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Regular Article

Restoration of typical HPA–SAM co-activation following psychosocial intervention among preadolescent youth living in poverty

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Abstract

Despite the added value of multisystem (relative to traditional single-system) approaches for characterizing biological processes linked to risk for psychopathology (e.g., neuroendocrine stress responsivity; Buss et al., 2019; Quas et al., 2014), no study to date has evaluated whether multisystem processes may serve as viable biological targets of intervention. Utilizing a multiple-levels-of-analysis approach (Cicchetti & Dawson, 2002), this person-centered study examined whether stress-adapted patterns of hypothalamus–pituitary–adrenal (HPA) axis and sympathetic-adrenomedullary (SAM) system co-activation were amenable to change following the Building a Strong Identity and Coping Skills intervention (BaSICS; Wadsworth et al., 2022). Preadolescents exposed to concentrated poverty ($n = 112$, $M_{age} = 11.78$ years, 57.1% female, 54% assigned to intervention; 40% Hispanic, 63% Black, 20% White) completed questionnaires and the Trier Social Stress Test at both pre- and posttest. Multitrajectory modeling of cortisol and alpha-amylase levels identified four pretest and posttest HPA-SAM co-activation profiles. At pretest, youth exhibiting *Asymmetric Nos. 1 & 2* HPA-SAM co-activation reported greater maladjustment relative to youth with *Symmetric Nos. 1 & 2* co-activation. Youth exhibiting *Asymmetric No. 1* co-activation at pretest were more likely to exhibit *Symmetric No. 1* co-activation following BaSICS relative to control. Findings highlight the potential of BaSICS to restore neuroendocrine stress response function in impoverished youth, pointing to HPA–SAM co-activation as a potential biological target of preventive intervention in this population.

Keywords: Adolescence; cortisol; alpha-amylase; multisystem; preventive intervention

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Introduction

Youth mental health disparities stem in part from the cumulative effects of chronic exposure to stressful life circumstances borne of inequality and marginalization, which both overwhelm a child's capacity to cope and access sources of support. Evidence increasingly shows that the roots of these disparities often take hold in children's developing brains and bodies (Choudhury et al., 2023), particularly in stress-sensitive neuroendocrine systems such as the hypothalamic–pituitary–adrenal (HPA) axis (as indexed by salivary cortisol; Evans & Kim, 2013; Guidi et al., 2021). When examined in laboratory-based settings using established stress-induction paradigms (e.g., Trier Social Stress Test-M; Yim et al., 2010), youth exposed to early adversity (e.g., poverty-related stress; PRS) largely exhibit HPA hypo-responsivity (i.e., blunting) to acute psychosocial stress (Koss & Gunnar, 2018; Ouellet-Morin et al., 2011). This early stress-related HPA alteration is associated with the later emergence of psychopathology, both with respect to internalizing (e.g., Heim et al., 2000; Raison & Miller, 2003) and externalizing (Alink et al., 2008; Laurent et al., 2014) forms of psychopathology.

In turn, preventive intervention researchers have sought to develop programs for stress-affected youth with the intention of restoring typical HPA rhythms (Slopen et al., 2014). Indeed, we developed the Building a Strong Identity and Coping Skills (BaSICS) program with this aim in mind (Wadsworth et al., 2022). BaSICS was designed to target stress-sensitive biological systems and psychosocial processes believed to contribute to risk for psychopathology related to PRS exposure. In accordance with the Adaptation to Poverty-related Stress model (APRS; Wadsworth, 2015; Wadsworth et al., 2023), BaSICS works to improve youths' engagement coping skills, foster their identity development, and teach strategies for taking collective action towards alleviating a commonly identified source of strain in their communities. One of BaSICS' central hypotheses is that learning how to individually and collectively cope with controllable (e.g., academic) and uncontrollable (e.g., environmental) stress, respectively, will help to restore efficient operation of the HPA axis in youth who contend with ongoing PRS exposure.

The current study aimed to both identify and address theoretical and methodological challenges to evaluating the efficacy of preventive interventions such as BaSICS in restoring typical neuroendocrine rhythms for preadolescent youth living in poverty. We first describe the limitations and advantages of traditional and contemporary analytic approaches to characterizing neuroendocrine stress response function in this population, and, thus, interpretable neuroendocrine targets of intervention.

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Next, we propose a theoretical model of multisystem stress response function in the context of PRS to provide conceptual clarity to classic single-system findings and hypothesize about comprehensive multisystem targets of intervention when studying PRS-exposed preadolescents. We then conduct an empirical test of this model, applying traditional and contemporary analyses to youth biological data collected prior to BaSICS delivery and then comparing results to determine the approach that conceptually and empirically characterized neuroendocrine response function in our sample. Lastly, we utilize the settled upon approach to evaluate the efficacy of BaSICS in optimizing neuroendocrine response function.

Characterizing neuroendocrine stress responsivity in youth living in poverty

According to current models of allostatic load, youths' stress-sensitive biological systems undergo a unique series of adaptions under conditions of chronic stress in an effort to maintain neuroendocrine homeostasis (e.g., Ellis & Del Giudice, 2019). In the face of ongoing uncontrollable stress, the HPA's feedback loops become more sensitized to stress exposure, resulting in initial-stage exaggerated reactivity referred to as *HPA hyper-responsivity*. Over time, the pituitary and hypothalamus respond to *HPA hyper-responsivity* (i.e., prolonged glucocorticoid production) with a breakdown in neuroendocrine signaling (e.g., compromised feedback loops), resulting in blunted reactivity referred to as *HPA hypo-responsivity* (de Rooij, 2013; Selye, 1950). Both hyper- and hypo-responsive HPA activation patterns have been associated with risk for psychopathology (Ellis & Del Giudice, 2019; Hartman et al., 2013; Lopez-Duran et al., 2015).

Although theory and evidence have both implicated and shown these two patterns to be associated with chronic stress exposure (with HPA blunting predominantly observed of preadolescents living in poverty; Ursache et al., 2015), studies of stress-affected youth have demonstrated weak and inconsistent cortisol response–maladjustment linkages (Raymond et al., 2018; Young et al., 2020). One question warranting further inquiry is whether traditionally-used approaches may contribute to this lack of clarity when studying this specific population (Buss et al., 2019). Take, for example, the utilization of multiple linear regression and summative cortisol reactivity score (e.g., Area Under the Curve – Increase (AUCi); Pruessner et al., 2003). If both theory and evidence suggest that significant cortisol reactivity–maladjustment relations exist at *both* ends of the cortisol reactivity distribution (i.e., *HPA hyper-responsivity, HPA hypo-responsivity*), this statistical approach might understandably return nonsignificant or weak cortisol reactivity effects (i.e., both high and low cortisol reactivity are associated with high maladjustment levels in this population). If so, conclusions drawn about the role HPA stress responsivity might play in PRS-exposed youths' risk for psychopathology may be erroneous.

Characterizing neuroendocrine stress responsivity in this way for youth living in poverty is perhaps even more challenging in the context of preventive intervention. Such programs (e.g., BaSICS) are classified by the populations they aim to serve; e.g., selective (i.e., known risk factor for the development of a psychopathology; e.g., living in poverty) and/or indicated (i.e., early to subclinical levels of psychopathology; e.g., emotional and behavior problems) samples (Garber et al., 2012). BaSICS was designed to reduce risk for the later emergence of severe internalizing psychopathology (e.g., depression, anxiety) in preadolescent youth living in poverty presenting with non-clinical to sub-threshold clinical internalizing symptom levels. Thus, when studying a sample such as ours, further consideration becomes necessary about whether variation in HPA activation prior to program delivery includes not only alterations in cortisol responsivity for high-risk youth described hitherto, but also more typical cortisol response patterns shown by lower risk youth (i.e., exposed to lower PRS levels, exhibiting fewer emotional and behavioral problems).

Further complicating matters, preventive intervention programs designed to move stress-sensitive biological rhythms intuitively target developmental periods characterized by enhanced plasticity of those biological systems (e.g., Dozier et al., 2018; Fisher et al., 2016). Indeed, our own work has focused specifically on restoring HPA stress response function in PRS-exposed youth during the preadolescent period, given that the pubertal transition is believed to open windows for environmentally induced changes in stress responsivity that promote youths' ability to utilize complex coping skills (Gunnar et al., 2019; Gunnar & Howland, 2022; Sisk & Gee, 2022). The issue here, however, is that periods of plasticity are inherently characterized by heterogeneity in neuroendocrine function. Thus, the existence of variation in cortisol responsivity tied not only to risk factor exposure (e.g., poverty) but also the developmental period of focus (e.g., preadolescence) creates additional difficulties for the use of the traditional approaches discussed hitherto, as these approaches may be ill-equipped to clearly illustrate this potential variation in both typical and atypical HPA stress response function in a single sample.

Recent studies have observed that cortisol responsivity exhibited by lower risk youth is often indistinguishable to that exhibited by their higher risk counterparts (Bendezú et al., 2022; Bendezú et al., 2022; Carosella et al., 2023; Wiglesworth et al., 2023). Lower risk preadolescents can possess weaker cortisol responsivity (e.g., fewer stressors to contend with, protects against neurotoxic effects of cortisol overexposure) referred to as *normative HPA non-responsivity* (van der Voorn et al., 2017). Lower risk preadolescents can also possess stronger cortisol responsivity (e.g., greater stressors as youth transition towards adolescence, supports more sophisticated coping) referred to as *normative HPA responsivity* (van der Voorn et al., 2017). Thus, in a sample such as ours, pre-intervention cortisol response–maladjustment links obtained from traditional approaches may be difficult to interpret because of the possibility that *both* safe-adapted (e.g., low-risk youth) and stress-adapted (e.g., high-risk youth) cortisol responses (which may appear similar and, thus, difficult to parse apart) exist at *both* lower (e.g., *normative HPA non-responsivity, HPA hypo-responsivity)* and higher (e.g., *normative HPA responsivity, HPA hyper-responsivity)* ends of the cortisol response distribution.

Identifying neuroendocrine stress response targets of preventive intervention

Thus far, we have outlined potential limitations of classic approaches to characterizing neuroendocrine function in preadolescents living in poverty. Given these limitations, it becomes necessary, then, to consider the appropriateness of specific neuroendocrine function outcomes of preventive intervention for this population. To date, studies assessing the ability of interventions to restore stress-adapted neuroendocrine rhythms have largely focused on the HPA alone and normalization of diurnal cortisol rhythms in young children exposed to early life stress (Boparai et al., 2018). Of those few studies that have utilized

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laboratory-based stressors, both increased and decreased cortisol responsivity intervention effects have been shown (Cohen et al., 2021; Luecken et al., 2015; Schuurmans et al., 2021). Notably, though each effect is interpreted as restoring typical HPA rhythms (i.e., remediating HPA hypo- or hyper-responsivity), these studies often do not characterize cortisol responsivity prior to program delivery by linking cortisol activation to indices of well-being or maladjustment (cf. Luecken et al., 2015). In our sample, utilization of traditional approaches and related difficulties with characterizing HPA stress responsivity prior to program delivery may restrict inference about whether program effects reflect movement towards or away from typical or atypical neuroendocrine function.

Difficulty characterizing neuroendocrine stress responsivity and, thus, identifying an interpretable neuroendocrine intervention outcome can also be observed in our earlier single-system studies of this sample. Joos et al., (2019) showed that youth at pretest were primarily composed of HPA nonresponders who, relative to HPA responders, presented with greater uncontrollable life events and psychological distress. However, differences between HPA responders and nonresponders on distress indices were small; e.g., scale scores within normal limits, weak HPA–distress associations. Nevertheless, the overall pattern of findings pointed to *cortisol responsivity* as *typical* and reflective of intact HPA axis function and *cortisol nonresponsivity* as *atypical* and reflective of blunted HPA axis function (Koss & Gunnar, 2018).

This single-system characterization, however, proved to be problematic, as it contradicted single-system findings from our later BaSICS efficacy evaluation (Wadsworth et al., 2020). Our preregistered neuroendocrine outcome was a *strengthening* of the cortisol response, signaling restoration youths' ability to marshal HPA-related resources for coping with PRS (Van der Voorn et al., 2017; Zimmer-Gembeck & Skinner, 2016). However, BaSICS youth unexpectedly demonstrated a *weakening* of the cortisol response relative to control. Based on these single-system findings, it was difficult to rule out the possibility of BaSICS-related iatrogenic effects vis-à-vis further blunting of HPA stress response. This quandary led us, and others (Buss et al., 2019; Quas et al., 2014), to consider more nuanced, comprehensive approaches to characterizing neuroendocrine stress response function and identifying neuroendocrine targets and outcomes of intervention.

