AN INVESTIGATION OF PARENTING RESPONSES TO TODDLER DISTRESS: INTERACTIONS BETWEEN PARENT PHYSIOLOGY, BEHAVIOUR, AND SOCIOEMOTIONAL CONTEXT

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ABSTRACT

This dissertation examined physiological, behavioural, and psychological aspects of parents' responses to children's distress across infancy and toddlerhood through a series of three studies. Study 1 is a systematic review and narrative synthesis of the literature that characterized parents' physiological responses to infants' and toddlers' (0-3 years) distress during experimental and naturalistic distress paradigms and examined concurrent associations between parents' physiological and behavioural responses. General trends in parents' physiological responses varied as a function of methodological factors including the physiological outcome (i.e., cortisol, cardiac outcomes, skin conductance, salivary alpha amylase), distress paradigm (e.g., fear-related distress, frustration-related distress), and baseline comparison condition used. Studies 2 and 3 used data from a sample of caregiver-toddler dyads (N=234) studied in a naturalistic high-distress context (i.e., toddler routine vaccination) to address the limitations and gaps in the literature identified in Study 1. Study 2 described the validation of a measure of insensitive (i.e., distress-promoting) caregiver behaviour during routine vaccination. Measure validity and reliability were investigated with correlations and autoregressive cross-lagged path analysis. Study 3 characterized the trajectory of caregivers' physiological (i.e., high-frequency heart rate variability) responses during routine vaccination and associations of the trajectory with parents' concurrent behaviour and psychological stress. Findings across all three studies are discussed in the context of the extant literature and relevant theoretical models. Clinical implications and directions for future research are offered.

DEDICATION

This work is dedicated to all the parents and parent figures who have so profoundly inspired me throughout my graduate training: to the parents who participated in this research and generously allowed me a window into their relationship with their child during a stressful moment, to the parents I've encountered through my clinical training, whose devotion to their children has led them to overcome extraordinary obstacles, and to my own parents, whose unwavering support of me has always fueled my curiosity and growth and provided the only proof I needed of how powerful parenting influences are.

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PUBLICATION DISCLOSURE

The studies comprising this dissertation (Chapters 2, 4, and 6) are currently published or under review for publication. Manuscript citations are provided below.

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DISSERTATION SYNOPSIS

During the first years of life, children develop foundational skills related to the expression and regulation of emotions that form the template for how they approach and manage stressors throughout childhood and adolescence (Bowlby, 1969/1982; Sameroff, 2010). Parents and other primary caregivers are the most significant social influences for the developing child (Sameroff, 2010). To date, progress toward understanding the mechanisms underlying parents' impact on children's emotion regulation has been limited by a narrow view of parents' influence on children which has overemphasized the impact of parents' sensitive behaviour while neglecting to consider how suboptimal parent behaviours and the physiological and psychological context underlying these behaviours contribute to these mechanisms (Samdan et al., 2020).

To address limitations of the existing literature, the current dissertation consisted of an in-depth analysis of the biological, behavioural, and psychological aspects of parents' responses to their child's distress across a range of distress contexts during infancy and toddlerhood in pursuit of three primary aims: (1) To synthesize the literature on parents' physiological responses to infants' and toddlers' (0-3 years) distress and how these responses relate to sensitive and insensitive parenting behaviour; (2) To validate a measure of parents' insensitive behaviour in a naturalistic high distress context; and (3) To examine associations among parents' physiological, behavioural, and psychological responses to toddler distress in a naturalistic high distress context. These aims were addressed through three studies that are either published or currently under peer review (Badovinac et al., 2023a; Badovinac et al., 2023b; Badovinac et al., 2023c). Studies are described in Chapters 2, 4, and 6. To facilitate understanding of the entire

dissertation, each study's primary aims, methodology, and key results are summarized in Appendix A.

Study 1 was a systematic review and narrative synthesis of studies that have measured parents' physiological responses to infants' and toddlers' distress. Methodological factors including different physiological outcomes (i.e., cortisol, cardiac outcomes, skin conductance, and salivary alpha amylase) and distress paradigms (e.g., fear-related distress, frustration-related distress) were examined. A synthesis of the studies' findings elucidated general trends in parents' physiological responses to their child's distress and associations with parenting behaviour as well as several methodological factors — such as the constraints on parents' behavioural and affective responses to their child imposed by the task as well as the type of baseline comparison condition used — that likely contributed to discrepant results across studies. Moreover, the synthesis showed that insensitive parent behaviour had stronger associations with parents' physiological responses to child distress than did sensitive parent behaviour.

Studies 2 and 3 built directly on key insights and gaps identified in Study 1. Both studies were based on data from a cohort of caregiver-toddler dyads who were observed in a naturalistic and universally standardized high distress context (toddler routine vaccinations) at 12, 18, or 24 months of age. Biological, behavioural, and psychological aspects of caregivers' responses to routine vaccination were discerned based on video and electrocardiography data collected prior to, during, and following the vaccination and self-reports of caregivers' psychological stress.

Study 2 described the validation of the Opportunities to Understand Childhood Hurt's Inoculation Evaluation – Research Version (OUCHIE-RV), a measure of insensitive parent behaviours that coded parental affect incongruence, parental attention disengagement, and parental physical distancing behaviours in response to toddlers' pain-related distress during

routine vaccination appointments. Analyses provided strong evidence for the reliability and validity of the OUCHIE-RV as a measure of distress-promoting parent behaviour.

Study 3 characterized the trajectory of caregivers' physiological (i.e., high-frequency heart rate variability [HRV]) responses during toddler vaccination and investigated other parental factors hypothesized to relate to physiological responses, including parents' insensitive and soothing behaviours, state anxiety, anxiety symptomology, and parenting stress. Contrary to hypotheses, results indicated minimal changes in parents' HRV from the pre-needle to post-needle period. Parenting stress was significantly associated with the trajectory of parents' HRV; however, there were no significant associations with parents' behaviour and other psychological stress measures.

Taken together, findings from the current dissertation support existing theoretical assertions and provide novel insights related to the mechanisms linking parents' self-regulatory abilities to children's self-regulatory outcomes. Notable themes to emerge across studies included the importance of parents' insensitive behaviour within emotion socialization processes and the importance of contextual and methodological factors in the design and interpretation of psychophysiological studies of parent-child interaction, as these factors can introduce nuance and heterogeneity to findings.

CHAPTER 1: INTRODUCTION

Parent socialization during the first years of life

Among the factors that shape children's social and emotional development, none has been more widely studied or considered more instrumental than parenting socialization (Bowlby, 1969/1982; Sameroff, 2010). Decades of research have provided support for parents' role as key socialization agents across all stages of child development, with parenting having the strongest influence on development during early childhood (Sameroff, 2010).

Within developmental psychology, among the most well-studied aspects of parenting is the socialization of emotion regulation skills (i.e., the ability to perform goal-directed monitoring and modulation of one's emotions; Thompson, 1994). Because children are not born with the ability to regulate their own emotions, they rely heavily on parents to provide external support needed to modulate strong emotions during the first years of life (Bowlby, 1969/1982; Kopp, 1989). This support from parents serves not only to scaffold emotion regulation during moments of distress, but also to provide a model of how emotions can be adaptively regulated that can then be adopted by the child over time and used in future distress contexts throughout their life (Bridgett et al., 2015). When parents consistently provide children with the support needed to express and cope with a range of emotions during these formative years of development, children are more likely to have better-developed skills related to the self-regulation of emotions, behaviour, and attention (Badovinac et al., 2021; Pallini et al., 2018), which underlie adaptive functioning across development. Given the profound influence of early parenting-related emotion socialization processes on adaptive developmental outcomes for children, gaining a comprehensive and multidimensional understanding of how these processes unfold has been highlighted as a research priority for developmental psychology (King et al., 2021).

Theoretical frameworks for parenting influences on emotion regulation

Several theoretical frameworks have been proposed to delineate mechanisms by which parents influence children's development broadly and emotion regulation abilities specifically. Bowlby's (1969/1982) Attachment Theory recognizes parent-child interactions in distressing contexts as the foundation for infants' development of emotion regulation. According to this view, infants are innately wired to signal their distress and seek proximity to parents as a strategy for having their emotional needs met. Ainsworth's (1974) concept of parental sensitivity and Biringen's (2000) Emotional Availability framework further elaborate Attachment Theory assertions and elucidate parents' contributions to infants' emotional outcomes. Both theories highlight how, through repeated interactions, parents' responses to infants' distress signals shape infants' capacity and strategies for emotion regulation, with patterns becoming more stable over the second year of life (Ainsworth et al., 1978). Specifically, sensitive and attuned parent behaviours, which communicate acceptance of and responsiveness to children's distress, support children's adaptive expression and regulation of emotions.

Like Attachment Theory, Sameroff's (2010) Unified Theory of Development also highlights the importance of the caregiving context in shaping development but situates the parent-child relationship within a larger ecological system in which influences are dynamic across child development. The Unified Theory suggests that parent-child interactions cannot be understood without reference to the broader geopolitical, community, school, social, and family contexts in which they exist, suggesting that understanding the parent's own individual circumstances is key to understanding the parent's response to their child and the subsequent implications for child outcomes. The dynamic and temporal aspects of the Unified Theory are illustrated by Sameroff's "ice-cream-cone-in-a-can" model (Sameroff & Fiese, 2000; see Figure

1), which describes how the influence of parents on children's self-regulation is strongest during infancy (i.e., when children rely entirely on external regulation by others; other-regulation) and lessens over time as the child takes on greater agency in regulating their own emotions and behaviour (self-regulation).

While the frameworks described above emphasize the significance of the parent (nested within their broader context) in shaping the developing child's emotion regulation abilities, they do not speak to the specific mechanisms through which the transition from other-regulation to self-regulation occurs. Insight into these mechanisms is offered by the Self-Regulation Intergenerational Transmission Model (Bridgett et al., 2015; see Figure 2), which purports that self-regulation abilities are transmitted across generations (i.e., from parent to child) via biological and social processes. According to this model, parents introduce their own self-regulatory abilities, defined in terms of their physiological and behavioural responses to stress and shaped by genetic programming and life experiences. Parents' self-regulatory abilities and deficits (e.g., psychopathology) directly influence parenting behaviour in response to child distress, which in turn influences the child's behavioural and physiological regulation from distress. Over time, children's responses to and regulation from distress become stable and are passed on to future generations through the same mechanisms. A notable feature of this model is its emphasis on physiological stress responses and regulation as offering valuable insights into the behavioural expression of parents' emotion regulation.

The theories outlined above converge on several key principles. First is the notion that parents, as primary caregivers, are key socialization agents in children's development of emotion regulation. Second, the influence of parents as socialization agents is not stable over time; it is strongest during the first years of life with more reliable associations being observed during the

second year of life (Kopp, 1989; Samdan et al., 2020; Ainsworth et al. 1978). Parents' influence gradually decreases over time due to the child's increasing regulatory independence and reliance on other social agents (e.g., peers, teachers; Valiente et al., 2020). Third, to fully appreciate the influence that parents have on children's emotion regulation, it is critical to study parents' behaviour in the context of their own self-regulatory abilities, operationalized from both biological and psychological perspectives. The current dissertation is grounded in these principles and focuses on individual differences in and associations among parents' behavioural, biological, and psychological responses to their child's distress during the second year of life (i.e., toddlerhood).

Knowledge and gaps related to parenting influences on toddler emotion regulation

To date, most research exploring parents' influence on infant and young child emotion regulation abilities has focused on parent behaviour. Consistent with theory, a recent systematic review (Samdan et al., 2020) suggested that associations between parent behaviour and child emotion regulation abilities strengthen during the second year of life, emphasizing that toddlerhood is an important time to observe these developmental processes unfolding. However, a notable limitation of this literature is the methodology used to assess parent behaviour, which has typically relied on naturalistic observation of parent-child interaction during play or has used structured laboratory procedures designed to induce moderate distress (Samdan et al., 2020), due to ethical concerns with inducing high distress in an experimental context. Because young children's reliance on parents for regulatory support increases as a function of distress experienced (Kopp, 1989), and children naturally have varying thresholds for distress due to temperamental factors (Stifter & Dollar, 2016), existing paradigms are not optimal for studying parents' contribution to children's regulation from high distress.

To better understand the influence of parent socialization factors on the development of young children's emotion regulation, researchers have turned to the context of early childhood routine vaccinations, which provides a naturalistic and ecologically valid paradigm for observing parents' response to their child's acute pain and its subsequent impact on children's emotion regulation. Unlike play-based naturalistic observation studies or structured laboratory procedures, the naturalistic pain context is notable in its propensity to elicit distress in both parent and child (Brown et al., 2018), increasing the situational demands on parents. Studies conducted in the pain context have yielded important insights into the specific parent behaviours that relate to infants' and toddlers' reactions to pain-related distress, as noted by a recent systematic review (Sobol-Kwapińska et al., 2020). For example, young children of parents who engage in more proximal soothing (Campbell et al., 2013) and sensitive caregiving behaviours (Atkinson et al., 2015; Din Osmun et al., 2014; Pillai Riddell et al., 2011) and less verbal reassurance (Cohen et al., 2005; Racine et al., 2012) display less pain-related distress following the painful stimulus.

Although encouraging progress has been made toward unpacking parents' influence on young children's emotion regulatory abilities in the context of pain and other distressing situations, there are significant gaps within the extant literature (Samdan et al., 2020; Sobol-Kwapińska et al., 2020). First, most studies examining the impact of parent behaviour on young children's regulatory abilities in pain have operationalized parent behaviour largely in terms of parental sensitivity, which tracks the presence or absence of positive or attuned aspects of parent behaviour such as responsiveness, support, and emotional availability, but does not generally capture less optimal parenting behaviours such as intrusiveness, unresponsiveness, and negative affect expression, that may occur in the context of other positive behaviours (Sobol-Kwapińska

et al., 2020). Given that multiple studies have shown that insensitive distress-promoting parenting behaviours can have a stronger influence on child distress than do positive behaviours (Badovinac et al., 2018; Brown et al., 2019; Campbell et al. 2018; Spagrud et al., 2008; Sweet & McGrath, 1998), this is a critical area of future investigation.

A second limitation of the extant literature is a limited application of the biopsychosocial model of development (see Samdan et al., 2020). Parent behaviour is an important observable aspect of parent-child interaction; however, it occurs in the context of parents' functioning across various other domains (e.g., biological, psychological, social). The biological substrates of parenting have garnered considerable interest within an emerging literature focused on parent-child physiological attunement (see Davis et al., 2018; Di Lorenzo et al., 2022). This literature has endeavoured to uncover patterns in the coordination of hypothalamic-pituitary-adrenal axis, autonomic nervous system, and neural activity between parents and children in the context of children's distress, which — as in the broader developmental psychology literature — is most often elicited in the context of experimental paradigms that elicit mild to moderate distress (Di Lorenzo et al., 2022). The pain context offers an ideal opportunity to apply a biopsychosocial perspective to the study of parent emotion socialization processes by examining parents' responses from biological, psychological, and behavioural perspectives.

Parenting influence on emotion regulation during painful procedures

Building on the foundation of Attachment Theory (Bowlby 1969/1982) and Sameroff's (2010) Unified Theory of Development, the Development of Infant Acute Pain Responding Model – Revised 2022 (DIAPR-R 2022; Pillai Riddell et al., 2022; see Figure 3) was developed to describe the biological, psychological, and social processes impacting children's experience of acute pain during infancy and early childhood. The DIAPR-R 2022 model focuses on the range

of factors that influence how parents respond to their child's pain and how this in turn relates to children's pain-related distress reactivity and regulation.

According to this model, infants' processing of pain begins before the painful event occurs and is influenced by infants' developing schemas of the sequence of events and associated emotions elicited during the painful event, as well as their developing templates for how reliably and effectively their primary caregivers meet their emotional needs more generally (i.e., attachment schemas). The painful event then initiates a sequence of events for the infant beginning with sensation and perception of the noxious event within the infant's central and peripheral nervous systems and ultimately results in the infant's behavioural expression of pain-related distress (e.g., crying, facial activity).

Concurrently to these unfolding events, a sequence of physiological, cognitive, and behavioural responses unfolds for the caregiver as they anticipate and react to their infant's pain-related distress. As illustrated in Figure 3, caregivers' cognitive schemas for pain and their autonomic nervous system reactions are hypothesized to impact caregivers' interpretation of their infant's pain-related distress which in turn leads to caregivers' behavioural responses to their distressed infant, and ultimately, their ability to support effective management of their infant's distress. More distal and systemic factors such as family dynamics, cultural beliefs, and caregivers' mental health also have the capacity to influence infant pain but are postulated to do so via the caregiver.

By bringing together the biological, psychological, and social aspects of parents' response to their child's distress under one theoretical framework, the DIAPR-R 2022 model (Pillai Riddell et al., 2022) addresses a need highlighted within the broader pediatric pain literature (Constantin et al., 2017), which is to consider the physiological context for parents'

responses to children's pain-related distress. The current dissertation examined the theoretical assertions of the DIAPR-R 2022 model during the toddlerhood period to contribute to an improved understanding of the mechanisms underlying parent emotion socialization processes across the early childhood period.

The current dissertation

The main goal of this dissertation was to advance our understanding of the biological, behavioural, and psychological substrates of parents' responses to children's distress during toddlerhood through a synthesis of existing research in the broader developmental psychology literature and the testing of novel hypotheses, informed by relevant theoretical models, in a naturalistic pain context. This goal was accomplished with three studies. The first study (Chapter 2; Badovinac et al., 2023a) is a systematic review and narrative synthesis of parents' physiological responses to infants' and toddlers' (0-3 years) distress and concurrent associations with parenting behaviour. The second study (Chapter 4; Badovinac et al., 2023b) describes the development and validation of an observational measure of parent distress-promoting (i.e., insensitive) behaviours enacted in response to toddlers' pain-related distress. The third study (Chapter 6; Badovinac et al., 2023c) characterizes parents' physiological responses during toddler vaccination, measured as high-frequency heart rate variability, and investigates concurrent associations with parenting behaviour and parent psychological stress. Chapters 3 and 5 are bridging chapters scaffolding the conceptual flow of the dissertation. Finally, given the multiple studies and analytic approaches, Appendix A briefly summarizes the primary aims, methodology, and results of each study for ease of synthesis.

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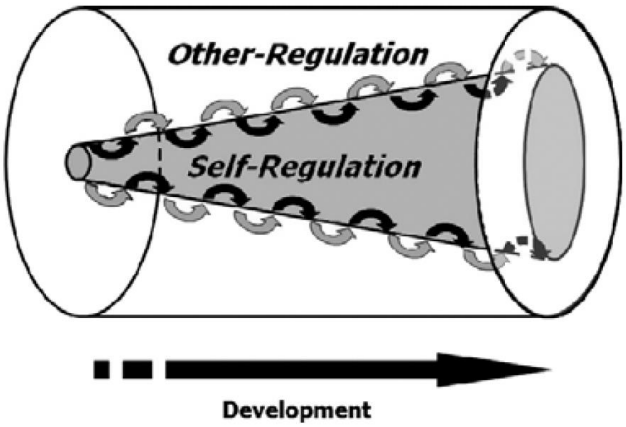
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Figure 1

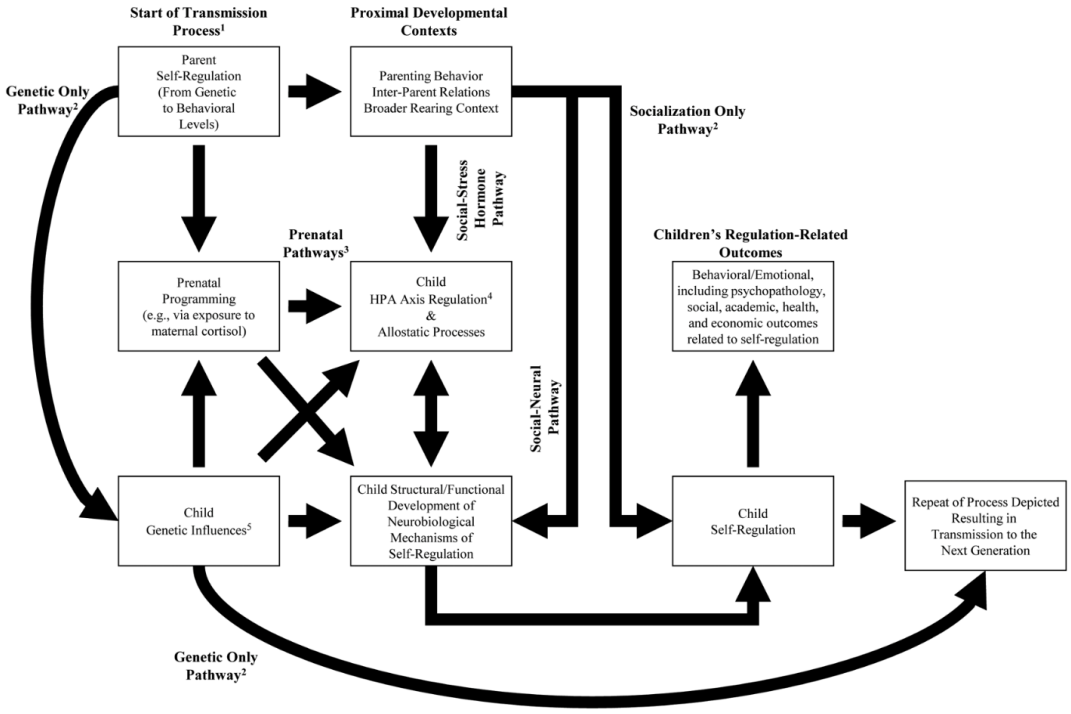
'Ice-cream-cone-in-a-can' model (Sameroff & Fiese, 2000).



Note: In the above figure, the bottom axis represents development from infancy to adulthood. The transition from "other"-regulation to "self"-regulation from infancy to adolescence and adulthood is depicted by the increasing size of the cone (and decreasing size of the surrounding space) as development progresses. The arrows represent the interdependent effects of the child and their environment, meaning that the actions of each influence the other.

Figure 2

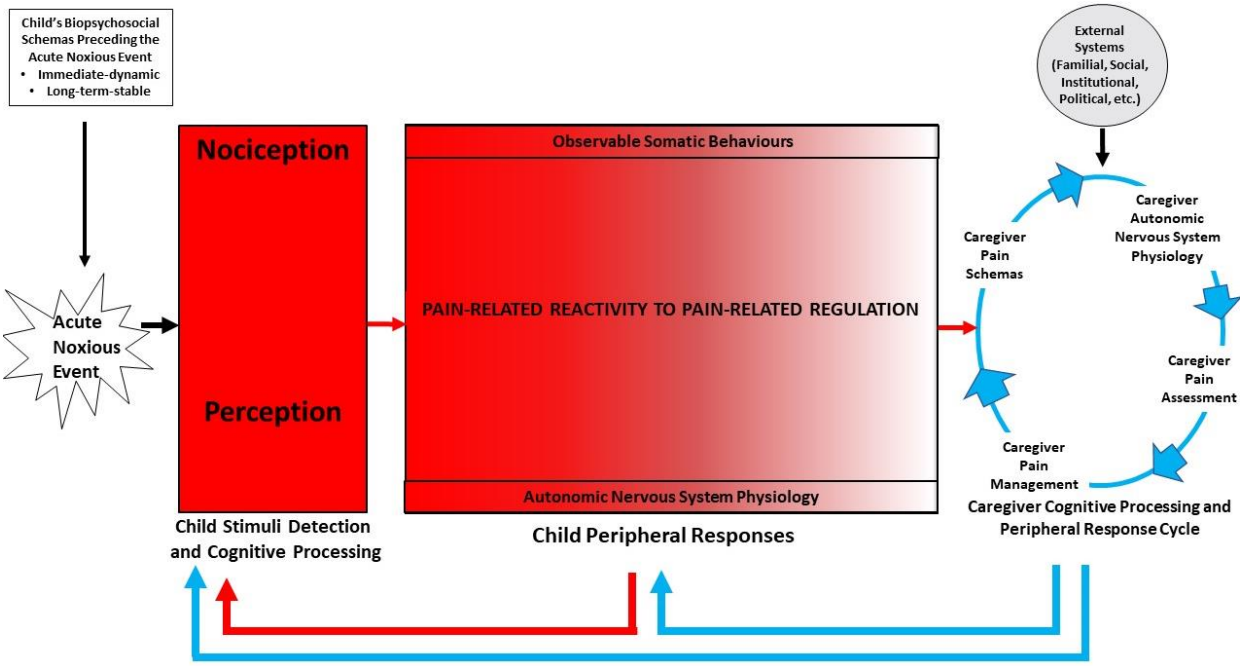
Self-regulation intergenerational transmission model (Bridgett et al., 2015).



Note: In the above figure, the biological (i.e., "genetics only") and environmental (i.e., "developmental contexts") pathways linking parents' self-regulatory capacities to children's self-regulatory capacities are depicted.

Figure 3

The Development of Infant Acute Pain Responding Model – Revised 2022 (DIAPR-R 2022; Pillai Riddell et al., 2022) model.



CHAPTER 2: PARENTS' PHYSIOLOGICAL REACTIVITY TO CHILD DISTRESS AND ASSOCIATIONS WITH PARENTING BEHAVIOUR: A SYSTEMATIC REVIEW[1]

1. Introduction

The ability to self-regulate emotions is a critical developmental skill that supports adaptive functioning across the lifespan (Robson et al., 2020; Thompson, 1994; Werner & Gross, 2010). While differences in temperament and other prenatal factors partly account for individual differences in this skill (Bridgett et al., 2015), parenting socialization processes, particularly during the first years of life, are primary mechanisms through which foundational emotional learning occurs (Bowlby, 1969; Kopp, 1989; Morris et al., 2017; Sameroff, 2010). During moments of distress, infants and children depend on parental support to process threat-related information and successfully modulate the associated emotions. Supporting this proposition, research has shown that parents' behavioural responses in distressing situations shape how children react to distress at both behavioural (Samdan et al., 2020) and physiological levels (Rattaz et al., 2022). Specifically, when parents respond to child distress with sensitive and attuned caregiving responses, children respond more adaptively to distress.

Theory and extant research highlight the dyadic nature of children's distress experiences during the first years of life. Yet, while children's behavioural (Ahola Kohut et al., 2012; Mesman et al., 2009; O'Neill et al., 2019) and physiological (Gunnar et al., 2009; Jansen et al., 2010; Jones-Mason et al., 2018; Puhakka & Peltola, 2020) responses to distress are well-characterized, considerably less is known about how parents are impacted during their child's

[1] Chapter 2 is the author's version of the published manuscript: Badovinac, S.D., Chow, C., Edgell, H., Flora, D.B., Di Lorenzo, M.G., & Pillai Riddell, R. (2023). Parents' Physiological Reactivity to Child Distress and Associations with Parenting Behaviour: A Systematic Review. *Neuroscience & Biobehavioural Reviews.* Advance online publication. https://doi.org/10.1016/j.neubiorev.2023.105229

distress. An emerging area of investigation has focused on characterizing parents' physiological responses during child distress, as measured by parents' hypothalamic-pituitary-adrenal (HPA) axis activity and autonomic nervous system (ANS) activity. From a biopsychosocial perspective, studying parents' physiological responses to their child's distress may offer key insights into the mechanisms subsuming parents' behavioural responses, and more specifically, their use of sensitive versus insensitive responses to their child's distress. For example, a parent's sub-optimal behavioural response could be driven by not accurately detecting their child's threat-related distress signals, detecting a threat but selecting a non-attuned behavioural response, or the parent themselves becoming emotionally dysregulated by the threat or by their child's distress signals, limiting their ability to monitor and respond to their child. Uncovering the physiological context for parenting behaviour supports a multidimensional understanding of parental emotion socialization processes, which has been highlighted as a research priority for developmental psychology that supports the National Institute of Mental Health's Research Domain Criteria (RDoC) initiative (King et al., 2021). The current paper presents a review and synthesis of this emerging area of research.

Current theory and research support the notion that observing the suffering of others invokes specific and marked emotional and physiological responses in the self (Krishnan et al., 2016; Stellar et al., 2015). Adults, including non-parents, reliably show changes in physiological arousal when faced with infant cries (Out et al., 2010). Among parents, responses may be more marked when hearing their own child in distress compared to an unfamiliar child (Wiesenfeld et al., 1981; Young et al., 2017). However, there are several other factors that may influence the magnitude of parents' physiological responses to their child's distress.

Perhaps the most salient methodological factor to consider is the context used to elicit the child's distress, which varies in terms of the extent to which the situation is naturalistic or contrived, as well as the type of threat it invokes. Laboratory-based stress paradigms used for infants and young children can be broadly differentiated between those designed to elicit child *fear*, either through an attachment-related threat (e.g., Still Face Procedure [Tronick et al., 1978]; Strange Situation Procedure [Ainsworth et al., 1978]) or due to exposure to novelty (e.g., approach by an unfamiliar adult or unpredictable toy [Goldsmith & Rothbart, 1996]), and those designed to elicit child *frustration*, either by interrupting and blocking the child's access to a desired toy (e.g., using a barrier or gentle physical restraint [Braungart-Rieker & Stifter, 1996; Goldsmith & Rothbart, 1996]) or through use of a dyadic task that requires parent and child to complete a challenging activity collaboratively under time constraint (e.g., Parent-Child Challenge Task [Lunkenheimer et al., 2017]). These tasks vary in terms of parents' role in causing distress as well as the degree to which parents' behaviour is constrained in the task, both of which likely impact their stress responses. Meta-analytic findings suggest that stressors involving an aspect of outcome unpredictability, uncontrollability, and social evaluation (i.e., threat to how one is perceived by others) elicit the largest acute physiological responses in the general population of adults (Dickerson & Kemeny, 2004). Both unpredictability and uncontrollability are generally limited in laboratory-based paradigms because parents are given the option to discontinue procedures at any time and procedures are typically terminated if the child becomes excessively distressed (e.g., Hibel et al., 2009; Mills-Koonce et al., 2009; Sturge-Apple et al., 2011). Accordingly, parents may exhibit greater physiological responses during naturalistic, relatively uncontrolled child distress-inducing situations, such as routine vaccinations and other painful procedures. Parents' role in naturalistic distress contexts is also

unscripted, which could lead to the perception of greater pressure to respond in the "right" way, particularly with onlookers present. It is also likely that the level of child distress elicited by different contexts would impact parents' responses. Infants consistently exhibit physiological reactivity to parent unavailability paradigms and physical stressors (e.g., blood draws, inoculations), whereas frustration and novelty paradigms have been found to elicit minimal reactivity (Gunnar et al., 2009; Puhakka & Peltola, 2020).

