boyce W (2011). 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. 10.1016/j.jecp.2011.03.004 [PubMed: 21524757]
- Bush NR and Boyce W, (2016). Differential sensitivity to context: Implications for developmental psychopathology In Cicchetti D (Ed.), *Developmental psychopathology*, Vol. 2 (pp. 107–137). Hoboken, NJ: John Wiley & Sons Inc.
- Calkins SD, & Keane SP (2004). Cardiac vagal regulation across the preschool period: Stability, continuity, and implications for childhood adjustment. *Developmental Psychobiology*, 45(3), 101–112. 10.1002/dev.20020 [PubMed: 15505799]
- Chen FR, Raine A, & Granger DA (2015). Tactics for modeling multiple salivary analyte data in relation to behavior problems: Additive, ratio, and interaction effects. *Psychoneuroendocrinology*, 51, 188–200. 10.1016/j.psyneuen.2014.09.027 [PubMed: 25462892]
- Cohen J, Cohen P, West SG, & Aiken LS (2014). *Applied multiple regression/correlation analysis for the behavioral sciences* (3rd edn.). Mahwah, NJ: Erlbaum.
- Collins LM, & Lanza ST (2009). *Latent class and latent transition analysis*. Hoboken, NJ: Wiley.
- Dahl RE, & Gunnar MR (2009). Heightened stress responsiveness and emotional reactivity during pubertal maturation: Implications for psychopathology. *Development and Psychopathology*, 21(1), 1–6. 10.1017/S0954579409000017 [PubMed: 19144219]

- Del Giudice M, Ellis BJ, & Shirlcliff EA (2011). The adaptive calibration model of stress responsivity. *Neuroscience & Biobehavioral Reviews*, 35(7), 1562–1592. 10.1016/j.neubiorev.2010.11.007 [PubMed: 21145350]
- Del Giudice M, Hinnant JB, Ellis BJ, & El-Sheikh M (2012). Adaptive patterns of stress responsivity: A preliminary investigation. *Developmental Psychology*, 48(3), 775. 10.1037/a0026519 [PubMed: 22148947]
- Dickerson SS, & Kemeny ME (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, 130(3), 355–391. 10.1037/0033-2909.130.3.355 [PubMed: 15122924]
- Doussard-Roosevelt JA, Montgomery LA, & Porges SW (2003). Short-term stability of physiological measures in kindergarten children: Respiratory sinus arrhythmia, heart period, and cortisol. *Developmental Psychobiology*, 43(3), 230–242. 10.1002/dev.10136 [PubMed: 14558045]
- Duncan GJ, Dowsett CJ, Claessens A, Magnuson K, Huston AC, Klebanov P, ... Japel C (2007). School readiness and later achievement. *Developmental Psychology*, 43(6), 1428. 10.1037/0012-1649.43.6.1428 [PubMed: 18020822]
- Ellis BJ, Oldehinkel AJ, & Nederhof E (2017). The adaptive calibration model of stress responsivity: An empirical test in the Tracking Adolescents' Individual Lives Survey study. *Development and Psychopathology*, 29(3), 1001–1021. 10.1017/S0954579416000985 [PubMed: 27772536]