Towards multisystem, person-centered clarification

Thus far, we have proposed that there potentially exist four groups of poverty-exposed youth who exhibit quantitatively similar yet qualitatively distinct cortisol responses: safe-adapted, low-risk (*normative HPA non-response, normative HPA response*); stress-adapted, high-risk (*HPA hyper-response, HPA hypo-response*). We have argued that their existence in the same sample likely interferes with traditional analytic efforts to characterize neuroendocrine stress responsivity, and thus, interpret neuroendocrine outcomes of preventive intervention. Here, we discuss how contemporary multisystem, person-centered approaches may help to clarify weak and inconsistent cortisol–maladjustment links identified in studies adopting classic approaches in this population and advance understanding about interpretable neuroendocrine outcomes.

Person-centered analytic approaches (e.g., Bergman & Magnusson, 1997; Block, 1971), such as Group-Based Trajectory Modeling (GBTM; Nagin, 2005), permit the identification of different subgroups of youth within a given sample who share unique trajectories (e.g., response patterns) on a single indicator of interest (e.g., cortisol). Once identified, these unique trajectories can be characterized by comparing subgroups on theory-driven correlates of interest (e.g., maladjustment). GBTM has facilitated identification of unique cortisol response trajectories and the correlates that characterize them (e.g., Giletta et al., 2015; Gunnar et al., 2009; Ji et al., 2016).

That said, as a single-system approach, GBTM is still limited by issues germane to the current study. As noted in Bendezú, Calhoun et al., (2022), GBTM may identify, for example, a single or multiple low cortisol response groups that are unknowingly comprised of *both* low-risk (*normative HPA non-response*) and high-risk (*HPA hypo-response*) youth. Indeed, in Gunnar et al. (2009), three GBTM-specified cortisol nonresponse groups were evenly composed of typically developing and early life stress exposed youth. To address this issue, recent studies have utilized multisystem extensions of GBTM (e.g., Multitrajectory Modeling, MTM; Nagin et al., 2018) to concurrently model systems that work in concert with the HPA to support coping (Bendezú et al., 2021, 2022; Carosella et al., 2023; Wiglesworth et al., 2023). These studies have shown MTM's ability to parse between low- and high-risk youth with identical cortisol response patterns by simultaneously attending to parallel stress response system processes.

Indeed, in Pham et al. (2023), we sought to strengthen inference about the existence of these four groups by simultaneously examining youths' HPA and sympathetic-adrenomedullary (SAM) system (as indexed by salivary alpha-amylase) TSST activation. MTM analyses of youth's cortisol and alpha-amylase levels identified four profiles of HPA–SAM co-activation: two low-risk *symmetrical* (Low HPA–Low SAM, High HPA–High SAM), two high-risk *asymmetrical* (High HPA[1]–Low SAM, Low HPA–High SAM). Connections to indices of stress exposure and psychological distress suggested that cortisol trajectories in symmetrical profiles reflected *normative HPA responsivity* and *nonresponsivity* while trajectories observed in asymmetrical profiles reflected *HPA hyper-responsivity* and *HPA hypo-responsivity*. Low HPA–Low SAM and Low HPA–High SAM youth exhibited indistinguishably low cortisol trajectories while differing in maladjustment. Group differences in stress exposure and psychological distress were also larger than that observed in Joos et al., (2019), with scale scores exceeding at-risk cutoffs for high-risk youth. These differences helped clarify our single-system intervention findings (Wadsworth et al., 2020), with the largest pretest differences observed between high-risk, asymmetrical High HPA[1]–Low SAM youth and low-risk, symmetrical Low HPA–Low SAM youth.

Restoration of HPA–SAM co-activation in preadolescents living in poverty

The current study was designed with this clarification in mind. Specifically, we test the proposition that BaSICS-related reductions in cortisol responsivity (Wadsworth et al., 2020) reflect a restoration of typical HPA response patterns by way of re-aligning *asymmetrica*l HPA–SAM co-activation toward *symmetrical* co-activation. Here, we integrate both theory and empirical evidence into a conceptual model of individual differences in preadolescent HPA–SAM co-activation in the context of

[1]High HPA–Low SAM youth displayed higher baseline cortisol levels than Low HPA–Low SAM, but lower baseline cortisol levels than High HPA–High SAM. These youth also displayed similar baseline cortisol levels to Low HPA–High SAM, but displayed pronounced cortisol reactivity whereas Low HPA–Low SAM and Low HPA–High SAM youth did not. Given the overall pattern of baseline cortisol and reactivity similarities and differences, a more parsimonious labeling convention for the High HPA–Low SAM group may be "Moderate HPA–Low SAM."

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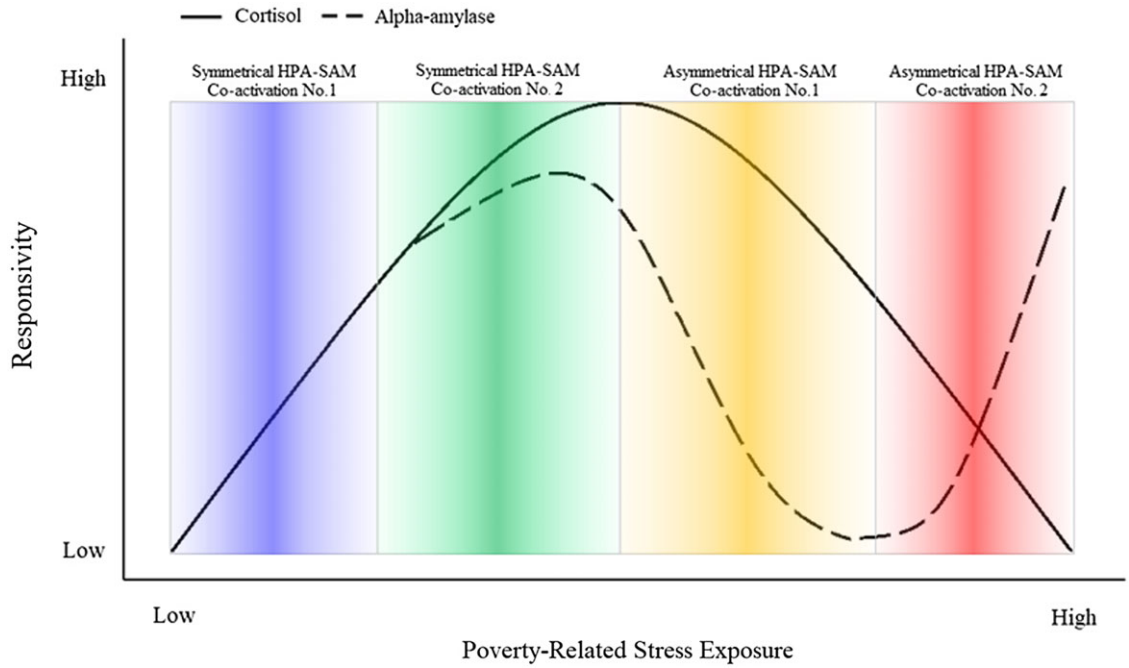

Figure 1. Theoretical model of HPA-SAM co-activation in preadolescent youth increasingly exposed to poverty-related stress.

poverty-related stress (PRS) exposure (Figure 1). Symmetrical HPA–SAM Co-activation Nos. 1 and 2 classifications reflect varying degrees of safe-adapted neuroendocrine responsivity characteristic of typically developing preadolescents. Asymmetrical HPA–SAM Co-activation Nos. 1 and 2 classifications reflect atypical, stress-adjusted neuroendocrine responsivity characteristic of PRS-exposed preadolescent youth.

Notably, within each classification, HPA–SAM co-activation exists on a continuum. This feature permits within-profile HPA and SAM response levels to differ across studies while signaling similar co-activation processes when validated though connections with maladjustment indices. The model also allows for moderate responses in identified profiles, such that a Moderate HPA–Moderate SAM profile might reflect Symmetrical No. 2 co-activation processes (i.e., normative HPA responsivity) while a High HPA–Moderate SAM or Moderate HPA–Low SAM profile might reflect Asymmetrical No. 1 processes (i.e., HPA hyper-responsivity).

The Symmetrical HPA–SAM Co-activation No. 1 classification reflects strong positive bidirectional feedback loops between the HPA axis and SAM system, each structurally and functionally linked to the hypothalamus, for youth rarely exposed to poverty-related stressors. In this classification, the HPA axis and SAM system perform in parallel, with strong positive bidirectional feedback loops facilitating effective cross-system communication and permitting the low to moderate cortisol response to down-regulate itself but also the low to moderate SAM response by suppressing its reflexive processes. Here, a Low HPA response might reflect *normative HPA nonresponsivity* described in the youth single-system HPA literature.

The Symmetrical HPA–SAM Co-activation No. 2 classification is conceptually similar to Symmetrical No. 1, though commensurate moderate to high HPA axis and SAM system responses are observed. These commensurate increases in HPA and SAM responsivity reflect the body's adaptation to more intermittent exposure to poverty-related stressors, signaling a well-balanced provision of additional neuroendocrine resources requisite for coping with stressors in more sophisticated and context-specific ways. Notably, initial disruptions of HPA–SAM co-activation and cross-system communication can be increasingly observed of youth exposed to more moderate PRS levels. In this profile, a Moderate to High HPA response is thought to reflect *normative HPA responsivity* described in the youth single-system HPA literature.

The Asymmetrical HPA–SAM Co-activation No. 1 classification signals the first-stage breakdown of HPA–SAM cross-system signaling, whereby asymmetry manifests as HPA responsivity that remains elevated while the SAM system shifts toward low responsivity. Elevated HPA responsivity initiated within and propagated by the hypothalamus and pituitary may reflect allostatic change in response to more frequent uncontrollable stress exposure. Repeated allostatic adaptation henceforth leads to sustained HPA over-activation. At the same time, decreased SAM responsivity may represent self-preserving allostatic adaptation in the face of neurotoxic sustained cortisol elevations, thereby protecting the body from noxious over-taxation and depletion of important cardiovascular, immunologic, and central nervous system resources. In this profile, a Moderate to High HPA response is believed to reflect atypical, stress-adapted *HPA hyper-responsivity* described in the single-system HPA literature.

Asymmetrical HPA–SAM Co-activation No. 2 reflects the second-stage breakdown of HPA-SAM cross-system signaling, whereby asymmetry manifests as low HPA responsivity while the SAM system shifts toward moderate to high responsivity. Low HPA responsivity may reflect further allostatic adaptation to more chronic PRS exposure, promoting longer-term survival by averting hypercortisolism-linked suppression of immunologic function, increasing catabolic pathways, and decreasing neurotoxic effects of cortisol overexposure. Moderate to High SAM responsivity can be viewed as a product of glucocorticoid resistance, and reduced cortisol suppression of SAM system activation that occurs in the presence of more typical HPA function. Chronic stress-adapted HPA response function then "spills over" to peripheral systems

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(e.g., SAM) which become over-taxed by the ongoing provision of biologically costly resources for managing PRS. In this profile, a Low to Moderate HPA response is thought to reflect atypical *HPA hypo-responsivity* (i.e., blunting) described in the youth single-system HPA literature.

Our model is not unlike other multisystem conceptualizations of stress response system (SRS) function; e.g., Adaptive Calibration Model (ACM; Del Giudice et al., 2011). First, each concern themselves with characterizing stress-adapted biological responsivity vis-à-vis consideration of multisystem SRS function. Second, each propose four multisystem profiles of stress responsivity that reflect functional organization and re-organization of the SRS to stressful life circumstance. Third, each hold that nonlinear relationships exist between stress exposure and the emergence of stress-adapted multisystem response patterns. Lastly, each suggest that developmental periods defined by SRS plasticity provide opportune windows for recalibration.

There are, however, notable points of divergence. First, our model accounts for symmetries as well as asymmetries in HPA and SNS[2] (of which the SAM system is a part) responsivity, whereas the ACM focuses largely on symmetries and asymmetries in parasympathetic nervous system (PNS) and SNS responsivity. Second, our model accounts for cortisol nonresponse observed of both typically developing and stress-affected youth (Gunnar et al., 2009; Ji et al., 2016), whereas the ACM accounts for cortisol nonresponse only in stress-affected youth; e.g., Unemotional (Type IV). Third, our model proposes that HPA and SNS activation increase in parallel in response to more moderate PRS exposure (i.e., shift from Symmetrical HPA–SAM Co-activation No. 1 to No. 2). The ACM proposes that HPA and SNS activation decrease in parallel under similarly stressful circumstances (i.e., shift from Sensitive Type I to Buffered Type II). Lastly, our model posits that asymmetries in HPA and SNS activation develop in stressful contexts and increase risk for psychopathology, whereas the ACM holds that symmetrically high and low HPA and SNS activation emerge in stressful environments and undergird the emergence of severe forms of psychopathology.