Equally important to consider is the outcome used to operationalize parents' stress responses. Acute stress responses are driven by the activity of two main physiological systems, including the HPA axis and the ANS. Salivary cortisol measurement in response to a stressor is commonly used as a marker of HPA axis reactivity. Cortisol typically increases in response to perceived threat or challenge, with peak reactivity in salivary measurements occurring 20 to 40 minutes post-challenge (Dickerson & Kemeny, 2004). The ANS, on the other hand, consists of two branches, the sympathetic and parasympathetic nervous systems, which operate co-actively (Berntson et al., 1993). Heart rate variability (HRV), also referred to as respiratory sinus arrhythmia despite some technical differences between the terms, is the most commonly used marker of ANS activity during psychosocial stressors and reflects parasympathetic control of the heart (Porges et al., 1994). Higher HRV levels at rest serve a "brake" function on the heart, whereas a decrease in HRV (i.e., HRV withdrawal) is considered adaptive in response to threat as it facilitates a shift to threat management (Porges, 2007). However, of relevance to caregiving situations, increases in HRV (i.e., HRV augmentation) are hypothesized to be adaptive and self-regulatory in situations requiring social engagement by supporting interaction with the environment (Beauchaine, 2001; Porges, 2007; Porges et al., 1994). Other commonly used measures of ANS activity include electrodermal activity (e.g., skin conductance level; reflective

of sympathetic nervous system activity), heart rate and heart period (which reflect joint sympathetic and parasympathetic influences), and salivary alpha amylase (sAA), which was more recently validated as a marker of sympathetic activity (Granger et al., 2007; Nater & Rohleder, 2009). Regardless of the stress outcome used, there are several methodological issues associated with data collection procedures that require consideration when interpreting findings of parents' stress reactivity. Factors such as the timing of baseline collection relative to arrival in the lab (Dickerson & Kemeny, 2004), postural changes across the task (e.g., changes from seated to standing; Quintana et al., 2016), the activity used as a baseline comparator (e.g., resting vs. dyadic interaction), and carry-over effects from completing a sequence of different laboratory tasks (Gunnar et al., 2009) can all impact the stress outcomes discussed above.

1.1 Current study

The current study aimed to accomplish two goals through use of systematic review and narrative synthesis of the extant literature:

- Aim 1: To characterize parents' physiological stress responses in reaction to their child's distress during infancy and early childhood (0-3 years).
- Aim 2: To examine concurrent associations between parents' physiological and behavioural responses in child distress contexts.

We focused specifically on the infancy and early childhood period (0-3 years) because parents are typically the primary socialization influences during this period (e.g., see Eisenberg et al., 1998) and thus play a central role in scaffolding children's adaptive emotion regulation in distress contexts. In addition, we aimed to investigate how methodological differences across studies, such as the types of distress tasks used, the type of stress outcome measure used and the timing of outcome collection relative to the task phases, study risk of bias, and sample

characteristics (e.g., child age) were related to outcomes. A narrative synthesis approach was selected (rather than meta-analytic synthesis) to allow for an in-depth discussion of trends across studies that accounted for the interacting influences of these methodological factors.

2. Methods

2.1. Search strategy and study selection

This review followed the systematic review methodology and reporting standards outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Page et al., 2021) and the American Psychological Association Journal Article Reporting Standards (JARS; Appelbaum et al., 2018). The review protocol was pre-registered in the International Prospective Register of Systematic Reviews (PROSPERO; #CRD42021252852; Pillai Riddell et al., 2021) prior to data extraction. A PRISMA Checklist is provided in Supplemental File 1.[2]

A systematic electronic literature search of four databases (CINAHL, Embase, Medline, and PsycINFO) was conducted with the assistance of an academic librarian using search terms related to parenting, physiological stress, and infant/child distress. An example search strategy is provided in Supplemental File 2.[3] The search was completed on October 11th, 2022. Following the search, additional articles were identified by screening the reference lists of included studies and through targeted Google Scholar alerts. Abstract screening, data extraction, and risk of bias assessments were conducted using Covidence (www.covidence.org).

Abstract screening methodology followed guidelines recommended by Polanin et al. (2019) and screening was completed by three reviewers (SB, CC, MD). Abstracts were

[2] Appendix B in the current dissertation.

[3] Appendix C in the current dissertation.

independently screened by reviewers, with 23% being screened by multiple reviewers. Percentage agreement exceeded 97% across all reviewer pairs and consensus on all disagreements was reached through discussion. To be retained for full-text review, abstracts were required to indicate that an infant or child distress task was completed and that parent physiological stress responses were assessed.

Full text review was completed by two authors (SB and CC). Each author independently reviewed studies to assess eligibility and each exclusion was double-checked by the other reviewer. Disagreements were rare and were resolved through consensus. Inclusion criteria were: 1) original peer-reviewed empirical article; 2) participating child aged 0 to 3 years (i.e., < 48 months); 3) procedures involve a contrived (i.e., laboratory) or naturalistic (e.g., painful procedure) paradigm that was intended or known to elicit child distress which was witnessed by the parent (i.e., parent is in the room or observing their child in real-time via monitor or one-way mirror); 4) analyzed parents' autonomic (e.g., cardiac, sAA, electrodermal activity) or HPA (e.g., cortisol) stress responses in reaction to the child distress task.[4] Details and citations of studies excluded at the full-text review stage are provided in Supplemental File 3.[5]

2.2. Data collection, risk of bias assessment, and synthesis

Following study selection, two authors (SB and CC) independently extracted data from included studies using a pre-constructed extraction template. The following methodological and

[4] These inclusion criteria reflect two changes from our pre-registered protocol. We had originally intended to include parents of children aged zero to five years and to include studies that used brain-based measurements (e.g., electroencephalogram [EEG], functional magnetic resonance imaging [fMRI]) as an indicator of parents' stress response. Given the large number of relevant studies identified during full-text review, relatively few of which focused on children in the preschool years or used brain-based measurement, these changes were made to allow for a more in-depth review of the extant literature.

[5] Appendix D in the current dissertation.

outcome data were collected: sample demographic characteristics, details of distress paradigm(s) studied, details of parent stress outcomes studied (i.e., operationalization, measurement parameters, data transformation), details of parent behaviour measurement (if applicable), and outcome data pertaining to parents' stress responses during the distress paradigm as well as statistical associations between parents' physiological stress responses and behavioural responses. If quantitative data were reported for outcomes (e.g., means and standard deviations, ANOVA results), these were used to calculate effect sizes (i.e., standardized mean differences [Cohen's *d*; Cohen, 1988]) to support synthesis of results across studies. When studies met inclusion criteria but were missing details on analysis outcomes, study authors were contacted by email and the relevant data were requested[6]. If insufficient data were available to calculate effect sizes, results were described based on the available information (e.g., trends in parents' responses as depicted in graphs, results of significance testing as reported by authors).

Because the timing of physiological outcome sampling varied across studies and outcome type, we used the following definitions to reflect parents' responses across various phases of the distress task. Effect sizes for *reactivity* indicate changes in outcome levels between baseline and the "peak stress" period of each task (e.g., Still Face episode of the Still Face Procedure, second separation of the Strange Situation Procedure, presentation of novel stimulus during novelty procedures). Effect sizes for *recovery* indicate changes in outcome levels between baseline and the re-engagement phase of the distress task when the parent was actively involved in soothing their distressed child. Designation of reactivity and recovery sampling times accounted for the time-lagged responses of cortisol (i.e., 20 to 40 minutes post-stressor; Dickerson & Kemeny,

[6] Sixteen authors were contacted to request supplementary data or clarification. Of these, seven authors responded and two provided additional data for use in this review.

2004) and sAA (i.e., 5 to 10 minutes post-stressor; Granger et al., 2007; Nater & Rohleder, 2009).

Given the lack of a gold-standard measure for assessing risk of bias in observational studies (Sanderson et al., 2007), an adapted risk of bias assessment tool was developed for this review informed by the NIH National Heart, Blood, and Lungs Institute (2022) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, Cochrane Collaboration's revised risk-of-bias tool for randomized trials (Sterne et al., 2019), and published guidelines for best practices in the measurement and analysis of physiological outcome measures (see Supplemental File 4[7] for further detail and the complete risk of bias tool). The tool evaluated each study's risk of bias as "low", "high", "unclear", or "not applicable" (Item 3 only; see below) in five domains. All studies were evaluated independently by two reviewers (SB and CC) and final risk of bias judgments were determined through consensus discussion. Domains included:

1. Validity and reliability of stress response measurement, including the collection of baseline physiological data, the clear definition of physiological outcome(s), the use of valid and reliable physiological measurement parameters, and the use of appropriate physiological data processing procedures.
2. Consideration of confounding variables relevant to physiological outcome measurement (i.e., parent sex, time of day, recent food intake, and medication use).
3. Validity and reliability of behavioural outcome measure (i.e., use of a validated or clearly described behaviour measure, evidence for adequate inter-rater reliability, and blinding of coders).

[7] Appendix E in the current dissertation.

4. Influence of missing data (i.e., discussion of missing participant data, including study attrition for longitudinal studies).
5. Definition and consistent application of inclusion/exclusion criteria.

Extracted results from the included studies were organized according to our two aims (characterizing parents' physiological stress responses to child distress [Aim 1] and exploring associations between parents' physiological stress responses and behavioural responses [Aim 2]). Each of these sections was further subdivided based on the specific stress outcome used (i.e., cortisol, HRV, other cardiac outcomes, sAA, and electrodermal activity), followed by the type of distress paradigm used (fear task, frustration task, additive fear and frustration, and naturalistic stressor). Narrative synthesis was used to consolidate and summarize results within each of these subsections (Popay et al., 2006). Synthesis involved a discussion of the general direction and magnitude of findings across studies based on study effect sizes and incorporating available study results (e.g., graphical results, results of significance tests) when effect sizes could not be calculated.

3. Results

The results of the systematic search and study selection process are summarized in Figure 1. In total, 55 studies were eligible for inclusion in the review.

3.1. Study characteristics

Characteristics of the 55 included studies are presented in Table 1. Studies used data from 37 unique samples, 18 of which were selected for specific parent (e.g., psychopathology, low income, k=16) or child (i.e., prematurity, k=2) risk factors. Cortisol (30 studies; 21 unique samples) and HRV (26 studies; 18 unique samples) were the most common stress outcomes

measured, with a minority of studies examining other cardiac outcomes[8] (10 studies; 9 unique samples), sAA (3 studies; 2 unique samples), and electrodermal activity (6 studies; 4 unique samples).

The included studies used 28 different distress paradigms to elicit child distress, which could be broadly differentiated between those designed to elicit child *fear* (including attachment-related fear [*k*=8] and distress to novelty [*k*=6]), those designed to elicit child *frustration* (including child-focused frustration [*k*=5] and dyadic frustration [*k*=4]), those designed to elicit aspects of *additive fear and frustration* (*k*=3), and *naturalistic stressors* (i.e., pain-related distress [*k*=2]). Details of the distress tasks, the associated parent behaviour constraints during the task, and the studies that used each task are provided in Supplemental File 6.[9]

Slightly fewer than half of the included studies (*k*=25) were judged to have a high risk of bias in at least one domain (see Table 2). Studies were most often judged to have a high risk of bias related to the reliability or validity of physiological outcome measurement (i.e., collection of baseline physiological data [*k*=11], clear definition of physiological outcome [*k*=2], physiological measurement parameters [*k*=10], or physiological data processing procedures [*k*=1]), followed by the risk of bias due to the consistent implementation of inclusion and exclusion criteria (*k*=6), the influence of missing data on results (*k*=5), and the validity or reliability of behavioural outcome measurement (*k*=1). No studies were judged to have a high risk of bias due to failing to consider key confounding variables.

3.2. Aim 1: Characterizing parents' stress responses

[8] Other cardiac outcomes included heart rate (Ham & Tronick, 2006, 2009; Lorber & O'Leary, 2005; Oppenheimer et al., 2013; Schechter et al., 2014), heart period (Busuito et al., 2019; Moore et al., 2009), sympathovagal balance (Sturge-Apple et al., 2011), pre-ejection period (Miller et al., 2015), and R-R interval (Van Puyvelde et al., 2021).

[9] Appendix F in the current dissertation.

Syntheses pertaining to Aim 1 are organized by biological outcome (cortisol, HRV, other cardiac outcomes, sAA, electrodermal activity). Within each of these sections, results are further sub-divided by the type of distress paradigm used. Summaries of key findings and risk of bias results for each outcome are presented in Table 3.

3.2.1. Cortisol

3.2.1.1. Fear paradigms

Parents' cortisol responses to their child's fear were measured in 20 studies of 12 unique samples in response to attachment- and novelty-related threats.

The Still Face Procedure (Crockett et al., 2013; Feldman et al., 2010; Khoury et al., 2021; Laurent et al., 2017; Morelius et al., 2015; Ramdas et al., 2021; Weisman et al., 2013) and adaptations of the Still Face Procedure (Feldman et al., 2010; Provenzi et al., 2019; Van Puyvelde et al., 2021) were the most common fear paradigms used to study parents' cortisol responses. Results consistently indicated a decrease in parental cortisol from the baseline to reactivity phases, including one study focused on fathers (Weisman et al., 2013), with effect sizes ranging from d= -0.86 to d= -0.08. The majority of these studies examined cortisol responses in parents of healthy infants, however, two focused on parents of pre-term (Morelius et al., 2015) and very pre-term (Provenzi et al., 2019) infants who were three to four months (corrected age) at the time of study participation. Parents in these studies also exhibited decreases in cortisol (d= -0.86 to d= -0.34), and an isolated finding was that parents of full-term infants exhibited a greater decline over time (d= -0.74) than parents of very pre-term infants (d= - 0.34; Provenzi et al., 2019).

Several studies examined parents' cortisol responses during attachment stressors involving separations and reunions, such as the standard lab-based Strange Situation Procedure

(Atkinson et al., 2013; Bader et al., 2021; Kern & Laurent, 2019; Khoury et al., 2016; Laurent et al., 2018; Laurent, Ablow, et al., 2011; Laurent et al., 2012; Laurent, Stevens, et al., 2011; Ludmer et al., 2017; Ramdas et al., 2021) or a comparable paradigm involving the Maternal Separation and Stranger Approach episodes of the Lab-TAB (Laurent et al., 2018; Ramdas et al., 2021; Volpe et al., 2020). Results again generally reflected declines in parent cortisol during the reactivity phase compared to baseline (*d*= -0.57 to *d*= -0.29). Among these studies was the largest study to date of fathers' stress responses during child distress (Bader et al., 2021), which found similar cortisol decreases from baseline to peak reactivity between mothers (*d*= -0.57) and fathers (*d*= -0.49). Only one of the samples studied displayed an increase in cortisol from baseline to peak stress (*d*= 0.27; Laurent et al., 2012). Growth modeling analyses based on this sample, which had been selected for low-income status and elevated risk for parenting problems, instead indicated that parents' cortisol reflected a quadratic curve characterized by an initial increase followed by a decrease approximately 45 minutes following the stressor (Laurent, Ablow, et al., 2011).

One study in this section (van Bakel & Riksen-Walraven, 2008) used a fear stressor that was designed to elicit distress to novelty, rather than attachment-related stress, with the key methodological difference with this type of task being that the parent is not generally the person causing the child's distress. Similar to other fear tasks, results reflected decreases in cortisol from baseline to reactivity. Cortisol decreases were larger for mothers who had been classified as "more sensitive" (*d*= -0.91) during a previous observation of parenting behaviour, compared to mothers classified as "less sensitive" (*d*= -0.71), although the effect for both groups was stronger than the effects reported above for studies examining attachment-related stress.

3.2.1.2. Frustration paradigms

Parents' cortisol responses to their child's frustration were measured in five studies of four unique samples using distress tasks designed to elicit child-focused or dyadic frustration.

All studies of child-focused frustration tasks found a relative decrease in parents' cortisol levels from baseline to reactivity (Atkinson et al., 2013; Bernard et al., 2017; Khoury et al., 2016; Luecken et al., 2019), regardless of whether the parent was the direct cause of the child's frustration (e.g., by removing or restricting access to a desired toy; Atkinson et al., 2013; Khoury et al., 2016) or was watching a researcher engage their child in a frustrating task (e.g., researcher gently restraining the child's arms; Bernard et al., 2017). Effect sizes were only available for two of the three samples in this section and ranged from d= -0.42 (Atkinson et al., 2013; Khoury et al., 2016) to d= -0.18 (Bernard et al., 2017).

One study measured cortisol levels during a dyadic frustration task. Parents in this study were reported to exhibit cortisol decreases in reaction to a discipline encounter with their toddler (Franz et al., 2021).

3.2.1.3. Additive fear and frustration paradigms

Six studies of four samples measured parents' cortisol responses following a series of child fear and frustration-based stressors completed consecutively over a short period of time. Because parents' cortisol responses to these paradigms would reflect their cumulative responses to their child's fear and frustration (due to the temporal non-specificity of salivary cortisol), these research designs are referred to here as additive fear and frustration paradigms.

Most studies in this section involved procedures designed to elicit child-focused frustration and distress to novelty across the various episodes. Parents typically had limited engagement in procedures, ranging from being instructed to sit beside their child while a researcher administered the procedures (Hibel et al., 2009; Hibel et al., 2015; Roque et al., 2012)

to being outside of the room and viewing their child participating in the study procedures via a monitor (Hendrix et al., 2018). Within all six of these studies, decreases in cortisol from baseline to post-task were reported (Cordero et al., 2017; Hendrix et al., 2018; Hibel et al., 2009; Hibel et al., 2015; Laurent et al., 2012; Roque et al., 2012), with effect sizes ranging from *d*= -1.46 to *d*= -0.16. One of these studies compared cortisol responses between mothers with secure attachments and mothers with insecure attachments and found that insecure mothers exhibited greater decreases in cortisol following the distress paradigm (Roque et al., 2012).

3.2.1.4. Naturalistic distress

Two studies measured parents' cortisol responses during naturalistic distress. Both studies examined parents' cortisol responses following a painful procedure in healthy infants, including a routine vaccination (Braarud & Stormark, 2006) and a heel stick blood draw (Spratt et al., 2016), and both had relatively small samples (*n*'s = 37 to 42). Spratt and colleagues (2016) reported a slight decrease in cortisol (*d*= -0.10), whereas Braarud and colleagues (2006) reported non-significant changes from baseline to post-procedure with no effect size available.

3.2.2. HRV

3.2.2.1. Fear paradigms

Parents' HRV responses to their child's fear were measured in 18 studies of 14 unique samples in response to attachment- and novelty-related threats.

As was the case for studies of parent cortisol, the Still Face Procedure was the most common paradigm used to study parents' HRV responses to their child's fear (Brown et al., 2021; Busuito et al., 2019; Feldman et al., 2010; Gao et al., 2022; Ham & Tronick, 2006; Lan et al., 2022; Leerkes et al., 2017; Mills-Koonce et al., 2009; Moore, 2009; Moore et al., 2009; Oppenheimer et al., 2013; Ostlund et al., 2017; Van Puyvelde et al., 2021; Xu & Groh, 2021).

During the Still Face episode, when parents were required to maintain a neutral facial expression through the entire episode, most studies reported relative increases or minimal changes in HRV during the Still Face episode (*d*= -0.08 to *d*= 0.66), compared to baseline. During the Reunion (i.e., recovery) episode, when parents could re-engage with and comfort their distressed infant, all studies found evidence for decreased HRV relative to baseline. The reunion episode tended to elicit a stronger HRV response than the Still Face episode, relative to baseline, and effect sizes ranged from *d*= -0.64 to *d*= 0.07. The tendency for decreased HRV from baseline to reunion is notable given that baseline conditions ranged from parents being seated without interacting with their child (Lan et al., 2022; Leerkes et al., 2017; Moore et al., 2009) to parents being asked to gaze quietly at their infant (Van Puyvelde et al., 2021) or interact with their infant (Busuito et al., 2019; Feldman et al., 2010; Gao et al., 2022; Xu & Groh, 2021). A possible interpretation of this trend is that parents are relatively less regulated (i.e., more physiologically aroused) when interacting with their distressed infant compared to low distress contexts.

Only two studies examined parents' HRV responses during separation-reunion paradigms (Hill-Soderlund et al., 2008; Schechter et al., 2014). Results were mixed, with one study finding a decrease (*d*= -0.25; Hill-Soderlund et al., 2008) in parents' HRV while they were separated from their infant and the other finding an increase (d= 0.5; Schechter et al., 2014) in HRV. These differences may be attributed to differences in the study populations (i.e., a community sample [Hill-Soderlund et al., 2008] versus a sample of mothers with a trauma history [Schechter et al., 2014]) or due to differences in parents' posture during the baseline condition. Namely, Schechter and colleagues (2014) compared HRV reactivity to a standing resting baseline to approximate the postural conditions of the Strange Situation Procedure separation episode more closely. Both

studies reported a relative decrease in parent HRV between baseline and the reunion episode; however, the only available effect size was very small (*d*= -0.09; Hill-Soderlund et al., 2008).

Studies that measured parents' HRV responses during tasks designed to elicit child distress to novelty also yielded mixed results (Augustine & Leerkes, 2019; Kiel et al., 2021; Leerkes et al., 2017). Increases in parents' HRV were found (*d*= 0.16 to 0.63) when children were approached for interaction by an unfamiliar adult (Augustine & Leerkes, 2019; Kiel et al., 2021), but a decrease was found when children were approached by a novel moving toy (*d*= -0.19; Leerkes et al., 2017).

3.2.2.2. Frustration paradigms

Parents' HRV responses to their child's frustration were measured in six studies of four unique samples using distress tasks designed to elicit child-focused frustration or dyadic frustration.

There were inconsistent findings regarding parents' HRV responses to child-focused frustration tasks. Across two studies that assessed the same sample of children during infancy and toddlerhood, mothers' HRV decreased from a resting baseline while a research assistant gently restrained her child's arms (*d*= -0.56; Leerkes et al., 2017) but increased during a toy removal task (*d*= 0.55; Augustine & Leerkes, 2019), relative to a play-based baseline episode.

Studies that examined dyadic frustration tasks also did not yield conclusive findings, likely due to between-study differences in the type of task used as well as how the baseline and reactivity conditions were defined, and a general paucity of data related to effect sizes. Three studies of two unique samples used the Parent-Child Challenge Task (PCCT), which required mother-toddler or father-toddler dyads to work together to complete a puzzle under time constraint (Fuchs et al., 2021; Lunkenheimer et al., 2017; Skoranski & Lunkenheimer, 2021). Results indicated relative increases or decreases in HRV that varied as a function of the baseline

condition (i.e., resting baseline vs. a non-challenging dyadic interaction) and the parent assessed (i.e., mother vs. father; Fuchs et al., 2021; Skoranski & Lunkenheimer, 2021). Effect sizes were available for only two studies and ranged from *d*= -0.25 to *d*= 0.1 (Fuchs et al., 2021; Lunkenheimer et al., 2017). The other study in this section observed mother-toddler dyads during a discipline encounter and found a relative decrease in parents' HRV, with no effect size available (Lorber & O'Leary, 2005).

3.2.3. Other cardiac outcomes

3.2.3.1. Fear paradigms

Parents' responses to their child's fear, as measured by alternative cardiac outcomes, were described in six studies of six unique samples in response to attachment-related threats. Studies of the Still Face Procedure measured parents' heart rate (Ham & Tronick, 2006; Oppenheimer et al., 2013) and R-R interval duration (Van Puyvelde et al., 2021), which is inversely related to heart rate. The Still Face episode elicited relative decreases in parents' heart rate (Ham & Tronick, 2006; Oppenheimer et al., 2013), with Oppenheimer (2013) reporting *d*= -0.38. Van Puyvelde (2021) found that heart period fluctuated minimally from baseline to the Still Face episode (*d*= -0.05 to *d*= -0.09); however, this sample had only 24 participants.

The two studies of separation-reunion procedures (e.g., the Strange Situation Procedure) used different measures of cardiac outcomes and both explored dynamics in mothers' cardiac responses throughout the procedure (Schechter et al., 2014; Sturge-Apple et al., 2011). Schechter and colleagues (2014) found relative decreases in mothers' heart rate between the separation (i.e., reactivity) and reunion episodes of the procedure (*d*= -0.76 to *d*= -0.66) after accounting for movement-related changes in heart rate by excluding the data collected while mothers exited and entered the room between episodes. In a supplemental analysis, the authors also found that

mothers diagnosed with interpersonal violence-related post-traumatic stress disorder (PTSD) exhibited a lower heart rate across the procedure, relative to both healthy controls and mothers with sub-threshold PTSD. Sturge-Apple and colleagues (2011) calculated mothers' sympathovagal balance, which reflects the ratio of sympathetic to parasympathetic nervous system activation. Mothers in this sample showed increases in sympathetic activation (i.e., increased sympathovagal balance) when separating from their children followed by decreases in sympathetic activation (i.e., decreased sympathovagal balance) upon reuniting.

3.2.3.2. Frustration paradigms

Only one study used an alternative cardiac outcome during a frustration-related stressor. This study, which measured mothers' heart rate during a mother-toddler discipline encounter, found a relative increase in mothers' heart rate compared to a resting baseline (Lorber & O'Leary, 2005).

3.2.4. sAA

3.2.4.1. Fear paradigms

Parents' sAA responses to their child's fear were measured in three studies of two unique samples in response to an attachment-related threat.

During the Strange Situation Procedure, studies found minimal declines in sAA levels between the baseline and reactivity phases (Hill-Soderlund et al., 2008; Laurent, Ablow, et al., 2011; Laurent et al., 2012), with effect sizes ranging from d = -0.11 to d= -0.07 (Hill-Soderlund et al., 2008; Laurent et al., 2012). One of these studies examined linear changes in sAA across the baseline, reactivity, and recovery phases of the Strange Situation Procedure (Laurent, Ablow, et al., 2011). Results indicated overall increases in sAA, with sAA levels at recovery being

higher than at baseline (*d*= 0.13; Laurent et al., 2012), which was postulated by the authors to reflect a delayed arousal response.

3.2.4.2. Additive fear and frustration paradigms

One study measured parents' sAA responses to an additive fear and frustration paradigm which included a series of tasks designed to elicit child distress to novelty and child-focused frustration (Laurent et al., 2012). Relative to baseline, mothers' sAA levels did not change during the reactivity phase (*d*= -0.01) and were marginally lower 20 minutes post-task (*d*= -0.1). Linear changes in sAA across the entire paradigm were near-zero.

3.2.5. Electrodermal activity

3.2.5.1. Fear paradigms

Parents' electrodermal activity responses to their child's fear were measured in four studies of three unique samples in response to attachment- and novelty-related threats.

Multiple studies reported substantial fluctuations in mothers' electrodermal activity, measured as skin conductance levels, during the Still Face Procedure (Busuito et al., 2019; Ham & Tronick, 2006; Leerkes et al., 2017). Mothers exhibited increases of *d*= 0.64 to *d*= 9.31 in skin conductance levels during the Still Face episode, relative to baseline, and similarly large increases in skin conductance levels during the reunion episode of the Still Face Procedure, relative to baseline (*d*= 0.8 to *d*= 9.08; Busuito et al., 2019; Leerkes et al., 2017), suggesting that parents' overall arousal increased throughout the task and remained high while they re-engaged with and soothed their infants during the reunion episode.

Mothers' responses to their children's novelty-related fear, although based on only one sample, indicated similar changes in skin conductance (Augustine & Leerkes, 2019; Leerkes et al., 2017). There were large increases in skin conductance levels while mothers observed their

child's fear in response to a novel toy (*d*= 7.32; Leerkes et al., 2017) and an interaction with an unfamiliar adult (*d*= 3.91; Augustine & Leerkes, 2019), compared to baseline.

3.2.5.2. Frustration paradigms

Parents' electrodermal activity responses to their child's frustration were measured in three studies of two unique samples using distress tasks designed to elicit child-focused or dyadic frustration. Studies that used child-focused frustration tasks reported large increases in mothers' skin conductance levels, compared to baseline, when mothers observed their child's frustration during an arm restraint procedure (*d*= 5.33; Leerkes et al., 2017) and a toy removal procedure (*d*= 2.78; Augustine & Leerkes, 2019). A mother-toddler discipline encounter was the only dyadic frustration task for which skin conductance responses were measured. Relative increases in skin conductance levels were also reported in this study; however, no effect sizes or statistical analysis results were provided (Lorber & O'Leary, 2005).

3.3. Aim 2: Associations between parents' physiological and behavioural responses

Syntheses pertaining to Aim 2 are organized by biological outcome (i.e., cortisol, HRV, other cardiac outcomes, and electrodermal activity; no studies examined associations with sAA). Within each of these sections, results are further sub-divided by the type of distress paradigm used. Summaries of key findings are presented in Table 3.

3.3.1. Cortisol

3.3.1.1. Fear paradigms

Only one study examined associations between parents' cortisol and behavioural responses to their child's fear; this study focused on attachment-related fear. Crockett and colleagues (2013) found that parents who exhibited severe disrupted communication (i.e., frightened, frightening, withdrawn, disoriented, or other odd behaviours) during the reunion

episode of the Still Face Procedure had lower overall cortisol levels across the baseline, reactivity, and recovery phases compared to mothers categorized as having moderate or non-disrupted communication (*d*= -0.86). However, the severe disrupted communication subgroup only included 3 of the 65 mothers in their sample, thus effect size results are unreliable.

3.3.1.2. Frustration paradigms

Only one study examined associations between parents' cortisol and behavioural responses during frustration paradigms and this study included a dyadic frustration paradigm. Franz (2021) found that mothers' change in cortisol levels (i.e., area under curve with respect to increase [AUC_i]) in reaction to a laboratory-based discipline encounter with their toddler was not correlated with their use of overreactive parenting behaviours (*r*= .02) or lax parenting behaviours (*r*= -.01) during the interaction.

3.3.1.3. Naturalistic distress

Only one study examined associations between parents' cortisol and behavioural responses to naturalistic distress and this study focused on infant routine vaccinations. Braarud and colleagues (2006) categorized mothers as "preparatory" or "contingent" based on whether they increased or decreased their use of soothing behaviours (i.e., physical contact and gaze to infant) from pre- to post-vaccination needle. They found no significant effect of group in predicting mothers' cortisol levels at baseline or after the needle (no effect sizes available).

3.3.2. HRV

3.3.2.1. Fear paradigms

Associations between parents' HRV and behavioural responses to their child's fear were measured in six studies of five unique samples during attachment-related and novelty-related stressors.

These studies reported no significant associations between parents' HRV and their behavioural responses during the Still Face Procedure, including their affective expression (i.e., positive, neutral, or negative affect; Busuito et al., 2019; Moore, 2009; Moore et al., 2009), positive and negative engagement with their infant (Ham & Tronick, 2009; Mills-Koonce et al., 2009), intrusiveness (Mills-Koonce et al., 2009), and withdrawn behaviour (Ham & Tronick, 2009). These studies examined associations between behaviour and either average HRV during the distress task (k=3 studies) or changes in HRV from baseline (k=2). Effect sizes were only reported by Mills-Koonce and colleagues (2009), who found near-zero associations between HRV withdrawal and both positive engagement (r= -.01) and intrusiveness (r= -.06).

During a novelty-related stressor, mothers' HRV withdrawal had a small, positive association (r= .11) with their level of sensitivity toward their toddler during novelty-related stressor (Augustine & Leerkes, 2019).

3.3.2.2. Frustration paradigms

Associations between parents' HRV and behaviour responses during child-focused and dyadic frustration tasks were measured in three studies of unique samples.

The only study that examined parent behaviour during a child-focused frustration task (i.e., toy removal) found a weak association between mothers' HRV withdrawal and sensitive parenting behaviour (r= .08; Augustine & Leerkes, 2019).