- El-Sheikh M, Kouros CD, Erath S, Cummings EM, Keller P, & Staton L (2009). Marital conflict and children's externalizing behavior: Interactions between parasympathetic and sympathetic nervous system activity. *Monographs of the Society for Research in Child Development*, 74(1), vii, 1–79.
- Essex MJ, Armstrong JM, Burk LR, Goldsmith HH, & Boyce WT (2011). Biological sensitivity to context moderates the effects of the early teacher-child relationship on the development of mental health by adolescence. *Development and Psychopathology*, 23(1), 149–161. 10.1017/S0954579410000702 [PubMed: 21262045]
- Essex MJ, Boyce WT, Goldstein LH, Armstrong JM, Kraemer HC, & Kupfer DJ. & Group, M. A. B. W (2002). The confluence of mental, physical, social, and academic difficulties in middle childhood. II: Developing the MacArthur Health and Behavior Questionnaire. *Journal of the American Academy of Child & Adolescent Psychiatry*, 41(5), 588–603. [PubMed: 12014792]
- Evans GW (2003). A multimethodological analysis of cumulative risk and allostatic load among rural children. *Developmental Psychology*, 39(5), 924. 10.1037/0012-1649.39.5.924 [PubMed: 12952404]
- Fox NA (Ed.) (1994). *The development of emotion regulation: Biological and behavioral considerations* (Vol. 59). Chicago: University of Chicago Press.
- Gatzke-Kopp L, & Ram N (2018). Developmental dynamics of autonomic function in childhood. *Psychophysiology*, 55(11), e13218. 10.1111/psyp.13218
- Gold PW, & Chrousos GP (2002). Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs low CRH/NE states. *Molecular Psychiatry*, 7(3), 254. [PubMed: 11920153]
- Goldberger AL, Amaral LA, Hausdorff JM, Ivanov PC, Peng C-K, & Stanley HE (2002). Fractal dynamics in physiology: Alterations with disease and aging. *Proceedings of the National Academy of Sciences*, 99(suppl 1), 2466–2472. 10.1073/pnas.012579499
- Goldstein DS, & Kopin IJ (2008). Adrenomedullary, adrenocortical, and sympathoneural responses to stressors: A meta-analysis. *Endocrine Regulations*, 42(4), 111. [PubMed: 18999898]
- Gordis EB, Granger DA, Susman EJ, & Trickett PK (2006). Asymmetry between salivary cortisol and alpha-amylase reactivity to stress: Relation to aggressive behavior in adolescents. *Psychoneuroendocrinology*, 31(8), 976–987. [PubMed: 16879926]
- Gunnar M, & Quevedo K (2007). The neurobiology of stress and development. *Annual Review of Psychology*, 58, 145–173. 10.1146/annurev.psych.58.110405.085605
- Gunnar MR, & Vazquez DM (2001). Low cortisol and a flattening of expected daytime rhythm: Potential indices of risk in human development. *Development and Psychopathology*, 13(3), 515–538. [PubMed: 11523846]
- Gunnar M, & Vazquez DM (2006). Stress neurobiology and developmental psychopathology In Cicchetti D & Cohen DJ (Eds.), *Developmental psychopathology*, Vol. 2 Hoboken, NJ: Wiley.