The current study: Aims and hypotheses

Aim 1

We sought to compare classic and contemporary analytic approaches in their capacity to characterize typical and atypical neuroendocrine response function in our pretest sample. We computed Area Under the Curve with respect to Ground (AUCg) and Increase (AUCi) scores for both pretest salivary cortisol and alpha-amylase data. We then utilized multiple linear regression models to examine these AUC scores as main and interactive predictors of youths' pretest self- and parent-reported internalizing and externalizing problems. We also utilized Group-Based Trajectory Modeling (GBTM) to identify distinct cortisol only and alpha-amylase only response trajectories. We intentionally limited GBTM model specification to two groups, an anticipated high and low group in each system so as to understand how lower or higher cortisol and alpha-amylase trajectories relate to maladjustment. Pham et al. (2023) had yet to be published at the time of writing the current manuscript. To avoid duplication and for ease of access, our pretest Multitrajectory Modeling (MTM) analytic plan and results are reported in the supplementary materials. We anticipated that stronger, more consistent links to pretest maladjustment indices would emerge with our pretest MTM approach relative to our AUC and GBTM approach.

Aim 2

We sought to examine whether youth who demonstrated atypical neuroendocrine response patterns prior to program delivery demonstrated more typical neuroendocrine response patterns thereafter, using the approach from Aim 1 that best characterized neuroendocrine function in our sample. We applied our Pham et al. (2023) approach to youth cortisol and alpha-amylase data collected at posttest. We expected to identify four posttest profiles similar to those identified at pretest just three months prior. We then examined the relationship between BaSICS assignment and posttest profile membership for youth who demonstrated atypical HPA–SAM Co-activation patterns prior to program delivery. We expected youth who demonstrated Asymmetrical profiles at pretest assigned to BaSICS to be more likely to exhibit Symmetrical profiles at posttest relative to their pretest Asymmetrical counterparts assigned to control.

To explore possible iatrogenic effects, we also examined the relationship between BaSICS assignment and posttest profile membership for youth exhibiting typical, Symmetrical patterns prior to program delivery. Specifically, we examined whether youth who exhibited Symmetrical profiles at pretest assigned to BaSICS were more likely to exhibit Asymmetrical profiles at posttest relative to their pretest Symmetrical counterparts assigned to control.

Method

Participants

One hundred twenty-nine parent-child dyads were recruited into the study. Sixteen dyads withdrew from the study upon randomization (13 intervention assigned, 3 control assigned) and one dyad withdrew prior to randomization. Parents who withdrew following randomization noted unforeseen scheduling conflicts with the bi-weekly intervention or disappointment in the condition they were assigned to. No significant differences on demographic and key study variable indices emerged between dyads who withdrew or remained in the study.

Of the remaining 112 youth ($M_{age} = 11.78$, $SD = 0.57$, 57.1% female), 61 were assigned to intervention and 51 assigned to the control group. With respect to race and ethnicity, 49% self-identified as mono-racial Black, 12% as mono-racial White, 16% as biracial, 3% as mono-racial Native American, 20% as Other, and 45% as Hispanic/Latino. The median number of adults and children living in the home was 2 and 3, respectively. Nearly 44% of caregivers were unemployed, with 41% of families receiving public assistance, 66% reporting food insecurity, and 24% receiving social security benefits. With respect to educational attainment, 29% of caregivers did not complete high school, 30% had a high school diploma/GED, 22% attended some college but did not receive a degree, and 19% received professional or associates degrees from technical or academic programs, and 4% received a bachelor or master's degree.

[2]While there is ongoing debate as to whether salivary alpha-amylase levels in the context of stress induction indicate activity of the sympathetic nervous system (SNS), parasympathetic nervous system (PNS), or a combination of both, some evidence suggests that salivary alpha-amylase levels may signal central noradrenergic activation (for review, see Ali & Nater, 2020). Our interpretation of salivary alpha-amylase as reflective of SNS activation was an intentional effort to remain consistent with the youth HPA–SNS co-activation literature (Jones et al., 2020).

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Recruitment and procedures

Participants were recruited from two high-poverty neighborhoods in a small metropolitan area in central Pennsylvania. Families were recruited in-person via recruitment staff (e.g., undergraduate research assistants, research coordinators) at schools within these two low-income communities, community health centers, and in partnership with cultural and spiritual agencies and institutions that serve those communities. Dyads who called to express interest in participating were screened by trained undergraduate students and research coordinators. Our study had the following inclusion criteria at time of screening: youth ages 10-12 years, youth fluency in English, parent fluency in English or Spanish, and family income at or below 200% of the federal poverty level. Exclusion criteria for this preventive intervention efficacy trial at time of screening was as follows: youth lifetime diagnosis of child autism spectrum disorder and/or intellectual disability as per parent report; youth current depression (Children's Depression Inventory, 2nd edition; Kovacs, 2015) or anxiety (Beck Anxiety Inventory; Beck et al., 1988) symptoms that met clinical cut-off criteria as per parent report of youth; youth enrollment in half to full day special education services. Parents reporting clinically elevated youth depression and/or anxiety symptoms were referred to community mental health agencies in the area.

Eligible dyads provided informed consent and were in turn provided a time slot beginning between 3 and 5 pm for which to complete their pretest assessment. This assessment took 3 hours to complete and consisted of two primary components: parents and youth completing a series of questionnaires (parents in one room, youth in a different room with a trained experimenter who read questions and remained with the youth for the duration of the assessment), Trier Social Stress Test-Modified (TSST-M; Yim et al., 2010). As per the TSST-M protocol, youth were instructed at screening and the day prior to their appointment to avoid eating a large meal and to abstain from brushing their teeth one hour before the assessment. They were also instructed to avoid having dairy or any sugary/acidic snacks twenty minutes before their assessment. However, in light of the duration of the assessment and the unique needs of our sample, youth were provided with a non-sugary snack and small amount of water upon arrival. Saliva samples were collected by the experimenter via passive drool techniques (Davis et al., 2002) at six time points. Following questionnaire administration (~40 min) and immediately prior to the start of the TSST-M, youth provided an initial saliva sample (+0 min from TSST-M start). During the TSST-M, youth parted with their experimenter and prepared (5 min) and delivered (5 min) a speech and completed a mental subtraction task (5 min) in front of an unresponsive "panel of experts" (i.e., study confederates unknown to participants). A second saliva sample was taken immediately thereafter (+15 min from TSST-M start). Youth were then provided musical instruments, art supplies, and toys, which their experimenter invited them to play with for 10 min while judges "scored their performance." A third saliva sample was taken thereafter (+25 min from TSST-M start). Youth were then interviewed by their experimenter for 10 min about the coping strategies they utilized during the TSST-M and while the judges were scoring their performance. A fourth saliva sample was collected (+35 min from TSST-M start). Next, youth followed along with an audio recording of a guided progressive muscle relaxation session (PMR). A fifth saliva sample was collected thereafter (+45 min from TSST-M start). Lastly, the experimenter administered any remaining questionnaires and invited the child to sit quietly for 10 min. A final sixth saliva sample was collected was collected (+55 min from TSST-M start). Experimenters then debriefed youth and families received $50 compensation. All procedures were approved by The Pennsylvania State University Institutional Review Board.

BaSICS youth attended two 2-hour sessions per week for 8 weeks. BaSICS aims to optimize youths' ability to successfully navigate the chronically stressful developmental contexts associated with living in poverty. Developed in accordance with the Adaptation to Poverty-Related Stress model (APRS; Wadsworth, 2015; Wadsworth et al., 2022), BaSICS adopts a multipronged approach to supporting youth living in poverty, one that (a) shores up knowledge about and capacity to utilize fundamental engagement coping skills, such as problem solving and emotion regulation, (b) fosters positive sociocultural identity via identity exploration, and by learning interpersonal problem solving, teamwork and cooperation, and (c) and provides new avenues for active coping via collaborative coping, which is comprised of social action and community engagement. These three "prongs" comprise the three components (modules) of BaSICS, which we propose will both treat psychopathology symptoms and impact stress biology, thereby improving youths' lives immediately and disrupting pathways to lifelong ill health.

Parent-child dyads were then scheduled for a posttest assessment. This assessment was completed by parent-child dyads approximately two weeks after the final BaSICS intervention session for that cohort, regardless of the whether they were assigned to intervention or control. The decision to use this specific length of time between pretest and posttest assessments was motivated by a desire to minimize practice effects of the TSST-M, following guidelines in the extant literature (10–12 weeks between pretest and posttest assessment; Petrowski et al., 2012). Of note, protocols and procedures used during posttest assessment were identical to pretest.

Measures

Cortisol and alpha-amylase

Saliva samples were stored in a −80°C freezer until sent to be assayed in duplicate at PSU's Core Biomarker Lab. Cortisol and alpha-amylase means for each sample were used. Intra- and inter-assay coefficients of variation for cortisol were 4.60% and 6.00%, respectively. Alpha-amylase intra- and inter-assay coefficients of variation were 5.47% and 4.70%, respectively.

Emotional and behavior problems

Parents and youth completed the Child Behavior Checklist (CBCL) and Youth Self-report (YSR), respectively (Achenbach & Rescorla, 2001), a 113-item and 112-item scale of youth behavior problems rated on a 3-point Likert scale (0 = "Never true" to 2 = "Very often true"). The YSR's Internalizing Problems ($M = 55.26$, $SD = 11.91$) and Externalizing Problems ($M = 48.16$, $SD = 9.88$) and CBCL Internalizing Problems ($M = 55.63$, $SD = 12.67$) and Externalizing Problems ($M = 55.55$, $SD = 12.38$) subscale scores were used in this study. Cronbach alphas for CBCL and YSR range from .90 (Internalizing Problems) to .94 (Externalizing Problems).

Covariates

Child age (years) and sex (0 = male, 1 = female) were included as primary study covariates in Aim 1 analyses. To consider the potential contribution of variables previously linked to HPA and SAM functioning, an additional secondary set of variables (see

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below) were examined. Parents reported on youth pubertal status using the Pubertal Development Scale (PDS; Petersen et al., 1988). Using a 4-point scale, boys' progression on height, facial hair, body hair, and voice changes (e.g., deepening) were each rated. Girls' development on height, body hair, and breast development were similarly rated, in addition to whether girls had started menstruation (1 = no; 4 = yes). Within-sex pubertal staging scores were calculated by averaging PDS items for boys ($M = 1.71$, $SD = 0.43$) and girls ($M = 2.53$, $SD = 0.63$). Parent-reported medications known to impact cortisol, alpha-amylase, or saliva assessment were coded (Granger et al., 2009; Rohleder & Nater, 2009). Parent-child dyad cohort number was also considered (0 = cohorts 1-5,
Pre Covid; 1 = cohorts 6-8, Post Covid). Saliva sample timing was considered and computed by subtracting youth's wake time from the time of the initial saliva assessment ($M = 9.50$ hr, $SD = 2.00$ hr).

Data preparation and preprocessing

Cortisol and alpha-amylase data

At pretest, 14 cortisol values were above three standard deviations from the grand mean: +0 min ($n = 3$), +15 min ($n = 2$), +25 min ($n = 4$), +35 min ($n = 3$), +45 min ($n = 3$), +55 min ($n = 2$). Seven alpha-amylase values were above three standard deviations from the grand mean: +0 min ($n = 2$), +15 min ($n = 1$), +25 min ($n = 0$), +35 min ($n = 1$), +45 min ($n = 2$), +55 min ($n = 1$). At posttest, 13 cortisol values were above three standard deviations from the grand mean: +0 min ($n = 2$), +15 min ($n = 2$), +25 min ($n = 2$), +35 min ($n = 3$), +45 min ($n = 1$), +55 min ($n = 3$). Five alpha-amylase values were above three standard deviations from the grand mean: +0 min ($n = 1$), +15 min ($n = 0$), +25 min ($n = 0$), +35 min ($n = 2$), +45 min ($n = 1$), +55 min ($n = 1$).

As recommended (Felt et al., 2017; Miller & Plessow, 2013), we applied a fourth root transformation to our pretest and posttest cortisol and alpha-amylase data. This approach also circumvented the need to winsorize outlier values that, in a repeated measures trajectory framework, may reflect yet to be discovered stress response patterns at the tail ends of the cortisol and alpha-amylase distributions (Bendezú & Wadsworth, 2018; Bendezú et al., 2022).

Analysis plan

Aim 1: Characterizing neuroendocrine stress response functioning

Three sets of analyses were used to achieve Aim 1. For our first two sets of analyses, pretest cortisol and alpha amylase Cortisol Area Under the Curve – Ground (AUCg) and Increase (AUCi) scores were computed using standard methods (Pruessner et al., 2003). Our primary (e.g., youth age, sex) and secondary (e.g., cohort, pubertal status, medication use, saliva sample timing) covariates were initially tested for inclusion in all three sets of analyses vis-à-vis links to neuroendocrine function. Primary covariates were retained irrespective of statistical significance.