Two studies examined associations between HRV and parenting behaviour during dyadic frustration tasks. In one study, mothers who exhibited greater increases in HRV during a discipline encounter tended to use fewer overreactive discipline strategies with their toddler (i.e., behaviour reflecting anger or irritation; r= -.18; Lorber & O'Leary, 2005). Miller and colleagues (2015) examined associations between maternal warmth and negativity and mothers' average

HRV levels during two collaborative tasks of varied difficulty. Mothers with higher HRV levels during the slightly less challenging collaborative task tended to engage in less negative behaviour (e.g., criticism, disapproval) towards their toddler (r= -.30). In contrast, HRV levels were very weakly correlated with mothers' negative behaviour during the more challenging dyadic task (r= -.08) and with maternal warmth during both tasks (r= .04 to r= .06).

3.3.2.3. Combined fear and frustration paradigms

Two studies of unique samples examined associations between parents' HRV and behavioural responses that had been averaged across fear and frustration paradigms. In both studies, mothers' sensitive parenting behaviours were very weakly correlated with HRV withdrawal across a series of attachment- and novelty-related fear and child-focused frustration tasks (r= -.04 to r= .09; Leerkes et al., 2016; Mills-Koonce et al., 2007).

3.3.3. Other cardiac outcomes

3.3.3.1. Fear paradigms

Associations between alternative cardiac outcomes and behavioural responses during fear tasks were examined by three studies of unique samples, with all studies focusing on attachment-related fear paradigms.

No significant associations were found between parents' affective responses (i.e., positive, neutral, or negative affect), positive or negative engagement, or withdrawn behaviour, and their average heart period (Busuito et al., 2019; Moore et al., 2009) or heart rate (Ham & Tronick, 2009) during the Still Face Procedure (no effect sizes available).

3.3.3.2. Frustration paradigms

Associations between alternative cardiac outcomes and behavioural responses during frustration tasks were examined by two studies of unique samples, with both involving dyadic frustration paradigms.

During a discipline encounter, mothers who exhibited greater increases in heart rate during a discipline encounter tended to engage in more overreactive discipline (r= .39; Lorber & O'Leary, 2005). During collaborative challenge tasks, mothers' average pre-ejection period (PEP) levels had small associations with their expressed warmth (r= .15 to r= .22) and negativity (r= -.08 to r= .10) towards their toddlers (Miller et al., 2015). As PEP levels are considered to reflect sympathetic nervous system activity (Sherwood et al., 1990), this finding suggests that more physiologically aroused mothers tended to exhibit more sensitive parenting behaviour.

3.3.4. Electrodermal activity

3.3.4.1. Fear paradigms

Associations between parents' electrodermal activity and behavioural responses during fear tasks were examined by two studies of unique samples focusing on attachment-related and novelty-related fear.

During the Strange Situation Procedure, parents' average skin conductance levels were not significantly correlated with their expression of positive or negative affect, according to one study (Busuito et al., 2019). When parents observed their toddler during a novelty-related fear task (i.e., interaction with stranger), greater increases in skin conductance levels from baseline (i.e., greater arousal) were associated with more sensitive parenting behaviours (r= .29; Augustine & Leerkes, 2019).

3.3.4.2. Frustration paradigms

Associations between parents' electrodermal activity and behavioural responses during frustration tasks were examined by two studies of unique samples in the context of child-focused and dyadic frustration.

During a child-focused frustration task (i.e., toy removal), mothers who exhibited greater increases in skin conductance levels from baseline tended to use more sensitive parenting behaviours when soothing their toddler (r= .17; Augustine & Leerkes, 2019). In contrast, parents' increases in skin conductance levels were not associated with their use of overreactive discipline during a discipline encounter (r= .05; Lorber & O'Leary, 2005).

3.3.4.3. Combined fear and frustration paradigms

One study examined associations between parents' electrodermal activity, averaged across attachment- and novelty-related fear and child-focused frustration tasks, and their behavioural responses within each individual task. Parents' average increases in skin conductance level across tasks were very weakly associated with their use of sensitive behaviour during a novelty task (r= .04), the Still Face Procedure (r= .09), and an arm restraint task (r= .14; Leerkes et al., 2016).

4. Discussion

To examine the biopsychosocial processes underlying parents' socialization of emotion in early childhood, the current study was the first systematic review of parents' physiological and behavioural responses to their child's distress. We reviewed studies examining parents' acute stress responses in various distress contexts across infancy and toddlerhood as assessed by HPA axis and ANS indicators (Aim 1) and reviewed how these responses related to parenting behaviours enacted in response to child distress (Aim 2). Our synthesis of the literature

highlighted patterns in the direction and magnitude of parents' stress responses and their associations with parents' behaviour, which are discussed in the sections that follow.

4.1. Aim 1: Parents' physiological stress responses to their child's distress

4.1.1. Cortisol

Cortisol was the most frequently studied stress outcome within the included studies and was typically assessed in relation to infants' or toddlers' attachment-related fear but was also assessed in relation to novelty-related fear and dyadic or child-focused frustration. Consistently across studies, parents exhibited small to moderate decreases in cortisol in response to their children's distress. This was an unexpected finding, given that meta-analytic findings indicate that children exhibit cortisol increases in response to social threat-related stressors (Gunnar et al., 2009; Puhakka & Peltola, 2020). One interpretation of this is that parents do not experience stress as a result of witnessing their child's distress. A second and more likely explanation is that parents' cortisol reactivity to stress is limited by elevated baseline cortisol levels that occur due to the novel setting and routine stressor of getting young children to any type of appointment. Collecting ecologically valid baseline cortisol samples has been highlighted as a challenge within the cortisol literature (Gunnar et al., 2009). Whereas stressor studies with adults commonly incorporate an extended period of relaxing or non-stressful activities (Kirschbaum et al., 1993), doing so is less feasible in laboratory studies involving infants and toddlers who are not able to tolerate long laboratory sessions (Gunnar et al., 2009). One of the reviewed studies found that baseline cortisol samples collected 10 minutes after arrival in the lab were higher (d= 0.73) than cortisol samples collected at home on another day at the same time of day (Cordero et al., 2017). Given that most of the included studies reported collecting baseline cortisol samples soon after

arrival into the lab, it is reasonable to assume that elevated baseline stress levels caused a ceiling effect that obscured the detection of cortisol reactivity to the distress paradigms across studies.

A notable trend in the two studies of naturalistic stressors was that, in contrast to the consistent decreases in cortisol seen in experimental distress paradigms, minimal changes in parents' cortisol levels were reported in response to the naturalistic stressors, which both involved routine painful procedures (Braarud & Stormark, 2006; Spratt et al., 2016). Given that these studies faced the same limitation of a relative lack of adaptation period preceding baseline sample collection, one potential interpretation of this finding is that parents shift less towards homeostasis (i.e., remaining stressed) in response to their child's pain-related distress. Spratt and colleagues' (2016) finding that nearly half of mothers chose to step out of the room during their infant's heel stick procedure lends behavioural evidence for this hypothesis. Despite naturalistic distress contexts offering an opportune setting for understanding parents' reaction to child distress, most work in this area to date has focused on parents of older children (Constantin et al., 2021; Constantin et al., 2022), and further research with parents of young children is warranted.

4.1.2. HRV

HRV has gained popularity within the developmental psychology literature owing to its conceptualization as a measure of self-regulatory efforts (Porges et al., 1994), and was the most commonly studied cardiac outcome among the included studies. Unlike salivary cortisol, which reflects a time-lagged response of the HPA axis to stress, HRV reflects moment-to-moment fluctuations in ANS activity, allowing for greater specificity for examining the effects of experimental manipulations. Among the reviewed studies, evidence of parents' HRV responses to child distress was inconsistent, which is likely attributable to heterogeneity in the types of distress paradigms utilized and the baseline condition that HRV reactivity was compared to.

During the Still Face Procedure and separation-reunion tasks, two distress paradigms that are designed to elicit moderate attachment-related fear responses in children, parents tended to exhibit HRV withdrawal, relative to baseline, when they were able to re-engage with their child (i.e., reunion phase of Still Face Procedure and Strange Situation Procedure). HRV withdrawal during the reunion portions of these tasks may reflect a physiological shift that allows access to resources for managing a threat (in this case, a brief rupture to the attachment relationship) at a time when these extra resources can be put to use. The fact that multiple studies reported HRV withdrawal during the reunion episode as compared to a baseline episode of normal parent-child play lends further support to HRV withdrawal underlying parents' caregiving response, since the only difference in behavioural demands between these two episodes is the need to respond to the distressed infant.

Limited data were available on parents' HRV changes during other distress tasks, including frustration tasks, and there were no consistent trends in terms of the general direction of HRV changes across studies based on task type, child age, or the participating parent (mother vs. father). Notably, studies varied in terms of how they operationalized parents' baseline HRV levels, which likely explains much of the heterogeneity in results. In low stimulation resting baseline conditions, parents watched a relaxing video (e.g., Fuchs et al., 2021) or were simply instructed to sit quietly (e.g., Lorber & O'Leary, 2005). In higher stimulation baseline conditions, dyads were given toys and parents were instructed to interact as they normally would with their child (e.g., Augustine & Leerkes, 2019) or dyads worked together on a puzzle without a time constraint before a time constraint was added in the challenge condition (e.g., Skoranski & Lunkenheimer, 2021).

4.1.3. Other stress outcomes

Other stress outcomes examined within the included studies were sAA, skin conductance levels, and alternative cardiac outcomes (e.g., heart rate, heart period). An understanding of parents' autonomic stress responses as measured by these outcomes remains incomplete, based on the available data, as studies using these outcomes tended to be characterized by considerable methodological heterogeneity and potential risk of bias.

At present, there is no evidence for changes in parents' sAA in response to children's distress. However, parents' sAA responses have only been studied in two unique samples to date and the issue of baseline samples not reflecting a true resting state, based on the timing of sample collection, is likely relevant in both cases. Other studies have suggested that adults exhibit increases in sAA in response to both physical and psychological stressors (Nater & Rohleder, 2009), and so an opportunity remains to further explore the application of sAA in developmental psychology contexts.

There is a stronger case for changes in skin conductance levels in response to infant and toddler distress. Although based on a small pool of studies that were identified as having concerns related to risk of bias, findings across studies suggested substantial increases in parents' skin conductance (i.e., sympathetic arousal), which were similar in magnitude across fear and frustration-related tasks. Given that skin conductance level responses have been shown to reflect reactivity to emotional stimuli (van Dooren & Janssen, 2012) and correlate with subjective ratings of emotional arousal (Lang et al., 1993), findings to date provide preliminary support for parents' sympathetic nervous system reactivity to child distress in the context of laboratory-based stressors.

4.2. Aim 2: Associations between parents' physiological and behavioural responses

The second aim of the current investigation was to examine how parents' stress reactivity related to their behavioural responses to their child's distress. Ultimately, fewer than one-quarter of the included studies reported on concurrent associations between parents' physiological stress responses and their observed parenting behaviour, and a high degree of methodological heterogeneity among these studies precludes clear conclusions**.** However, two emerging trends are notable.

First, stronger associations between parents' physiological and behavioural responses tended to occur in the context of dyadic frustration tasks. One potential explanation for this finding is that the dyadic frustration tasks used in the included studies involved longer periods of unconstrained interaction between the parent and their distressed child, compared to fear-eliciting tasks during which parents were typically required to refrain from interacting with their distressed child until the distressing stimulus was removed, after which there was a brief reunion interaction. Extended periods of interaction between parents and their distressed child, such as during dyadic or collaborative parent-child tasks, may offer greater insights into parents' repertoire of behavioural strategies and how their behaviour evolves in response to fluctuating child distress levels from peak reactivity through to recovery. Since few studies coded parent behaviour during prolonged interactions in fear contexts, further research is needed to determine the extent to which distress type (i.e., fear vs. frustration) differentially impacts parents' stress response-behaviour associations.

Second, stronger associations emerged between measures of parents' ANS activity and their use of suboptimal or insensitive behaviour. Insensitive parent behaviour, defined within an attachment framework (Ainsworth et al., 1978), reflects parent behaviours that are non-attuned with the child's current emotional state. Parents' lower HRV levels, smaller increases in HRV,

and larger increases in heart rate in response to child distress were associated with higher levels of insensitive behaviours (e.g., negativity towards child, use of overreactive discipline). This finding supports theoretical assertions in the infant pain literature (Pillai Riddell et al., 2022) regarding potential mechanisms underlying parents' use of insensitive behaviours by suggesting that parents who were less able to regulate their own arousal were more likely to use suboptimal soothing behaviours that reflected a dysregulated emotional state. Considering the trends in parents' ANS responses identified in Aim 1, a preliminary interpretation is that while parents generally exhibit increased sympathetic activity and decreased parasympathetic activity when engaging with their distressed child, appropriate and attuned caregiving responses are predicated on parents being able to modulate or limit their own stress responses. Collectively, these results suggest that measuring parent responses across multiple stress outcomes and coding both sensitive and insensitive aspects of parent behaviour are important for understanding parents' responses to their child's distress.

4.3. Risk of Bias and Methodological Recommendations for Future Research

The nuances and complexity of physiological data collection and the many methodological factors that can have a strong impact on study findings necessitated the development of a risk of bias tool that examined specific sources of potential bias with relevance to the current study. Informed by exemplars and standards recommended for psychophysiological research, our risk of bias measure identified that nearly half of the reviewed studies evidenced high risk of bias in at least one domain.

High bias risk was most often related to the way that authors defined, collected, or analyzed physiological outcome measures. For example, many studies either did not collect resting baseline physiological data or used a baseline or comparator condition that would be

likely to elicit parents' cognitive or emotional arousal (e.g., reading to, playing with, or solving a puzzle with their child, or providing a cortisol sample shortly after the completion of a trauma assessment). While there are often compelling reasons for including a non-resting baseline – for example, to differentiate between parents' stress responses during a normal interaction with their child compared to a distressing interaction – this approach contributes to heterogeneity in how changes from baseline can be interpreted across studies, thereby limiting the generalizability and consolidation of study findings. Other factors contributing to high risk of bias included reporting high levels of attrition or missing participant data without examining mechanisms of missing data (e.g., associations with sociodemographic factors) and inconsistent or post-hoc implementation of inclusion and exclusion criteria (e.g., excluding dyads in which children showed atypical behavioural responses; Braarud & Stormark, 2006; Lorber & O'Leary, 2005), which further limit study generalizability and can lead to biased effect estimates.

Based on the high number of studies with either high or unclear risk of bias across domains, we offer the following recommendations to enhance the validity of future investigations of physiological outcomes in developmental psychology contexts. First, as discussed above, authors should aim to collect valid "resting" baseline observations which allows for a period of acclimation to measurement equipment and accounts for the time-lagged responses of the physiological outcome, when applicable (e.g., cortisol). Second, whenever possible, participants should be asked to refrain from confounding influences (e.g., food and drink intake, exercise, medication) prior to study participation to minimize measurement error and eliminate confounds. At minimum, authors should measure and control for these variables in analyses. Third, authors should report and investigate the presence of missing data, including missing data due to attrition. Missing data is common in physiological studies (e.g., due to

insufficient saliva production, movement artifacts, etc.) and cannot necessarily be assumed to be missing completely at random. For example, one study found that mother-child dyads with resistant attachments had a higher likelihood of having missing data, due to the children removing electrodes (Hill-Soderlund et al., 2008). Fourth, we recommend that authors consult published guidelines on best practices for the measurement and analysis of physiological outcomes when designing, conducting, analyzing, and reporting physiological outcomes (Boucsein et al., 2012; Laborde et al., 2017; Quintana et al., 2016; Rohleder & Nater, 2009; Task Force, 1996).

In addition to the methodological limitations described above, our review uncovered several areas in need of future investigation to support a better understanding of the mechanisms underlying parenting responses. For example, despite global trends reflecting fathers' increasing role in primary caregiving responsibilities (Cabrera et al., 2000), fathers continue to be underrepresented in this body of research. Evolutionary theory (Möller et al., 2013) and preliminary data (Fuchs et al., 2021; Skoranski et al., 2021) support differences in how mothers and fathers respond to their child's distress that are reflected at a physiological level. Future investigations should examine how these differences present as a function of physiological outcome and distress context, as well as their implications for caregiving behaviours. Furthermore, studies examining concurrent associations between parents' physiological and behavioural responses in the context of child distress are much needed. In light of the current findings, studies that minimize constraints to parents' behaviour and code both positive (i.e., sensitive) and sub-optimal (i.e., insensitive) aspects of parents' behaviour, based on consideration of how parent behaviours align with the child's current state, reflect a particular gap. Finally, future studies should account for key clinical variables including parents' current

psychiatric symptoms, attachment representations, and parenting experience, which have been demonstrated to impact on adults' stress physiology even in community (i.e., non-clinical) samples (Leerkes et al., 2016, 2017; Out et al., 2010; Roque et al., 2012).

4.4. Limitations and Conclusions

Our findings should be considered in the context of some potential limitations. First, in keeping focus on parents' physiological and behavioural responses exclusively, the influence of child behaviour and physiology were not accounted for but likely strongly contribute to parents' responses. Given that multiple reviews have focused on characterizing infants' and children's physiological responses to distress paradigms (Gunnar et al., 2009; Jansen et al., 2010; Jones-Mason et al., 2018; Puhakka & Peltola, 2020; Waxman et al., 2020) as well as parent-child physiological attunement during distress paradigms (Davis et al., 2018; Di Lorenzo et al., 2022), a review dedicated to understanding parents' biological and behavioural responses adds important perspective to our knowledge of parent-child interaction dynamics. However, we acknowledge the dyadic nature of this interaction. In addition, while we opted to exclude studies using brain-based measures of parents' stress responses (e.g., EEG, fMRI) due the very few studies identified, we acknowledge that brain-based measurement offers a unique perspective into the mechanisms underlying parenting responses and encourage future reviews to incorporate this emerging area of research.

In conclusion, our review provides a comprehensive synthesis of the literature examining how parents respond to their child's distress during early childhood from both a biological and behavioural perspective. Findings build on existing theory concerning the intergenerational transmission of self-regulatory abilities from parents to children and highlight methodological

limitations in the existing literature that should be addressed in future work to facilitate further synthesis of knowledge within the field.

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Table 1

Characteristics of included studies.

Research group	Reference	Sample	Special characteristics	Child age (range or mean)	Distress paradigm(s)	Biological outcome(s)
Atkinson	(Atkinson et al., 2013)	297 mothers		16 and 17 months	Strange Situation Procedure Toy Frustration Task	Cortisol
	(Khoury et al., 2016)	297 mothers		16 and 17 months	Strange Situation Procedure Toy Frustration Task	Cortisol
	(Ludmer et al., 2017)	296 mothers		17 months	Strange Situation Procedure	Cortisol
Durham Child Health and Development Study	(Hill-Soderlund et al., 2008)	132 mothers		13 months	Strange Situation Procedure	sAA HRV
	(Mills-Koonce et al., 2007)	148 mothers		6 months	Still Face Procedure Lab-TAB Arm Restraint	HRV
	(Mills-Koonce et al., 2009)	175 mothers		7 months	Still Face Procedure	HRV
	(Moore, 2009)	152 mothers		6 months	Still Face Procedure (with emotion exposure)	Heart Period HRV
Family Life Project	(Hibel et al., 2009)	702 mothers	Low income, rural families	5 to 13 months	Lab-TAB Mask Presentation, Barrier Task, and Arm Restraint	Cortisol
	(Hibel et al., 2015)	1141 mothers		7, 15, and 24 months	Lab-TAB Mask Presentation, Barrier Task, and Arm Restraint	Cortisol
From Pregnancy to Parenting Your First Baby project	(Laurent, Ablow, et al., 2011)	86 mothers	Low income, selected for risk for parenting problems	17 months	Strange Situation Procedure	sAA Cortisol
	(Laurent, Stevens, et al., 2011)	22 mothers		18 months	Strange Situation Procedure	Cortisol

	(Laurent et al., 2012)	86 mothers		18 months	Strange Situation Procedure Lab-TAB Fear and Frustration Tasks	sAA Cortisol
	(Oppenheimer et al., 2013)	81 mothers		3 to 7 months	Still Face Procedure	HRV Heart Rate
	(Ostlund et al., 2017)	95 mothers		3 to 7 months	Still Face Procedure	HRV
Ham/Tronick	(Ham & Tronick, 2006)	12 mothers		5 months	Still Face Procedure	Skin Conductance Level HRV Heart Rate
	(Ham & Tronick, 2009)	18 mothers		5 months	Still Face Procedure	HRV Heart Rate
Laurent	(Kern & Laurent, 2019)	47 mothers	Low income	12 months	Strange Situation Procedure	Cortisol
	(Laurent et al., 2017)	73 mothers		6 months	Still Face Procedure	Cortisol
	(Laurent et al., 2018)	54 mothers		18 months	Lab-TAB Maternal Separation and Stranger Approach Tasks	Cortisol
	(Ramdas et al., 2021)	73 mothers		6, 12, and 18 months	Still Face Procedure Strange Situation Procedure Lab-TAB Maternal Separation and Stranger Approach Tasks	Cortisol
	(Volpe et al., 2020)	79 mothers		6, 12, and 18 months	Still Face Procedure Strange Situation Procedure Lab-TAB Maternal Separation and Stranger Approach Tasks	Cortisol
Leerkes	(Augustine & Leerkes, 2019)	208 mothers		13 months	Stranger in costume Toy Removal Variation	Skin Conductance Level HRV
	(Leerkes et al., 2016)	211 mothers		6 months	Novel Toy Approach Prolonged Arm Restraint Still Face Procedure	Skin Conductance Level HRV
	(Leerkes et al., 2017)	230 mothers		6 months	Novel Toy Approach Prolonged Arm Restraint Still Face Procedure	Skin Conductance Level HRV
Lunkenheimer 1	(Lunkenheimer et al., 2017)	96 mothers		3 years	Parent Child Challenge Task	HRV

Lunkenheimer 2	(Fuchs et al., 2021)	71 mothers 47 fathers	Socioeconomic risk (low income, Child Protective services involvement, or life stress)	3 years	Parent Child Challenge Task	HRV
	(Skoranski & Lunkenheimer, 2021)	126 mothers 87 fathers		3 years	Parent Child Challenge Task	HRV
Fetal Neurobehavioral Development and Postnatal Continuity	(Busuito et al., 2019)	140 mothers		6 months	Still Face Procedure	Skin Conductance Level HRV Heart Period
Unique	(Moore et al., 2009)	48 mothers		6 to 8.5 months	Still Face Procedure	HRV
Unique	(Bader et al., 2021)	141 mothers 125 fathers		12 and 13 months	Strange Situation Procedure	Cortisol
Unique	(Brown et al., 2021)	47 mothers	Public welfare-involved families	6 to 14 months	Still Face Procedure	HRV
Unique	(Bernard et al., 2017)	182 mothers	Parent psychological risk (exposure to intimate partner violence)	11 to 15 months	Lab-TAB Arm Restraint	Cortisol
Unique	(Braarud & Stormark, 2006)	37 mothers		3 months	Needle (Routine Vaccination)	Cortisol
Unique	(Cordero et al., 2017)	37 mothers	Parent psychological risk (sub-sample with PTSD related to interpersonal violence)	12 to 42 months	Modified Cromwell Procedure	Cortisol
Unique	(Crockett et al., 2013)	63 mothers	Low income	4 months	Still Face Procedure	Cortisol
Unique	(Feldman et al., 2010)	53 mothers		6 months	Still Face Procedure Still Face + Touch Procedure	Cortisol HRV
Unique	(Franz et al., 2021)	78 mothers	Parent psychological risk (exposure to trauma)	18 to 36 months	Discipline Encounter Protocol	Cortisol

Unique	(Gao et al., 2022)	106 mothers	Parent psychological risk (sub-sample with high levels of self-rated emotion dysregulation)	6 months	Still Face Procedure	HRV
Unique	(Hendrix et al., 2018)	233 mothers	Parent psychological risk (history psychiatric illness, most commonly depression)	4 to 7 months	Arm Restraint and Noise Burst	Cortisol
Unique	(Khoury et al., 2021)	150 mothers	Parent psychological risk (sub-sample with exposure to childhood abuse, neglect and/or domestic violence)	4 months	Still Face Procedure	Cortisol
Unique	(Kiel et al., 2021)	120 mothers		2 to 3 years	Clown Task	HRV
Unique	(Lan et al., 2022)	204 mothers	Low income	4 to 8 months	Still Face Procedure	HRV
Unique	(Lorber & O'Leary, 2005)	93 mothers		2 to 3 years	Discipline Encounter Protocol Phone Task	Skin Conductance Level HRV Heart Rate
Unique	(Luecken et al., 2019)	204 mothers	Low-income Mexican-American mothers	12 weeks	Lab-TAB Arm Restraint	Cortisol
Unique	(Miller et al., 2015)	83 mothers		3.5 years	Puzzle Task Origami Task	HRV Pre-ejection period
Unique	(Morelius et al., 2015)	32 mothers	Preterm infants	4 months corrected age	Still Face Procedure	Cortisol
Unique	(Provenzi et al., 2019)	109 mothers	Child risk (health risk; half of sample very preterm)	3 months corrected age	Double Still Face Procedure	Cortisol
Unique	(Roque et al., 2012)	51 mothers		18 to 26 months	Emotion Regulation Paradigm	Cortisol

Unique	(Schechter et al., 2014)	54 mothers	Parent psychological risk (sub-samples with PTSD related to interpersonal violence and sub-threshold PTSD)	18 to 48 months	Separation-Reunion Procedure	Heart Rate HRV
Unique	(Spratt et al., 2016)	42 mothers		1 month	Needle (Heel Stick)	Cortisol
Unique	(Sturge-Apple et al., 2011)	153 mothers	Half low-income families	17 to 19 months	Strange Situation Procedure	Sympathovagal balance
Unique	(van Bakel & Riksen-Walraven, 2008)	81 mothers 2 fathers		15 months	Stranger/Robot Procedure	Cortisol
Unique	(Van Puyvelde et al., 2021)	33 mothers		3 to 8 weeks	Still Face Procedure (with Gentle Touch Stimulation)	Cortisol HRV R-R Interval
Unique	(Weisman et al., 2013)	35 fathers		4 to 8 months	Still Face Procedure	Cortisol
Unique	(Xu & Groh, 2021)	139 mothers		6 months	Still Face Procedure	HRV

Note: HRV = Heart Rate Variability; PTSD = Post-Traumatic Stress Disorder; sAA = salivary alpha amylase

Table 2

Risk of bias of included studies.

Reference	Validity and reliability of physiological measures	Consideration of key confounding variables	Validity and reliability of behavioural measures	Influence of missing data	Implementation of inclusion/exclusion criteria	Item(s) contributing to high risk of bias of physiological outcome
(Atkinson et al., 2013)						
(Augustine & Leerkes, 2019)						Collection of baseline physiological data Physiological measurement parameters
(Bader et al., 2021)						
(Bernard et al., 2017)						
(Braarud & Stormark, 2006)						
(Brown et al., 2021)						Physiological measurement parameters
(Busuito et al., 2019)						Collection of baseline physiological data
(Cordero et al., 2017)						
(Crockett et al., 2013)						
(Feldman et al., 2010)						Collection of baseline physiological data
(Franz et al., 2021)						Collection of baseline physiological data
(Fuchs et al., 2021)						Physiological measurement parameters
(Gao et al., 2022)						Collection of baseline physiological data Physiological measurement parameters
(Ham & Tronick, 2006)						Collection of baseline physiological data Clear definition of physiological outcome(s)
(Ham & Tronick, 2009)						Collection of baseline physiological data Clear definition of physiological outcome(s)
(Hendrix et al., 2018)						
(Hibel et al., 2009)						
(Hibel et al., 2015)						
(Hill-Soderlund et al., 2008)						Physiological measurement parameters
(Kern & Laurent, 2019)						
(Khoury et al., 2016)						
(Khoury et al., 2021)						
(Kiel et al., 2021)						Physiological measurement parameters
(Lan et al., 2022)						
(Laurent, Ablow, et al., 2011)						
(Laurent, Stevens, et al., 2011)						
(Laurent et al., 2012)						Collection of baseline physiological data
(Laurent et al., 2017)						

(Laurent et al., 2018)						
(Leerkes et al., 2016)						Physiological measurement parameters
(Leerkes et al., 2017)						Physiological measurement parameters
(Lorber & O'Leary, 2005)						Physiological measurement parameters Physiological data processing procedures
(Ludmer et al., 2017)						
(Luecken et al., 2019)						
(Lunkenheimer et al., 2017)						Collection of baseline physiological data
(Miller et al., 2015)						Collection of baseline physiological data
(Mills-Koonce et al., 2007)						
(Mills-Koonce et al., 2009)						
(Moore, 2009)						
(Moore et al., 2009)						
(Morelius et al., 2015)						
(Oppenheimer et al., 2013)						
(Ostlund et al., 2017)						
(Provenzi et al., 2019)						
(Ramdas et al., 2021)						
(Roque et al., 2012)						
(Schechter et al., 2014)						
(Skoranski & Lunkenheimer, 2021)						
(Spratt et al., 2016)						
(Sturge-Apple et al., 2011)						Collection of baseline physiological data Physiological measurement parameters
(van Bakel & Riksen-Walraven, 2008)						
(Van Puyvelde et al., 2021)						
(Volpe et al., 2020)						
(Weisman et al., 2013)						
(Xu & Groh, 2021)						

Note. Red shading indicates high risk of bias, yellow indicates unclear risk of bias, green indicates low risk of bias, and grey indicates non-applicable domain.

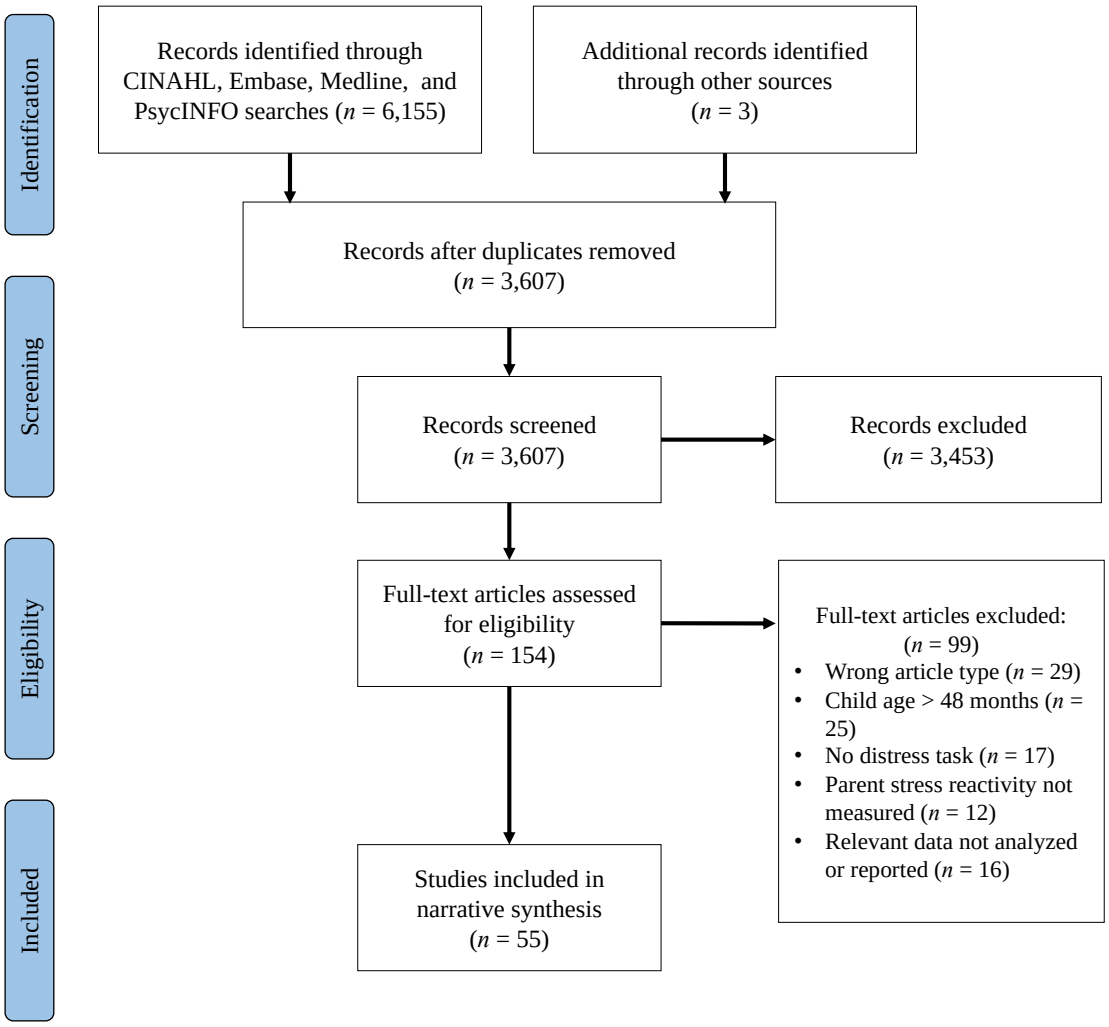
Table 3. Summary of review findings.