- 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. 10.1176/appi.ajp.160.9.1566
- Lipsitz LA, & Goldberger AL (1992). Loss of complexity and aging. *JAMA*, 267(13), 1806–1809. 10.1001/jama.1992.03480130122036 [PubMed: 1482430]
- 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). New York, NY: John Wiley & Sons Inc.
- Masyn KE (2013). Latent class analysis and finite mixture modeling In Little TD (Ed.), *The oxford handbook of quantitative methods*, Vol. 2 New York, NY: Oxford University Press.
- McEwen BS (1998). Stress, adaptation, and disease. Allostatic 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. 10.1016/S0018-506X(02)00024-7 [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), 25–39. 10.1037/0033-2909.133.1.25 [PubMed: 17201569]
- Moore GA, & Calkins SD (2004). Infants' vagal regulation in the still-face paradigm is related to dyadic coordination of mother-infant interaction. *Developmental Psychology*, 40(6), 1068–1077. 10.1037/0012-1649.40.6.1068 [PubMed: 15535757]
- Muthén LK, & Muthén BO (1998-2017). *Mplus User's Guide* (8th edn.). Los Angeles, CA: Muthén & Muthén.
- Oberski D (2016). Mixture models: Latent profile and latent class analysis In Robertson J & Kaptein M (Eds.), *Modern statistical methods for HCI: A modern look at data analysis for HCI research* (pp. 275–287). Cham, Switzerland: Springer International Publishing.
- Obradovi 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. 10.1017/S0954579410000672 [PubMed: 21262042]
- Obradovic J, Bush NR, Stamperdahl J, Adler NE, & Boyce WT (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. 10.1111/j.1467-8624.2009.01394.x [PubMed: 20331667]
- Parent S, Lupien S, Herba CM, Dupere V, Gunnar MR, & Seguin JR (2019). Children's cortisol response to the transition from preschool to formal schooling: A review. *Psychoneuroendocrinology*, 99, 196–205. 10.1016/j.psyneuen.2018.09.013 [PubMed: 30253327]
- Perry NB, Calkins SD, Nelson JA, Leerkes EM, & Marcovitch S (2012). Mothers' responses to children's negative emotions and child emotion regulation: The moderating role of vagal suppression. *Developmental Psychobiology*, 54(5), 503–513. 10.1002/dev.20608 [PubMed: 22072217]
- Porges SW (1997). Emotion: An evolutionary by-product of the neural regulation of the autonomic nervous system. *Annals of the New York Academy of Sciences*, 807, 62–77. 10.1111/j.1749-6632.1997.tb51913.x [PubMed: 9071344]
- Porges SW (2007). The polyvagal perspective. *Biological Psychology*, 74(2), 116–143. 10.1016/j.biopsycho.2006.06.009 [PubMed: 17049418]
- Porges SW, Doussard-Roosevelt JA, Lourdes Portales A, & Suess PE (1994). Cardiac vagal tone: Stability and relation to difficultness in infants and 3-year-olds. *Developmental Psychobiology*, 27(5), 289–300. 10.1002/dev.420270504 [PubMed: 7926281]
- Porges SW, & Furman SA (2011). The early development of the autonomic nervous system provides a neural platform for social behaviour: A polyvagal perspective. *Infant and Child Development*, 20(1), 106–118. 10.1002/icd.688 [PubMed: 21516219]