In our first set of analyses, requisite covariates and pretest cortisol and alpha-amylase AUCg scores were entered in our regression models in a single step, with each of four models predicting one of four outcomes of interest: Internalizing Problems (youth-report, parent-report) Externalizing Problems (youth-report, parent-report). Then, a cortisol and alpha-amylase AUCg interaction term was added to each of the four models in a second step. Cortisol and alpha amylase AUCg scores were grand mean centered prior to computing the interaction term. Steps in our second set of analyses of cortisol and alpha-amylase AUCi scores mirrored our first set.

In our third set of analyses, two Group-Based Trajectory Models (GBTMs) were used to explore potential within-person profiles of HPA axis only and SAM system only stress responsivity. GBTM and Multitrajectory Modeling (MTM) share near identical iterative steps for a) identifying the best fitting model, b) evaluating model adequacy, and c) testing trajectory distinction. As such, this process outlined in Pham et al. (2023) is provided in our supplementary materials. After obtaining the final GBTM solution for HPA axis only and SAM system only models, we conducted two separate MANCOVAs which examined GBTM profile differences in levels of psychopathology while controlling for requisite primary and secondary covariates.

Lastly, we compared the overall pattern of findings obtained from our pretest regression and GBTM analyses with findings from our pretest MTM analyses (see supplementary materials). This comparison facilitated decision-making about the interpretability of each prospective target for evaluating BaSICS effects on neuroendocrine stress response function.

Aim 2: BaSICS effects on posttest HPA–SAM co-activation profile membership

To identify posttest HPA–SAM Co-activation profiles, our Multitrajectory Modeling (MTM) approach reported in Pham et al. (2023) (see supplementary materials) was applied in identical fashion to the corresponding posttest cortisol and alpha-amylase data. After specifying the best fitting model, evaluating model adequacy, and distinguishing profile trajectories, we compared and contrasted our identified posttest HPA–SAM Co-activation profiles against our pretest profiles (see supplementary materials) for points of convergence and divergence.

We then examined the association between experimental condition and posttest HPA–SAM Co-activation profile membership for youth exhibiting asymmetrical (e.g., to test BaSICS efficacy effects) and symmetrical (e.g., to test BaSICS iatrogenic effects) HPA–SAM Co-activation profiles at pretest. To our knowledge, the only TSST study to date that has applied a person-centered approach to identify and longitudinally track neuroendocrine stress response profiles utilized cross-tab analysis for examining longitudinal changes in profile membership over time (Ji et al., 2016). However, our design complicated implementation of such analyses to the *sample as a whole*. Our study involved an experimental manipulation, precluding conclusions about more basic longitudinal change patterns in HPA–SAM Co-activation. To address this issue, but also our secondary aim, we conducted similar cross-tab analysis to examine changes in profile membership, yet as a function of random assignment to BaSICS or control for each pretest *subgroup individually*. For each pretest subgroup, we plotted probabilities of posttest profile membership (e.g., rows) conditional on assignment to BaSICS or control (e.g., columns). We then applied chi-square analyses of these probabilities to determine statistical significance.

Post hoc analyses

To provide a more comprehensive view of our stress responsivity findings, we explored whether differences in behavioral reactivity (e.g., youth-reported negative affectivity responses) could be observed across our pretest and posttest profiles. A question in the literature remains as to whether HPA non-responsivity reflects a lack of experienced distress to the TSST (i.e., the TSST was not

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successful at eliciting stress responses in certain youth). Following Campbell and Ehlert (2012), we created pretest (α = .85) and posttest (α = .98) negative affect scores (i.e., averaged anger, sadness, and nervousness scores obtained via self-report at T1–T4 on a 5-point Likert scale measure) and compared pretest and posttest profiles on baseline levels as well as reactivity indices (i.e., difference scores for T1 and T2 negative affect values).

To better understand whether similar profile–psychopathology linkages could be found in our posttest HPA–SAM Co-activation profiles, we utilized MANCOVA to examine posttest profile membership to posttest psychopathology associations (e.g., youth- and parent-reported Internalizing and Externalizing Problems). Primary (e.g., youth age, sex) and secondary (e.g., cohort, pubertal status, medication use, saliva sample timing) covariates were initially tested for inclusion in our MANCOVA model, with covariates significantly associated with posttest profile membership retained. Primary covariates were retained irrespective of statistical significance.

Results

Table 1 provides descriptive statistics and bivariate correlations for pretest and posttest cortisol and alpha amylase data. At both pretest and posttest, cortisol levels were positively correlated (r = .44–.95) as were alpha-amylase levels (r = .55–.90). At both pretest and posttest, between-person associations for cortisol and alpha-amylase were largely nonsignificant (95.4%). Youth internalizing problems and externalizing problems were not significantly associated at the bivariate level with pretest or posttest cortisol or alpha-amylase levels.

Aim 1: Characterizing neuroendocrine stress response functioning

Area under the curve with respect to ground (AUCg) and increase (AUCi)

Table 2 displays parameter estimates for regression models predicting youth- and parent-reported Internalizing and Externalizing Problems from our neuroendocrine variables of interest. During our initial test of primary (e.g., youth age, sex) and secondary (e.g., cohort, pubertal status, medication use, saliva sample timing) covariate – AUCg main and interactive linkages, no statistically significant effects emerged ($B_{\_covariates}$ = −0.064–0.149, $SE_{\_covariates}$ = 0.001–0.118, $p_{\_covariates}$ = .07–.80). Similarly, no statistically significant effects emerged when examining primary (e.g., youth age, sex) and secondary (e.g., cohort, pubertal status, medication use, saliva sample timing) covariate – AUCi main and interactive linkages ($B_{\_covariates}$ = -0.197–0.032, $SE_{\_covariates}$ = 0.001–0.127, $p_{\_covariates}$ = .07–.98). Youth sex and age were retained in our first (AUCg) and second (AUCi) set of analyses. As shown in Table 2, no significant main or interactive effects for cortisol and alpha-amylase AUCg or AUCi scores predicting youth- and parent-reported internalizing and externalizing problems emerged in either set of analyses.

Group-based trajectory modeling (GBTM)

Table 3 displays parameter estimates, adequacy indices, and trajectory distinction results (i.e., differing subscripts) for our GBTM analysis on pretest cortisol only and alpha-amylase only levels. GBTM specification results supported our predetermined two-profile solution for cortisol and alpha-amylase (Figure 2): cortisol two- to one-profile comparison [$2\log_e(B_{10})$ = 314.08], alpha-amylase two- to one- profile comparison [$2\log_e(B_{10})$ = 118.84]. As per Nagin (2005), a systematic examination of model adequacy indices suggested that the two-profile cortisol only and alpha-amylase only solutions fit the data well. The Low HPA profile (n = 93) displayed a cortisol trajectory characterized by significantly lower baseline levels and significantly less pronounced quadratic reactivity relative to the cortisol trajectory identified in the High HPA profile (n = 19). The Low SAM profile (n = 61) displayed an alpha-amylase trajectory characterized by significantly lower baseline levels and non-significantly different quartic reactivity relative to the alpha-amylase trajectory identified in the High SAM profile (n = 51).

During our initial test of primary (e.g., youth age, sex) and secondary (e.g., cohort, pubertal status, medication use, saliva sample timing) covariate – cortisol GBTM linkages, there were largely no significant differences among the two HPA profiles with respect to our primary and secondary covariates: youth age ($F(1,101) = 1.43$, $p = .24$), sex ($\chi^2(1) = 0.15$, $p > .25$), cohort ($\chi^2(1) = 3.14$, $p = .08$), pubertal status ($F(1,91) = 1.925$, $p = .17$), medication use ($\chi^2(1) = 0.17$, $p > .25$) and saliva sample timing ($F(1,99) = 1.021$, $p > .25$). Youth age and sex were controlled for in our subsequent MANCOVAs analyses which examined cortisol only GBTM profile differences in levels youth- and parent-reported internalizing and externalizing problems. Covariance matrices between profiles were assumed equal for the purposes of MANCOVA (*Box's M* = 4.79, $p > .25$).

The association between HPA profile membership and youth- and parent-reported internalizing and externalizing problems was nonsignificant; Wilk's Lambda = 0.97, $F(4,69) = 0.51$, $p > .25$. A series of Levene's F tests suggested that the homogeneity of variance assumption was satisfied: youth-reported internalizing problems ($F(1,75) = 0.27$, $p > .25$), youth-reported externalizing problems ($F(1,75) = 2.13$, $p = .15$), parent-reported internalizing problems ($F(1,75) = 1.31$, $p > .25$), parent-reported externalizing problems ($F(1,75) = 1.06$, $p > .25$). Follow-up ANCOVAs revealed nonsignificant associations between HPA profile membership and each of our four psychopathology indices (Figure 3): youth-reported internalizing problems ($F(1,72) = 1.26$, $p > .25$) and externalizing problems ($F(1,72) = 1.35$, $p = .25$), parent-reported internalizing problems ($F(1,72) = 0.01$, $p > .25$) and externalizing problems ($F(1,72) = 0.21$, $p > .25$).

No statistically significant covariate – alpha-amylase GBTM linkages emerged: youth age ($F(1,101) = 1.03$, $p > .25$), sex ($\chi^2(1) = 1.43$, $p > .25$), cohort ($\chi^2(1) = 1.00$, $p > .25$), pubertal status ($F(1,91) = 0.74$, $p > .25$), medication use ($\chi^2(1) = 1.19$, $p > .25$), and saliva sample timing ($F(1,99) = 3.38$, $p > .25$). Youth age and sex were controlled for in our subsequent MANCOVAs analyses which examined alpha-amylase only GBTM profile differences in levels youth- and parent-reported internalizing and externalizing problems. Covariance matrices between profiles were assumed equal for the purposes of MANCOVA (*Box's M* = 17.82, $p = .08$).

The association between SAM profile membership and youth- and parent-reported internalizing and externalizing problems was nonsignificant; Wilk's Lambda = 1.00, $F(4,79) = 0.11$, $p > .25$. The overall pattern of results obtained from a series of Levene's F tests suggested that the homogeneity of variance assumption was satisfied: youth-reported internalizing problems ($F(1,84) = 0.17$, $p > .25$), youth-reported externalizing problems ($F(1,84) = 220.61$, $p = .001$),[3] parent-reported internalizing problems

[3]As per Howell (2009), no standard deviation value was four times larger than the smallest standard deviation value, suggesting that follow-up ANCOVAs conducted were robust to potential violations of the homogeneity of variance assumption indicated by Levene's F test.

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Table 1. Descriptives and bivariate correlations for key study variables

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	*M*	*SD*	*Min*	*Max*
1. sC + 0 min TSST start	—	.73*	.45*	.57*	.73*	.71*	.37*	.20	.13	.26*	.16	.14	.08	.09	.01	.54
2. sC + 15 min TSST start	.92*	—	.70*	.64*	.60*	.74*	.20	.12	.11	.20	.11	.08	.07	.05	.02	.27
3. sC + 25 min TSST start	.72*	.82*	—	.88*	.46*	.72*	.05	−.01	.01	.08	−.03	−.09	.07	.06	.02	.32
4. sC + 35 min TSST start	.51*	.66*	.85*	—	.44*	.84*	.01	.01	−.03	.06	−.05	−.07	.07	.07	.01	.34
5. sC + 45 min TSST start	.51*	.65*	.81*	.95*	—	.50*	.40*	.15	.12	.19	.12	.08	.07	.10	.01	.83
6. sC + 55 min TSST start	.61*	.76*	.92*	.85*	.84*	—	.06	.03	.01	.11	.01	−.03	.06	.05	.01	.22
7. sAA + 0 min TSST start	−.01	−.01	−.09	−.03	−.04	−.09	—	.82*	.74*	.72*	.60*	.57*	101.1	77.11	11.40	405.6
8. sAA + 15 min TSST start	−.01	.03	−.03	−.03	−.02	−.02	.63*	—	.81*	.67*	.51*	.55*	137.9	96.12	12.50	396.8
9. sAA + 25 min TSST start	−.01	−.02	−.07	−.11	−.11	−.06	.66*	.83*	—	.86*	.57*	.59*	113.7	76.94	11.91	346.7
10. sAA + 35 min TSST start	−.02	−.03	−.10	−.11	−.07	−.09	.72*	.75*	.80*	—	.72*	.74*	96.00	67.47	11.32	294.2
11. sAA + 45 min TSST start	−.04	−.03	−.10	−.02	−.02	−.08	.74*	.66*	.74*	.84*	—	.90*	98.87	82.30	11.50	399.4
12. sAA + 55 min TSST start	.01	.02	−.04	−.01	.01	−.03	.77*	.69*	.77*	.84*	.83*	—	99.34	81.60	9.50	388.1
M	0.08	0.08	0.08	0.09	0.07	0.06	107.0	178.6	118.7	119.1	106.3	107.7				
SD	0.08	0.07	0.08	0.11	0.08	0.06	83.57	121.1	79.72	87.60	87.00	74.23				
Min	0.02	0.02	0.01	0.02	0.01	0.01	2.92	23.60	12.76	5.64	10.43	5.48				
Max	0.59	0.52	0.57	0.82	0.65	0.48	498.0	640.5	358.6	547.8	565.3	465.6				

Note. sC = salivary cortisol. sAA = salivary alpha-amylase. TSST = Trier Social Stress Test. Coefficients below the diagonal reflect correlations between pretest cortisol and alpha-amylase values. Coefficients above the diagonal reflect correlations between posttest cortisol and alpha-amylase values. Descriptives underneath the correlation matrix correspond to pretest cortisol and alpha-amylase values. Descriptives to the right of the correlation matrix correspond to posttest cortisol and alpha-amylase values.
*$p < .05$.