Aim 1	**Summary**
Cortisol	Nearly all studies assessing parents' cortisol responses to their child's distress found decreases in cortisol levels, compared to baseline, with most effect sizes between *d*= 0.2 and 0.8. This finding was consistent across attachment-related fear paradigms, distress to novelty fear paradigms, child-focused frustration paradigms, and additive fear and frustration paradigms, but was not replicated in the two studies that used naturalistic stress paradigms, both of which found minimal changes in cortisol. Approximately one third of studies in this section were rated as having a high risk of bias in at least one domain and risk of bias status did not relate to differences in findings across studies. Studies also varied on the location of data collection (i.e., in home vs. in lab), however, no clear trends emerged related to location.
HRV	Studies measuring parents' HRV responses to child distress were heterogeneous in terms of the comparator condition used as a baseline and constraints on parents' behaviour during their child's distress. Across fear paradigms, a consistent finding was a relative decrease in HRV during attachment-related stressors when parents re-engaged with their distressed child, with most effect sizes between *d*= 0 and 0.6. Results from frustration paradigms did not reflect consistent trends and limited effect sizes were available. Most studies in this section were rated as exhibiting high risk of bias, most often for failing to collect resting physiological data. However, the trends noted for fear paradigms were replicated in low risk of bias studies.
Other cardiac outcomes	Studies measuring parents' cardiac responses to child distress using other outcomes were methodologically heterogeneous and all but one had a high risk of bias in at least one domain. Some evidence suggested that parents' heart rate tended to decrease during the Still Face episode of the Still Face Procedure, as would be expected based on the episode's behavioural constraints. In addition, two studies examining dynamics in parents' cardiac responses during separation-reunion procedures found decreases in heart rate and sympathetic activation, respectively, between separations and reunions.
sAA	Few studies have examined fluctuations in parent sAA in response to child distress. The limited data available suggest minimal sAA changes in response to children's attachment-related stress and additive fear and frustration. However, two of the three studies of sAA were judged to have a high risk of bias in at least one domain and all studies collected baseline sAA samples soon after arrival in the lab, which may have impacted the validity of the baseline sample.
Electrodermal activity	All studies of electrodermal activity used skin conductance levels as the primary outcome. Trends were consistent across studies and reflected relative increases in skin conductance levels (i.e., increases in parents' physiological arousal) in response to attachment-related fear, novelty-related fear, child-focused frustration, and dyadic frustration. Effect sizes for fear and frustration tasks consistently indicated substantial effects and ranged from *d*= 0.64 to 9.31 across studies. However, all included studies were judged to have a high risk of bias in at least one domain.
Aim 2	
Cortisol	Studies in this section were methodologically heterogeneous and limited by relatively small sample sizes and high risk of bias in at least one domain for two of three studies. Overall, minimal evidence emerged for associations between parents' cortisol and behavioural responses to their child's distress.

HRV	Studies in this section examined associations between parents' HRV levels or changes (i.e., augmentation or withdrawal) and a range of sensitive and insensitive behavioural responses to child distress. Minimal associations between parents' HRV responses and behavioural responses emerged, however, two studies linked higher parental HRV with lower use of insensitive behaviour during dyadic frustration tasks (r= -.18 to -0.3). More than half of the studies in this section were judged to have a high risk of bias in at least one domain, including both studies that reported effects.
Other cardiac outcomes	Among the five studies that examined alternative cardiac outcomes in relation to parents' behaviour, no significant associations or effect sizes were reported for fear tasks. Among studies of dyadic frustration, higher levels of physiological arousal, as measured by heart rate and PEP, were associated with greater use of insensitive parenting behaviour (r= -.08 to .39) and parental warmth (r= .15 to .22). However, most studies in this section were judged to have a high risk of bias in at least one domain, including both studies that found effects.
Electrodermal activity	Some evidence emerged for small positive associations (r= .05 to .29) between greater physiological arousal as measured by skin conductance levels and sensitive parenting behaviours during child-focused frustration and novelty-related fear. However, all four studies in this section were rated to have a high risk of bias in at least one domain.

Figure 1

PRISMA flow chart.



CHAPTER 3: INVESTIGATING PHYSIOLOGY-BEHAVIOUR ASSOCIATIONS IN NATURALISTIC DISTRESS CONTEXT

Study 1 reviewed and synthesized a burgeoning area of research exploring the physiological substrates of parenting a child in distress. To date, several reviews have focused on the respective impacts of parents' behavioural responses (Samdan et al., 2020; Sobol-Kwapińska et al., 2020) and physiological responses (Davis et al., 2018; Di Lorenzo et al., 2022; Rattaz et al., 2020) on children's regulation from distress. Yet, a basic understanding of normative parent physiological responses to child distress (e.g., the direction and magnitude of change in physiological outcomes) — and how these responses may be reflected in parenting behaviour — has been limited. Parents' physiological responses to distressing situations are considered an indicator of parents' own underlying self-regulatory abilities which, along with behavioural responses, are key variables in pathways linking parental influences to children's self-regulatory outcomes (Bridgett et al., 2015). Study 1 reviewed the extant literature on how parents' self-regulatory physiology during a stressful situation with their child relates to their parenting behaviours towards their distressed child.

A narrative synthesis approach was used to summarize the literature so that the various sources of methodological heterogeneity identified across studies as well as relevant sources of study bias could be integrated into the discussion of trends across studies. Several findings emerged which both furthered an understanding of what shapes parents' physiological responses to their child's distress and highlighted key methodological barriers and gaps in the literature that continue to limit progress towards an improved understanding of these responses. Key findings from Study 1 that lay the foundations for the research questions and hypotheses addressed in Studies 2 and 3 are discussed below.

The first aim of Study 1 was to characterize parents' physiological stress responses to their child's distress. Parents' physiological responses as measured by cortisol, cardiac outcomes (e.g., heart rate variability [HRV], heart rate), salivary alpha amylase, and skin conductance were considered. HRV responses were the second most-commonly studied physiological outcome (after cortisol) and offered the most consistent and compelling evidence for a normative parent physiological response to child distress. This finding is likely due to the temporal specificity of cardiac outcome measurement which makes cardiac outcomes favourable for capturing moment-to-moment fluctuations in parents' physiological reactivity. A key finding from Study 1 was that parents exhibit decreases in HRV (i.e., vagal withdrawal), relative to baseline, when re-engaging with their distressed child immediately after an attachment stressor (i.e., a brief period of parental unavailability). The fact that parents tend towards vagal withdrawal in this controlled, experimental context in response to their child's mild to moderate distress suggests that, at some level, parents experience their child's distress as a threat to their own homeostasis requiring additional physiological resources to manage. A lack of studies (only two of the 55 included studies) of child distress in a naturalistic setting was a significant limitation of the extant literature that leaves questions concerning generalizability to real life parent-child interactions under distressing circumstances.

The second aim of Study 1 was to examine how parents' physiological responses relate to their concurrent behavioural responses. Less than one-quarter of the included studies examined how parents' physiological responses relate to their concurrent parenting behaviours, underlining the need for further work in this area. The first conclusion was that parents' physiological reactivity was more strongly associated with parents' use of *insensitive* behaviour, compared to *sensitive* behaviour, such that parents with greater increases in physiological arousal or smaller

regulatory (i.e., HRV) responses used more insensitive behaviour. Insensitive behaviours are those that are not attuned with the child's current needs and can have a stronger influence on children's recovery from distress than more positive or sensitive aspects of parent behaviour (Badovinac et al., 2018). The second conclusion was that parents' physiology and behaviour had stronger associations in the context of dyadic frustration tasks, which are designed to elicit stress in both the parent and the child, than distress tasks used in most other reviewed studies.

Based on Study 1, the extant literature consists of very little research that characterizes parents' physiological responses to their child's distress in naturalistic contexts and investigates concurrent associations with parenting behaviour. Studies 2 and 3 — presented in Chapters 4 and 6, respectively — are observational cohort studies that build directly on Study 1 by targeting this gap and drawing on the conclusions gleaned from Study 1. Both studies are based on a cohort of parent-toddler dyads who were observed during a highly distressing and acutely painful distressing event (i.e., toddlers' routine vaccinations) that is known to be stressful for parents (Bernard & Cohen, 2006) as well as toddlers. Study 2 (Chapter 4) describes the development and validation of an observational measure of parents' insensitive behaviour (i.e., behaviour that promotes toddler distress). Study 2, in turn, laid the foundation for Study 3 (Chapter 6), which brings together physiological, behavioural, and psychological aspects of parents' responses to toddlers' distress during routine vaccination.

Study 2 builds on findings from Study 1 and the broader pediatric pain literature which suggest that insensitive parenting behaviours are an important component of parents' responses to their child's distress that have a significant influence on children's distress levels (Sobol-Kwapińska et al., 2020) and appear to relate to parents' underlying physiological state. Existing measures used to characterize parents' use of insensitive behaviours in response to children's

distress in a pain context have been criticized for a primary or exclusive focus on parents' verbalizations, which does not capture non-verbal parent behaviours such as sub-optimal facial expressions, proximity, and eye contact that are known to contribute to children's distress (Bai et al., 2018). To address this limitation, Study 2 developed and provided evidence for the validity of a measure of a broader range of parents' distress-promoting behaviour during routine vaccination.

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CHAPTER 4: A MEASURE OF CAREGIVERS' DISTRESS-PROMOTING BEHAVIOURS DURING TODDLER VACCINATION: VALIDATION OF THE OUCHIE-RV[1]

Introduction

Parents and other primary caregivers[2] play a central role in supporting infants' and young children's ability to cope with pain-related distress (Sobol-Kwapińska et al., 2020). Efforts to better understand caregivers' influence on acute pain outcomes in early childhood have led to the development of behavioural coding systems which characterize and quantify various aspects of caregiving behaviour during painful medical procedures, such as the Child-Adult Medical Procedure Interaction Scale (CAMPIS; Blount et al., 1989) and the Measure of Adult and Infant Soothing and Distress (MAISD; Cohen et al., 2005). Most coding systems focus on measuring frequently observed aspects of caregiver behaviour to examine how individual behaviours or clusters of behaviours relate to child pain outcomes. However, these coding systems have been suggested to be limited by a lack of a theoretical foundation and an underrepresentation of caregiver non-verbal behaviours (Bai et al., 2018). Therefore, the current study aimed to provide evidence to support the validity of a new researcher-oriented version of a measure of caregiver behaviour during toddler vaccination, the **O**pportunities to **U**nderstand **C**hildhood **H**urt's **I**noculation **E**valuation – **R**esearch **V**ersion (OUCHIE-RV), that addresses limitations of existing coding systems, incorporates current theory and research concerning the impact of insensitive or distress-promoting caregiver behaviours on pain-related distress (Pillai Riddell et al., 2022;

[1] Chapter 4 is the author's version of the published manuscript: Badovinac, S.D., Flora, D.B., Edgell, H., Flanders, D., Garfield, H., Weinberg, E., Savlov, D., & Pillai Riddell, R. (2023). A measure of caregivers' distress-promoting behaviors during toddler vaccination: Validation of the OUCHIE-RV. *Journal of Pediatric Psychology.* Advance online publication. https://doi.org/10.1093/jpepsy/jsad050

[2] The terms parent and caregiver are used interchangeably within the current manuscript.

Sobol-Kwapińska et al., 2020), and conforms to best practice guidelines for the development of behavioural coding systems in pediatric psychology (Chorney et al., 2015).

Historical and theoretical foundations of the OUCHIE tools

The predecessor to the current OUCHIE-RV tool was the OUCHIE – Clinical Version (OUCHIE-CV; Pillai Riddell, Gennis et al., 2018). The fundamental difference between the current tool and its predecessor is that the earlier version was a clinical tool intended for *in vivo* (i.e., scored as the appointment was taking place) use by health professionals providing vaccinations, whereas the current measure is intended for more fine-grained *post hoc* coding based on video footage. The previous version focused on the presence or absence of eight core caregiver behaviours that exacerbated infant distress and were not captured by existing observational tools. These behaviours were identified based on consultation with experts in observational coding of caregiver sensitivity or infant pain-related distress, observation of thousands of infant vaccination appointments, and a series of discussion groups with clinicians who provide vaccinations (see Pillai Riddell, Gennis et al., 2018 for more detail). The current measure (OUCHIE-RV) evolved from this foundation to provide more fine-grained data on the frequency *and* intensity of these distress-promoting behaviours for intended use in research contexts. Moreover, it evolved to focus on three behavioural domains (i.e., affect incongruence, attention diversion, physical distance) that were derived from the eight discrete behaviours.

The OUCHIE tools draw on core theoretical frameworks within the developmental psychology literature (i.e., Ainsworth's [1974] concept of parental sensitivity and the Emotional Availability framework [Biringen, 2000]) and the pediatric pain literature (i.e., the Development of Infant Acute Pain Responding- Revised model [DIAPR-R 2022; Pillai Riddell et al., 2022]). The Emotional Availability framework and Ainsworth's concept of parental sensitivity, which

are both grounded in Attachment Theory (Bowlby, 1969/1982), define dimensions of caregiving responses that influence the quality of caregiver-child interactions in distress and non-distress contexts (Ainsworth et al., 1974; Biringen, 2000). A fundamental principle of both frameworks is that caregiver behaviour must be understood in the caregiver-child dyadic context. According to this view, most discrete behaviours are not inherently sensitive or insensitive; rather, the appropriateness of a behaviour is defined by the degree of attunement or non-attunement between the child's signaled need and the caregiver's contingent response. This principle underlies a core feature of the OUCHIE tools, which is that caregiver behaviours are only coded when the child is in *moderate to high pain-related distress*. According to Attachment Theory, moderate to high distress behaviours (e.g., crying) are clear signals from the child of an acute attachment need for caregiver proximity and comfort. Focusing on moments of moderate to high distress allows for theoretically informed assumptions regarding which specific caregiver behaviours support or undermine adaptive regulation of pain-related distress.

The OUCHIE-RV behaviour domains reflect caregiver responses that, based on theory and decades of pediatric pain research, have been demonstrated or hypothesized to maintain or exacerbate child distress in acute pain contexts (e.g., routine vaccinations). Fundamentally, the behaviours were selected because they communicate a lack of recognition or contingent responding on the part of the caregiver to the child's distress signaling, presumably leading to a maintenance or escalation of distress. Moreover, OUCHIE-RV behaviours may also provide insight into caregivers' internal experiences of the vaccination context. For example, the DIAPR-R 2022 model (Pillai Riddell et al., 2022) delineates the biological, psychological, and social factors underlying caregivers' behavioural responses to infants' acute pain and suggests that

caregivers' physiological and emotional responses, triggered by witnessing their child's distress, may directly impact caregivers' behavioural responses to their child in pain.

The current study

The current study reports on the development and psychometric evaluation of the OUCHIE-RV. The study had two primary aims:

1. To examine the reliability of the OUCHIE-RV based on interrater reliability (Aim 1a) and internal consistency (Aim 1b).
2. To examine the concurrent validity of the OUCHIE-RV based on associations with toddler pain-related distress.

Exploratory aims of the study included examining associations between the OUCHIE-RV and other aspects of caregivers' response to their child's painful procedure, including their use of soothing behaviours (i.e., physical proximity, rocking, and verbal reassurance), self-reported state anxiety, and measures of physiological arousal (i.e., heart rate) and regulation (i.e., high-frequency heart rate variability).

We hypothesized that findings would provide support for the concurrent validity of the OUCHIE-RV as a measure of caregiver distress-promoting behaviour, based on positive associations between OUCHIE-RV composite scores (higher values of which reflect greater frequency and/or intensity of caregiver distress-promoting behaviour) and toddlers' pain-related distress. Regarding exploratory analyses, we expected that OUCHIE-RV composite scores would have positive associations with caregiver behaviours known to promote infant distress (i.e., verbal reassurance; Sobol-Kwapińska et al., 2020), negative associations with caregiver behaviours known to reduce child distress (i.e., physical comfort, rocking), positive associations

with caregivers' state anxiety and physiological arousal, and negative associations with caregivers' physiological regulation.

Methods

Participants

Participants were drawn from a larger longitudinal cohort-sequential study (*N*=234) that followed healthy, typically developing toddlers and their caregiver during routine vaccination appointments across the second year of life (12, 18, and/or 24 months). Exclusion criteria included prematurity (<37 weeks gestation), neonatal intensive care unit stay during infancy, suspected or confirmed developmental delay, chronic illness, and caregiver self-reporting a lack of fluency in English. The current study used a subsample of 223 dyads with video data available for at least one appointment. For dyads who participated at multiple time points, only data from the final participation point were included in the current analyses to support a more even distribution of toddlers across the second year of life (i.e., 12, 18, 24 months). Dyads' participation at a single time point (vs. multiple time points) was not significantly related to demographic variables (i.e., caregiver age, education, relation to child, ethnicity, or toddler sex).

In the analyzed sample (*N*=223), toddlers (53% male) were on average 18 months old (*M*=18.2, *SD*=4.6). Caregivers ranged in age from 20 to 62 years (*M*=36.2, *SD*=5.3) and were primarily mothers (80%), but also included fathers (19%) and grandparents (1%). Additional demographic details are in Table 1.

Procedure

Ethical approval was obtained from the Research Ethics Board at the participating university. Recruitment and data collection occurred in two large community pediatric clinics in urban areas of a large, multicultural city (Toronto, Canada). Caregivers of toddlers scheduled for

a vaccination appointment were made aware of the study upon entering the pediatric clinic. If the caregiver agreed to be approached by researchers, a research assistant explained the study and screened for inclusion and exclusion criteria. Informed consent was obtained from all participating caregivers. All data collection occurred between December 2015 and December 2019 by research assistants who were blinded to study hypotheses.

During the appointment, caregiver-toddler dyads were videorecorded and both members of the dyad were connected to MindWare wireless ambulatory monitors (MW1000A), which recorded electrocardiography (ECG) data at a sampling rate of 500 Hz. Three ECG electrodes were placed on each caregiver and toddler over the right clavicle, under the bottom left rib, and under the bottom right rib (ground electrode). MindWare Biolab software (version 3.3) was used for continuous ECG acquisition and The Observer XT software was used to synchronize video and cardiac data capture. Video and cardiac data were collected beginning two minutes before the vaccination needle was given and ending up to five minutes after the vaccination needle. Caregivers were asked to rate their state anxiety at the beginning of the recording period (pre-needle) and at the end (post-needle). Once ECG monitoring equipment was in place, dyads were observed with minimal interference from the research team. As per standard practice in the participating clinics, all caregivers held their toddler during the vaccination. Caregivers were able to move around unimpeded by the ECG monitoring equipment; however, given the small size of the clinic rooms, most caregivers' locomotion was minimal. Vaccinations administered during the appointments included pneumococcal conjugate, meningococcal conjugate, measles/mumps/rubella, varicella, and diptheria/tetanus/pertussis/polio/haemophilus influenzae type B [DTaP-IPV-Hib]. Following their participation, caregivers received a pamphlet outlining evidence-based needle pain management strategies. A schematic of data collection timelines is

provided in Figure 1. All data processing and coding were completed in lab using The Observer XT and MindWare HRV software (version 3.1.5) by separate coding teams who were blinded to participant data on other measures and study hypotheses. Data are available upon request.

The current analysis involves caregiver soothing behaviour and toddler pain-related distress, caregiver cardiac responses, and caregiver state anxiety. Previous studies of this cohort have included toddlers' self-regulatory behaviours (Gennis et al., 2022) and behavioural and physiological reactivity (Waxman et al., 2020; Waxman et al., 2021) and caregiver-toddler physiological attunement (Di Lorenzo-Klas et al., 2023a; Di Lorenzo-Klas et al., 2023b).

Measures

Demographic questionnaire

A demographic questionnaire asked about caregiver age, self-reported heritage culture, education, relation to child, and toddler age and sex. Caregivers' self-reported heritage culture was coded into the ethnic and cultural categories defined by Statistics Canada (2021), including North American, European, Caribbean, Latin/Central/South American, African, Oceanian, and "other" ethnic and cultural origins (e.g., Jewish, Christian, Muslim). Caregivers were also asked to rate the extent to which their way of life reflected mainstream North American culture and their heritage culture (respectively) on a 0 to 10 scale. This measure of acculturation allows researchers to better understand the extent to which mainstream North American culture and caregivers' own heritage culture are reflected in caregivers' daily life. It was adapted (see Pillai Riddell et al., 2018) from the Vancouver Index of Acculturation (Ryder et al., 2000) and Berry's (1992) bidimensional model of acculturation. Higher scores reflect greater identification with mainstream or heritage culture.

Caregiver distress-promoting behaviour

Measure development and coder training. Caregivers' use of distress-promoting behaviour was measured using the OUCHIE-RV. Development of the OUCHIE-RV followed best practice guidelines for the development and modification of behavioural coding systems in pediatric psychology (Chorney et al., 2015), the relevant steps of which are described below.

To ensure content validity of the OUCHIE-RV, item generation was informed by theory, prior research, and the clinical and research experience of the research team (see introduction). The OUCHIE-CV behaviours (Pillai Riddell, Gennis et al., 2018) were classified into one of the three OUCHIE-RV behaviour domains (i.e., affect incongruence, attention diversion, physical distance)[3] which were coded during discrete epochs across the post-needle period. This approach was chosen to balance capturing themes in caregiver behaviours with achieving temporal specificity, given our goal of developing a tool for use in research contexts.

Affect incongruence codes the frequency and intensity of caregiver affective responding that is inappropriate or incongruent in response to a distressed child. Affect incongruence may be communicated verbally (through the content or tone of vocalizations) or non-verbally (through facial expression) and may suggest fearful, angry, overly positive, or completely restricted (i.e., flat) caregiver affect. *Attention diversion* codes the frequency and intensity of caregivers diverting their attention away from their distressed child (e.g., by ignoring their child's bids for attention or shifting their attention to someone else in the room), determined based on how caregivers direct their gaze, vocalizations, and other actions. *Physical distance* codes the frequency and intensity of lapses in caregivers' close physical contact with their distressed child

[3] Initially, we planned to code four domains of parent distress-promoting behaviour. The fourth domain (intrusive action, including the items "forceful" and "face cover" from the OUCHIE-CV) was dropped from the coding scheme due to a low base rate in the current sample.

(e.g., caregiver separating from distressed toddler or holding toddler away from caregiver's body in a way that prevents chest-to-chest contact).

A preliminary coding manual was developed and piloted with a team of undergraduate psychology student coders, a clinical psychology graduate student (SB), and a clinical health psychologist and behavioural scientist (RPR) by coding an initial subset of the sample. Operational definitions for the behaviour domains were revised during the pilot coding phase and the coding manual was finalized. Coding was completed by one graduate student primary coder with extensive behavioural coding experience and two undergraduate psychology student coders with no prior behavioural coding experience prior to the pilot coding described above. Training occurred over an approximately three-month period during which the lead coder (SB) provided weekly coding assignments requiring approximately three hours of weekly coding and coding discrepancies were reviewed during a 1-hour weekly consensus meeting. A description of the coding scheme and calculation of OUCHIE-RV composite scores follows.

Coding of distress-promoting behaviour during toddler moderate to high distress. As aforementioned, only caregiver behaviour that occurred during the toddler's moderate to high distress was coded. To ensure that coders could reliably distinguish no or low distress from moderate to high distress, toddlers' distress state (i.e., 0 = *no or low distress* , 1 = *moderate or high distress*) was coded during each 30-second epoch, based on the toddler's vocalizations (i.e., the presence of full-lunged crying) using a definition from an established behavioural pain scale (Taddio et al., 1995). To measure the frequency and intensity of each of the three behaviour domains (i.e., affect incongruence, attention diversion, and physical distance) over time, each of the three domains was rated on a 0 to 2 scale (0 = *no evidence for the domain,* 1 = *some evidence for the domain,* 2 = *marked* [i.e., high intensity] *or pervasive* [i.e., high frequency] *evidence for*

the domain) every 30 seconds during the three minutes after the vaccination needle. The full coding scheme is presented in Supplemental File 1.[4] Coding time typically ranged from 10 to 20 minutes per video for trained coders. Twenty percent of the dataset was double-coded and reliability with the primary coder was examined (see results section).

Calculation of composite scores. An overall OUCHIE-RV composite score was calculated for each of the first three minutes post-needle (i.e., Post 1, Post 2, and Post 3). Composite scores were calculated by averaging over all three behaviour domains for the two epochs within each minute. Epochs during which toddlers were not in a state of moderate to high distress were not factored into the calculated score. Composite scores range from 0 to 2 and higher scores indicate more frequent or intense use of distress-promoting behaviour in response to toddler distress during that particular minute.

Caregiver physiological arousal and regulation

ECG data were processed using MindWare HRV 3.1.5 software, which derived caregiver heart rate (HR) based on the identification of R-waves (Berntson et al., 1997) and high-frequency heart rate variability (HRV) based on spectral analysis of RR intervals (i.e., the intervals between successive heart beats or R waves) using frequency bands within the range of spontaneous respiration for adults (0.12 to 0.40 [Cacioppo et al., 2000]). Manual data inspection and artifact editing (i.e., in the event of software misidentification or equipment malfunction) was conducted by coders who were trained by an experienced primary coder and impacted less than 5% of data for all participants. Interrater reliability with the primary coder, calculated on a randomly selected 20% of the sample, was strong (intraclass correlations [ICC] ranging from 0.96 to 0.99). Caregiver HR (reported as beats per minute [BPM]) and HRV (reported as the natural logarithm

[4] Appendix G in the current dissertation.

of milliseconds squared) were calculated for consecutive 30-second epochs during the minute before the needle and the three minutes post-needle, which were then averaged within each minute to yield average caregiver HR and HRV at Baseline, Post 1, Post 2, and Post 3. Caregiver HR was used to index caregivers' physiological arousal and HRV was used to index caregivers' physiological regulation (Appelhans & Luecken, 2006).

Caregiver posture

Because posture can influence physiological responses (Berntson et al., 2016), caregiver posture was coded from video footage throughout the same time frame as cardiac data collection for use as a covariate in subsequent analyses. Postural position (i.e., seated or standing) was continuously coded and used to calculate the percentage of time spent standing at Baseline, Post 1, Post 2, and Post 3.

Caregiver pre- and post-needle state anxiety

Caregivers rated their state anxiety on two occasions — once pre-needle and a second time approximately three minutes post-needle — by verbally responding to the question: "How worried are you right now on a scale of 1 to 10, where 1 is 'no worry at all' and 10 is 'the most worry possible'?", asked by a research assistant. Higher scores reflect more state anxiety. Previous research has supported the validity of subjective ratings of distress as a measure of acute emotional discomfort (Tanner, 2012).

Caregiver soothing behaviours

Caregiver soothing behaviours were coded using the MAISD (Cohen et al., 2005), a behavioural coding system used to code the frequency of discrete caregiver behaviours. Three soothing behaviours were analyzed in the current study, including physical comfort (i.e., rubbing, patting, or massaging child), rocking (i.e., swaying or bouncing child), and verbal

reassurance (e.g., making reassuring comments to child such as “it’s ok”). Each behaviour was coded as present or absent during 5-second epochs beginning immediately after the needle and continuing for three minutes. Proportion scores for each behaviour, reflecting the proportion of epochs during which the behaviour was observed out of all codable epochs, were calculated for Post 1, Post 2, and Post 3. Scores range from 0 to 1 and higher scores reflect more frequent use of the soothing behaviour. Coding was conducted by three undergraduate students who were trained by an experienced post-graduate primary coder. Interrater reliability, calculated as single-measures ICCs based on a randomly selected 20% of videos coded by the primary coder, ranged from 0.8 to 0.93 for physical comfort, 0.96 to 0.99 for rocking, and 0.81 to 0.95 for verbal reassurance across Post 1, Post 2, and Post 3.

Toddler pain-related distress

Toddler distress was measured using the Face, Legs, Activity, Cry, Consolability (FLACC) scale (Merkel et al., 1997). The FLACC is a behavioural coding system used to code the intensity of behavioural distress as indicated by five behaviours, including toddler facial expression, leg movement, activity level, crying, and consolability (reverse-scored). Each behaviour was rated on a 0-2 intensity scale during 15-second epochs beginning one minute before the needle and continuing for three minutes after the needle. Composite scores for Baseline, Post 1, Post 2, and Post 3 were calculated as the sum of all five behaviours across the epochs within each minute. Scores range from 0 to 40 and higher scores reflect more behavioural distress. Coding was conducted by a team of undergraduates who were trained by an experienced graduate student primary coder. Single-measures ICCs, based on a randomly selected 20% of the videos coded by the primary coder, ranged from 0.90 to 0.94 across Baseline, Post 1, Post 2, and Post 3.

Analysis plan

In preliminary analyses, caregiver gender, education level, and age, and toddler age and sex, were examined as potential covariates of OUCHIE-RV scores using correlations.

Aim 1: Reliability of the OUCHIE-RV

To address Aim 1a, we examined interrater reliability between the primary coder and each secondary coder for the OUCHIE-RV composite scores and toddler distress state variables based on the twenty percent of the dataset that was double-coded. Two-way random effects single measures ICCs examined interrater reliability for OUCHIE-RV composite scores and kappa coefficients examined interrater reliability for the dichotomous toddler distress state variables for each of the six 30-second epochs. Thresholds of 0.7 and 0.6 have been proposed to reflect adequate reliability for ICCs (Mitchell, 1979) and kappa coefficients (Horner, 2005) respectively. To address Aim 1b (i.e., internal consistency), we calculated correlations between each composite score (e.g., OUCHIE-RV Post 1) and the behaviour domain scores used to derive the composite score (e.g., Affect Incongruence Post 1, Attention Diversion Post 1, Physical Distance Post 1).

