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## Early Human Development

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



# Exposure to intimate partner violence in utero and infant internalizing behaviors: Moderation by salivary cortisol-alpha amylase asymmetry



Cecilia Martinez-Torteya<sup>a,\*</sup>, G. Anne Bogat<sup>b</sup>, Joseph S. Lonstein<sup>b</sup>, Douglas A. Granger<sup>c,d</sup>, Alytia A. Levendosky<sup>b</sup>

- <sup>a</sup> Department of Psychology, DePaul University, USA
- <sup>b</sup> Department of Psychology, Michigan State University, USA
- <sup>c</sup> Institute for Interdisciplinary Salivary Bioscience Research, University of California, Irvine, USA
- <sup>d</sup> Johns Hopkins University School of Nursing, School of Medicine, and Bloomberg School of Public Health, USA

#### ARTICLE INFO

# Keywords: Intimate partner violence Prenatal stress Cortisol sAA Internalizing Externalizing

#### ABSTRACT

Guided by the main tenets of contemporary models of the developmental origins of health and disease, this study evaluated whether individual differences in reactivity of the hypothalamic-pituitary-adrenal (HPA) axis and Sympathetic Nervous System (SNS) moderate the effect of prenatal exposure to trauma on internalizing and externalizing behaviors during infancy. Participants were a community sample of 182 mothers (M age = 25 years, 43% Caucasian, 33% Black/African American, 24% Biracial/Other) and their infants (59% girls; M age = 11.8 months). Each mother completed questionnaires that assessed IPV experienced during pregnancy and also reported on her infant's behavior problems. Infant saliva samples (later assayed for cortisol and sAA) were collected before and after a frustrating task (i.e., arm restraint). Results revealed that the association between in utero IPV and infant internalizing behaviors was most pronounced for infants with asymmetrical HPA-SNS (i.e., high-cortisol and low-sAA) reactivity to frustration, and least pronounced for infants with symmetrical HPA-SNS (i.e., low-cortisol and low-sAA or high-cortisol and high-sAA) reactivity to frustration. Higher levels of externalizing behavior, in contrast, were associated with higher levels of prenatal IPV but unrelated to either cortisol or sAA reactivity to stress. Findings replicate documented associations between maternal IPV exposure during pregnancy and offspring risk. Moreover, findings advance our understanding of individual differences in the developmental origins of health and disease and provide additional evidence that assessing multiple stress biomarkers contributes to a more comprehensive understanding of individual vulnerability to adversity.

#### 1. Introduction

A large body of literature highlights the detrimental effects of negative gestational experiences, including exposure to prenatal stress, on many aspects of development [1]. Of note, some studies identify intimate partner violence (IPV) that mothers experience during pregnancy as a particularly adverse stressor for their children [2,3,4,5]. IPV creates a stressful, unpredictable, and dangerous environment for pregnant women that includes both acute traumatic events and chronic anticipation of abusive behaviors. Only a few investigators have examined its effects on offspring, despite the fact that IPV occurs frequently during pregnancy [6] and that its prenatal effects may be even more pronounced and long lasting than those of milder or less chronic pregnancy stressors (e.g., stressful life events) [7]. These studies document a significant association between prenatal IPV exposure and

The fields studying neural, psychological and behavioral development are just now beginning to understand individual differences in young children's outcomes after prenatal stress exposure (i.e., multifinality) [9]. Contemporary models of development propose that biological predispositions can make individuals more or less sensitive to environmental inputs, and that distinct profiles of physiological reactivity and regulation are most beneficial in different contexts [10,11]. In theory, children who are more biologically susceptible to environmental influences have the worst outcomes in high-risk environments, but show the best outcomes in supportive and enriched environments [10,11]. Aligned with these predictions, research has documented

birth outcomes (low birth weight) [2], stress response alterations [4], temperamental difficulties [3] and internalizing (e.g., sad, inhibited) and externalizing (e.g., oppositional, aggressive, rule-breaking, impulsive) behaviors during infancy [4] and childhood [8].

<sup>\*</sup> Corresponding author at: 2219 N Kenmore Ave., Suite 420, Chicago, IL 60614, USA. E-mail address: cmart121@depaul.edu (C. Martinez-Torteya).

interactions between indices of stress response activity and environmental adversity, including family and sociodemographic risk [12,13]. Emerging research on prenatal stress is also consistent with the tenets of these models, such that biological (i.e., genetic) predispositions moderate the effect of maternal stress during pregnancy on infant negative emotionality [14] and childhood externalizing problems [15]. Although interrelated, prenatal exposure to IPV and high physiological arousal during early life may similarly interact to shape infant behavioral outcomes.

The psychobiology of the stress response is multi-faceted and involves coordination among several physiological systems, including but not limited to the Hypothalamic-Pituitary-Adrenal (HPA) axis activity and Sympathetic branch of the Autonomic Nervous System (SNS) [16,17]. The SNS orchestrates the "fight or flight" response to stress through the effects of catecholamines (i.e., adrenaline, noradrenaline) and is thought to represent a defensive reaction in response to situations where the individual is effectively and appropriately mobilizing resources to deal with challenge. Activation of this system leads to a fast response across multiple systems in the body, including enhanced cardiovascular tone, respiratory flow, blood flow to muscles, and elevated blood glucose [18]. Salivary alpha amylase (sAA), an enzyme released in response to sympathetic activation, is widely used as a valid peripheral marker of SNS activity [19]. The Hypothalamic-Pituitary-Adrenal (HPA) axis is a relatively slower, but longer acting system, that is thought to reflect a "defeat" reaction (HPA activity increase in response to circumstances where the individual is overwhelmed, withdraws, and is distressed). Threat recognition leads to secretion and release of the corticotropin-releasing hormone (CRH) by the hypothalamus, which stimulates release of adrenocorticotropin hormone (AC-TH) by the pituitary, and leads to cortisol release by the adrenal cortex. Cortisol exerts its effects throughout the brain and body inducing enhanced glucose metabolism, immunosuppression, and changes in cognition, memory, and emotion [20]. Some evidence suggests a normative dampening of the cortisol response during the first year of life [21]; however, studies document that infants exposed to psychosocial risk display cortisol mobilization to stressors [22,23,24] and that infant cortisol reactivity is relatively stable across laboratory stressors and in the short term [25]. Less is known about the infant sAA response, but research documents increases 5 to 10-minute post-stress among 12month-old infants [26].