Table 2. Parameter estimates (standard errors) for multiple linear regressions predicting Time 1 parent and youth reported internalizing and externalizing problems from Time 1 youth cortisol and alpha-amylase A) Area Under the Curve – Ground (AUCg) and B) Area Under the Curve – Increase (AUCi) scores

		Internalizing Problems (Parent Report)		Externalizing Problems (Parent Report)		Internalizing Problems (Youth Report)		Externalizing Problems (Youth Report)	
		Main effects	Interactive effects	Main effects	Interactive effects	Main effects	Interactive effects	Main effects	Interactive effects
A)	Youth sex	−0.117 (2.697)	−0.117 (2.713)	−4.195 (2.579)	−4.195 (2.594)	−1.110 (2.541)	−1.156 (2.547)	−2.416 (2.146)	−2.429 (2.159)
	Youth age	−1.084 (2.314)	−1.802 (2.342)	−4.201 (2.213)	−1.544 (2.239)	−3.974 (2.130)	−4.054 (2.136)	−2.722 (1.799)	−2.743 (1.811)
	sC AUCg	0.337 (0.282)	0.336 (0.286)	0.144 (0.270)	0.137 (0.274)	−0.307 (0.260)	−0.273 (0.264)	−0.239 (0.220)	−0.229 (0.224)
	sAA AUCg	−0.021 (0.046)	−0.021 (0.046)	−0.015 (0.044)	−0.016 (0.044)	0.001 (0.043)	0.004 (0.044)	0.009 (0.037)	−0.010 (0.037)
	sC AUCg × sAA AUCg		−0.001 (0.011)		−0.002 (0.011)		0.009 (0.011)		0.003 (0.009)
B)	Youth sex	0.301 (2.732)	0.235 (2.792)	−3.629 (2.570)	−4.014 (2.615)	−1.339 (2.546)	−0.881 (2.592)	−2.425 (2.147)	−2.054 (2.186)
	Youth age	−2.345 (2.308)	−2.381 (2.336)	−4.470 (2.270)	−4.677 (2.389)	−3.549 (2.125)	−3.376 (2.133)	−2.305 (1.792)	−2.165 (1.799)
	sC AUCi	−0.113 (0.466)	−0.122 (0.473)	−0.454 (0.438)	−0.502 (0.443)	0.324 (0.424)	0.365 (0.426)	0.152 (0.357)	0.185 (0.359)
	sAA AUCi	−0.005 (0.077)	−0.051 (0.077)	−0.049 (0.072)	−0.051 (0.072)	−0.017 (0.070)	−0.015 (0.070)	−0.047 (0.059)	−0.045 (0.059)
	sC AUCi × sAA AUCi		0.004 (0.033)		0.026 (0.031)		−0.028 (0.029)		−0.022 (0.024)

Note. sC = salivary cortisol; sAA = salivary alpha-amylase. Youth sex coded 0 for boys and 1 for girls. *$p < .05$.

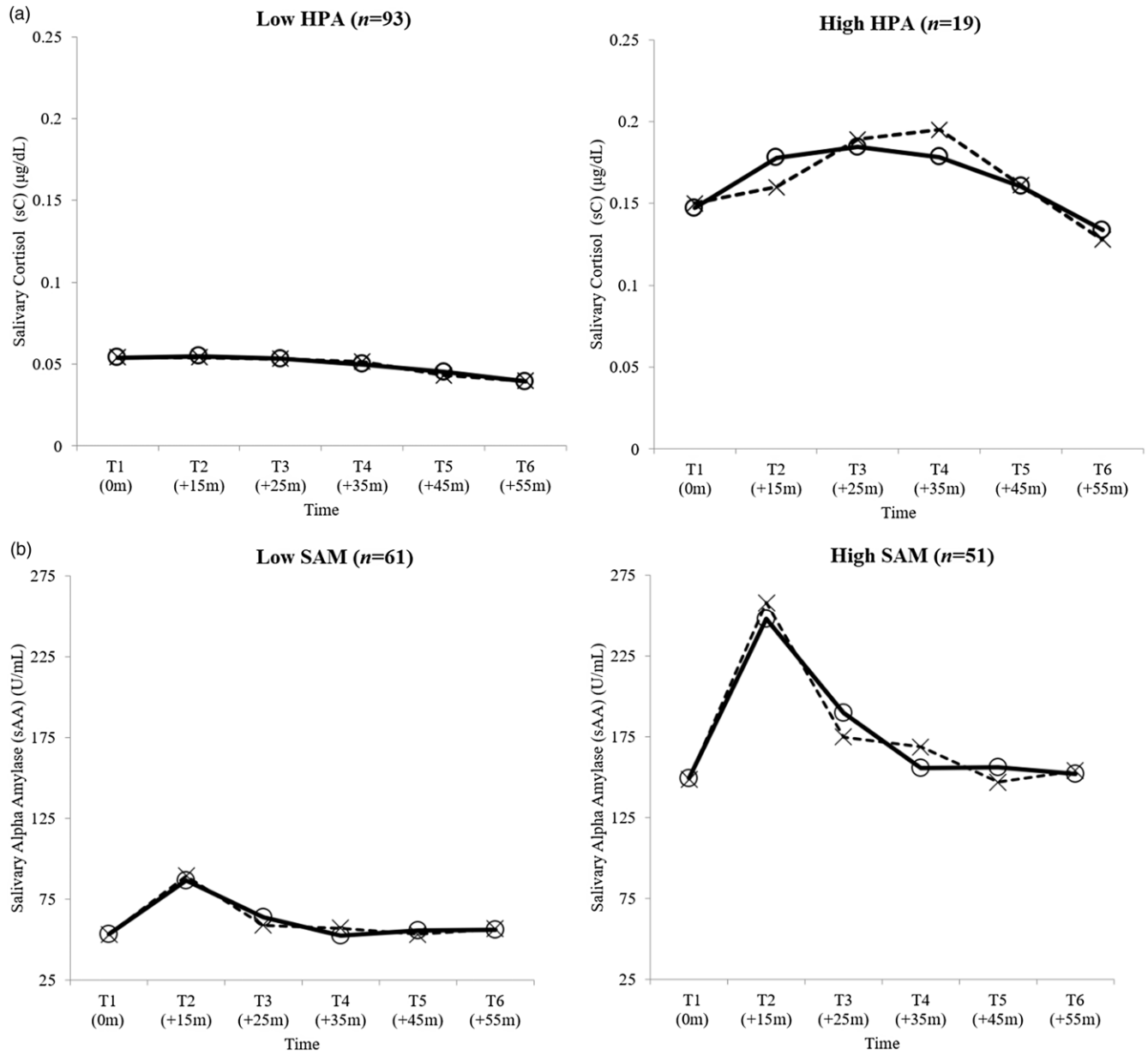

Figure 2. Actual versus predicted salivary cortisol and alpha-amylase trajectories for the final a) hpa only and b) sam only pretest two-group solutions. *Note*. Actual trajectories denoted with dotted lines. Predicted trajectories denoted by solid lines. Reverse transformed values presented for ease of interpretation and cross-study communication. Values in parentheses reflect the number of children assigned to each group.

($F(1,84) = 0.414$, $p > .25$), parent-reported externalizing problems ($F(1,84) = 0.006$, $p > .25$). Follow-up ANCOVAs revealed nonsignificant associations between SAM profile membership and each of our four psychopathology indices (Figure 3): youth-reported internalizing problems ($F(1,72) = 1.26$, $p > .25$) and externalizing problems ($F(1,72) = 21.35$, $p = .25$), parent-reported internalizing problems ($F(1,72) = 0.01$, $p > .25$) and externalizing problems ($F(1,72) = 0.21$, $p > .25$).

Aim 2: BaSICS effects on posttest HPA–SAM co-activation profile membership

Profiles of posttest HPA–SAM co-activation

Based on the results of our Aim 1 analyses, our Aim 2 analyses proceeded under the assumption that our MTM identified HPA–SAM Co-activation profiles reflected interpretable targets of intervention. Thus, we explored the existence of HPA–SAM Co-activation profiles at posttest, anticipating that these posttest profiles would be similar to those identified at pretest.

Table 4 displays parameter estimates, adequacy indices, and trajectory distinction analysis results (i.e., differing subscripts) for our MTM analysis of posttest cortisol and alpha-amylase levels. Results obtained from MTM specification supported a four-profile solution (Figure 4): two- to one-profile comparison [$2\log_e(B_{10}) = 230.03$], three- to two-profile comparison [$2\log_e(B_{10}) = 148.76$], four- to three-profile comparison [$2\log_e(B_{10}) = 75.8$]. As per Nagin (2005), our model adequacy indices suggested that the final four-profile solution fit the data well.

The identified posttest profiles were similar to those identified at pretest: Symmetrical HPA–SAM Co-activation

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Table 3. Parameter estimates (standard errors) and model adequacy indices for final A) HPA only and B) SAM only prestest two-group solutions

			$AvePP_j$	OCC_j	$Prob_j$	$Prop_j$	*Ratio*
A)	Low HPA ($n = 93$)		.989	92.214	.828	.830	0.998
	Intercept	0.482* (0.007)^{A}					
	Linear	0.001 (0.001)					
	Quadratic	−0.001* (0.001)^{a}					
	High HPA ($n = 19$)		.960	23.902	.171	.169	1.012
	Intercept	0.619* (0.008)^{B}					
	Linear	0.003* (0.001)					
	Quadratic	−0.001* (0.001)^{b}					
B)	Low SAM ($n = 61$)		.973	39.505	.553	.544	1.017
	Intercept	2.706* (0.055)^{A}					
	Linear	0.091* (0.021)					
	Quadratic	−0.007* (0.002)					
	Cubic	0.001* (0.001)					
	Quartic	−0.001* (0.001)^{a}					
	High SAM ($n = 51$)		.949	18.524	.447	.455	0.982
	Intercept	3.497* (0.066)^{B}					
	Linear	0.111* (0.023)					
	Quadratic	−0.007* (0.002)					
	Cubic	0.001* (0.001)					
	Quartic	−0.001* (0.001)^{a}					

Note. $AvePP_j$ = Average posterior probability; OCC_j = Odds of correct classification; $Prob_j$ = Probability of group assignment; $Prop_j$ = Proportion of children assigned to each group; *Ratio* = Ratio of $Prob_j$ to $Prop_j$. Upper-case superscripts denote significant differences in intercept estimates. Lower-case superscripts denote significant differences in polynomial estimates. *$p < .05$.

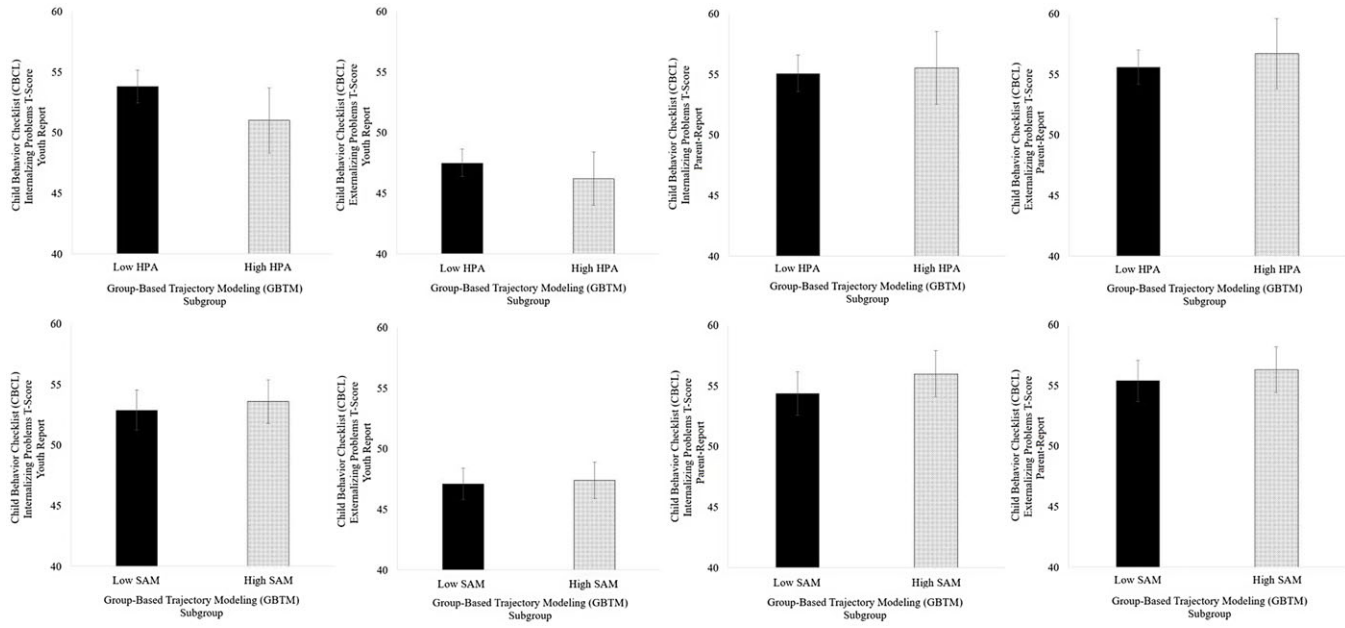

Figure 3. Plotted means and standard error bars for risk and mental health indices for final A) HPA only and B) SAM only pretest two-group solution. *Note*. No significant differences emerged across subgroups.