Aim 2: Validity of the OUCHIE-RV

To address Aim 2, we first calculated correlations between OUCHIE-RV composite scores and toddler pain-related distress. To further evaluate Aim 2 and determine the variance accounted for in toddlers' pain-related distress by the OUCHIE-RV over and above toddlers' previous distress behaviour, we estimated an autoregressive cross-lagged path analysis model. This type of analysis is ideal for examining the interactive influences of two variables over time because it allows for examination of three types of relationships within the same model, including: (1) *predictive within-measure* relationships (e.g., prediction of OUCHIE-RV Post 2

composite score from OUCHIE-RV Post 1 composite score), (2) *predictive between-measure* relationships (e.g., prediction of FLACC Post 2 from OUCHIE-RV Post 1 composite score), and (3) *concurrent (residual) between-measure* relationships (e.g., association between OUCHIE-RV Post 2 composite score and FLACC Post 2 after accounting for prediction from OUCHIE-RV Post 1 and FLACC Post 1). Toddlers' pre-needle pain-related distress (FLACC Baseline) was included in the model as a predictor of Post 1 OUCHIE-RV and FLACC since it can impact on subsequent toddler and caregiver behaviour (Waxman et al., 2020). Multiple indices assessed model fit, including the comparative fit index (CFI), Tucker-Lewis index (TLI), and root mean square error of approximation (RMSEA). Conventional benchmarks of RMSEA < .06, TLI > 0.90, and CFI > 0.90 were used to evaluate model fit (Bentler & Bonett, 1983; Hu & Bentler, 1999).

Exploratory aims: Associations with other aspects of caregiver responses

To address our exploratory aims, we calculated correlations between OUCHIE-RV composite scores and toddler pain-related distress, caregiver state anxiety, caregiver physiological arousal and regulation, and soothing behaviours (i.e., physical comfort, rocking, and verbal reassurance).

The autoregressive cross-lagged path analysis model (Aim 2) was estimated in R (R Core Team, 2022) using the *lavaan* package (Rosseel, 2012). Maximum likelihood estimation was used, which allows for the inclusion of cases with missing data on outcomes. All other statistical analyses were conducted in SPSS (Version 28) using pairwise deletion to address missing data. Alpha levels of .05 were used for all statistical tests.

Results

Data checking was performed by screening all outcome variables for evidence of outliers (> 3 standard deviations from the mean). A small number of outliers were identified, the removal of which did not substantially impact statistical outcomes. Thus, outliers were retained. Rates of missing data ranged from 5 to 7% for self-report and behavioural variables (most often due to blocked video footage) and from 32 to 33% for physiological variables (most often due to equipment failure).[5] Missingness was not significantly associated with caregiver age, education, relation to child, ethnicity, or toddler sex.

Sample characteristics are in Table 1 and descriptive statistics for all primary variables are in Table 2. Participating caregivers reflected a high level of educational attainment, a wide range of self-reported heritage cultures, and moderate to high acculturation to North American culture (see Table 1). OUCHIE-RV scores were not associated with caregiver gender, education level, or age, or toddler age or sex, based on correlations (p>.05).

Aim 1: Reliability of the OUCHIE-RV

Interrater reliability for the dichotomous OUCHIE-RV toddler distress codes, calculated as kappa coefficients, ranged from 0.86 to 0.97. Interrater reliability for the continuous OUCHIE-RV composite scores, calculated as ICCs, ranged from 0.77 to 0.85 across coding pairs. This suggested strong interrater reliability.

Regarding internal consistency, behaviour domain-total correlations ranged from r=.60 to .74 at Post 1, from r=.57 to .78 at Post 2, and from r=.70 to 0.78 at Post 3 (all p's <.001), suggesting moderate to strong positive associations between each OUCHIE-RV behaviour domain and the overall OUCHIE-RV composite score within each minute.

[5] Missing physiological data rates exceeding 20-30% are common among studies that measure cardiac data during conditions other than a resting state (Lan et al., 2022; Mills-Koonce et al., 2009; Sturge-Apple et al., 2011).

Aim 2: Validity of the OUCHIE-RV

Correlations between the three OUCHIE-RV composite scores and toddler pain-related distress are in Table 3. OUCHIE-RV composite scores generally had significant, small positive associations with toddlers' pain-related distress within concurrent (r =.28 to .36) and subsequent minutes (r =.24).

To further examine associations between the three OUCHIE-RV composite scores and toddlers' pain-related distress, we estimated an autoregressive cross-lagged path analysis model. The model fit the data adequately (CFI=0.97, TLI=0.92, RMSEA=0.08). Results are in Figure 2 and Table 4. *Predictive within-measure* path results indicated that the OUCHIE-RV Post 1 composite score significantly predicted the OUCHIE-RV Post 2 composite score. In addition, toddler pain-related distress at each minute significantly predicted toddler pain-related distress in the subsequent minute. *Predictive between-measure* path results indicated that caregivers' use of distress-promoting behaviour did not significantly predict subsequent toddler pain-related distress. However, higher toddler pain-related distress at Baseline and Post 1 significantly predicted higher caregiver distress-promoting behaviour at Post 1 and Post 2, respectively. *Concurrent between-measure* path results indicated significant residual associations between caregivers' distress-promoting behaviour and toddler pain-related distress within each of the three post-needle minutes.

Exploratory aims: Associations with other aspects of caregiver responses

Correlations were calculated between OUCHIE-RV composite scores and caregiver state anxiety, caregiver physiological arousal, and soothing behaviours (i.e., physical comfort,

rocking, and verbal reassurance), the results of which are reported in Table 3.[6] OUCHIE-RV composite scores had small to moderate negative correlations with caregivers' concurrent use of physical comfort (r =-.34 to -.24) and rocking (r=-.36 to -.19) and negligible to small associations with caregivers' use of verbal reassurance (r=.06 to .12). Correlations between OUCHIE-RV composite scores and caregivers' state anxiety (r=-.02 to .09), physiological arousal (r=-.15 to .05), and physiological regulation (r=-.04 to .13) were generally negligible.

Discussion

The current study introduced the OUCHIE-RV, a novel observational measure of caregivers' distress-promoting behaviour during toddler vaccination that is based on coding caregivers' verbal and non-verbal behaviours in reaction to their toddlers' distress. Results provide evidence for the validity and reliability of the OUCHIE-RV as a tool for quantifying the frequency and intensity of caregivers' distress-promoting behaviour during toddler vaccination.

Aim 1: Reliability of the OUCHIE-RV

To explore measure reliability, Aim 1 examined interrater agreement and internal consistency. Results suggested that the OUCHIE-RV can be reliably coded by a team of undergraduate students with training by an experienced coder, supporting the feasibility of the measure's use in other research and clinical contexts. Each behavioural domain of the OUCHIE-RV had moderate to strong positive associations with OUCHIE-RV composite scores, which were similar in magnitude across the three minutes post-needle. This suggests that associations between each composite score and the behavioural domains used to derive the score are

[6] Caregiver posture (i.e., percentage of time in a standing position) was examined as a covariate in analyses involving HR and HRV. Because its inclusion did not alter results, results are reported without the covariation of caregiver posture.

internally consistent across time. These findings provide strong evidence for the reliability of the OUCHIE-RV.

Aim 2: Validity of the OUCHIE-RV

After confirming measure reliability, we proceeded to our primary aim of examining the relationship between the OUCHIE-RV and toddler pain-related distress. To examine the concurrent validity of the OUCHIE-RV as a measure of caregivers' distress-promoting behaviours, Aim 2 tested the hypothesis that the OUCHIE-RV would be positively associated with toddlers' pain-related distress. Results provided support for this hypothesis. As predicted, OUCHIE-RV composite scores for each minute of the post-needle period were significantly associated with greater concurrent and subsequent pain-related distress, with small to medium-sized correlations.

To obtain a more nuanced understanding of these relationships across the three minutes following the vaccination needle, a cross-lagged model was used to estimate how much variance the OUCHIE-RV explained in toddlers' pain-related distress after accounting for toddlers' distress and caregivers' distress-promoting behaviour in the previous minute. Results showed that within each minute, more frequent or intense caregiver distress-promoting behaviour was still significantly associated with greater concurrent toddler distress, providing further support for OUCHIE-RV behaviours as distress-promoting. Despite the small to moderate bivariate correlations between OUCHIE-RV in a given minute and toddler distress in the subsequent minute that were identified in preliminary analyses, caregiver behaviour in a given minute did not predict toddler distress in a subsequent minute beyond what was already predicted by concurrent caregiver behaviours when investigated in the cross-lagged model. This finding is consistent with the DIAPR-R 2022 model, which posits that caregiver and infant are each

reacting to and influencing the other's responses on a moment-to-moment basis through dyadic feedback loops (Pillai Riddell et al., 2022). Furthermore, greater toddler distress at baseline and during the first minute post-needle significantly predicted more caregiver distress-promoting behaviour within the subsequent minute. Since infants with higher levels of anticipatory (i.e., pre-needle) distress typically take longer to regulate following the needle (Waxman et al., 2020), one interpretation is that caregivers themselves become dysregulated by the initial signs of their child's dysregulation, resulting in non-attuned soothing behaviours.

Exploratory aims: Associations with other aspects of caregiver responses

Exploratory aims of the current study were to examine associations between the OUCHIE-RV and other aspects of caregivers' psychological, physiological, and emotional responses within the vaccination context. Results indicated partial support for hypotheses. As predicted, the OUCHIE-RV had significant negative associations with measures of caregivers' proximal soothing behaviours (i.e., physical comfort, rocking), which were small to moderate in magnitude. Proximal soothing responses are considered to reflect a prototypical sensitive caregiving response (e.g., Biringen, 2000), and so the finding of small to moderate-sized negative associations with the OUCHIE-RV could suggest that distress-promoting caregiver behaviour reflects a unique dimension of caregiver behaviour, rather than simply reflecting the absence of sensitive behaviour. The hypothesized positive association between the OUCHIE-RV and caregivers' use of verbal reassurance (e.g., saying "You're okay") was largely unsupported, with correlations in the negligible to small range. Previous research suggests that verbal reassurance can be soothing when used sparingly but distress-promoting when used at high frequency (Racine et al., 2012), even when verbal reassurance occurs in the context of other sensitive verbal responses (Campbell et al., 2018). Given that frequent verbal reassurance is only

one form of affect incongruence captured within the OUCHIE-RV composite score, this finding may suggest that this particular behaviour is less often accompanied by other aspects of distress-promoting behaviours. Additionally, the fact that verbal reassurance as coded by the MAISD captures all use of reassuring statements by caregivers during the post-needle period, regardless of whether the timing or intensity of these statements would likely be attuned or non-attuned to the child's needs, may also underlie the relatively small associations with the OUCHIE-RV composite scores.

Caregivers' distress-promoting behaviour was not significantly associated with caregivers' self-reported state-anxiety or measures of their physiological arousal and regulation. Previous research in an acute pain context has linked parents' use of distress-promoting behaviours with lower baseline HRV and higher state catastrophizing during child venipuncture (Constantin et al., 2022). Similarly, findings from non-pain related laboratory-based stressors suggest that higher levels of parents' physiological arousal and lower levels of regulation are associated with greater use of distress-promoting parenting behaviour (Lorber & O'Leary, 2005; Miller et al., 2015). The absence of these associations in our sample of caregivers with relatively low socioeconomic risk may suggest that factors other than high arousal and low regulatory capacity (e.g., lack of knowledge about the impact of behaviours) are primarily driving caregivers' use of distress-promoting behaviours.

Clinical implications

Parent-focused interventions are an important tool used to improve pain outcomes in infants and toddlers (Pillai Riddell et al., 2018) and several findings from the current study can inform future intervention work. For example, caregivers' distress-promoting behaviour was not associated with their state anxiety or physiological responses but was predicted by toddlers'

distress during previous epochs. This suggests that distress-promoting behaviours may reflect caregivers' well-intentioned but non-attuned soothing response. Initiatives to educate caregivers on the impact of caregiving behaviours (Kain et al., 2007; Pillai Riddell et al., 2018) may be expected to be fruitful and broadly relevant as first-line interventions in vaccination contexts alongside more targeted intervention focused on supporting caregivers' emotion regulation. Importantly, education initiatives should focus on providing caregivers with a repertoire of adaptive soothing responses that can be trialed and adapted in response to toddlers' reactions. We found that caregiver distress-promoting behaviour in a given minute did not predict *future* toddler distress, suggesting that caregivers can adapt initially unsuccessful behavioural responses without carryover effects to the remainder of the interaction.

Limitations and future directions

Strengths of the current study include the use of a universally relevant and standardized pain context and the recruitment of a large culturally diverse sample of healthy toddlers and caregivers. However, several limitations should be considered. First, the high educational attainment of participating caregivers and our focus on healthy, typically developing toddlers may impact on the generalizability of the OUCHIE-RV. Although the domains of distress-promoting parent behaviours coded by the OUCHIE-RV are grounded in theory and empirical evidence drawn from socioeconomically diverse samples, supporting their generalizability, future studies should examine the validity of the OUCHIE-RV in samples characterized by more socioeconomic diversity as well as for caregivers of children with developmental disabilities, medical comorbidities or traumatic medical experiences, and other factors that may impact on how toddlers communicate pain-related distress and how caregivers interpret and respond to their child's pain-related distress. Second, due to our grounding in Attachment Theory, we only coded

caregiver behaviour that occurred following the painful stimulus (i.e., post-needle) as this is when the toddlers' needs are not ambiguous. However, we acknowledge that caregivers' behaviour prior to the needle may impact toddlers' subsequent distress behaviour. Including toddlers' baseline distress behaviour as a covariate within the cross-lagged path analysis, as we have done, would be expected to partly, but not completely, account for this influence. Another potential limitation of the study is that results may not generalize to dyads in which the toddler expressed no or low distress post-vaccination (i.e., behavioural response characteristic of an avoidant attachment style). However, this was very rare in our study (~5%). Finally, because data for the current study were collected prior to the COVID-19 pandemic, future research should examine whether pandemic-related changes in healthcare practices (e.g., masking requirements) may impact the usability or validity of the OUCHIE-RV. Emerging evidence suggests that face masks hamper the accurate detection of certain emotions (e.g., happiness) more than others (e.g., fear; Carbon, 2020; McCrackin et al., 2021), which may have implications for both coder reliability and the extent to which toddlers discern and react to caregivers' facial expressions.

Conclusions

We have presented a novel behavioural coding scheme, grounded in Attachment Theory, that captures verbal and non-verbal aspects of caregiver behaviours that promote toddler pain-related distress. Our results provide support for the reliability and validity of the OUCHIE-RV as a measure of caregivers' distress-promoting behaviour. We found that when caregivers respond to toddlers' moderate to high pain-related distress in a way that communicates a lack of recognition or misinterpretation of the child's distress signals, such as through non-contingent affect, maintaining physical space between themselves and their child, or diverting their attention

away from their distressed child, toddlers respond by maintaining or escalating their pain-related distress. The OUCHIE-RV supports a better understanding of the aspects of caregivers' behavioural responses that impact on young children's coping during painful procedures and offers an empirically and theoretically grounded research tool for the objective assessment of caregiver behavioural responses in future research.

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Table 1

Demographic characteristics (N=223).

	M (SD) or *%*
Child sex (%)	
Male	53
Female	47
Relationship to child (%)	
Mother	80
Father	19
Grandparent	1
Caregiver education (%)	
Graduate School or Professional Training	48
University Graduate (4 years)	34
Partial University (at least 1 year)	2
Trade School/Community College	14
High School Graduate	1
Self-reported heritage culture (%)	
North American	22
Asian	24
European	25
Latin, Central, or South American	4
African	1
Caribbean	1
Oceanian	1
Other ethnic/cultural origins	8
Mixed	14
Self-reported acculturation to North American culture [a]	7.9 (2.0)
Self-reported acculturation to self-reported heritage culture [a]	6.3 (2.8)

[a] Ranges from 0 to 10, with higher scores reflecting greater identification with mainstream North American or self-reported heritage culture.

Table 2

Descriptive statistics for study variables.

	n	Mean (SD)	Range
OUCHIE-RV composite scores			
OUCHIE-RV Post 1	201	0.88 (0.45)	0-2
OUCHIE-RV Post 2	134	0.74 (0.45)	0-1.83
OUCHIE-RV Post 3	97	0.63 (0.47)	0-2
Toddler pain-related distress			
FLACC Baseline	217	8.26 (9.33)	0-39
FLACC Post 1	222	23.61 (9.2)	0-40
FLACC Post 2	221	14.92 (11.14)	0-36
FLACC Post 3	219	11.37 (11.1)	0-39
Caregiver state anxiety			
Pre-needle	220	2.43 (2.5)	0-10
Post-needle	221	1.83 (2.34)	0-9
Caregiver physiological arousal and regulation			
HR Baseline	157	93.76 (14.39)	37.06-131.28
HR Post 1 (bpm)	158	92.77 (14.81)	62.38-153.29
HR Post 2 (bpm)	159	91.49 (14.67)	62.02-151.48
HR Post 3 (bpm)	158	90.32 (14.03)	57.57-139.42
HRV Baseline (ln[ms^2])	157	4.76 (1.2)	1.1-9.16
HRV Post 1 (ln[ms^2])	158	4.94 (1.18)	2.06-7.46
HRV Post 2 (ln[ms^2])	158	4.84 (1.21)	2.06-8.06
HRV Post 3 (ln[ms^2])	158	4.73 (1.16)	1.74-7.74
Caregiver soothing behavior			
Physical Comfort Post 1	223	0.57 (0.29)	0-1
Physical Comfort Post 2	223	0.42 (0.31)	0-1
Physical Comfort Post 3	222	0.36 (0.3)	0-1
Rocking Post 1	223	0.31 (0.32)	0-1
Rocking Post 2	223	0.31 (0.35)	0-1
Rocking Post 3	222	0.27 (0.35)	0-1
Verbal Reassurance Post 1	218	0.24 (0.21)	0-0.92
Verbal Reassurance Post 2	219	0.12 (0.16)	0-0.75

Verbal Reassurance Post 3	217	0.09 (0.13)	0-0.75

Note: FLACC = Face, Legs, Activity, Cry, Consolability scale; HR = heart rate; HRV = heart rate variability; OUCHIE-RV = Opportunities to Understand Childhood Hurt's Inoculation Evaluation — Research Version; bpm = beats per minute; ln(ms^2)= natural logarithm of milliseconds squared.

Table 3

Correlations between OUCHIE-RV composite scores and toddler and caregiver variables.

	OUCHIE-RV Post 1			OUCHIE-RV Post 2			OUCHIE-RV Post 3		
	n	*r*	*p*	*n*	*r*	*p*	*n*	*r*	*p*
Toddler pain-related distress									
FLACC Baseline	195	**0.21**	**0.004**	128	0.15	0.1	94	0.07	0.49
FLACC Post 1	200	**0.28**	**<.001**	134	**0.18**	**0.04**	97	-0.04	0.69
FLACC Post 2	199	**0.24**	**<.001**	134	**0.29**	**<.001**	97	-0.03	0.79
FLACC Post 3	197	**0.22**	**0.002**	133	**0.24**	**0.01**	97	**0.36**	**<.001**
Caregiver state anxiety									
Pre-needle	198	0.09	0.23	133	0.03	0.7	96	-0.02	0.89
Post-needle	199	0.05	0.46	132	0.04	0.69	95	-0.01	0.93
Caregiver physiological arousal and regulation									
HR Baseline	138	0.02	0.78	96	-0.04	0.72	69	-0.15	0.23
HR Post 1	138	0.03	0.7	95	-0.04	0.73	68	-0.14	0.25
HR Post 2	139	0.05	0.59	96	-0.06	0.6	68	-0.13	0.31
HR Post 3	138	0.02	0.83	95	-0.09	0.4	67	-0.12	0.34
HRV Baseline	138	0.1	0.24	96	0.13	0.22	69	0.04	0.75
HRV Post 1	138	0.02	0.78	95	-0.01	0.93	68	0.1	0.41
HRV Post 2	138	0.08	0.38	95	0.03	0.79	67	0.05	0.71
HRV Post 3	138	0.03	0.7	95	-0.04	0.73	67	0.08	0.53
Caregiver soothing behaviors									
Physical Comfort Post 1	201	**-0.28**	**<.001**	134	**-0.23**	**0.01**	97	-0.09	0.36
Physical Comfort Post 2	201	**-0.24**	**<.001**	134	**-0.34**	**<.001**	97	-0.1	0.35
Physical Comfort Post 3	200	**-0.21**	**0.002**	134	-0.15	0.08	97	**-0.24**	**0.02**
Rocking Post 1	201	**-0.19**	**0.01**	134	**-0.21**	**0.01**	97	**-0.31**	**0.002**
Rocking Post 2	201	**-0.16**	**0.03**	134	**-0.31**	**<.001**	97	**-0.21**	**0.04**
Rocking Post 3	200	-0.14	0.06	134	**-0.24**	**0.004**	97	**-0.36**	**<.001**
Verbal Reassurance Post 1	196	0.09	0.2	132	0.14	0.11	95	-0.08	0.45
Verbal Reassurance Post 2	197	0.13	0.08	132	0.12	0.18	95	-0.15	0.14
Verbal Reassurance Post 3	195	-0.01	0.95	132	0.07	0.42	95	0.06	0.58

Note: FLACC = Face, Legs, Activity, Cry, Consolability scale; HR = heart rate; HRV = heart rate variability; OUCHIE-RV = Opportunities to Understand Childhood Hurt's Inoculation Evaluation — Research Version.
Significant correlations are bolded.

Table 4

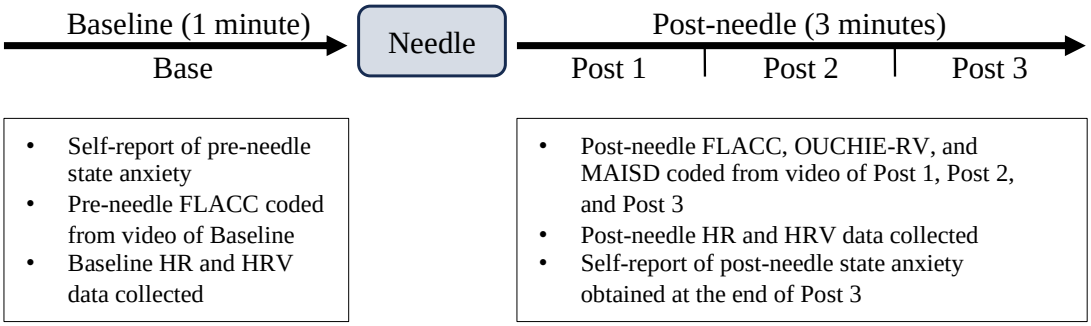
Estimates for autoregressive cross-lagged path analysis model of relations between OUCHIE-RV composite scores and toddler pain-related distress.

	Standardized estimate	Unstandardized estimate	*z*	*p*
Predictive within-measure paths				
FLACC Base → FLACC 1	0.37	0.36	7.25	<.001
FLACC Post 1 → FLACC Post 2	0.6	0.72	11.60	<.001
FLACC Post 2 → FLACC Post 3	0.67	0.66	10.31	<.001
OUCHIE-RV Post 1 → OUCHIE-RV Post 2	0.41	0.46	4.88	<.001
OUCHIE-RV Post 2 → OUCHIE-RV Post 3	0.19	0.17	1.57	.12
Predictive between-measure paths				
FLACC Base → OUCHIE-RV Post 1	0.23	0.01	3.1	.002
FLACC Post 1 → OUCHIE-RV Post 2	0.34	0.02	2.50	.01
FLACC Post 2 → OUCHIE-RV Post 3	0.01	0	0.12	.90
OUCHIE-RV Post 1 → FLACC Post 2	0.07	1.69	1.25	.21
OUCHIE-RV Post 2 → FLACC Post 3	0.06	1.20	0.80	.43
Concurrent between-measure paths				
OUCHIE-RV Post 1 ↔ FLACC Post 1	0.27	1.01	3.29	.001
OUCHIE-RV Post 2 ↔ FLACC Post 2	0.34	1.21	3.34	.001
OUCHIE-RV Post 3 ↔ FLACC Post 3	0.37	1.30	3.69	<.001

Note: FLACC = Face, Legs, Activity, Cry, Consolability scale; OUCHIE-RV = Opportunities to Understand Childhood Hurt's Inoculation Evaluation — Research Version.

Figure 1

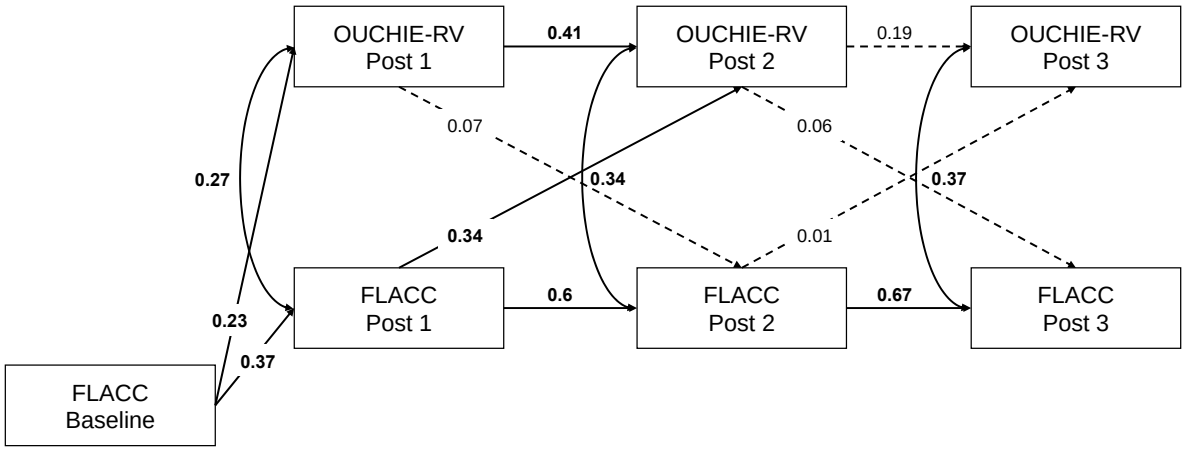
Schematic overview of data collection during the vaccination appointment.



Note: FLACC = Face, Legs, Activity, Cry, Consolability scale; HR = heart rate; HRV = heart rate variability; OUCHIE-RV = Opportunities to Understand Childhood Hurt's Inoculation Evaluation — Research Version; MAISD = Measure of Adult and Infant Soothing and Distress.

Figure 2

Autoregressive cross-lagged path analysis model of relations between OUCHIE-RV composite scores and toddler pain-related distress.



Note: FLACC = Face, Legs, Activity, Cry, Consolability scale; OUCHIE-RV = Opportunities to Understand Childhood Hurt's Inoculation Evaluation — Research Version. Standardized regression coefficients reported. Double-headed arrows reflect concurrent associations and single-headed arrows reflect predictive associations. Bolded paths are significant at $p<.05$. Comparative fit index (CFI)=0.97, Tucker-Lewis index (TLI)=0.92, root mean square error of approximation (RMSEA)=0.08, n=217.

CHAPTER 5: TOWARDS AN EXAMINATION OF BIOLOGICAL, BEHAVIOURAL, AND PSYCHOLOGICAL ASPECTS OF PARENT RESPONSES TO TODDLER PAIN

Study 2 addressed the need highlighted in Study 1 to consider parents' use of insensitive behaviour and the lack of studies in the literature examining parent verbal and non-verbal responses to child distress in naturalistic contexts. As several aspects of parents' insensitive behaviour present non-verbally and are not captured by existing observational measures used in pediatric pain contexts (Bai et al., 2018), Study 2 examined the validity of an observational measure intended to quantify parent behaviours that promote or maintain toddlers' distress during routine vaccination: the Opportunities to Understand Childhood Hurt's Inoculation Evaluation – Research Version (OUCHIE-RV). This measure was developed by revising an existing clinical checklist tool (the Opportunities to Understand Childhood Hurt's Inoculation Evaluation – Clinical Version; Pillai Riddell, Gennis, et al., 2018) such that more fine-grained data on the frequency and intensity of various distress-promoting behaviours across the various phases of toddler distress could be acquired. The revised measure coded the frequency and intensity of parent distress-promoting behaviour within three domains: affect incongruence, attention diversion, and physical distance. Primary analyses in Study 2 focused on providing evidence for the reliability and validity of the OUCHIE-RV as a critical intermediary step leading up to the next chapter's (i.e., Study 3) examination of how insensitive behaviours and other aspects of parents' behavioural and psychological responses relate to parents' HRV responses and trajectories during toddler vaccination.

Drawing on guidelines for the development of behavioural coding systems in pediatric psychology (Chorney et al., 2015), reliability was first examined. Results provided evidence for adequate reliability of the OUCHIE-RV based on inter-rater reliability and internal consistency.

Next, associations between the OUCHIE-RV and toddlers' pain-related distress were examined. This analysis provided key validity evidence for the OUCHIE-RV, which was developed to measure parent behaviours that were hypothesized to promote or maintain toddler distress during vaccination. As hypothesized, the OUCHIE-RV had significant, positive correlations with toddlers' distress within concurrent and subsequent minutes. Building on this finding using a cross-lagged model — which supports an examination of potential causality in the associations between two variables — provided further evidence for the validity of the OUCHIE-RV as a measure of parent distress-promoting behaviour. Results showed that, even after accounting for the predictive power of toddler distress measured during previous minutes, parent distress-promoting behaviour as measured by the OUCHIE-RV remained as a significant correlate of toddler distress within each minute. This finding confirmed that the OUCHIE-RV effectively serves its primary aim as a measure of parents' distress-promoting behaviour. Another noteworthy finding was that higher levels of toddler distress at baseline and during the first minute post-needle predicted more parent distress-promoting behaviour in subsequent minutes, which suggests that insensitive behaviour can also present as a *reaction* to a highly distressed toddler, and not just as a cause of toddler distress.

Keeping with a main goal of this dissertation to achieve a multifaceted understanding of the various aspects of parents' responses to their toddlers' pain-related distress, associations between the OUCHIE-RV and other aspects of caregivers' behavioural, psychological, and physiological responses were examined in exploratory analyses. The OUCHIE-RV had significant small to moderate negative associations with parents' use of physical comfort and rocking and negligible to small associations with verbal reassurance. Associations between the

OUCHIE-RV and parents' state anxiety during vaccinations and their heart rate and heart rate variability (HRV) were negligible and non-significant.

While Study 2 produced preliminary data concerning how OUCHIE-RV scores were associated with parents' average HRV levels based on simple correlations, Study 3 used a more sophisticated statistical approach (i.e., growth curve modeling) to examine how distress-promoting and soothing parental behaviours, as well as parents' psychological stress, relate to parents' HRV levels and trajectories of response during toddler vaccination. Bringing together key findings and identified gaps discerned in Study 1 and a newly validated measure of parents' distress-promoting behaviour developed in Study 2, Study 3 characterized parents' physiological responses in a naturalistic distress setting and investigated other behavioural and psychological parent factors hypothesized to relate to physiological responses. Specifically, Study 3 investigated parents' HRV responses during toddler vaccination, further contextualized by parents' state anxiety, anxiety symptomology, parenting stress, and both insensitive and sensitive aspects of parent behaviour.