- Qu Y, Tan M, & Kutner MH (1996). Random effects models in latent class analysis for evaluating accuracy of diagnostic tests. *Biometrics*, 52, 797–810. [PubMed: 8805757]
- Quas JA, Yim IS, Oberlander TF, Nordstokke D, Essex MJ, Armstrong JM, ... Boyce WT (2014). The symphonic structure of childhood stress reactivity: Patterns of sympathetic, parasympathetic, and adrenocortical responses to psychological challenge. *Development and Psychopathology*, 26, 963–982. [PubMed: 24909883]
- Rash JA, Thomas JC, Campbell TS, Letourneau N, Granger DA, Giesbrecht GE, & Team, A. P. S. (2016). Developmental origins of infant stress reactivity profiles: A multi-system approach. *Developmental Psychobiology*, 58(5), 578–599. 10.1002/dev.21403 [PubMed: 26956370]
- 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. 10.1016/S0193-3973(00)00051-4
- Roubinov DS, Boyce WT, & Bush NR (2018). Informant-specific reports of peer and teacher relationships buffer the effects of harsh parenting on children's oppositional defiant disorder during kindergarten. *Development and Psychopathology*, 32(1), 163–174.
- Roubinov DS, Bush NR, Hagan MJ, Thompson J, & Boyce WT (2019). Associations between classroom climate and children's externalizing symptoms: The moderating effect of kindergarten children's parasympathetic reactivity. *Development and Psychopathology*, 1–12. 10.1017/S095457941900052X
- Rudolph CD, Rudolph AM, Hostetter MK, Lister GL, & Siegel NJ (2003). *Rudolph's pediatrics* (21st edn.). New York: McGraw-Hill.
- Salomon K, Matthews KA, & Allen MT (2000). Patterns of sympathetic and parasympathetic reactivity in a sample of children and adolescents. *Psychophysiology*, 37(6), 842–849. 10.1111/1469-8986.3760842 [PubMed: 11117464]
- Sapolsky RM, Romero LM, & Munck AU (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrine Reviews*, 21(1), 55–89. 10.1210/edrv.21.10389 [PubMed: 10696570]
- Schulting AB, Malone PS, & Dodge KA (2005). The effect of school-based kindergarten transition policies and practices on child academic outcomes. *Developmental Psychology*, 41(6), 860–866. 10.1037/0012-1649.41.6.860 [PubMed: 16351333]
- Shader TM, Gatzke-Kopp LM, Crowell SE, Jamila Reid M, Thayer JF, Vasey MW, Beauchaine TP (2018). Quantifying respiratory sinus arrhythmia: Effects of misspecifying breathing frequencies across development. *Development and Psychopathology*, 30(1), 351–366. 10.1017/S0954579417000669 [PubMed: 28554343]
- Stratakis CA, SChrousos GP(1995). Neuroendocrinology and pathophysiology of the stress system. *Annals of the New York Academy of Sciences*, 771, 1–18. 10.1111/j.1749-6632.1995.tb44666.x [PubMed: 8597390]
- Suess PE, Porges SW, & Plude DJ (1994). Cardiac vagal tone and sustained attention in school-age children. *Psychophysiology*, 31(1), 17–22. 10.1111/j.1469-8986.1994.tb01020.x [PubMed: 8146250]
- Tein J-Y, Coxe S, & Cham H (2013). Statistical power to detect the correct number of classes in latent profile analysis. *Structural Equation Modeling*, 20(4), 640–657. 10.1080/10705511.2013.824781 [PubMed: 24489457]
- Ulrich-Lai YM, & Herman JP (2009). Neural regulation of endocrine and autonomic stress responses. *Nature Reviews Neuroscience*, 10(6), 397–409. 10.1038/nrn2647 [PubMed: 19469025]
- Ursache A, Blair C, & Raver CC (2012). The promotion of self-regulation as a means of enhancing school readiness and early achievement in children at risk for school failure. *Child Development Perspectives*, 6(2), 122–128. 10.1111/j.1750-8606.2011.00209.x [PubMed: 32226480]
- van den Bos E, & Westenberg PM (2015). Two-year stability of individual differences in (para)sympathetic and HPA-axis responses to public speaking in childhood and adolescence. *Psychophysiology*, 52(3), 316–324. 10.1111/psyp.12337 [PubMed: 25267560]
- West SG, Taylor AB, & Wu W (2012). Model fit and model selection in structural equation modeling. In Hoyle RH (Ed.), *Handbook of structural equation modeling* (pp. 209–231). New York: Guilford Press.