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Table 4. Parameter estimates (standard errors) and model adequacy indices for final HPA–SAM multitrajectory modeling posttest four-group solution

	Salivary Cortisol	Salivary Alpha-Amylase	$AvePP_j$	OCC_j	$Prob_j$	$Prop_j$	*Ratio*
Symmetrical No.1 ($n = 37$)			.914	31.906	.328	.330	0.994
Intercept	0.459* (0.009)^{A}	2.807* (0.098)^{A}					
Linear	−0.001* (0.001)^{a}	0.029* (0.014)					
Quadratic		−0.001* (0.001)					
Cubic		0.001* (0.001)^{a}					
Symmetrical No.2 ($n = 12$)			.998	1349.36	.109	.107	1.019
Intercept	0.700* (0.016)^{D}	3.456* (0.127)^{B}					
Linear	−0.002* (0.001)^{b}	0.011 (0.010)					
Quadratic		−0.001† (0.001)$^{-}$					
Asymmetrical No.1 ($n = 36$)			.922	35.672	.324	.321	1.009
Intercept	0.559* (0.011)^{C}	2.911* (0.067)^{A}					
Linear	−0.002* (0.001)^{a}	−0.004* (0.002)$^{-}$					
Asymmetrical No.2 ($n = 27$)			.926	34.747	.239	.241	0.992
Intercept	0.502* (0.014)^{B}	3.585* (0.100)^{B}					
Linear	−0.001* (0.001)^{a}	0.037* (0.016)					
Quadratic		−0.002* (0.001)					
Cubic		0.001* (0.001)^{b}					

Note. $AvePP_j$ = Average posterior probability; OCC_j = Odds of correct classification; $Prob_j$ = Probability of group assignment; $Prop_j$ = Proportion of children assigned to each group; *Ratio* = Ratio of $Prob_j$ to $Prop_j$. Upper-case superscripts denote significant differences in intercept estimates within the biological index. Lower-case superscripts denote significant differences in polynomial estimates within the same biological index. $^{\dagger}p = .12$. $^{*}p < .05$.

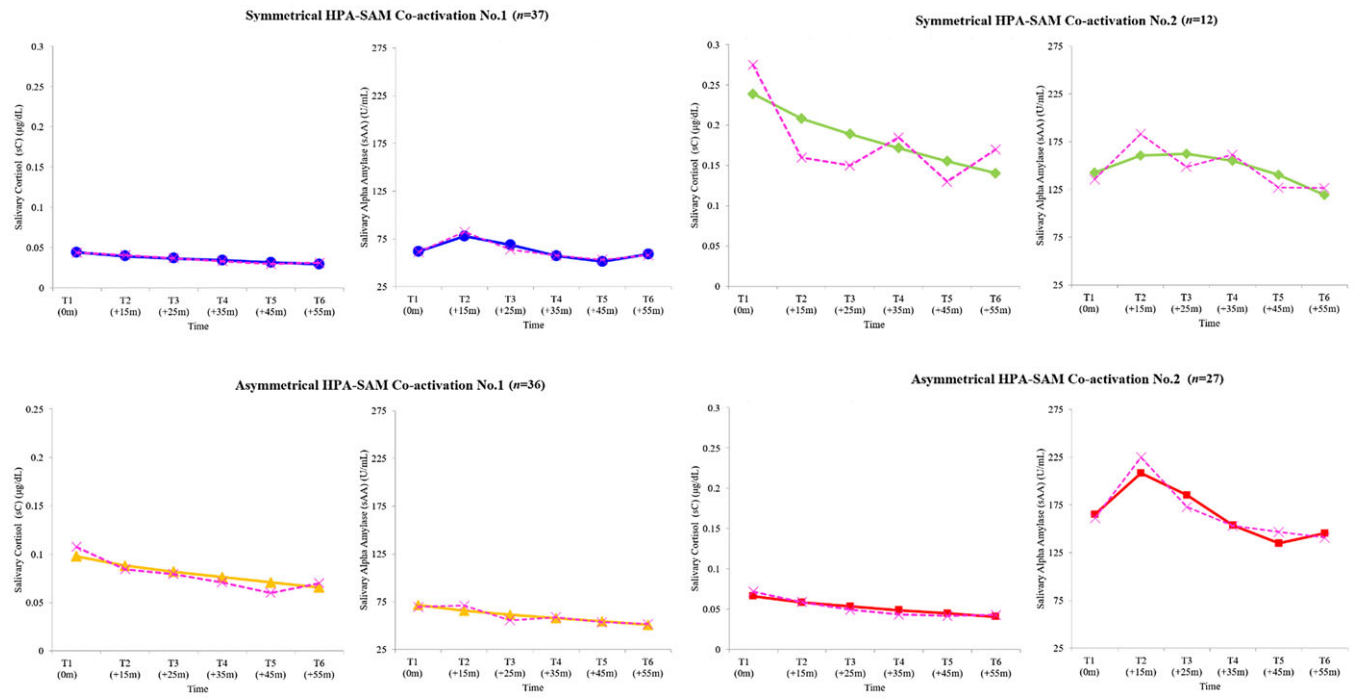

Figure 4. Actual versus predicted cortisol and alpha-amylase trajectories for the final posttest HPA–SAM four-group solution. *Note*. Actual trajectories denoted with dotted lines. Predicted trajectories denoted by solid lines. Reverse transformed values presented for ease of interpretation and cross-study communication. Values in parentheses reflect the number of children assigned to each group.

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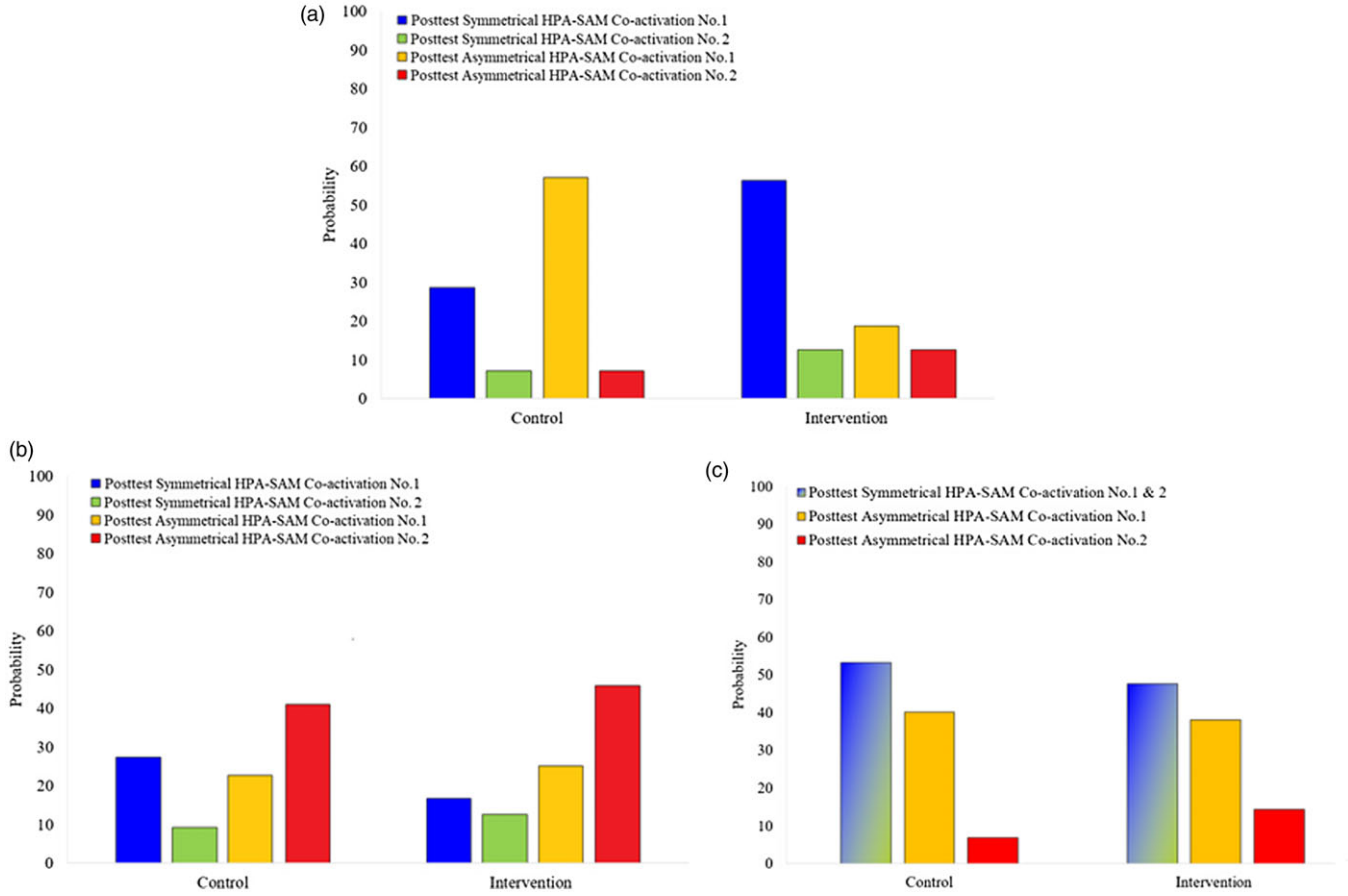

Figure 5. Plotted probabilities of posttest HPA–SAM co-activation profile membership for pretest A) Asymmetrical HPA-SAM co-activation No. 1, B) Asymmetrical HPA-SAM co-activation No. 2, and C) Symmetrical HPA-SAM co-activation Nos. 1 & 2 Youth assigned to BaSICS and control.

No. 1 ($n = 37$), Symmetrical HPA–SAM Co-activation No. 2 ($n = 12$), Asymmetrical HPA–SAM Co-activation No. 1 ($n = 36$), Asymmetrical HPA–SAM Co-activation No. 2 ($n = 27$). There were, however, two notable pretest-posttest differences observed. First, both cortisol and alpha-amylase baseline values observed in our posttest Symmetrical HPA–SAM Co-activation No. 2 (*cortisol_t*(22) = 8.573, $p < .001$; *alpha amylase_t*(22) = 9.100, $p < .001$) and Asymmetrical HPA–SAM Co-activation No. 1 profiles (*cortisol_t*(64) = 16.916, $p < .001$; *alpha amylase_t*(64) = 12.079, $p = .01$) were more elevated than that observed at pretest. Second, cortisol and alpha-amylase reactivity parameter estimates for these two profiles at posttest reflected more non-reactivity relative to that observed at pretest: Symmetrical HPA–SAM Co-activation No. 2 (pretest cortisol = negative quadratic, posttest cortisol = negative linear; pretest alpha-amylase = negative quartic, posttest alpha-amylase = negative quadratic); Asymmetrical HPA–SAM Co-activation No. 1 (pretest cortisol = negative quadratic, posttest cortisol = negative linear; pretest alpha-amylase = positive cubic; posttest alpha-amylase = negative linear).

BaSICS assignment and posttest HPA–SAM co-activation profile membership

Pretest asymmetrical HPA–SAM co-activation No. 1. Probabilities of membership in each individual posttest profile by intervention status are plotted in Figure 5A. A follow up chi-square test was significant ($\chi^2(1) = 4.20$, $p = .04$). As expected, pretest Asymmetrical HPA–SAM Co-activation No.1 youth assigned to BaSICS were approximately two times more likely to become members of posttest Symmetrical HPA–SAM Co-activation No. 1 ($n = 9$) relative to their counterparts in control ($n = 4$). Still further, pretest Asymmetrical HPA–SAM Co-activation No. 1 youth assigned to control were approximately three times more likely to remain members of Asymmetrical HPA–SAM Co-activation No. 1 at posttest ($n = 8$) relative to their BaSICS counterparts ($n = 3$).