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CHAPTER 6: CAREGIVERS' PHYSIOLOGICAL RESPONSES DURING TODDLER VACCINATIONS: ASSOCIATIONS WITH PSYCHOLOGICAL AND BEHAVIOURAL RESPONSES[1]

Introduction

Painful experiences are a common and inevitable aspect of daily life for young children. Healthy children receive upwards of 20 vaccination needles during the first two years of life as part of routine care (Centers for Disease Control and Prevention, 2023). Vaccinations are a source of significant distress for most children, with most toddlers exhibiting moderate to high levels of pain-related distress behaviours post-needle (Waxman et al., 2021). Although needle pain is generally brief, with most toddlers recovering within three minutes of the vaccination needle (Waxman et al., 2021), children who struggle to regulate pain-related distress or who form distressing memories of painful procedures in early childhood are at an increased risk of long-term negative outcomes such as needle anxiety and avoidance of medical procedures (Kennedy et al., 2008).

The International Association for the Study of Pain's conceptualization of pain emphasizes the influence of social factors on how pain is experienced and coped with (Raja et al., 2020). In early childhood — a stage defined by emerging abilities to speak, self-regulate, and comprehend the world — children are highly influenced by the social context of their primary caregiver. Theory and longitudinal evidence suggest that caregivers' responses to children's pain reflect a complex interplay of biological, psychological, and social factors (Pillai Riddell et al.,

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2022). These include proximal influences, such as caregivers' acute emotional state, pain management behaviours, and stress physiology, and more distal factors, such as caregivers' mental health and parenting experiences. However, the literature on the interplay of parental factors is sparse. The current study provides an in-depth analysis of caregivers' physiological response to toddlers' acute pain by examining relationships with caregivers' observed behaviours and self-reported psychological stress.

Caregivers' physiological responses to child pain and distress

Several investigations have measured caregivers' physiological responses during interactions with their distressed child to better understand how caregivers' experiences of their child's distress are reflected biologically. A recent review (Badovinac et al., 2023a) highlighted considerable heterogeneity in findings across studies, due in part to differences in the type of physiological outcome used and the type of child distress elicited by the task (e.g., fear, frustration, pain), among other factors.

Heart rate variability (HRV) is a commonly used physiological marker of caregivers' physiological responses (Badovinac et al., 2023a). High-frequency HRV reflects the activity of the parasympathetic branch of the autonomic nervous system. At rest, higher HRV indicates higher parasympathetic control which serves a "brake" function on the heart. In the context of stress, a decrease in HRV from baseline (i.e., vagal withdrawal) is an adaptive response to threat by supporting increased sympathetic and decreased parasympathetic nervous system activity for the purpose of threat management (Porges, 2007). Conversely, increases in HRV from baseline are hypothesized to be adaptive in situations requiring social engagement by activating neural pathways involved in social behaviours (e.g., emotional expression, gaze, attention to human voice; Porges, 1994; Porges, 2007).

Caregivers' physiological responses to laboratory distress paradigms with infants and toddlers

Most studies investigating caregivers' HRV responses to their infants' and toddlers' distress have focused on laboratory-based distress paradigms. Typically, these studies elicit attachment-related fear in infants and toddlers with paradigms that make the caregiver briefly unavailable to their infant or toddler (e.g., through physically separating the dyad or restricting the caregiver's emotional responding to the child). Studies typically report a pattern of caregivers' vagal withdrawal, relative to baseline, when caregivers reunite with and respond to their distressed infant (Busuito et al., 2019; Hill-Soderlund et al., 2008; Lan et al., 2022; Leerkes et al., 2017; Schechter et al., 2014). This suggests that caregivers experience children's attachment-related distress as a threat to homeostasis requiring a shift in physiological resources to manage.

Caregivers' physiological responses to procedural pain-related distress with infants and toddlers

Research examining caregivers' physiological responses to their children's pain-related distress is limited (Badovinac et al., 2023a). Two studies of school-aged children found that caregivers exhibit vagal withdrawal while observing their child perform the Cold Pressor Task (Constantin et al., 2022a; Vervoort et al., 2014), suggesting that pain-related laboratory-based distress tasks evoke similar physiological responses in caregivers as other laboratory-based distress tasks. However, these findings may not generalize to naturalistic contexts, which differ from laboratory-based tasks in that they do not constrain caregivers' availability to respond to their child's distress and they involve a degree of uncontrollability for caregivers (as procedural pain, unlike separation distress, cannot be instantaneously discontinued). Painful procedures such as routine vaccination provide a context to study caregivers' naturalistic physiological and

behavioural responses in a situation that more closely approximates the caregiving demands of everyday life.

The first study of caregivers' physiological responses to toddlers' pain-related distress discerned groups of caregiver-toddler dyads based on physiological attunement patterns, as indexed by caregiver and toddler HRV during routine vaccination (Di Lorenzo-Klas et al., 2023a). Within most dyads, caregivers showed relatively stable HRV levels from baseline to three minutes post-needle. Although this study focused on identifying trajectories of dyadic responding (as opposed to specifically caregivers' responding), it prompts a question of the factors that contribute to individual differences in caregivers' HRV responses. The only other study of caregivers' HRV during procedural pain focused on caregivers of school-aged children undergoing venipuncture (Constantin et al., 2022b) and found decreases in caregivers' HRV pre-, during, and post-venipuncture, relative to a resting baseline.

Associations between caregivers' physiological, psychological, and behavioural responses to children's pain-related distress

A notable gap in the literature concerns how caregivers' physiological responses relate to psychological and behavioural aspects of caregivers' responses. Within the pain context, caregivers' state anxiety (i.e., self-report measure of their psychological stress during their child's pain) has received the most attention to date. There is evidence that caregivers who self-report higher pre-needle and lower post-needle state anxiety exhibit less adaptive co-regulatory patterns with their toddlers during vaccination (Di Lorenzo-Klas et al., 2023b); however, another study found that caregivers' state anxiety was minimally associated (*r*'s = -.13 to 0) with their HRV reactivity during venipuncture in school-aged children (Constantin et al., 2022b).

To date, no studies have examined how caregivers' physiological responses relate to their concurrent soothing behaviours in response to their infants and toddlers' pain. In other toddler distress contexts, higher average caregiver HRV during toddlers' distress and increased HRV from baseline in response to toddlers' distress have been associated with caregivers' use of fewer overreactive discipline strategies (Lorber & O'Leary, 2005) and other negative parenting behaviours (e.g., criticism and disapproval; Miller [2015]). In contrast, among caregivers of school-aged children, lower caregiver HRV has been associated with greater use of coping-promoting behaviours (e.g., child-directed humor, non-procedure related talk, encouragement of coping behaviours), and not associated with their use of distress-promoting behaviours (e.g., criticism, verbal reassurance, apology; Constantin et al., 2022a) during the Cold Pressor Task.

Inconsistencies in the operationalization of HRV responses are a challenge across psychophysiological research and potentially contribute to mixed findings across studies (Beauchaine, 2001). Many studies define HRV reactivity as changes (i.e., difference scores) in average HRV levels between baseline and the various phases of a distress task. While difference scores denote the direction and magnitude of change in HRV elicited by a stressor, they do not capture the dynamics of change *throughout* the stressor, including the recovery trajectory. Moving beyond difference scores and using statistical approaches that characterize the direction, magnitude, and trajectory of HRV responses across time can offer insight into individual differences in HRV responses and how they relate to other aspects of individuals' emotional and behavioural responses.

The current study

Most investigations of caregivers' responses to their child's pain have focused on observed caregiving behaviours. Research consistently shows that caregivers who respond to

their child's pain with more sensitive behaviour and less insensitive behaviour have children who are better able to regulate pain (for a review, see Samdan et al., 2020), yet less is known about what underlies caregivers' use of appropriate and inappropriate soothing behaviours. Examining caregivers' physiological responses to child pain and their relation to caregivers' behaviours and self-reported stress is therefore an important area of research. To our knowledge, the current study is the first to characterize the dynamics of caregivers' HRV responses and associations with caregiver behavioural and psychological responses during vaccination pain.

Our first aim was to characterize caregivers' physiological response to toddlers' pain-related distress during vaccination. This aim was first addressed in preliminary analyses that examined the direction and magnitude of change in average HRV from baseline to post-stressor, based on standardized mean differences, to facilitate comparison of our results to previous studies using this approach. We hypothesized that caregivers would exhibit a pattern of decreased HRV (i.e., vagal withdrawal) from baseline to post-stressor. Next, we used growth curve modeling to examine the trajectory of HRV responses throughout the stressor (i.e., across the post-needle period). Growth curve modeling involves the specification of latent variables representing the magnitude of caregivers' initial HRV (i.e., HRV intercept latent variable) and the change in caregivers' HRV responses across the post-needle period (i.e., HRV slope latent variable). We defined the HRV intercept latent variable as the first minute post-needle — corresponding with toddlers' highest levels of pain-related distress and reflecting caregivers' initial reactivity to and early regulation from their toddlers' distress — and the HRV slope latent variable as the trajectory of HRV across the first three minutes post-needle. We hypothesized that caregivers would exhibit the lowest HRV levels during the first minute post-needle and an

overall pattern of increasing HRV throughout the three minutes post-needle (i.e., positive HRV slope latent variable), corresponding with toddlers' recovery from pain-related distress.

Our second aim was to examine how caregivers' physiological responses — represented by the HRV intercept and slope from the first aim — relate to caregivers' concurrent behaviour and psychological stress. Behaviour was defined in terms of caregivers' use of soothing behaviours and distress-promoting behaviours and psychological stress was characterized in terms of caregivers' state anxiety (i.e., anxiety reported during the vaccination appointment) and general stress levels (i.e., self-reported parenting stress and anxiety symptoms for the two weeks surrounding the appointment). We hypothesized that lower caregiver HRV during the initial reactivity and early regulation phase of caregivers' response (i.e., lower HRV intercept) and slower regulation of HRV (i.e., smaller increases in HRV slope) would relate to less optimal behavioural and psychological responses, including fewer soothing behaviours, more distress-promoting behaviours, and higher levels of state anxiety, parenting stress, and anxiety symptoms.

Methods

Participants

Participants were drawn from a larger longitudinal cohort-sequential study that followed healthy, typically developing toddlers and their caregivers during routine vaccination appointments across the second year of life (12, 18, and 24 months; see Di Lorenzo-Klas et al., 2023a, for further details). The current study used a subsample of 194 caregiver-toddler dyads with physiological data available for at least one appointment. For dyads with data available at multiple time points, only the final participation point was included in the current analyses. Caregiver age, education, relation to child, and ethnicity and toddler sex were not significantly

associated with dyads' participation at a single (vs. multiple) time points, based on point-biserial correlations and chi-square tests (p's > .05).

In the analyzed sample (N = 194), toddlers (54% male) were on average 18 months old (M= 17.6, SD= 4.4). Caregivers ranged in age from 20 to 62 years (M= 36, SD= 5.2) and were primarily mothers (81%), but also included fathers (18%) and grandparents (1%). Additional demographic details are in Table 1.

Procedure

Ethical approval was obtained from the Research Ethics Board at York University. Caregivers of toddlers scheduled for a vaccination appointment were made aware of the study upon entering the pediatric clinic. If the caregiver agreed to be approached by researchers, a research assistant explained the study and conducted screening for inclusion and exclusion criteria (see Di Lorenzo-Klas et al., 2023a). Written informed consent was obtained from caregivers who agreed to participate. Recruitment and data collection occurred between December 2015 and December 2019 by research assistants who were blinded to study hypotheses.

Before the appointment, caregivers were asked to complete a demographic questionnaire. During the appointment, caregiver-toddler dyads were videorecorded and were connected to MindWare wireless ambulatory monitors (MW1000A) which recorded electrocardiography (ECG) data at a sampling rate of 500 Hz. Three ECG electrodes were placed on each caregiver and toddler, including one placed over the right clavicle, one placed under the bottom left rib, and one ground electrode placed under the bottom right rib. MindWare Biolab software (version 3.3) was used for continuous ECG acquisition and The Observer XT software synchronized video and cardiac data capture. Video and cardiac data were collected for two minutes before the

vaccination needle and up to five minutes after the vaccination needle was given. Caregivers were asked to rate their state anxiety at the beginning (pre-needle) and at the end (post-needle) of the recording period. Once ECG monitoring equipment was in place, dyads were observed with minimal interference from the research team. As per standard clinical practice in the participating clinics, all caregivers held their toddler during the vaccination. Caregivers' movement was unimpeded by the wireless ECG monitoring equipment. However, given the small size of the clinic rooms, caregivers did not move around significantly during the appointment. At the end of the appointment, caregivers received a pamphlet outlining evidence-based pain management strategies. Following the appointment, caregivers were contacted by phone and administered measures of self-reported general psychological distress and parenting stress. Most caregivers (i.e., 70%) completed phone measures within three weeks of the appointment. Processing and coding of data was completed in lab using The Observer XT software and MindWare HRV software (version 3.1.5) by separate coding teams who were blinded to participant data on other measures and were unaware of study hypotheses.

The current analysis involves caregiver physiological responses, soothing behaviour, and psychological stress (i.e., self-reported anxiety and parenting stress). Previous studies of this cohort have reported on toddlers' self-regulatory behaviours (Gennis et al., 2022) and behavioural and physiological reactivity (Waxman et al., 2020; Waxman et al., 2021) and caregiver-toddler physiological attunement (Di Lorenzo-Klas et al., 2023a; Di Lorenzo-Klas et al., 2023b).

Measures

Demographic questionnaire

A demographic questionnaire collected information about caregiver age, education, relation to child, and toddler age and sex. It also asked caregivers to report the extent to which caregivers' way of life reflected mainstream North American culture on a scale from 0 to 10. This rating was adapted (see O'Neill et al., 2016) from the Vancouver Index of Acculturation (Ryder et al., 2000) and higher scores reflect greater identification with mainstream culture.

Caregiver high-frequency HRV

ECG data were edited using MindWare HRV 3.1.5 software, which derived caregiver high-frequency HRV based on spectral analysis of RR intervals (i.e., the intervals between successive heart beats or R waves; Berntson et al., 1997) using frequency bands within the range of spontaneous respiration for adults (0.12 to 0.40 [Cacioppo et al., 2000]). Manual inspection of data and editing of artifacts was conducted by coders who were trained by an experienced primary coder. Editing of artifacts (e.g., due to software misidentification or equipment malfunction) occurred in consultation with the primary coder and impacted less than 5% of data for all participants. Interrater reliability with the primary coder, calculated on a randomly selected 20% of the sample, indicated strong reliability (intraclass correlations [ICC] from 0.96 to 0.99). Caregiver HRV was calculated for consecutive 30-second epochs during the minute before the vaccination needle (i.e., baseline) and three minutes post-needle, which were then averaged within each minute to yield average HRV at Baseline, one minute post-needle (Post 1), two minutes post-needle (Post 2), and three minutes post-needle (Post 3). All analyses included caregiver posture (i.e., percentage of time spent standing, coded concurrently from video footage) as a covariate due to its influence on HRV levels (Berntson et al., 2016).

Caregiver pre- and post-needle state anxiety

Caregivers rated their state anxiety on two occasions (once prior to the toddler's needle and a second time approximately three minutes after the needle) by verbally responding to the question: "How worried are you right now on a scale of 1 to 10, where 1 is 'no worry at all' and 10 is 'the most worry possible'?", asked by a research assistant. Higher scores reflect more state anxiety. Subjective ratings of distress have been previously validated as a measure of acute emotional discomfort (Tanner, 2012).

Caregiver anxiety symptoms

Caregivers' anxiety symptoms were self-reported using the anxiety scale of the Brief Symptom Inventory (BSI), a 53-item questionnaire used to evaluate psychological distress that has been validated in clinical and non-clinical adult populations (Derogatis & Melisaratos, 1983). T-scores are reported (i.e., standardized scores based on population mean = 50 and SD = 10), with higher scores on the anxiety scale reflecting more intense recent symptoms of anxiety.

Parenting stress

Caregivers completed the Parenting Stress Index – 4th Edition, Short Form (PSI-4-SF; Abidin et al., 2012), a 36-item questionnaire used to evaluate stress related to the parent-child relationship. It consists of three subscales including parental distress (i.e., feelings of burden, distress, and support associated with the parenting role), parent-child dysfunctional interaction (i.e., extent to which interactions with child are rewarding or stressful), and difficult child (i.e., perception of child as having a difficult temperament). Subscale scores are combined to generate the Total Stress Index T-score, used in the current study, with higher scores reflecting more parenting stress.

Caregiver soothing behaviours

Caregiver soothing behaviours were coded from video footage of vaccination appointments using the Measure of Adult and Infant Soothing and Distress (MAISD; Cohen et al., 2005), a behavioural coding system used to code the occurrence of discrete caregiver behaviours. Four soothing behaviours were analyzed, including distraction (i.e., directing child's attention elsewhere by making faces, pointing, etc.), physical comfort (i.e., rubbing, patting, or massaging child), rocking (i.e., swaying or bouncing child), and verbal reassurance (e.g., making reassuring comments to child such as "it's ok"). Each behaviour was coded as present or absent during 5-second epochs throughout the three minutes post-needle. Proportion scores, reflecting the proportion of epochs during which the behaviour was observed out of all codable epochs, were calculated. Scores can range from 0 to 1 and higher scores reflect more frequent use of the soothing behaviour across the three minutes. Coding was conducted by three undergraduate coders who were trained by an experienced post-graduate primary coder. Interrater reliability, calculated as single-measures ICCs based on a randomly selected 20% of videos coded by the primary coder, ranged from 0.8 to 0.93 for physical comfort, 0.96 to 0.99 for rocking, and 0.81 to 0.95 for verbal reassurance across Post 1, Post 2, and Post 3 for coder pairs.

Caregiver distress-promoting behaviours

Caregiver distress-promoting behaviours were coded from video footage of vaccination appointments using the Opportunities to Understand Childhood Hurt's Inoculation Evaluation – Research Version (OUCHIE-RV; Badovinac et al., 2023b). The OUCHIE-RV codes caregivers' use of three domains of distress-promoting behaviour in response to child distress, including affect incongruence (e.g., verbal or non-verbal behaviours reflecting non-attuned affect, such as fearful, angry, overly positive, and/or restricted affect), attention diversion (i.e., attending away from distressed child, such as by speaking to someone else in the room), and physical distance

(i.e., lapses in physical contact between caregiver and distressed child, such as putting down the distressed child). Each behaviour domain was rated on a 0 to 2 scale during 30-second epochs spanning three minutes post-needle. Scores across behaviours and epochs were averaged, resulting in an overall OUCHIE-RV composite score representing distress-promoting behaviour during the three minutes post-needle. Composite scores range from 0 to 2 and higher scores indicate more frequent or intense use of distress-promoting behaviour in response to toddler distress. Coding was conducted by two undergraduate coders who were trained by an experienced graduate student primary coder. Interrater reliability, calculated as single-measures ICCs based on a randomly selected 20% of videos coded by the primary coder, ranged from 0.77 to 0.85 across coding pairs.

Analysis plan

Preliminary analyses included the calculation of descriptive statistics and correlations among all primary variables. Missing data rates were calculated and demographic factors potentially associated with missing data were examined using point-biserial correlations and chi-square tests.

To address our first aim, we first examined the direction and magnitude of change in HRV from Baseline through Post 3 through calculation of standardized mean differences (Cohen's *d*). Next, unconditional growth curve models (Bollen & Curran, 2006) were used to characterize the mean and variability of caregivers' HRV *during the first minute post-needle* (i.e., initial reactivity and early regulation of HRV, reflected by the intercept latent variable) and the mean and variability of caregivers' HRV *across the three minutes post-needle* (i.e., regulatory trajectory of HRV, reflected by the slope latent variable). The unconditional growth model modeled the linear change in HRV across the three minutes post-needle (i.e., Post 1, Post

2, and Post 3). The Tucker-Lewis Index (TLI), Comparative Fit Index (CFI), root mean square error of approximation (RMSEA), and standardized root mean squared residual (SRMR) were used to assess model fit (see Bollen & Curran, 2006).

To address our second aim, conditional models were estimated, which involves regressing the intercept and slope latent variables onto predictor variables, allowing for an examination of how caregivers' initial reactivity and early regulation (intercept) and regulatory trajectories (slope) in HRV relate to other aspects of caregivers' behavioural and psychological responses. Two conditional growth curve models were estimated. The first conditional model (Model 1) examined how caregivers' *concurrent behavioural responses* (i.e., behaviour during the three minutes post-needle) predicted the HRV intercept and slope latent variables; the specific predictors included were distraction, physical comfort, rocking, verbal reassurance, and distress-promoting behaviours. The second conditional model (Model 2) examined how *caregiver stress variables* predicted the HRV intercept and slope latent variables; the specific predictors included were caregivers' pre-needle state anxiety, post-needle state anxiety, anxiety symptoms, and parenting stress. Both models included caregivers' baseline (i.e., pre-needle) HRV and posture (i.e., percentage of time spent in a standing position) as covariates of the HRV intercept and slope latent variables.

Growth curve models were estimated in R (R Core Team, 2022) using the *lavaan* package (Rosseel, 2012). Robust maximum likelihood estimation was used, which allows for the inclusion of incomplete cases and produces model fit statistics and standard error estimates that are robust to non-normality. Alpha = .05 was used for all statistical tests.

Results

Descriptive statistics and preliminary analyses

Variables were approximately normally distributed, with the exception of the MAISD distraction variable, which showed significant positive skew. Distraction was thus dichotomized such that scores of 0 reflected no use of distraction and scores of 1 reflected any use of distraction. Rates of missing data ranged from 0.5% to 14.9% across variables. Missingness was not significantly associated with caregiver age, education, relation to child, ethnicity, or child sex, based on chi-square tests and point-biserial correlations ($p>.05$). Descriptive statistics and correlations among all primary variables are in Table 2 and sample mean HRV levels from Baseline to Post 3 are depicted in Figure 1. Sample mean HRV levels reflected negligible changes in HRV from baseline to Post 1 (d = 0.08), from Post 1 to Post 2 (d = -0.09), and from Post 2 to Post 3 (d = -0.03; see Figure 1). Caregiver posture was significantly correlated with HRV at Post 1, Post 2, and Post 3 (r=-.25 to -.14, $p<.05$) and parenting stress was significantly correlated with HRV at Post 3 (r=.17, $p<.05$; see Table 2). HRV levels were not significantly correlated with caregiver age or sex ($p>.05$).

Unconditional growth curve model

Model estimates are in Table 3. A linear growth model of caregiver post-needle HRV provided a good fit to the data (CFI = 1.00; TLI = 1.01; RMSEA = 0.00; SRMR = 0.01). Caregiver HRV slightly decreased from Post 1 to Post 3 (unstandardized mean of latent slope factor = -0.06, p=.049), reflecting a general trend of vagal withdrawal from Post 1 to Post 3. Variance estimates suggested substantial inter-individual variability in the level of HRV at Post 1 (intercept latent variable variance = 1.12, $p<.001$) and non-significant variability in the amount of HRV change from Post 1 to Post 3 (slope latent variable variance = 0.05, p=.41).

Conditional growth curve models

Model 1: Behavioural responses across the vaccination

Estimates for the conditional growth curve model of caregiver HRV and behavioural responses post-needle are in Table 4. Caregivers' baseline HRV and posture were included as covariates. Baseline HRV was significantly positively associated with the HRV intercept latent variable (standardized B = 0.63, unstandardized B = 0.54, $p<.001$) but not the HRV slope (standardized B = -0.02, unstandardized B = -0.004, $p=.91$). The HRV intercept and slope latent variables were not significantly associated with caregiver posture or caregivers' behavioural responses during the post-needle period (see Table 4).

Model 2: Caregiver stress

Estimates for the conditional growth curve model of caregiver HRV and caregiver stress variables are in Table 5. As in Model 1, caregivers' baseline HRV remained significantly positively associated with the HRV intercept latent variable (standardized B = .62, unstandardized B = 0.51, $p<.001$) but not the HRV slope (standardized B = -.03, unstandardized B = -0.01, $p=.88$). Caregiver posture was significantly associated with the HRV intercept latent variable (standardized B = -.17, unstandardized B = -0.004, $p=.01$) but not the HRV slope (standardized B = .01, unstandardized B = 0.00, $p=.95$). Parenting stress was significantly positively associated with the HRV slope latent variable (standardized B = .47, unstandardized B = 0.02, $p=.003$), indicating that caregivers who reported higher levels of parenting stress showed a pattern of less vagal withdrawal across the post-needle period. Finally, caregiver state anxiety and anxiety symptoms did not have significant unique associations with the HRV intercept or slope latent variables (see Table 5).

Discussion

For the first time in the literature, this study investigated relationships between caregivers' physiological responding to their toddlers' vaccination and both their behavioural

responses and self-reported stress. We characterized caregivers' HRV responses in terms of the direction and magnitude of change from baseline and the trajectory of caregivers' HRV responses during toddler vaccination (Aim 1) and examined concurrent associations between caregivers' HRV responses (i.e., initial reactivity and early regulation of HRV and regulatory trajectories of HRV) and their behaviour and self-reported stress (Aim 2).

Aim 1 elucidated caregivers' HRV responses throughout toddlers' pain-related distress. Preliminary analyses characterized the direction and magnitude of change from pre- to post-needle based on the standardized mean difference in HRV from Baseline to Post 1, with results indicating negligible changes (d=0.08). Next, the intercept and slope of caregivers' HRV responses across the post-needle period — reflecting caregivers' initial reactivity and early regulation and regulatory trajectory of HRV — were examined using growth curve modeling. A linear growth model fit the data well and reflected a slight decrease in caregiver HRV from the early to late phases of toddlers' pain-related distress. These findings did not support hypotheses, as we had expected to see a pattern of vagal withdrawal from baseline to post-needle and a trend of increasing caregiver HRV across the three minutes post-needle corresponding with toddlers' recovery from pain-related distress.

The finding of minimally fluctuating caregiver HRV from baseline in response to toddlers' distress is discrepant from previous studies which have reported vagal withdrawal in response to children's attachment-related distress (Busuito et al., 2019; Hill-Soderlund et al., 2008; Lan et al., 2022; Leerkes et al., 2017; Schechter et al., 2014) and pain-related distress (Constantin et al., 2022a; Constantin et al., 2022b; Vervoort et al., 2014). Two factors may explain this discrepancy. First, previous studies in a pain context have compared caregivers' HRV reactivity to a resting or low-demand baseline condition during which caregivers were not

interacting with their child (Constantin et al., 2022a; 2022b; Vervoort et al., 2014). In comparison, baseline data in this study were collected during the minute before the needle, during which caregivers could interact freely with their toddler. Demands for social interaction during the pre-needle period in combination with the possibility that caregivers were coping with anticipatory distress (their own or their child's) related to the needle may have led to a stress response in caregivers that preceded their child's pain. This interpretation is supported by previous research showing that parents' state anxiety during their child's pain is more strongly associated with parents' ratings of their child's *anticipatory* distress than their *pain-related* distress (Kaluza et al., 2021). Thus, a longer period of baseline data collection may have been needed to capture the onset of caregivers' stress response.

A second potential explanation is that the demands on caregivers within the context of vaccination are different from other distress contexts. During attachment stressors, because the caregiver's unavailability is the cause of the distress, the caregiver's reengagement with the child would be expected to lead to a prompt resolution of the child's distress and return to normal caregiver-child interaction (Badovinac et al., 2023a). During vaccination, because the child's pain persists even after the removal of the needle, there is a greater demand on caregivers to attune to their child's distress behaviours, attempt various soothing behaviours, and monitor the child's response to soothing behaviours in order to regulate the child's distress. Maintaining stable HRV levels throughout the onset and course of toddler distress may support the ongoing social engagement behaviours (Porges et al., 2003) needed to maintain toddlers' gaze and decode their evolving distress levels by attending to toddlers' vocalizations and facial expression.

Aim 2 contextualized caregivers' HRV responses with their concurrent behavioural responses and psychological stress. Conditional growth curve models were used to examine how

behavioural and psychological variables related to the HRV intercept (initial reactivity and early regulatory response post-needle) and slope (change over the three minutes post-needle) latent variables, while controlling for caregivers' baseline HRV levels and posture. Contrary to hypotheses, associations between caregivers' HRV responses and their concurrent use of soothing behaviours or distress-promoting behaviours were non-significant. Only one previous study has examined associations between caregivers' HRV levels and their concurrent use of soothing behaviours in a pain context; this study found a negative correlation between caregivers' use of coping-promoting behaviours and their concurrent HRV levels during a Cold Pressor Task (Constantin et al., 2022a). In our results, of the caregiver behaviour variables examined, rocking had the strongest correlations with caregiver HRV (r=-.12 to -.13; see Table 2) but was not significantly associated with the HRV intercept or slope latent variables alongside other aspects of soothing and distress-promoting behaviours in the conditional growth curve model. Although results from both studies reflect a pattern of negative relationships between caregivers' parasympathetic activity levels and their use of soothing behaviours during child distress, evidence is insufficient to draw clear conclusions. Because of the nuanced and complex ways in which caregivers may use and combine soothing and distress-promoting behaviours in the context of their child's distress (Campbell et al., 2018), further research (e.g., using cross-lagged path analysis) may be needed to better understand the reciprocal associations between caregiver physiology and behaviour.

The final conditional growth curve model examined associations between caregivers' HRV responses and self-reported stress, including state anxiety during the vaccination and recent anxiety and stress symptoms as assessed by the BSI and the PSI, while controlling for baseline HRV levels and posture. Results provided partial support for hypotheses. Although caregivers'

state anxiety and recent anxiety symptoms were not significantly associated with the HRV intercept or slope latent variables, parenting stress was significantly associated with the HRV slope latent variable. Specifically, caregivers who reported higher levels of parenting stress exhibited less vagal withdrawal over the course of the post-needle period. One possible explanation for this finding is that caregivers with higher levels of parenting stress needed to maintain higher HRV levels across the post-needle period as a self-regulatory effort to deal with their child's ongoing distress (Beauchaine, 2001). Higher parenting stress levels may ensue from having a child with more negative emotionality and who is less easily soothed, therefore requiring more active engagement and soothing from their caregiver particularly during times of distress. However, it is also possible that, due to higher chronic stress levels, these caregivers have less of a "stress reserve" available to activate a stress response (e.g., vagal withdrawal) during their child's distress. To further explore this hypothesis, future work could investigate how individual differences in caregiver stress and physiology relate to toddlers' temperament and pain-related distress behaviour.

Limitations

Owing to practical constraints of conducting research in a pediatric primary care setting, our baseline physiological data – collected over the three minutes pre-needle and analyzed for the minute immediately preceding the needle – do not reflect a true "resting" baseline that is common practice in psychophysiological research (Quintana & Heathers, 2014). Acquiring resting baseline data is a challenge across psychophysiological parent-child interaction studies (Badovinac et al., 2023a) that complicates the interpretation of HRV reactivity findings. Given that minimal changes were found between caregivers' Baseline and Post 1 HRV, caregivers' Baseline HRV data may have reflected an anticipatory stress response to their child's impending

pain-related distress and may not be directly comparable to lab-based studies that include a resting baseline.