Zisner AR, & Beauchaine TP (2016). Psychophysiological methods and developmental psychopathology In Cicchetti D (Ed.), *Developmental psychopathology* (pp. 834–882). New York, NY: John Wiley & Sons Inc.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Research Highlights

- Latent profile analysis evaluated children's multisystem activity in three biological systems: the parasympathetic nervous system, sympathetic nervous system, and hypothalamic pituitary adrenal axis.
- In fall and spring of children's kindergarten year, three distinct and consistent profiles of multisystem physiological activity emerged.
- Latent transition analysis uncovered children's patterns of stability and change across the school year.
- Multisystem profile membership over the course of the kindergarten year was associated with children's socioemotional outcomes.

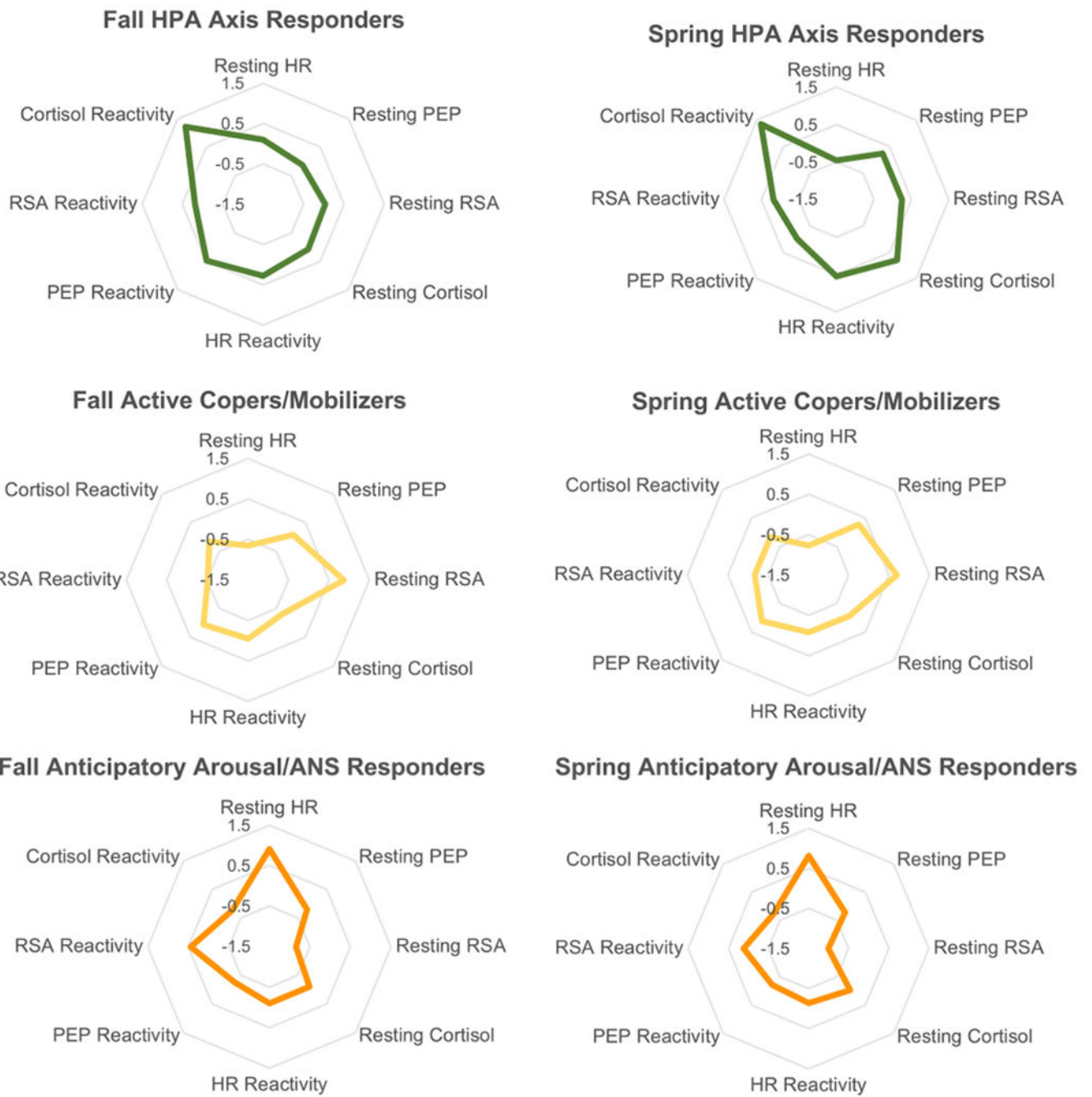


FIGURE 1. Graphical representation of 3-class latent profile analysis models in fall and spring using standardized averages of latent indicator means