Pretest asymmetrical HPA–SAM co-activation No. 2. Probabilities of membership in each individual posttest HPA–SAM Co-activation profile by intervention status are plotted in Figure 5B. A follow-up chi-square test was nonsignificant ($\chi^2(1) = 0.24$, $p > .25$).

Pretest symmetrical HPA–SAM co-activation Nos. 1 & 2.[4] Probabilities of membership in individual posttest HPA–SAM Co-activation profile by intervention status are plotted in Figure 5C. A follow-up chi-square test was nonsignificant ($\chi^2(1) = 0.59$, $p > .25$).

[4]Iatrogenic effects for the Symmetrical HPA–SAM Co-activation No. 2 profile could not be evaluated given the small subgroup sample size, with expected counts falling below five in all cells. A composite pretest Symmetrical HPA–SAM Co-activation profile and composite posttest Symmetrical HPA–SAM Co-activation profile and were created by combining Symmetrical HPA–SAM Co-activation Nos. 1 & 2 profiles at each time point.

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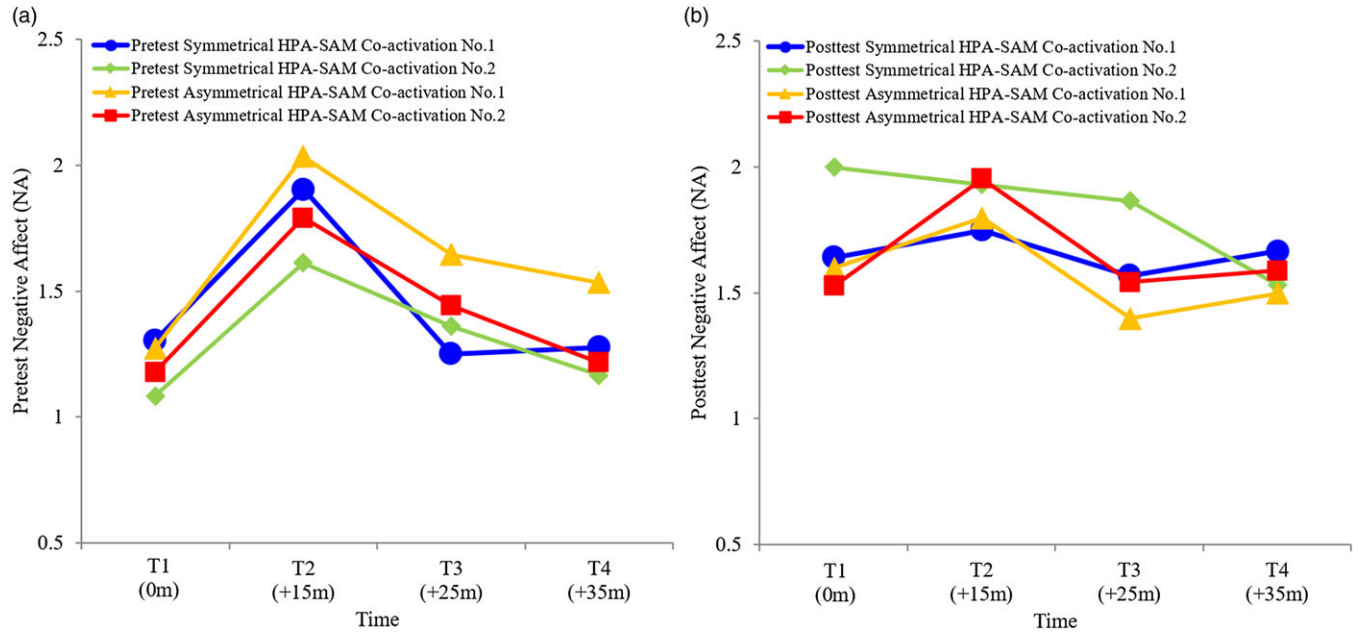

Figure 6. Average youth-reported negative affect scores for each a) pretest and b) posttest HPA–SAM co-activation profile.

Post hoc analyses

Pretest and posttest negative affect responsivity

Figure 6 depicts pretest and posttest youth-reported negative affect scores obtained over the course of the TSST (T1–T4) for each pretest and posttest HPA–SAM Co-activation profile. With respect to pretest negative affect responsivity, percent increase from baseline to peak negative affect scores for each profile are as follows: Symmetrical HPA–SAM Co-activation No. 1 (45.7%), Symmetrical HPA–SAM Co-activation No. 2 (48.3%), Asymmetrical HPA–SAM Co-activation No. 1 (59.7%), Asymmetrical HPA–SAM Co-activation No. 2 (51.9%). With respect to posttest negative affect responsivity, percent increase from baseline to peak negative affect scores for each profile are as follows: Symmetrical HPA–SAM Co-activation No. 1 (6.64%), Symmetrical HPA–SAM Co-activation No. 2 (-3.35%), Asymmetrical HPA–SAM Co-activation No. 1 (17.7%), Asymmetrical HPA–SAM Co-activation No. 2 (27.8%).

At pretest, no significant differences in negative affect baseline levels (all $p > .17$) or reactivity scores (difference between T2 and T1 negative affect values) (all $p > .25$) emerged among the profiles. At posttest, with the exception of negative affect reactivity scores for Symmetrical HPA–SAM Co-activation No. 2 and Asymmetrical HPA–SAM Co-activation No. 2 (*reactivity score_t*$(25) = -2.560$, $p = .02$), no significant differences in negative affect baseline levels (all $p > .21$) or reactivity scores (all $p > .16$) emerged among the profiles.

A unique pattern of significant differences comparing pretest and posttest baseline levels and reactivity scores emerged. Consistent with our comparison of cortisol and alpha-amylase baseline and reactivity estimates, Symmetrical HPA–SAM Co-activation No. 2 (*baseline_t* $(22) = 3.150$, $p = .01$; *difference score_t*$(22) = 2.330$, $p = .03$) and Asymmetrical HPA–SAM Co-activation No. 1 profiles (*baseline_t*$(64) = 2.053$, $p = .04$; *difference score_t*$(64) = 2.935$, $p = .01$) negative affect baseline levels and reactivity (difference between T2 and T1 negative affect scores) were more elevated and less pronounced, respectively, than that observed at pretest.

Posttest HPA–SAM profile linkages to youth- and parent-reported psychopathology

There were no significant differences among the four posttest HPA–SAM Co-activation profiles with respect to our primary (youth age, sex) and secondary variables (cohort, pubertal status[5]) variables: child age ($F(3,99) = 0.16$, $p > .25$), sex ($\chi^2(3) = 3.225$, $p > .25$), cohort ($\chi^2(3) = 2.813$, $p > .25$), pubertal status ($F(3,57) = 0.06$, $p > .25$). Child age and sex were retained and controlled for in all MANCOVA analyses. Covariance matrices between profiles were assumed equal for the purposes of MANCOVA (*Box's M* $= 19.06$, $p > .25$).

The association between posttest HPA–SAM Co-activation profile membership and posttest youth-reported and parent-reported internalizing and externalizing problems was not significant; Wilk's Lambda $= 0.80$, $F(12,161) = 1.061$, $p > .25$). A series of Levene's F tests suggested that the homogeneity of variance assumption was satisfied: youth-reported Internalizing Problems ($F(3,60) = 0.51$, $p > .25$), youth-reported Externalizing Problems ($F(3,60) = 1.88$, $p = .14$), parent-reported Internalizing Problems ($F(3,60) = 0.99$, $p > .25$), parent-reported Externalizing Problems ($F(3,60) = 1.33$, $p > .25$). Omnibus tests obtained from our follow-up ANCOVAs revealed no significant associations between posttest HPA–SAM Co-activation profile membership and posttest psychopathology indices: youth-reported Internalizing Problems ($F(3,58) = 1.10$, $p > .25$), youth-reported Externalizing Problems ($F(3,58) = 0.29$, $p > .25$), parent-reported Internalizing Problems ($F(3,58) = 0.57$, $p > .25$), parent-reported Externalizing Problems ($F(3,58) = 1.45$, $p > .25$). Estimated marginal means, standard errors bars, and the results of Fisher's LSD tests comparing profile mean estimates are depicted in Figure 7. No significant differences in psychopathology emerged across posttest HPA–SAM Co-activation profiles.

[5]Medication use and saliva sample timing (e.g., wake time) were not collected at posttest.

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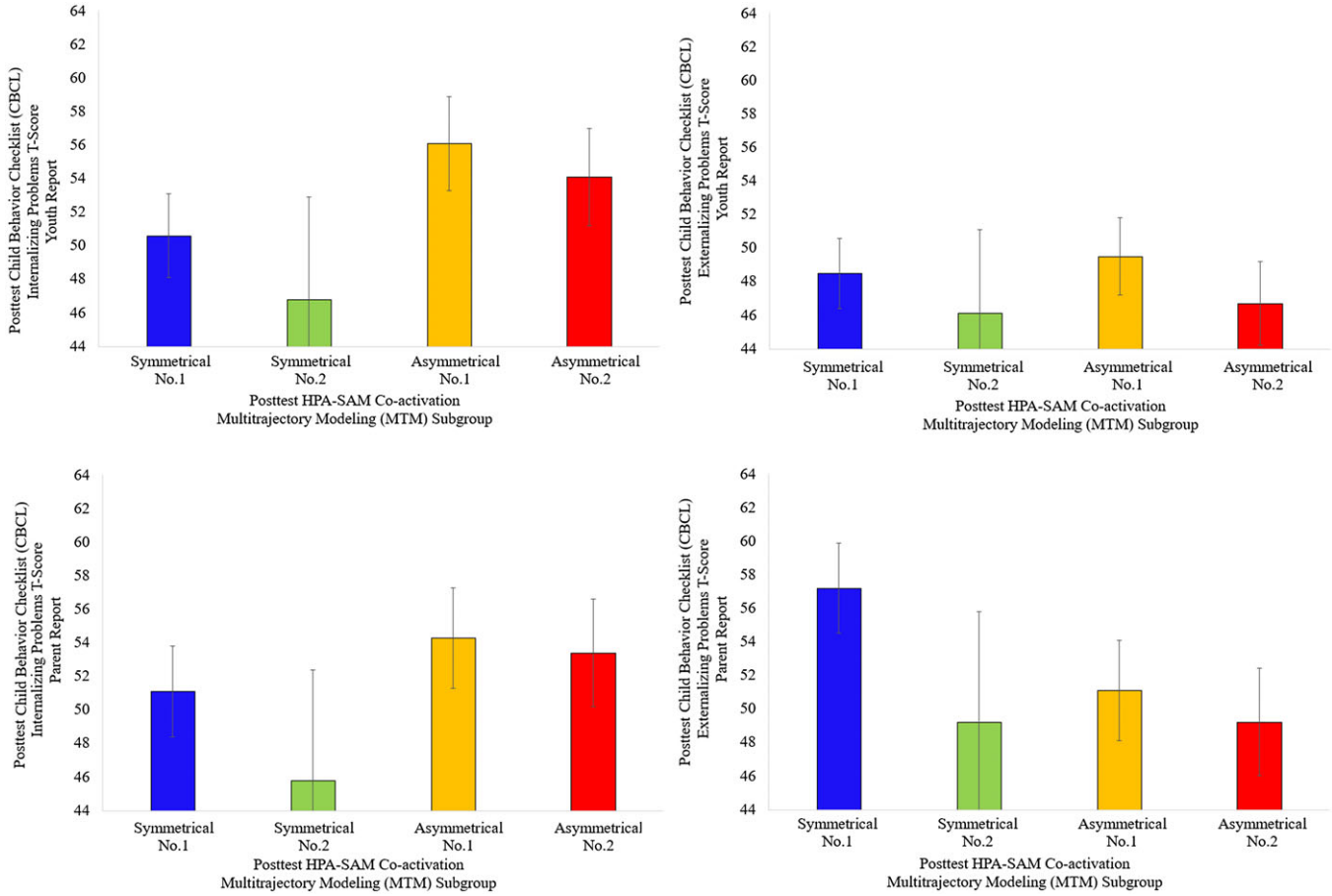

Figure 7. Plotted means and standard error bars for internalizing and externalizing problems for final HPA–SAM posttest four-group solution. *Note*. No significant differences emerged across subgroups.