Second, in line with the high educational attainment and low psychological distress symptomology of caregivers in our sample (see Table 1), generalizability to caregivers with sociodemographic risk related to low education or clinical levels of psychopathology may be limited, as these factors can impact both resting HRV and HRV reactivity to stressors (Laborde et al., 2017). Future work should aim to characterize the caregivers' physiological responding to their child's pain using a more socioeconomically diverse sample.

Finally, data on caregivers' food intake, general physical activity levels, and medication use were not collected. Controlling for these factors is recommended due to their influence on HRV (Laborde et al., 2017; Quintana et al., 2016). Given that growth curve modeling focuses on within-person change — as opposed to traditional statistical approaches that examine individual deviations from the sample mean — food intake, activity levels, and medication use, which remain stable within participants throughout the data collection period, would not be expected to confound results but may have contributed to individual differences in baseline HRV intercept levels.

Conclusion

The current study examined associations between caregivers' physiological, psychological, and behavioural responses to toddlers' pain-related distress. Using a universally standardized, naturalistic stressor, we have described typical physiological responses, operationalized using a marker of parasympathetic nervous system activity, in a culturally diverse sample of caregivers. Results indicated minimal changes in caregivers' parasympathetic activity levels from baseline to post-needle and a trend of slightly decreasing parasympathetic

activity levels across the post-needle period. Our examination of parenting behaviours and psychological stress as potential correlates of parasympathetic responses suggested that caregivers with more parenting stress showed less vagal withdrawal across the post-needle period. This work contributes to an improved understanding of caregivers' experiences of their toddlers' pain and can inform future research focused on leveraging caregivers as the primary intervention for supporting children during painful experiences.

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Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Data availability statement

The data analyzed during the current study are not publicly available as ethical approval was not granted for open access data sharing. Data are available from the corresponding author on reasonable request.

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Table 1.

Demographic characteristics (N= 194).

	M (SD) or *%*
Child sex (%)	
Male	54
Female	46
Relationship to child (%)	
Mother	81
Father	18
Grandparent	1
Caregiver education (%)	
Graduate School or Professional Training	47
University Graduate (4 years)	35
Partial University (at least 1 year)	2
Trade School/Community College	15
High School Graduate	1
Self-reported heritage culture (%)	
North American	24
Asian	23
European	27
Mixed	12
Other	14
Self-reported acculturation to North American culture[a]	7.9 (2.1)

[a]Ranges from 0 to 10; higher scores reflect greater identification with mainstream North American culture.

Table 2.

Descriptive statistics and correlations among study variables (n = 194).

	n	Mean (SD) or %	Range	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.
1. High-frequency HRV Base	183	4.74 (1.22)	1.1-9.16													
2. High-frequency HRV Post 1	186	4.84 (1.22)	1.73-7.46	.57*												
3. High-frequency HRV Post 2	186	4.73 (1.22)	1.99-8.06	.55*	.73*											
4. High-frequency HRV Post 3	186	4.69 (1.18)	1.74-7.74	.58*	.74*	.78*										
5. Posture (time standing)	190	68.33 (43.75)	0-100	-.14	-.23*	-.25*	-.24*									
6. Distraction	189	34.4[a]		.06	-.01	-.13	-.01	.16*								
7. Physical comfort	189	0.45 (0.24)	0-1	-.08	.01	-.03	-.02	.01	-.05							
8. Rocking	189	0.31 (0.31)	0-1	-.09	-.12	-.13	-.13	.47*	.05	.27*						
9. Verbal reassurance	188	0.14 (0.14)	0-0.61	.08	.01	.003	.02	.03	.23*	.16*	.09					
10. Distress-promoting behaviour	174	0.74 (0.4)	0-1.75	.06	-.03	.02	-.03	.03	.21*	-.36*	-.19*	.05				
11. Pre-needle state anxiety	191	2.5 (2.52)	0-10	.03	.08	.13	.1	-.01	-.04	.1	.04	.06	.002			
12. Post-needle state anxiety	193	1.91 (2.39)	0-9	.11	.09	.1	.08	.1	.08	.12	0.11	.05	-.03	.52*		
13. Anxiety symptoms	168	47.77 (8.97)	38-71	.11	.11	.05	.12	.03	.04	-.09	-.1	-.08	.04	.16*	.02	
14. Parenting stress	167	43.9 (6.72)	33-65	.08	-.01	.08	.17*	-.01	-.08	-.02	.02	-.07	-.05	.25*	.13	.35*

Note: HRV = high-frequency heart rate variability. Base = baseline.

[a]Percentage reported (i.e., percentage of caregivers who used distraction).

*p<.05

Table 3.

Unconditional growth curve model for caregiver high-frequency heart rate variability (HRV; N=189).

Variable	Unstandardized estimate	SE	*Z*	*p*
Intercept latent variable				
Mean	4.82	0.09	54.92	<.001
Variance	1.12	0.16	6.89	<.001
Slope latent variable				
Mean	-0.06	0.03	-1.97	.049
Variance	0.05	0.06	0.83	0.41

Note. Comparative Fit Index = 1.00, Tucker-Lewis Index = 1.01, root mean square error of approximation = 0.00, standardized root mean squared residual = 0.008

Table 4.

Conditional growth curve model examining associations between caregiver high-frequency heart rate variability (HRV) intercept and slope and caregiver behaviours (Model 1; N=160).

Predictor	Standardized Estimate	Unstandardized Estimate	SE	*Z*	*p*
Intercept					
Baseline HRV	**0.63**	**0.54**	**0.08**	**6.74**	**<.001**
Posture	-0.11	-0.003	0.002	-1.4	0.16
Distraction	-0.1	-0.2	0.19	-1.1	0.27
Physical comfort	0.08	0.33	0.35	0.93	0.35
Rocking	0.002	0.01	0.29	0.03	0.98
Verbal reassurance	-0.03	-0.22	0.7	-0.32	0.75
Distress-promoting behaviour	0.003	0.01	0.2	0.04	0.97
Slope					
Baseline HRV	-0.02	-0.004	0.03	-0.11	0.91
Posture	0.01	0	0.001	0.05	0.96
Distraction	0.14	0.07	0.07	1	0.32
Physical comfort	-0.03	-0.03	0.15	-0.19	0.85
Rocking	-0.13	-0.11	0.12	-0.88	0.38
Verbal reassurance	-0.03	-0.05	0.24	-0.21	0.84
Distress-promoting behaviour	-0.06	-0.04	0.08	-0.5	0.62

Note. Comparative Fit Index = 1.00, Tucker-Lewis Index = 1.00, root mean square error of approximation = 0.00, standardized root mean squared residual = 0.01. Significant predictors (p<.05) are bolded.

Table 5.

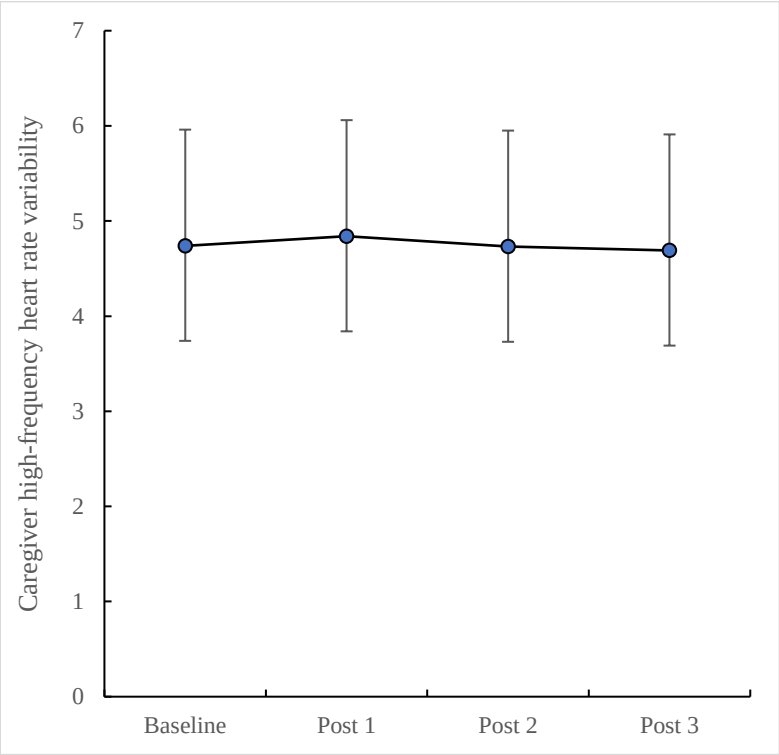
Conditional growth curve model examining associations between caregiver high-frequency heart rate variability (HRV) intercept and slope and caregiver stress variables (Model 2; N=151).

Predictor	Standardized Estimate	Unstandardized Estimate	SE	*Z*	*p*
Intercept					
Baseline HRV	**0.62**	**0.51**	**0.07**	**7.17**	**<.001**
Posture	**-0.18**	**-0.004**	**0.002**	**-2.52**	**0.01**
Pre-needle state anxiety	0.02	0.01	0.04	0.2	0.84
Post-needle state anxiety	0.05	0.02	0.04	0.6	0.55
Anxiety symptoms	0.07	0.01	0.01	1.00	0.32
Parenting stress	-0.1	-0.02	0.01	-1.34	0.18
Slope					
Baseline HRV	-0.03	-0.01	0.03	-0.16	0.88
Posture	0.01	0	0.001	-0.06	0.95
Pre-needle state anxiety	0.11	0.01	0.02	0.65	0.52
Post-needle state anxiety	-0.06	-0.01	0.02	-0.29	0.77
Anxiety symptoms	-0.16	-0.004	0.004	-1.13	0.26
Parenting stress	**0.47**	**0.02**	**0.01**	**3.00**	**0.003**

Note. Confirmatory Factor Index = 1.00, Tucker-Lewis Index = 1.01, root mean square error of approximation = 0.00, standardized root mean squared residual = 0.01. Significant predictors (p<.05) are bolded.

Figure 1.

Caregivers' high-frequency heart rate variability (HRV) levels from baseline to three minutes post-needle.



Notes: Units of measurement are the natural logarithm of milliseconds squared. Error bars reflect standard deviations.

CHAPTER 7: CONCLUSIONS

During the first years of life, when children are in the earliest stages of acquiring the developmental skills needed to navigate the world around them, their experiences are filtered through the experiences of their primary caregivers (Sameroff, 2010). Over time, proximity, emotionally invested care, and the generally attuned responding of caregivers, particularly during moments of children's distress, help children develop a view of others as supportive and trustworthy and of themselves as competent and worthy of care (Ainsworth et al., 1978; Bowlby, 1969/1982). Sensitive caregiving and the resultant socio-emotional foundations established for children exposed to sensitive caregiving result in many positive developmental outcomes (Badovinac et al., 2021; Fearon et al., 2010; Groh et al., 2012; Pallini et al., 2018). Although biopsychosocial approaches have come to dominate theoretical frameworks guiding the study of developmental psychology (Sameroff, 2010), our understanding of caregivers' influence on child outcomes has been restricted by limited consideration of the concurrent biological, behavioural, and psychological factors underlying caregivers' responses to their children's distress (Constantin et al., 2017; Samdan et al., 2020). This dissertation addresses this limitation by providing an in-depth investigation of the biological, behavioural, and psychological aspects of caregivers' responses to children's distress across infancy and toddlerhood.

This dissertation consisted of a series of three studies. Study 1 synthesized findings from studies of parents' physiological responses to infants' and toddlers' distress during experimental and naturalistic distress paradigms, examined concurrent associations between parents' physiological and behavioural responses, and identified methodological limitations and gaps within the extant literature. Studies 2 and 3 built on gaps identified in Study 1 related to the need for studies of naturalistic distress contexts, the importance of studying parents' insensitive

behaviours, and our enduring lack of understanding how parents' physiological responses relate to their behavioural and psychological responses. Appendix A provides a two-page summary of the objectives, analyses, and results for each study. A general discussion of the key themes, insights, and implications of this dissertation is presented in the current chapter.

Integrative synthesis

Characterizing physiological aspects of parenting responses

Characterizing parents' physiological responses to their children's distress was a central objective of the current dissertation. Study 1 examined the literature on parents' physiological responses across a range of experimental and naturalistic distress contexts and Study 3 focused on parents' physiological responses within the naturalistic high-distress context of toddler routine vaccinations. These studies offered insights into how parents respond physiologically to their children's distress across a range of contexts that varied in the type and intensity of child distress elicited.

A central theme to emerge across these studies was that contextual and methodological factors are key contributors to the heterogeneity in research findings related to parents' physiological responses to their child's distress. For example, caregivers reliably exhibited a pattern of vagal withdrawal in response to their child's *attachment-related distress* (i.e., distress related to caregiver separation or unavailability) which was not consistently observed during distress paradigms involving *frustration-related distress* (Study 1) or during toddler *pain-related distress* (Study 3). One possible explanation for these differences is that attachment-related stress, which effectively reflects stress caused by the caregiver, elicits a more reliable and marked physiological response due to the emotional implications of caregivers' awareness of their causative role in their child's response. However, it is important to consider that research

involving other types of distress paradigms (e.g., frustration, distress to novelty, pain) tended to be more methodologically heterogeneous than research on attachment-related distress. Mixed findings among non-attachment related distress paradigms occurred in the context of differences in the extent of parental involvement in causing children's distress, constraints on how parents could respond during the task, and most notably, differences in the baseline comparison used for parents' physiological reactivity, which ranged from a resting baseline condition to parents playing with their child during baseline. Study 1 offered several methodological recommendations to guide study design and enhance comparability across future studies.

Study 3, which characterized parents' high-frequency heart rate variability (HRV) responses during toddlers' pain-related distress, did not find the hypothesized pattern of vagal withdrawal that would reflect parents' physiological stress (i.e., decreased parasympathetic input) to their children's high levels of distress. Instead, changes in parents' HRV following the vaccination needle were minimal compared to their pre-needle baseline. Based on findings from Study 1, as well as previous research suggesting that parents' pre-needle HRV is higher than during a resting baseline but not different from post-needle HRV during pediatric venipuncture in older children (Constantin et al., 2022), this finding suggests that pre-needle baseline data may not capture the onset of parents' stress responses during toddlers' routine vaccination. This finding highlights that, in addition to the distress context being studied, both the nature and timing of baseline data collection can impact the meaning of results.

Insensitive parent behaviour as a key contributor within emotion socialization processes

Revealing the mechanisms underlying parent emotion socialization processes was another major objective of this dissertation. Guided by theoretical assertions concerning how parental factors relate to parental responses and child outcomes during children's distress

generally (Bridgett et al., 2015) and pain-related distress specifically (Pillai Riddell et al., 2022), Studies 1, 2, and 3 each offered insights into various stages of emotion socialization processes.

Study 1 reviewed the literature on how parents' physiological and behavioural responses were associated in the context of children's distress across infancy and toddlerhood. Parents' insensitive behaviour had stronger associations with their physiological reactivity than did their sensitive behaviour, with greater increases in physiological arousal and smaller regulatory responses relating to more insensitive behaviour. Study 2 demonstrated that greater frequency and intensity of parents' insensitive behaviour (i.e., affect incongruence, attention diversion, physical distance) were associated with higher levels of toddlers' pain-related distress within each phase of the post-needle period, even after controlling for toddlers' previous distress levels. The magnitude of positive associations between parent insensitive behaviours and toddler pain-related distress in Study 2 ranged from $r = .27$ to $r = .37$, which is roughly double the magnitude of negative associations identified between children's pain-related distress and the most powerful positive parent behaviours (i.e., emotional availability, distraction) in a recent meta-analysis (r = -.1 to -.15; Sobol-Kwapińska et al., 2020). Taken together, these findings highlight the importance of parent insensitive behaviour within emotion socialization processes as a variable that reflects parents' own emotional state and communicates to children how attuned parents are to their emotional needs.

In Study 3, we did not find evidence for hypothesized associations between parents' insensitive behaviour and parents' HRV levels or trajectories during routine vaccination when insensitive behaviours were examined in growth curve models alongside other parent soothing behaviours (e.g., physical comfort, rocking, verbal reassurance) and after controlling for parents' baseline HRV and posture. Similarly, correlations between insensitive behaviour and mean HRV

levels at baseline and throughout the post-needle period were negligible in Study 2 (r=-.04 to .13). This discrepancy may relate to how HRV was defined and measured within the current studies. As discussed above and in Study 3 (Chapter 6), our results — when considered in the context of previous research — suggest that the timeline of our data collection (i.e., collecting baseline data one minute pre-needle) may not have captured the onset of parents' distress related to their child's painful procedure. Given that maladaptive HRV responses have been defined in terms of the changes in HRV from typical or resting levels (Beauchaine, 2001), it is possible that defining parents' HRV responses in relation to a resting baseline would have yielded more insight into the reactive and self-regulatory physiological processes that relate more strongly to parent behaviour.

Clinical implications

Several findings from the current dissertation have implications for clinical settings. First, consistent with previous studies of the vaccination context (Badovinac et al., 2018; Campbell et al., 2018), our findings highlight the strong impact that parents' insensitive behaviours have on children's pain-related distress. When parents responded to their toddlers' pain-related distress in a way that communicated a lack of recognition or misinterpretation of children's distress, such as through incongruent affect (e.g., fear, frustration, overly positive or overly restricted affect), denying their child's need for proximity, and diverting their attention away from their distressed child, toddlers maintained higher levels of behavioural distress. The association between insensitive parent behaviour and toddlers' pain-related distress as determined in Study 2 was stronger than meta-analytic effect sizes linking sensitive parent behaviour and children's pain-related distress (Sobol-Kwapińska et al., 2020). This finding emphasizes that teaching parents what *not to do* in response to their child's pain-related distress is at least as important as teaching

parents what *to do* (Pillai Riddell et al., 2022). Parent education initiatives delivered in the context of well-baby and well-child visits are important for translating knowledge regarding best practices for pain management (Pillai Riddell et al., 2018), and recommendations to avoid the insensitive parent behaviours measured by the OUCHIE-RV should be incorporated into education initiatives to support more sensitive and attuned parenting responses to children's pain. Health professionals who provide vaccinations to caregiver-child dyads who are at greater psychosocial risk (e.g., due to mental illness, low socioeconomic status, maltreatment risk) may consider more intensive interventions such as Circle of Security Parenting or Attachment and Biobehavioural Catch-Up, which can be delivered in the context of well-baby and well-child visits and lead to improvements in parental sensitivity (Bergström et al., 2020).

Second, our findings build on previous evidence indicating that the onset of parents' stress responses to their child's pain-related distress precedes children's pain (Constantin et al., 2022; Kaluza et al., 2021). Given that parents' own anticipatory distress has been shown to relate to higher levels of children's procedural pain (Campbell et al., 2017), this finding emphasizes the importance of parents monitoring and managing their own emotional distress as a strategy to support positive pain outcomes for their children. An additional implication to consider is how parents' anticipatory stress levels may impact their engagement in the well-baby appointment. In addition to the vaccination procedure, well-baby appointments involve information gathering and sharing between parents and health professionals which support assessment and monitoring of children's development and overall functioning. Clinicians should be alert to indicators of elevated parental anxiety, consider how this anxiety may impact parents' ability to engage in the appointment (Mamedova et al., 2019), and be prepared to offer evidence-based strategies for

managing parents' state anxiety (e.g., parental education, therapeutic parent-child play; see Santapuram et al., 2021).

Third, we found that factors that are distal to the vaccination context have important implications for how parents respond to their toddlers' pain-related distress. In Study 3, parents' self-reported parenting stress levels were significantly associated with their HRV trajectories across the post-needle period, suggesting that parents' day-to-day stress related to their role as a parent impacts the physiological stress reserve that parents have available when responding to acute stressors. This limited stress reserve would be expected to impact parents' capacity to respond to their children's emotions in the context of other stressors beyond the pain context. As a strategy to support the child and their caregiving system, it is important for clinicians to make use of well-baby visits as an opportunity to check-in on caregivers' general well-being and consider when a referral to a mental health professional may be warranted.

Theoretical implications

Findings from the current dissertation support and build on key theoretical frameworks guiding the study of parent emotion socialization processes during the first years of life. The validation of the OUCHIE-RV (Study 2) tested foundational principles of Ainsworth's (1974) sensitivity framework and Biringen's (2000) Emotional Availability framework. These frameworks, which are both grounded in Attachment Theory (Bowlby, 1969/1982), posit that young children rely on close physical proximity and contingent, emotionally attuned responding provided by a primary caregiver to adaptively regulate their distress. Conversely, when caregiver behaviour expressly communicates a misinterpretation or lack of attuned responsiveness, children struggle to regulate distress. This pattern was supported by Study 2's findings, which showed that higher levels of parent insensitive behaviour, as communicated through incongruent

affect (i.e., fearful, angry, overly positive, or flat affect), diverting attention away from their distressed toddler, or denying their toddler's need for close physical proximity, led to toddlers maintaining higher levels of behavioural distress. This finding also provides further support for the DIAPR-R 2022 model (Pillai Riddell et al., 2022) by showing that parent behaviour continues to impact toddlers' pain-related distress outcomes during the second year of life.

Both the DIAPR-R 2022 model (Pillai Riddell et al., 2022) and the Self-Regulation Intergenerational Transmission Model (Bridgett et al., 2015) posit that parents' physiological responses to their children's distress directly impact parents' behavioural responses. Our results provided partial support for this hypothesis. Study 1's synthesis of the literature provided evidence for small associations between parents' physiological responses and parenting behaviours, yet Study 3 found that parents' initial HRV responses to toddler vaccination and the trajectories of their HRV responses across time were not significantly associated with parents' use of sensitive or insensitive behaviours in response to their toddlers' pain-related distress. Future research that examines physiology-behaviour associations may help illuminate the directional associations between parent physiological responses and their use of sensitive and insensitive soothing behaviours. Given Study 3's finding of limited variability in parent HRV from pre-needle to post-needle, future work should test the hypothesis that parents' physiological response precedes their child's pain-related distress through the collection of resting baseline data. Studying parents' reactivity from a resting baseline may provide more insights into how parents' physiological responses relate to their behavioural responses.

Finally, Study 3's finding of significant associations between caregivers' self-reported parenting stress (i.e., stress related to the parenting role) and their trajectories of physiological responding to their toddlers' pain-related distress support theoretical assertions described within

the DIAPR-R 2022 model concerning the impact of distal factors on parental responding in the context of routine vaccination. As stress related to the parenting role could arise due to a variety of systemic factors (e.g., the division of caregiving responsibilities among primary caregivers, perceived support in the caregiving role, culturally-laden expectations for parents), this finding underscores the importance of considering how factors beyond the pain context impact parenting responses.

Limitations

The findings of the current dissertation should be contextualized based on the following limitations. First, the composition of the cohort analyzed for Studies 2 and 3 was characterized by a high level of educational attainment and normative levels of psychopathology symptoms and was primarily comprised of mothers. Thus, the generalizability of findings to samples with sociodemographic risk related to low education or psychopathology may be limited. Moreover, as fathers take on an increasing role in primary caregiving responsibilities within North American societies (Kalil et al., 2014) — presumably including scheduling and caregiving during vaccination appointments — ensuring that fathers are represented in this work is an important future area of study. Of note, while caregiver biological sex cannot be considered equivalent to socialized gender roles of mother or father, caregiver sex was not significantly associated with primary outcomes in Studies 2 or 3. Second, it is possible that parents' physiological and behavioural responses to child distress, as investigated in Studies 1 and 3, were impacted by individual differences in how children responded to the distressing situation. This dissertation was focused primarily on parenting; specifically, it examined the biological, behavioural, and psychological aspects of parenting in distress contexts. Accordingly, a detailed examination of the dyadic processes unfolding in distress contexts was beyond the scope of the

current work. Third, caregivers' HRV responses can be impacted by a multitude of factors, some of which (e.g., food intake, physical activity levels, medication use, attachment history; Laborde et al., 2017; Roque et al., 2012) were not accounted for in Studies 2 and 3 yet may have contributed to individual differences in caregivers' HRV responses.

Directions for future research

Based on the findings and limitations discussed above, several directions for future research are offered. While Studies 2 and 3 focused on characterizing the dynamics of caregiver responses to toddler vaccination pain at a single timepoint during the second year of life, future work should explore other proximal and distal factors that potentially predict or are predicted by the physiological, behavioural, and psychological aspects of caregiver responses discussed in this dissertation. These variables may include caregiver and child factors such as toddler anticipatory and post-needle distress, temperament, and socioemotional functioning, and caregiver physiological, behavioural, and psychological responses collected at previous, concurrent, or subsequent timepoints (see the DIAPR-R 2022 model; Pillai Riddell et al., 2022). Cognitive aspects of caregiver responses to child distress such as caregivers' attributions for children's distress (e.g., attributing infants' crying to hunger vs. the distressing stimulus) are an understudied domain that has been linked to parents' physiological and behavioural responses in other distress contexts (Leerkes et al., 2016). Statistical approaches such as structural equation modeling offer value in representing the interrelationships and pathways involving multiple predictors and outcomes and have been used in experimental distress contexts to study mechanisms linking caregivers' physiological, emotional, cognitive, and behavioural responses to child outcomes (Leerkes et al., 2016; Lorber & O'Leary, 2005). The frequency and standardized nature of routine vaccinations during infancy and toddlerhood (i.e., 20 or more

vaccinations during the first two years of life; Centers for Disease Control and Prevention, 2022) offers a rich opportunity to study these processes as they unfold longitudinally across early development.

Studies employing physiological markers of caregiver or child responses to distress should carefully consider methodological factors such as the context (i.e., resting baseline vs. parent-child interactive baseline) and timing (i.e., following a period of acclimation if using outcomes such as cortisol that demonstrate time-lagged responses) of baseline data collection, characterization of physiological outcomes (e.g., analyzing sample means or change scores, modeling outcome trajectories), and the confounding impact of specific task demands (e.g., constraining parents' emotional or behavioural responses [e.g., Tronick et al., 1978], requiring movement or changes in posture [e.g., Ainsworth et al., 1978]). These factors, as well as others discussed in Chapter 2, have important implications for the validity and interpretability of the resulting data.

Furthermore, as highlighted throughout this work, studies of non-maternal caregivers (e.g., fathers, grandparents) continue to be underrepresented in the literature despite the increased role of these caregivers in primary child-rearing responsibilities (Cabrera et al., 2000; Kalil et al., 2014). Studies should fill this gap by directly comparing caregiving responses as a function of caregiving role (e.g., see Fuchs et al. 2021; Skoranski et al., 2021) in order to test evolutionary hypotheses regarding functional differences in responses across caregivers (Möller et al., 2013) while considering broader issues such as how a historical focus on "mothering" has impacted on the availability of theoretical models and measurement tools to assess "fathering" (Cabrera et al., 2018).

Finally, this dissertation has contributed a theoretically grounded research tool (the OUCHIE-RV) with strong reliability and validity evidence for quantifying parents' insensitive behaviours during toddler vaccination. Future work can build on this effort by examining the reliability and validity of the OUCHIE-RV in other contexts, such as infant and preschool vaccination, other acute pain contexts (e.g., venipuncture, lumbar puncture, wound dressing changes), and other experimental distress contexts.

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APPENDIX A

Summary of Objectives, Analyses, and Results

Study 1: Parents' Physiological Reactivity to Child Distress and Associations with Parenting Behaviour: A Systematic Review

Objective: To synthesize the literature regarding parents' physiological responses to their child's (0-3 years) distress and how they relate to parenting behaviours.

Analysis: A search yielded 3,607 records. Fifty-five studies met inclusion criteria and underwent narrative synthesis and risk of bias assessment. This involved describing the direction, magnitude (standardized effect sizes), and consistency of findings, contextualized by studies' risk of bias.

Results:

- Among studies of parents' physiological responses to child distress, cortisol (k = 30) and heart rate variability (HRV; k = 26) were the most common outcomes studied, with findings indicating:
    - Small to moderate decreases in *cortisol* in response to laboratory-based child fear and frustration tasks.
    - Decreases in *HRV* during the reunion phase of child attachment fear tasks — compared to baseline — and inconsistent findings for other types of distress.
    - Substantial increases in *skin conductance levels* during fear and frustration tasks, with high risk of bias in relevant studies being an important caveat.
    - No evidence for changes in *salivary alpha amylase*, based on two studies.
- Less than one quarter of studies (k = 13) examined how parent physiological responses relate to concurrent parenting behaviours, with two preliminary trends emerging:
    - Parental physiological reactivity was more strongly associated with parents' use of *insensitive behaviour*, compared to sensitive behaviour. Specifically, less modulation of physiological responses (e.g., greater increases in arousal, smaller regulatory responses) related to more insensitive behaviour.
    - *Dyadic frustration tasks*, which are designed to stress both dyad members and which involve more opportunity to observe unconstrainted parent-child interaction, more often elicited parent physiology-parent behaviour associations.
- Several methodological considerations for future research were elucidated, such as:
    - "Baseline" comparison conditions varied considerably (e.g., resting vs. parent-child interaction), likely contributing significantly to mixed findings.
    - Parents' physiological responses to child distress in naturalistic settings are understudied.

Study 2: A measure of caregivers' distress-promoting behaviours during toddler vaccination: Validation of the OUCHIE-RV

Objective: Examine the reliability and validity of the OUCHIE-RV as an observational measure of caregivers' distress-promoting behaviour during toddler vaccination.

Analyses: Measure reliability was examined through interrater reliability (kappa coefficients [κ], intraclass correlations [ICC]) and internal consistency (correlations). Validity was examined through correlations and autoregressive cross-lagged path analysis.

Results:

- Strong interrater reliability (κ = 0.86 to 0.97; ICC = 0.77 to 0.85) and internal consistency (*r* = 0.57 to 0.78) for OUCHIE-RV composite scores.
- Evidence for concurrent validity based on associations between OUCHIE-RV composite scores and toddler pain-related distress:
    - Correlation analyses: significant small associations within concurrent (*r* =.28 to .36) and subsequent minutes (*r* =.24).
    - Autoregressive cross-lagged path analysis:
        - Toddler distress at Baseline and Post 1 predicted higher *subsequent* OUCHIE-RV at Post 1 (β= .23) and Post 2 (β= .34), respectively. Toddler distress at Post 2 did not predict OUCHIE-RV at Post 3 (β= .01).
        - OUCHIE-RV did not predict *subsequent* toddler distress (β= .06 to .07).
        - OUCHIE-RV and toddler distress were *concurrently* associated at Post 1 (*r*= .27), Post 2 (*r*= .34), and Post 3 (*r*= .37).
- Exploratory associations (OUCHIE-RV composite scores and other caregiver factors):
    - OUCHIE-RV composite scores had small to moderate correlations with caregivers' concurrent use of physical comfort (*r* =-.34 to -.24, *p*<.05) and rocking (*r*=-.36 to -.19, *p*<.05) and negligible to small associations with verbal reassurance (*r*=.06 to .12, *p*>.05).
    - OUCHIE-RV composite scores had negligible associations with caregivers' state anxiety (*r*=-.02 to .09, *p*>.05), physiological arousal (*r*=-.15 to .05, *p*>.05), and physiological regulation (*r*=-.04 to .13, *p*>.05).

Study 3: Parents' physiological responses during toddler vaccinations: Associations with psychological and behavioural responses

Objective: Characterize caregivers' physiological responses (i.e., HRV) to toddler vaccination and how these responses relate to caregivers' concurrent behaviour and psychological stress.