Despite having somewhat different functions, the SNS and HPA axis are highly interconnected: hypothalamic CRH neurons and noradrenargic neurons can become co-activated, as they respond to the same neurochemicals and can also modulate each other's activity through reciprocal neural connections [18]. Thus, a multi-system measurement approach is needed to more accurately operationalize the activity of the biological components of the stress response [27,28]. Bauer, Quas, & Boyce [18] delineated two competing models of HPA/ ANS coordination. The "additive" effects model assumes joint activity that "totals" moderate levels of arousal is optimal, such that a stress response characterized by moderate activation of both systems, or high activation of one system accompanied by low activation of another represents an adaptive response, while joint high activation or de-activation that leads to excessive or not enough arousal, respectively, is maladaptive. The second model proposes "interactive" effects, so that the systems have complimentary functions and disassociations in activity (i.e., activation of only one system) reflect inefficient coordina-

A few studies have tested these alternative models of coordination by measuring salivary levels of cortisol and alpha-amylase, which can be collected using non-invasive methods, are relatively inexpensive to assay, and have strong associations with more direct indices of SNS and HPA axis activity [29,30]. However, the results of these studies have been inconsistent and difficult to interpret because the study designs, participants, behavioral measures, and saliva sampling strategies (e.g., diurnal rhythm, stress-reactivity, basal levels) are very different. Three

studies suggest that "asymmetrical" activity between these two stress response systems is associated with better cognitive and behavioral outcomes, while "symmetrical" activation is generally associated with psychosocial problems [31,32,33]. However, these studies differ on the specific patterns that confer risk for internalizing and externalizing behaviors (e.g., low cortisol paired with low sAA reported by Chen et al. [31], and Gordis et al. [33]; high cortisol paired with high sAA reported by El-Sheikh et al. [32]). In contrast, one study [34] found that highcortisol combined with low-sAA reactivity was associated with more attention, anxiety, depressive symptoms, and social problems among school-aged children and adolescents. As a result, the association between HPA and SNS functioning and internalizing or externalizing behaviors during childhood is poorly understood. This is particularly true for infants, as no study to date has evaluated links between HPA and SNS multi-system activation to a stressor and infant socioemotional outcomes.

Interactions between children's physiological stress reactivity and their environment may help explain some of these discrepant findings. However, only two studies to date have evaluated associations between multi-system coordination as moderators of environmental risk and no study has focused on early childhood. Koss et al. [35] evaluated the interaction between marital conflict, HPA and SNS reactivity among a community sample of second graders. Results showed that children with a profile of high sAA and low cortisol activity in response to a stressor (viewing conflict vignettes) were most affected by marital discord; cortisol/sAA coordination moderated the effect of marital conflict on children's concurrent internalizing, and later (7th grade) internalizing and externalizing problems. Similarly, Chen et al. [36] evaluated cortisol/sAA coordination as a moderator of the effect of parental harsh discipline on child internalizing and externalizing behaviors among a large sample of inner-city 11-12 year olds. Results showed that for boys, harsh discipline was associated with more internalizing and externalizing problems for those with asymmetric HPA-SNS activity (i.e., high-cortisol and low-sAA or low-cortisol and highsAA). These findings suggest that specific profiles of HPA-SNS activity may enhance susceptibility to environmental risk, but it is hard to tease apart the effects of stress system activity and environmental risks, as HPA and SNS functioning are themselves shaped by environmental inputs throughout childhood [21].

A focus on the prenatal context and infant outcomes can help minimize these bidirectional effects that child biological sensitivity and environmental factors may exert on each other over time. Although infant socioemotional problems remain understudied, it is important to address internalizing and externalizing problems among this age group, as infants growing up in high risk environments can experience clinically significant impairment [37]. One study found that 35% of 12- to 18-month-olds referred to protective services for child maltreatment allegations have clinically significant behavioral and emotional problems [38]. Moreover, high levels of internalizing and externalizing problems during infancy persist in the short term (1 year later) [39,40] and predict later emotional and behavioral disorders (school age) [41], particularly among children exposed to high levels of family stress [42].

#### 1.1. Present study

The present study evaluated the <u>combined effects</u> of prenatal adversity as well as stress-related HPA axis and SNS reactivity as predictors of internalizing and externalizing behaviors when infants were about 12-month-old infants. With only a handful of studies with older children to guide predictions [35,36], we expected a significant interaction between prenatal IPV exposure and cortisol/sAA coordination, such that asymmetrical coordination combined with high levels of prenatal IPV would be associated with more infant internalizing and externalizing behaviors. Because previous studies reported gender effects on HPA and SNS links to behavioral outcomes among older children [36], infant sex was assessed as a potential covariate. Other

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