Discussion

This investigation highlighted the strengths and limitations of classic and contemporary approaches to characterizing neuroendocrine stress response function and evaluating preventive interventions designed to move such neuroendocrine function when studying preadolescents living in poverty. Our previous multisystem, person-centered analysis of youth cortisol and alpha-amylase data helped characterize typical and atypical neuroendocrine stress response function in our sample prior to BaSICS program delivery (Pham et al., 2023), whereas our more traditional analytic approaches in the current study could not. Certain pretest HPA–SAM co-activation profiles identified in Pham et al., appeared to be amenable to BaSICS-related change in ways that helped clarify earlier single-system findings from our initial efficacy evaluation (Wadsworth et al., 2020). Youth exhibiting the atypical, Asymmetric HPA–SAM Co-activation No. 1 profile at pretest assigned to BaSICS were twice as likely to exhibit Symmetric HPA–SAM Co-activation No. 1 at posttest relative to control. Notably, youth exhibiting the atypical, Asymmetrical HPA–SAM Co-activation No. 1 profile at pretest assigned to control were three times as likely to exhibit Asymmetrical HPA–SAM Co-activation No. 1 at posttest relative to BaSICS. It is, however, important to note that not all high-risk youth assigned to BaSICS made the shift towards symmetric HPA–SAM co-activation (i.e., Asymmetrical HPA–SAM Co-activation No. 2). Our findings highlight the potential benefits of adopting multisystem, person-centered approaches when studying preadolescent youth living in poverty, both with respect to characterizing typical and atypical neuroendocrine rhythms as well as identifying suitable (i.e., interpretable) neuroendocrine stress response targets of preventive intervention.

Characterizing neuroendocrine stress responsivity in preadolescents living in poverty

Our efforts to link neuroendocrine stress response function to either youth- or parent-reported indices of maladjustment with our more traditional analytic approaches were largely unsuccessful. This could, at least in part, be attributed to the existence of both typical and atypical cortisol responses at both lower and higher ends of the cortisol response distribution within our sample. Indeed, our pretest multisystem, within-person profiles identified in Pham et al. (2023) and links to maladjustment suggest as much; e.g., low-risk Low HPA–Low SAM youth and high-risk Low HPA–High SAM youth demonstrated cortisol trajectories that were indistinguishable with respect to low baseline levels and less pronounced response patterning. Statistical approaches that can parse between quantitative similar typical and atypical cortisol responses may be necessary when studying a poverty-exposed preadolescents, where the presence of typical cortisol non-responsivity is just as much to be expected as "blunted" cortisol responsivity. This distinction is also of great importance to the evaluation of preventive interventions designed to restore typical

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neuroendocrine function, as movement towards lower cortisol responsivity can signal either therapeutic or iatrogenic effects. With respect to the latter, our small sample size in Symmetrical HPA–SAM Co-activation No. 2 precluded examination of such iatrogenic effects. Thus, our study requires replication with larger sample sizes.

Notably, efforts to link stress response function to maladjustment using traditional analyses were unsuccessful when alpha-amylase was examined in isolation. Relative to cortisol, less is known about SAM responsivity and its role in youth risk for psychopathology (Jones et al., 2020), with studies reporting non-significant (Allwood et al., 2011; El-Sheikh et al., 2008; Gordis et al., 2006), weak positive (Koss et al., 2014), and weak negative (Susman et al., 2010) alpha-amylase–maladjustment associations. One consideration worthy of additional inquiry is whether both typical and atypical SAM response patterns exist at both tail ends of the alpha-amylase distribution. Insight into this prospect can be gleaned from our prior work (Pham et al., 2023), where low-risk Low HPA–Low SAM and high-risk High HPA–Low SAM youth showed indistinguishably low baseline alpha-amylase levels and only subtle differences in responsivity. Additional empirical support for this argument would suggest that both HPA axis and SAM system function are equally important and indispensable factors in characterizing neuroendocrine stress responsivity in poverty-exposed preadolescents, with further clarity gleaned about each's role in risk for psychopathology from analytic approaches that model these systems in tandem.

BaSICS-related restoration of typical HPA–SAM co-activation patterns

By identifying HPA–SAM co-activation as a suitable (i.e., interpretable) biological target of our current evaluation, our multisystem, person-centered analyses helped strengthen inference regarding BaSICS capacity to restore typical neuroendocrine stress response function, most notably by parsing apart those specific youth in our sample for whom this therapeutic effect emerged. Specifically, youth exhibiting the atypical Asymmetrical No. 1 profile prior to BaSICS program delivery were more likely to exhibit the Symmetrical No. 1 profile at posttest relative to their counterparts assigned to control, who were more likely to exhibit the Asymmetrical No. 1 profile at posttest relative to their counterparts assigned to BaSICS. This effect, however, is preliminary and should be interpreted with caution, particularly given the small number of youth exhibiting the Asymmetrical No. 1 profile at pretest which, thus, warrants replication with larger sample sizes. Nevertheless, to our knowledge, the current study is the first to a) evaluate a psychosocial intervention by examining pre- and posttreatment related changes in multisystem stress responsivity and b) demonstrate a significant intervention effect. Furthermore, that a coping skill and empowerment-based intervention (i.e., BaSICS) supported what appears to be a restoration of stress-sensitive biological system functioning for early adolescents living in extreme poverty is of additional critical importance. Reversing stress-response system adaptations to poverty-related stress during the neuroplastic pubertal period could have profound implications for impoverished youth whose life trajectories might otherwise be rather grim.

Once again, not all youth assigned to BaSICS made the shift from asymmetric to symmetric HPA–SAM co-activation, however. For youth exhibiting the Asymmetrical HPA–SAM Co-activation No. 2 profile at pretest, there was no indication that their membership in any of the symmetrical or asymmetrical profiles at posttest varied as a function of being assigned to either BaSICS or control. This may be due to the fact that youth exhibiting the Asymmetrical HPA–SAM Co-activation No. 2 profile at pretest presented with the greatest levels of PRS-exposure in the sample (Pham et al., 2023). It is, thus, possible that the Asymmetric HPA–SAM Co-activation No. 2 profile reflects a more pathological, and perhaps treatment resistant, form of PRS-adapted HPA–SAM co-activation (e.g., cortisol blunting, HPA hypo-activation). If so, one consideration worthy of additional empirical attention whether restoration of typical HPA–SAM co-activation patterns proceeds more slowly for these youth relative to their less PRS-exposed peers with Asymmetrical No. 1 profiles, with therapeutic effects perhaps emerging at later time points. This contention is supported by our proposed model of HPA–SAM co-activation for youth living in poverty and warrants longitudinal investigation with additional timepoints.

Our findings have implications for future evaluation of preventive interventions designed to move biological rhythms for stress-affected youth. Given the substantial heterogeneity that characterizes neuroendocrine function in poverty-exposed youth, multisystem analysis may reflect a more thorough and, thus, judicious approach for testing biological re-programing intervention effects. Without consideration of peripheral biomarker (e.g., alpha-amylase) and system (e.g., SAM) activation, it might have been difficult to interpret whether BaSICS-related decreases in cortisol reflected movement towards more typical or atypical neuroendocrine function. Given that even the most efficacious programs do not lead to symptom improvement for everyone (Weisz et al., 2006), it is possible that biological mechanisms underlying those symptoms may also show improvement only for some individuals. Multisystem approaches may provide a more comprehensive illustration of neuroendocrine stress responsivity, with this enhanced ability to distinguish between typical and atypical neuroendocrine stress response patterns providing a platform for clearer interpretation of preventive intervention effects.

Additional considerations

Our findings provide additional clarity about how preadolescents living in poverty respond to laboratory-based stressors. Previous studies of typically developing and stress affected children using person-centered modeling of single-system HPA response function have found each of their samples to be primarily composed of cortisol nonresponders (e.g., Gunnar et al., 2009; Ji et al., 2016), leading researchers to question the efficacy of the TSST in eliciting a stress response in either population. Our examination of negative affect reactivity scores at pretest suggested that youth in each profile responded with increases in subjective distress (>10% increase from baseline; Gordis et al., 2006), irrespective of whether they exhibited a cortisol response, suggesting that they viewed the TSST as stressful. Furthermore, by modeling cortisol and alpha-amylase responsivity simultaneously, our study further addresses this question by showing that youth in each profile at pretest responded to the TSST with their own unique HPA–SAM co-activation pattern. Alpha-amylase responsivity was observed in both Symmetrical No. 1 and Asymmetrical No. 2 profiles at pretest, despite exhibiting indistinguishably nonresponsive cortisol levels. Concurrent consideration of subjective distress and SAM system activation may, thus, help to reconceptualize what is considered "nonresponse" in the literature.

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It is worth noting that, for specific profiles, cortisol and alpha-amylase response trajectories appeared to differ in certain respects at pre- and posttest. Relative to pretest, higher baseline cortisol levels and linear declining responsivity as well as higher alpha-amylase baseline levels and less pronounced/blunted responsivity were observed in both the Symmetrical HPA–SAM Co-activation No. 2 and Asymmetrical HPA–SAM Co-activation No. 1 co-activation profiles at posttest. One possibility may be that observed differences are attributable to factors related to the study design. Youth with penchants towards neuroendocrine stress responsivity at pretest (e.g., reactive responders) may have exhibited an anticipatory stress response to being informed that they were to undergo the TSST–M again upon arrival to their posttest visit. Indeed, relative to pretest, youth in each of these profiles reported higher baseline levels of negative affect prior to the start of the TSST and exhibited more blunted/attenuated negative affect responsivity at posttest. Multisystem, person-centered analyses that concurrently model subjective stress responsivity in addition to HPA and SAM responsivity may be needed to further adjudicate this claim. Furthermore, future research utilizing the TSST-M protocol to examine biological re-programming of neuroendocrine stress response function may also consider modifications to experimental procedures to account for anticipatory stress responses.

Lastly, HPA–SAM co-activation profile connections to maladjustment indices were not significant at posttest. It is possible that these nonsignificant results reflect an inability replicate or sustain our pretest findings. One additional possibility may be that these nonsignificant posttest profile–maladjustment linkages reflect the effects of BaSICS. Our preventive intervention was designed to provide high-risk youth with the psychosocial competencies necessary to cope with controllable and uncontrollable stressors and overcome pathophysiological predispositions. BaSICS may have weakened the relations between HPA–SAM Co-activation and emotional and behavioral problems in this poverty exposed sample of preadolescent youth. Replication with larger sample sizes is needed to adjudicate this claim.

Limitations and future directions

The current study has limitations that offer several directions for future research. First, our sample size was relatively small for a person-centered design, which may have limited power to detect correlate and intervention effects for youth in smaller subgroups. Research with larger samples is needed to further validate the profiles and better understand which profiles are amenable to BaSICS-related change. Second, as is common with Group-Based Trajectory Modeling (Nagin, 2005) and Multitrajectory Modeling (Nagin et al., 2018), covariate effects in these models were estimated after youth were classified into subgroups. Future investigations may wish to adjust for covariates during model specification. Third, there are other potential multisystem analytic avenues by which research might arrive at similar conclusions drawn from our person-centered approaches. For example, researchers might consider the addition of curvilinear effects for cortisol, alpha-amylase, and their interaction in regression frameworks to characterize neuroendocrine function in studies of poverty-exposed youth. Fourth, although our multisystem approach is perhaps an improvement over more traditional single bio-marker approaches, the inclusion of additional biological stress response indices may clarify stress response heterogeneity in this population even further (Ellis et al., 2017). Inclusion of pre-post parallel parasympathetic nervous system (PNS) activation would permit tests of the Adaptive Calibration Model (ACM; Del Giudice et al., 2011) and examination of whether coping and empowerment based preventive intervention for preadolescents living in poverty help to move hypothesized stress response system profiles; e.g., shifts from Vigilant (Type III) and/or Unemotional (Type IV) towards Sensitive (Type I) and/or Buffered (Type II). To our knowledge, no study to date has demonstrated psychosocial intervention related changes in ACM profile membership. Fifth, though our identification of profiles at pre- and posttest permitted examination of BaSICS-related changes in HPA–SAM co-activation over time, an improvement over previous biological re-programing studies (e.g., Dozier et al., 2018; Fisher et al., 2016), we were unable to test whether changes in HPA–SAM co-activation mediate (i.e. mechanistic action) the association between BaSICS assignment and symptoms reduction due to sample size limitations. It will be important for future research to examine whether changes in HPA–SAM co-activation that follow from BaSICS explain changes in youth behavior. Lastly, the BaSICS RCT was unfortunately impacted by the COVID-19 pandemic, which limited final enrollment numbers and interfered with assessment at 6- and 12-month follow-up. Future intervention studies that follow youth across multiple follow-up time points may be poised to examine whether restored HPA–SAM co-activation patterns are maintained over time and whether such maintenance further contributes to symptom reduction in parallel.

Conclusion

Utilizing a novel person-centered, multisystem approach, the current study illustrates how BaSICS, an intervention designed to enhance skills for coping with poverty-related stress among early adolescents at-risk for internalizing psychopathology, supports the restoration of typical patterns of HPA–SAM co-activation. This study highlights HPA–SAM co-activation as a suitable (i.e., interpretable) biological target of preventive intervention for preadolescent youth living in poverty, one that should be examined in future experimental therapeutics studies seeking to remediate atypical neuroendocrine stress response rhythms. It further highlights the potential for the culturally affirmative, strength-building BaSICS preventive intervention to address the needs and improve the life chances of stress-exposed youth living in poverty.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954579424001172.

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Competing interests. No conflict.

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