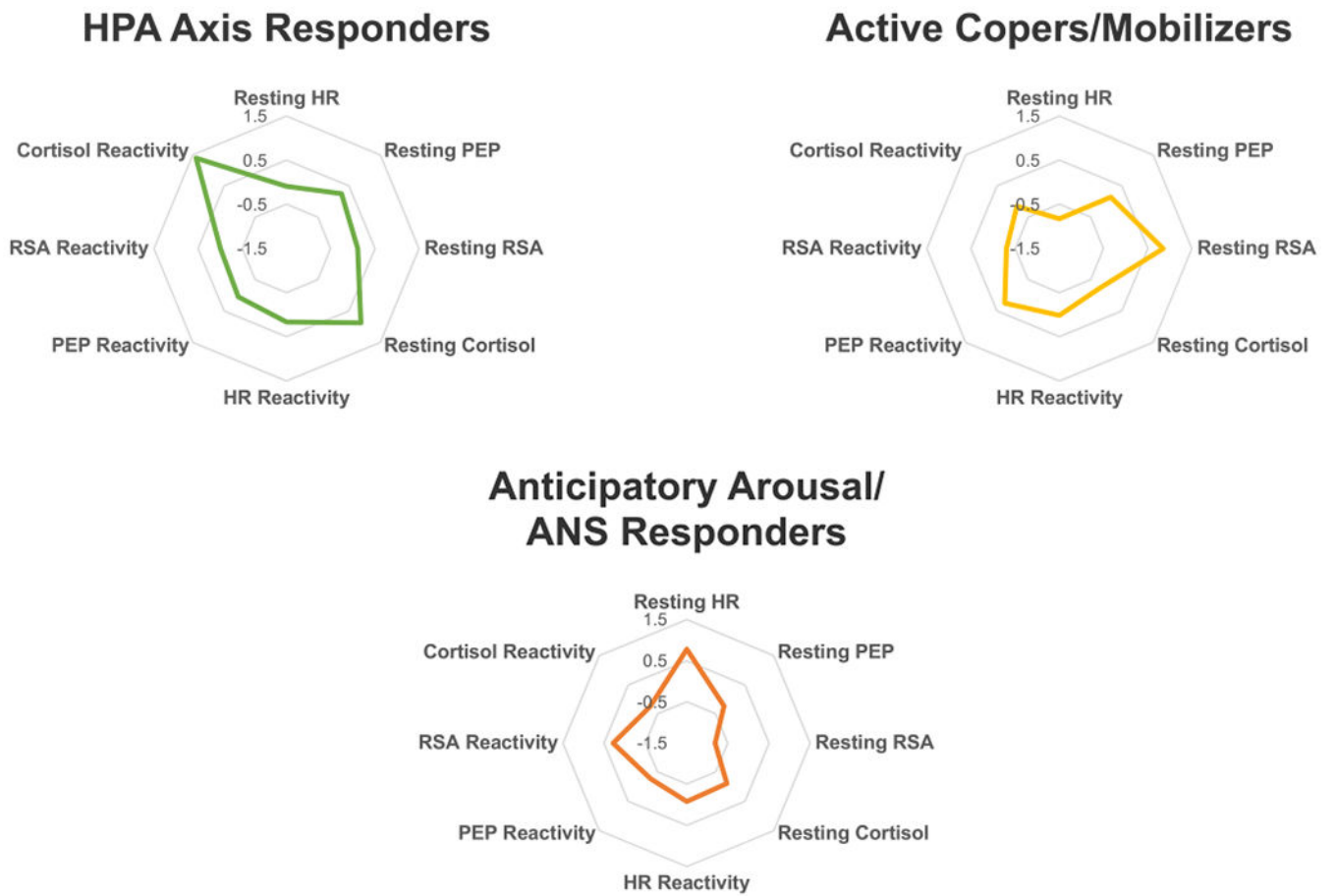


FIGURE 2. Graphical representation of 3-profile latent transition model using standardized averages of latent indicator means

Profile-specific ns, latent-indicator means, and confidence intervals of latent-indicator means for final 3-class fall, spring, and latent transition analysis models

TABLE 1

	Fall	Spring	Latent transition model
HPA Axis Responders	$n = 55^a$	$n = 56$	Fall $n = 42$ /Spring $n = 54$
Resting HR	95.14 (92.35, 97.94)	90.46 (88.81, 92.11)	93.48 (92.29, 94.66)
Resting PEP	78.15 (77.02, 79.28)	80.25 (79.02, 81.48)	80.36 (79.53, 81.19)
Resting RSA	6.86 (6.62, 7.11)	7.06 (6.86, 7.27)	6.94 (6.80, 7.07)
Baseline Cortisol	0.67 (0.60, 0.74)	0.83 (0.78, 0.88)	0.85 (0.81, 0.89)
HR Reactivity	0.13 (0.02, 0.23)	0.25 (0.11, 0.40)	0.07 (-0.03, 0.17)
PEP Reactivity	-0.19 (-0.29, -0.09)	0.01 (-0.12, 0.13)	-0.02 (-0.07, 0.04)
RSA Reactivity	-0.09 (-0.22, 0.05)	-0.08 (-0.21, 0.06)	0.00 (-0.09, 0.09)
Cortisol Reactivity	2.84 (1.97, 3.72)	3.17 (2.13, 4.21)	3.28 (2.52, 4.04)
Active Copers/Mobilizers	$n = 144$	$n = 144$	Fall $n = 136$ /Spring $n = 133$
Resting HR	88.85 (87.75, 89.95)	87.94 (86.41, 89.46)	87.36 (86.40, 88.33)
Resting PEP	79.31 (78.70, 79.93)	80.43 (79.54, 81.32)	79.71 (79.13, 80.29)
Resting RSA	7.66 (7.54, 7.77)	7.49 (7.32, 7.65)	7.64 (7.53, 7.75)
Baseline Cortisol	0.59 (0.56, 0.61)	0.64 (0.62, 0.66)	0.60 (0.59, 0.62)
HR Reactivity	-0.03 (-0.09, 0.03)	-0.04 (-0.16, 0.08)	0.00 (-0.06, 0.07)
PEP Reactivity	-0.02 (-0.07, 0.04)	-0.05 (-0.09, 0.00)	-0.10 (-0.14, -0.05)
RSA Reactivity	0.22 (0.16, 0.27)	0.07 (-0.03, 0.18)	0.13 (0.07, 0.19)
Cortisol Reactivity	-0.65 (-0.93, -0.38)	-0.66 (-0.87, -0.46)	-0.59 (-0.72, -0.46)
Anticipatory Arousal/ANS Responders	$n = 135$	$n = 126$	Fall $n = 159$ /Spring $n = 150$
Resting HR	101.85 (100.71, 102.98)	101.03 (99.82, 102.24)	100.74 (99.80, 101.68)
Resting PEP	77.78 (77.13, 78.44)	77.69 (76.92, 78.47)	77.63 (77.06, 78.21)
Resting RSA	6.03 (5.90, 6.15)	5.87 (5.73, 6.01)	6.05 (5.94, 6.17)
Baseline Cortisol	0.63 (0.60, 0.67)	0.65 (0.62, 0.68)	0.63 (0.61, 0.65)
HR Reactivity	-0.05 (-0.10, 0.01)	-0.07 (-0.15, 0.01)	-0.04 (-0.08, 0.00)
PEP Reactivity	0.11 (0.06, 0.16)	0.09 (0.04, 0.14)	0.11 (0.07, 0.15)

	Fall	Spring	Latent transition model
RSA Reactivity	-0.19 (-0.26, -0.12)	-0.05 (-0.14, 0.04)	-0.12 (-0.18, -0.07)
Cortisol Reactivity	-0.78 (-0.98, -0.58)	-0.93 (-1.14, -0.73)	-0.87 (-0.99, -0.75)

Note: Models estimate four covariances between resting and reactivity indicators (baseline HR and HR reactivity, baseline PEP and PEP reactivity, baseline RSA and RSA reactivity, and baseline cortisol and cortisol reactivity)

^aThe *rs* within the table reflect the final profile sizes based on most likely profile membership (Muthén & Muthén, 1998–2017). *M*plus also provides *rs* based on the estimated model, which account for participants' estimated probabilities of class membership (all of which were above 0.90 in the present analyses). The *rs* based on the estimated model are as follows for the HPA Axis Responders profile, Active Copers/Mobilizers Profile, and Anticipatory Arousal/ANS Responders profile, respectively: Fall LPA: 66.95, 138.49, 128.55; Spring LPA: 64.12, 137.55, 124.33; Fall LTA: 50.02, 135.03, 151.94; Spring LTA: 67.53, 128.83, 140.64).

TABLE 2

Transitional probabilities from the latent transition analysis model

Spring Latent Profiles			
Fall Latent Profiles	HPA Axis Responders (<i>n</i> = 54)	Active Copers/Mobilizers (<i>n</i> = 133)	Anticipatory Arousal/ANS Responders (<i>n</i> = 150)
HPA Axis Responders (<i>n</i> = 42)	0.57	0.27	0.16
Active Copers/Mobilizers (<i>n</i> = 136)	0.09	0.68	0.23
Anticipatory Arousal/ANS Responders (<i>n</i> = 159)	0.18	0.15	0.67

Note: Transitional probabilities characterize the likelihood of specific transitions among the three latent multisystem profiles from fall to spring of the kindergarten year. Probabilities on the diagonal reflect stability in class membership and probabilities off the diagonal reflect change in class membership. For each status, *n* reflects the model-estimated status size.