Analyses: Descriptive statistics; growth curve model

Results:

- Mean HRV levels reflected a negligible increase HRV from baseline to Post 1 (*d* = 0.08) and negligible decreases from Post 1 to Post 2 (*d* = -0.09) and Post 2 to Post 3 (*d* = -0.03).
- HRV decreased from Post 1 to Post 3 (mean of latent slope factor = -0.06, *p*=.049). There was substantial inter-individual variability in HRV intercepts (*p*<.001) and non-significant variability in HRV slopes (*p*=.41).
- In Model 1, HRV intercept and slope latent variable were not associated with caregiver behaviour including rocking (β = -.13 to .002), physical comfort (β = -.03 to .08), verbal reassurance (β = -.03), and distress-promoting behaviour (β = -.06 to .003), after accounting for baseline HRV and caregiver posture.
- In Model 2, parenting stress was associated with the HRV slope latent variable (β = .47, *p*=.003), but not the HRV intercept latent variable (β = -.10). State anxiety (β = -.06 to .11) and anxiety symptoms (β = -.16 to .07) were not associated with HRV intercept or slope latent variables.

APPENDIX B

PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Section 1
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Section 1.1
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Section 2.1
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Section 2.1
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supp. File 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Section 2.2
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Section 2.2
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Section 2.2
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.2
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Section 2.2
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5).	Section 2.2

Section and Topic	Item #	Checklist item	Location where item is reported
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Section 2.2
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	NA
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Section 1.1 & 2.2
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Section 2.2
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	NA
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Supp. File 3
Study characteristics	17	Cite each included study and present its characteristics.	Section 3.1; Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Section 3.1; Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Sections 3.2 – 3.3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 3
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Table 3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Sections 3.2 – 3.3
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	NA

Section and Topic	Item #	Checklist item	Location where item is reported
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	NA
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Section 4
	23b	Discuss any limitations of the evidence included in the review.	Section 4.4
	23c	Discuss any limitations of the review processes used.	Section 4.4
	23d	Discuss implications of the results for practice, policy, and future research.	Section 4.3
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Section 2.1
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Section 2.1
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Section 2.1
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Section 6
Competing interests	26	Declare any competing interests of review authors.	Title Page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Supp. File 5

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

APPENDIX C

Example Search Terms and Pairings (PsycINFO database)

#	Searches
1	Parent Child Relations/ or Father Child Relations/ or Mother Child Relations/ or Parenting/
2	("child mother relation*" or "child parent relation*" or "child parent spatial pattern*" or "father child relation*" or "father infant relation*" or "father-child relation*" or "maternal fetal relation*" or "maternal patterns of care" or "maternal-fetal relation*" or "mother child interaction*" or "mother child relation*" or "mother fetus relation*" or "mother infant interaction*" or "mother infant relation*" or "mother-child interaction*" or "mother-child relation*" or "mother-fetus relation*" or "mother-infant interaction*" or "mother-infant relation*" or "parent child correlation" or "parent child relation*" or "parent infant bonding" or "parent infant relation*" or "parental role*" or "parent-child relation*" or "parenting").tw.
3	Mothers/ or Fathers/
4	(father or fathers or mother or mothers or dyad*).tw.
5	or/1-4
6	Hypothalamic Pituitary Adrenal Axis/ or ("adrenal hypophyseal axis" or "adrenohypophyseal axis" or "diencephalon adrenal axis" or "hypophyseal adrenal axis" or "hypophyseal adrenal system" or "hypophyseal adrenocortical system" or "hypophyseoadrenocortical system" or "hypophysis adrenal axis" or "hypophysis adrenal cortex system" or "hypophysis adrenal function" or "hypophysis adrenal gland" or "hypophysis adrenal system" or "hypophysoadrenal axis" or "pituitary adrenal axis" or "pituitary adrenal function" or "pituitary adrenal system" or "pituitary adrenocortical function" or "pituitary adrenocortical regulation" or "pituitary adrenocortical system" or "pituitary gland adrenal gland axis" or "pituitary-adrenal system").tw.
7	Parasympathetic Nervous System/ or ("acetyl cholinergic system" or "cholinergic mechanism" or "cholinergic nerve system" or "cholinergic nervous system" or "cholinergic pathway" or "cholinergic receptor system" or "parasympathetic nerve plexus" or "parasympathetic nerve system" or "parasympathetic nervous system" or "parasympathetic nervous systems" or "parasympathetic system" or "parasymphatic nervous system").tw.
8	Heart Rate/ or ("cardiac chronotropism" or "cardiac chronotropy" or "cardiac frequency" or "cardiac rate" or "cardiac rates" or "heart frequency" or "heart rate" or "heart rates" or "pulse rate" or "pulse rates" or "ventricle rate" or "ventricle rates").tw.
9	Sympathetic Nervous System/ or ("adrenergic mechanism" or "adrenergic nerve system" or "adrenergic nervous system" or "adrenergic regulatory mechanism" or "adrenergic system" or "beta adrenergic system" or "ortho sympathetic nervous system" or "orthosympathetic nervous system" or "sympathetic nerve system" or "sympathetic nervous system" or "sympathetic system" or "sympathic nervous system" or "sympathicoadrenal system" or "sympathoadrenal system" or "vasomotor system" or "vasomotor systems").tw.
10	Hydrocortisone/ or ("11 epicortisol" or 11-epicortisol or acticort or "aeroseb hc" or "aeroseb-hc" or ala-cort or ala-scalp or alfacort or algicortis or "alpha derm" or alphaderm or anucort-hc or anumed-hc or anutone-hc or aquanil hc or balneol-hc or barseb hc or beta-hc or biacort or cetacort or cobadex or colocort or "compound f" or "cordicare lotion" or coripen or "cort dome" or cort-dome or cortef or "cortef cream" or cortenema or cortibel or corticorenol or cortifair or cortifan or cortiphate or cortisol or cortisole or cortispray or cortoderm or cortril or cotacort or covocort or cremicort-h or cutaderm or "dermacrin hc lotion" or dermaid or "derm-aid cream" or dermocare or dermocortal or dermolate or dioderm or eczacort or "ef cortelan" or efcortelan or egocort or eksalb or eldecort or emo-cort or epicort or epicortisol or ficortril or filocot or flexicort or glycort or gly-cort or "hc no. 1" or "hc no. 4" or h-cort or hebcort or "hemorrhoidal hc" or hemril-30 or "hemril-hc uniserts" or hi-cor or hidrotisona or hycor or hycort or hydracort or hydrasson or "hydro ricortex" or hydrocort or hydrocorticosteroid or hydrocortisate or hydrocortison or hydrocortisone or hydrocortisonum or hydrocortisyl or hydrocortone or hydrogalen or hydrokort or hydrokortison or hydro-rx or hydrotopic or hysone or hytisone or hytone or "incortin h" or "instacort 10" or kyypakkaus or "lacticare hc" or lacticare-hc or "lemnis fatty cream hc" or lenirit or "medihaler cort" or "medihaler duo" or medrocil or mildison or "mildison fet krem" or "mildison lipocream" or mildison-fatty or "mitocortyl demangeaisons" or munitren or "nogenic hc" or novohydrocort or nutracort or optef or "otosone f" or penecort or plenadren or prepcort or "prevex hc" or "pro cort" or procort or proctocort or "procto-kit 1%" or "procto-kit 2.5%" or "proctosert hc" or proctosol-hc or proctosone or procutan or rectasol-hc or rectocort or rederm or sanatison or scalp-aid or

	schericur or "schericur 0.25%" or "scherosone f" or "sistral hydrocort" or skincalm or stie-cort or "substance m" or synacort or texacort or triburon-hc or unicort or vasocort).tw.
11	("SA nodal arrhythmia" or "SA node arrhythmia" or "sinoatrial arrhythmia" or "sinoatrial arrhythmias" or "sinoatrial node arrhythmia" or "sino-atrial node arrhythmia" or "sinus arrhythmia" or "sinus arrhythmias" or "sinus arrhythmica" or "sinus node arrhythmia" or "sinus node syndrome").tw.
12	Autonomic Nervous System/ or ("automatic nervous system" or "autonomic nerve system" or "autonomic nervous system" or "autonomic nervous systems" or "autonomic system" or "autonomous nervous system" or "involuntary nervous system" or "neuroautonomic system" or "neurovegetative system" or "organic nervous system" or "splanchnic nervous system" or "systema nervosum autonomicum" or "vegetative nervous system" or "vegetative nervous systems" or "vegetative system" or "visceral nervous system" or "visceral nervous systems").tw.
13	Galvanic Skin Response/ or ("cutaneous galvanic response" or "electric skin response" or "electrodermal response" or "electrodermal responses" or "galvanic skin reflex" or "galvanic skin response" or "galvanic skin responses" or "GSR" or "psychogalvanic reflex" or "psychogalvanic skin reflex" or "skin conductance response" or "skin electric conductance" or "skin galvanic response" or "skin potential response").tw.
14	("adrenal cortex" or "adrenal cortical activity" or "adrenal cortical activities" or "adrenal cortical system" or "adrenal cortical systems" or "adrenal gland cortex" or "adreno cortical activity" or "adreno cortical activities" or "adrenocortical activity" or "adrenocortical activities" or "adrenocortical system" or "adrenocortical systems" or "adrenocortical tissue" or "cortex glandulae suprarenalis").tw.
15	Saliva/ or (spittle or saliva or salivas).tw.
16	("parotid amylase" or "parotid amylases" or "saliva alpha amylase" or "saliva alpha amylases" or "saliva amylase" or "saliva amylases" or "salivary alpha amylase" or "salivary alpha amylases" or "salivary alpha amylase" or "salivary alpha amylases" or "salivary alpha-amylase" or "salivary alpha-amylases" or "salivary amylase" or "salivary amylases" or "salivary gland amylase" or "salivary gland amylases").tw.
17	("diencephalohypophyseal system" or "diencephalohypophyseal systems" or "diencephalohypophysis system" or "diencephalohypophysis systems" or "hypophyseal hypothalamic system" or "hypophyseal hypothalamic systems" or "hypophyseal portal system" or "hypophyseal portal systems" or "hypophysis hypothalamus system" or "hypophysis hypothalamus systems" or "hypothalamic hypophyseal axis" or "hypothalamic hypophyseal system" or "hypothalamic hypophyseal systems" or "hypothalamic neurohypophyseal system" or "hypothalamic neurohypophyseal systems" or "hypothalamic neuropituitary system" or "hypothalamic neuropituitary systems" or "hypothalamic pituitary axis" or "hypothalamic pituitary system" or "hypothalamic pituitary systems" or "hypothalamic pituitary unit" or "hypothalamic-pituitary unit" or "hypothalamo hypophysary axis" or "hypothalamo hypophyseal connection" or "hypothalamo hypophyseal system" or "hypothalamo hypophyseal systems" or "hypothalamo hypophyseal tract" or "hypothalamo neuropituitary system" or "hypothalamo neuropituitary systems" or "hypothalamo pituitary axis" or "hypothalamo pituitary system" or "hypothalamo pituitary systems" or "hypothalamohypophyseal axis" or "hypothalamohypophyseal neurosecretory system" or "hypothalamohypophyseal neurosecretory systems" or "hypothalamohypophyseal system" or "hypothalamohypophyseal systems" or "hypothalamo-hypophyseal system" or "hypothalamo-hypophyseal systems" or "hypothalamohypophysis axis" or "hypothalamohypophysis system" or "hypothalamohypophysis systems" or "hypothalamoneurohypophyseal system" or "hypothalamoneurohypophyseal systems" or "hypothalamopituitary axis" or "hypothalamopituitary function" or "hypothalamopituitary system" or "hypothalamopituitary systems" or "hypothalamus hypophyseal axis" or "hypothalamus hypophyseal system" or "hypothalamus hypophyseal systems" or "hypothalamus hypophysis" or "hypothalamus neurohypophysis system" or "hypothalamus neurohypophysis systems" or "hypothalamus neuropituitary system" or "hypothalamus neuropituitary systems" or "hypothalamus pituitary gland axis" or "hypothalamus pituitary system" or "hypothalamus pituitary systems").tw.
18	"respiratory sinus arrhythmia".tw.
19	Human Biological Rhythms/ or ("circadian clock" or "circadian clocks" or "circadian cycle" or "circadian fluctuation" or "circadian periodicity" or "circadian rhythmicity" or "circadian variation" or "day night rhythm" or "diurnal cycle" or "diurnal fluctuation" or "diurnal pattern" or "diurnal rhythm" or "diurnal rhythmicity" or "diurnal variation" or "diurnal variations" or "nychtohemeral" or "circadian rhythm" or "circadian rhythms" or "diurnal rhythm" or "diurnal rhythms" or "nycthemeral rhythm" or "nycthemeral rhythms" or "nyctohemeral rhythm" or "nyctohemeral rhythms" or "twenty four hour rhythm" or "twenty-four hour rhythm" or "twenty-four hour rhythms" or "biological rhythm" or "biological rhythms").tw.

20	vagus nerve/ or ("cranial nerve x" or "nerve x" or "nerve xs" or "pneumogastric nerve" or "pneumogastric nerves" or "tenth cranial nerve" or "tenth cranial nerves" or "regeneration nervi vagi" or "tenth cranial nerve" or "vagal nerve" or "vagal receptor" or "vagosympathetic trunk" or vagus).tw.
21	homeostasis/ or (autoregulation or homeostasis or "homeostatic equilibrium" or "homeostatic mechanism" or homoeostasis or homoiostasis).tw.
22	("adrenal hypophyseal axis" or "adrenohypophyseal axis" or "diencephalon adrenal axis" or "hypophyseal adrenal axis" or "hypophyseal adrenal system" or "hypophyseal adrenal systems" or "hypophyseal adrenocortical system" or "hypophyseal adrenocortical systems" or "hypophyseoadrenocortical system" or "hypophyseoadrenocortical systems" or "hypophysis adrenal axis" or "hypophysis adrenal cortex system" or "hypophysis adrenal cortex systems" or "hypophysis adrenal function" or "hypophysis adrenal gland" or "hypophysis adrenal gland system" or "hypophysis adrenal gland systems" or "hypophysoadrenal axis" or "pituitary adrenal axis" or "pituitary adrenal function" or "pituitary adrenal system" or "pituitary adrenal systems" or "pituitary adrenocortical function" or "pituitary adrenocortical regulation" or "pituitary adrenocortical system" or "pituitary adrenocortical systems" or "pituitary gland adrenal gland axis" or "pituitary-adrenal system" or "pituitary-adrenal systems").tw.
23	exp electroencephalography/ or ("alpha activit*" or "alpha rhythm" or "alpha rhythms" or "alpha wave" or "alpha waves" or "beta activit*" or "beta rhythm" or "beta rhythms" or "beta wave" or "beta waves" or "brain activity" or "brain electric activit*" or "brain electrical activit*" or "brain wave" or "brain waves" or "brainwave" or "brainwaves" or "delta activit*" or "delta rhythm" or "delta rhythms" or "delta wave" or "delta waves" or "e.e.g." or EEG or electroencephalogram or electroencephalograms or electroencephalography or "electric encephalography" or "electrical encephalography" or "electro encephalography" or "electric encephalogram" or "electrical encephalogram" or "electro encephalogram" or "gamma activit*" or "gamma rhythm" or "gamma rhythms" or "gemma wave" or "gemma waves" or "theta activit*" or "theta rhythm" or "theta rhythms" or "theta wave" or "theta waves").tw.
24	("cortical synchronisation" or "cortical synchronization").tw.
25	or/6-24
26	psychological stress/
27	distress/
28	emotions/
29	physiological arousal/
30	(distress* adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
31	(stress* adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
32	(negativ* adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
33	(emotion* adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
34	((cries or crying) adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
35	(arous* adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
36	(sensitiv* adj3 (infan* or newborn? or "new born*" or baby* or babies or toddler? or child* or pediatric* or paediatric* or peadiatric*)).tw.
37	self-regulation.tw.
38	or/26-37
39	5 and 25 and 38
40	limit 39 to english language

APPENDIX D

Details of studies excluded at full-text review

#	Reference	Year	Reason for Exclusion
1	Axfors, C., Bränn, E., Henriksson, H. E., Hellgren, C., Kallak, T. K., Fransson, E., ... & Skalkidou, A. (2019). Cohort profile: the Biology, Affect, Stress, Imaging and Cognition (BASIC) study on perinatal depression in a population-based Swedish cohort. *BMJ open*, *9*(10), e031514.	2019	Wrong article type (review, dissertation, or conference proceeding)
2	Granger, D. A., Kivlighan, K. T., Blair, C., El-Sheikh, M., Mize, J., Lisonbee, J. A., ... & Schwartz, E. B. (2006). Integrating the measurement of salivary α-amylase into studies of child health, development, and social relationships. *Journal of Social and Personal relationships*, *23*(2), 267-290.	2006	Wrong article type (review, dissertation, or conference proceeding)
3	Jamieson, B., Dryer, A., & Atkinson, L. (2021). Maternal Parasympathetic Regulation During Dyadic Stress: Associations With Emotional Availability, Maternal Depressive and Anxiety Symptoms, and Infant Distress. *Biological Psychiatry*, *89*(9), S386.	2021	Wrong article type (review, dissertation, or conference proceeding)
4	Kimmel, M., Kachouei, S. A., Grewen, K., Azcarate-Peril, A., Skalkidou, A., Fransson, E., ... & Meltzer-Brody, S. (2021). Maternal and Infant Autonomic Nervous System Dysfunction. *Biological Psychiatry*, *89*(9), S335.	2021	Wrong article type (review, dissertation, or conference proceeding)
5	Bader, L., Tan, L., Gonzalez, R., Provenzi, L., & Volling, B. L. (2020). Adrenocortical attunement betweeen infants and their fathers and mothers. *Psychoneuroendocrinology*, *119*, 105023.	2020	Wrong article type (review, dissertation, or conference proceeding)
6	Epperson, C. N., Hantsoo, L. V., Ewing, G., Podcasy, J., Kim, D., & Sammel, M. D. (2017, October). Stressed Mom, Stressed Baby: Exploring Mechanisms for Intergenerational Transmission of Parental Early Life Stress. In *64th Annual Meeting*. AACAP.	2017	Wrong article type (review, dissertation, or conference proceeding)
7	Kasparian et al., (2017) Biopsychosocial contributions to risk and resilience in infants with complex congenital heart disease and their parents. 7th World Congress of Pediatric Cardiology & Cardiac Surgery Abstracts. (2017). *Cardiology in the Young*, *27*(S4), S1-S653. doi:10.1017/S104795111700110X	2017	Wrong article type (review, dissertation, or conference proceeding)
8	Epperson, C., Morrison, K., Hantsoo, L. V., Ewing, G., Podcasy, J., Sammel, M. D., & Bale, T. L. (2017). 91. Maternal Early Life Adversity: Impact on Offspring Stress Responsiveness. *Biological Psychiatry*, *81*(10), S38.	2017	Wrong article type (review, dissertation, or conference proceeding)
9	Drury, S. S. (2016). 37.4 THE ORANGE-COLORED FUTURE IS NOW: EPIGENETICS AND THE ROLE OF THE NEW SCIENCES IN UNDERSTANDING AND ADDRESSING CHILD AND ADOLESCENT MENTAL HEALTH DISPARITIES. *Journal of the American Academy of Child & Adolescent Psychiatry*, *10*(55), S57-S58.	2016	Wrong article type (review, dissertation, or conference proceeding)
10	Costa et al. (2015) Physiological reactions during parent-infant interactions. THE INTERNATIONAL MARCÉ SOCIETY FOR PERINATAL MENTAL HEALTH BIENNIAL SCIENTIFIC CONFERENCE. *Arch Womens Ment Health* **18**, 269–408 (2015). https://doi.org/10.1007/s00737-014-0488-6	2015	Wrong article type (review, dissertation, or conference proceeding)

11	Simeonova et al. (2014). Opportunities and challenges in establishing the emory longitudinal cohort of offspring of mothers with bipolar disorder (ELCOM-BD). http://dx.doi.org/10.1111/bdi.12189	2014	Wrong article type (review, dissertation, or conference proceeding)
12	Glover et al. (2013). Effects of prenatal anxiety, depression and stress on fetal and child development. Mechanisms and questions. http://dx.doi.org/10.1007/s00737-013-0355-x	2013	Wrong article type (review, dissertation, or conference proceeding)
13	Howell et al. (2012). Prenatal cocaine predicts postpartum negative affect, maternal sensitivity and autonomic activity. https://doi.org/10.1016/j.biopsych.2012.02.012	2012	Wrong article type (review, dissertation, or conference proceeding)
14	Swain et al., (2010) Parental brain function and structure: Effects of early life experience, contemporaneous breastfeeding, correlations with behavior and changes in the early postpartum. Poster Session III. *Neuropsychopharmacol 35* (Suppl 1), S297–S408. https://doi.org/10.1038/npp.2010.218	2010	Wrong article type (review, dissertation, or conference proceeding)
15	Gonzalez, A., Levitan, R., Pereira, J., Goldberg, S., & Atkinson, L. (2008). P.8.b.002 Early maternal experience, maternal sensitivity, infant emotion regulation and HPA function. European Neuropsychopharmacology - EUR NEUROPSYCHOPHARMACOL. 18. 10.1016/S0924-977X(08)70900-3.	2008	Wrong article type (review, dissertation, or conference proceeding)
16	Mörelius, E., Örtenstrand, A., Theodorsson, E., & Frostell, A. (2016). OC09–Early maternal contact has an impact on preterm infants' brain systems that manage stress.	2016	Wrong article type (review, dissertation, or conference proceeding)
17	Nichols, K., Gergely, G., & Fonagy, P. (2001). Experimental protocols for investigating relationships among mother-infant interaction, affect regulation, physiological markers of stress responsiveness, and attachment. *Bulletin of the Menninger Clinic*, *65*(3: Special issue), 371-379.	2001	Wrong article type (review, dissertation, or conference proceeding)
18	Wu, Q. (2018). *Maternal Emotion Socialization and Child Emotion Regulation in At-Risk Populations*. The Ohio State University.	2021	Wrong article type (review, dissertation, or conference proceeding)
19	Jog, M. (2020). *Secure Base Script Knowledge and Vagal Regulation as Predictors of Maternal Sensitivity to Distress* (Doctoral dissertation, Lehigh University).	2021	Wrong article type (review, dissertation, or conference proceeding)
20	Skoranski, A. M. (2019). *Modeling Profiles of Mothers' and Fathers' Mental Health and Stress Physiology and Physiological Coregulation with Preschool-Aged Children*. The Pennsylvania State University.	2021	Wrong article type (review, dissertation, or conference proceeding)
21	Hertz, R. M. (2019). *Mindfully parenting the next generation: Maternal history of child maltreatment, stress, and infant attachment* (Doctoral dissertation, University of Oregon).	2020	Wrong article type (review, dissertation, or conference proceeding)
22	Richardson, P. A. (2018). *Fathering and Toddler Emotion Regulation: Intergenerational Caregiving and Parasympathetic Processes*. Wayne State University.	2019	Wrong article type (review, dissertation, or conference proceeding)

23	Rouse, M. H. (2013). *Physiological Mediators of Parenting Behaviors in Mothers with Low to Moderate Depression Symptoms* (Doctoral dissertation, Emory University).	2014	Wrong article type (review, dissertation, or conference proceeding)
24	Martin, L. F. (2013). *Affective Attunement and Adrenocortical Attunement as Pathways Between Intimate Partner Violence and Child Behavior Problems*. Michigan State University. Psychology.	2014	Wrong article type (review, dissertation, or conference proceeding)
25	Hogue, U. T. (2011). *Childhood externalizing behaviour and parent-child interaction: associations among cortisol reactivity, emotion, child and parent psychopathology*. Library and Archives Canada= Bibliothèque et Archives Canada, Ottawa.	2011	Wrong article type (review, dissertation, or conference proceeding)
26	Kivlighan, K. T. (2007). Dyadic Stress Vulnerability in Mother-Infant Dyads: Sympathetic Nervous System and Adrenocortical Reactivity to Infant Challenge.	2009	Wrong article type (review, dissertation, or conference proceeding)
27	Lorber, M. F. (2004). *Does negative sentiment override predict overreactive maternal discipline?*. State University of New York at Stony Brook.	2005	Wrong article type (review, dissertation, or conference proceeding)
28	Sethre-Hofstad, L. M. (1997). *Maternal sensitivity, cortisol, and emotion regulation: Relations between maternal and child response to stress*. The University of New Mexico.	1998	Wrong article type (review, dissertation, or conference proceeding)
29	Hessl, D. R. (1997). *Fathering young children: Maternal depression, paternal mental health, and marital adjustment as determinants of involvement and parenting*. University of Washington.	1998	Wrong article type (review, dissertation, or conference proceeding)
30	Davis, M., Suveg, C., & Shaffer, A. (2015). The value of a smile: Child positive affect moderates relations between maternal emotion dysregulation and child adjustment problems. *Journal of Child and Family Studies*, *24*, 2441-2452.	2015	Wrong age (mean or range > 48 months)
31	Ruttle, P. L., Serbin, L. A., Stack, D. M., Schwartzman, A. E., & Shirtcliff, E. A. (2011). Adrenocortical attunement in mother–child dyads: Importance of situational and behavioral characteristics. *Biological Psychology*, *88*(1), 104-111.	2011	Wrong age (mean or range > 48 months)
32	Blankenship, S. L., Chad-Friedman, E., Riggins, T., & Dougherty, L. R. (2019). Early parenting predicts hippocampal subregion volume via stress reactivity in childhood. *Developmental Psychobiology*, *61*(1), 125-140.	2019	Wrong age (mean or range > 48 months)
33	Deater-Deckard, K., & Bell, M. A. (2017). Maternal executive function, heart rate, and EEG alpha reactivity interact in the prediction of harsh parenting. *Journal of Family Psychology*, *31*(1), 41.	2017	Wrong age (mean or range > 48 months)
34	Deater-Deckard, K., Li, M., & Bell, M. A. (2016). Multifaceted emotion regulation, stress and affect in mothers of young children. *Cognition and Emotion*, *30*(3), 444-457.	2016	Wrong age (mean or range > 48 months)
35	Shih, E. W., Quiñones-Camacho, L. E., & Davis, E. L. (2018). Parent emotion regulation socializes children's adaptive physiological regulation. *Developmental psychobiology*, *60*(5), 615-623.	2018	Wrong age (mean or range > 48 months)

36	Lunkenheimer, E., Busuito, A., Brown, K. M., Panlilio, C., & Skowron, E. A. (2019). The interpersonal neurobiology of child maltreatment: Parasympathetic substrates of interactive repair in maltreating and nonmaltreating mother–child dyads. *Child maltreatment*, *24*(4), 353-363.	2019	Wrong age (mean or range > 48 months)
37	Shaffer, A., Whitehead, M., Davis, M., Morelen, D., & Suveg, C. (2018). A model-based cluster analysis of maternal emotion regulation and relations to parenting behavior. *Family process*, *57*(3), 707-718.	2018	Wrong age (mean or range > 48 months)
38	Wells, J. N., Skowron, E. A., Scholtes, C. M., & DeGarmo, D. S. (2020). Differential physiological sensitivity to child compliance behaviors in abusing, neglectful, and non-maltreating mothers. *Development and psychopathology*, *32*(2), 531-543.	2020	Wrong age (mean or range > 48 months)
39	Smith, J. D., Woodhouse, S. S., Clark, C. A., & Skowron, E. A. (2016). Attachment status and mother–preschooler parasympathetic response to the strange situation procedure. *Biological psychology*, *114*, 39-48.	2016	Wrong age (mean or range > 48 months)
40	Ostfeld-Etzion, S., Golan, O., Hirschler-Guttenberg, Y., Zagoory-Sharon, O., & Feldman, R. (2015). Neuroendocrine and behavioral response to social rupture and repair in preschoolers with autism spectrum disorders interacting with mother and father. *Molecular autism*, *6*(1), 1-13.	2015	Wrong age (mean or range > 48 months)
41	Feldman, R., Vengrober, A., Eidelman-Rothman, M., & Zagoory-Sharon, O. (2013). Stress reactivity in war-exposed young children with and without posttraumatic stress disorder: relations to maternal stress hormones, parenting, and child emotionality and regulation. *Development and Psychopathology*, *25*(4pt1), 943-955.	2013	Wrong age (mean or range > 48 months)
42	Schechter, D. S., Zeanah Jr, C. H., Myers, M. M., Brunelli, S. A., Liebowitz, M. R., Marshall, R. D., ... & Hofer, M. A. (2004). Psychobiological dysregulation in violence-exposed mothers: Salivary cortisol of mothers with very young children pre-and post-separation stress. *Bulletin of the Menninger Clinic*, *68*(4), 319-336.	2004	Wrong age (mean or range > 48 months)
43	Ravindran, N., Zhang, X., Green, L. M., Gatzke-Kopp, L. M., Cole, P. M., & Ram, N. (2021). Concordance of mother-child respiratory sinus arrythmia is continually moderated by dynamic changes in emotional content of film stimuli. *Biological Psychology*, *161*, 108053.	2021	Wrong age (mean or range > 48 months)
44	Skoranski, A. M., Skowron, E. A., Nekkanti, A. K., Scholtes, C. M., Lyons, E. R., & DeGarmo, D. S. (2022). PCIT engagement and persistence among child welfare-involved families: Associations with harsh parenting, physiological reactivity, and social cognitive processes at intake. *Development and psychopathology*, *34*(4), 1618-1635.	2021	Wrong age (mean or range > 48 months)
45	Vervoort, T., Karos, K., Johnson, D., Sütterlin, S., & Van Ryckeghem, D. (2019). Parental emotion and pain control behaviour when faced with child's pain: the emotion regulatory role of parental pain-related attention-set shifting and heart rate variability. *Pain*, *160*(2), 322-333.	2019	Wrong age (mean or range > 48 months)
46	Factor, R. S., Swain, D. M., & Scarpa, A. (2018). Child autism spectrum disorder traits and parenting stress: The utility of using a physiological measure of parental stress. *Journal of Autism and Developmental Disorders*, *48*, 1081-1091.	2018	Wrong age (mean or range > 48 months)

47	Borelli, J. L., Rasmussen, H. F., John, H. K. S., West, J. L., & Piacentini, J. C. (2015). Parental reactivity and the link between parent and child anxiety symptoms. *Journal of Child and Family Studies*, *24*, 3130-3144.	2015	Wrong age (mean or range > 48 months)
48	Lunkenheimer, E., Busuito, A., Brown, K. M., & Skowron, E. A. (2018). Mother–child coregulation of parasympathetic processes differs by child maltreatment severity and subtype. *Child maltreatment*, *23*(3), 211-220.	2018	Wrong age (mean or range > 48 months)
49	Sreekrishnan, A., Herrera, T. A., Wu, J., Borelli, J. L., White, L. O., Rutherford, H. J., ... & Crowley, M. J. (2014). Kin rejection: social signals, neural response and perceived distress during social exclusion	2014	Wrong age (mean or range > 48 months)
50	Vervoort, T., Trost, Z., Sütterlin, S., Caes, L., & Moors, A. (2014). Emotion regulatory function of parent attention to child pain and associated implications for parental pain control behaviour. *PAIN®*, *155*(8), 1453-1463.	2014	Wrong age (mean or range > 48 months)
51	Gatzke-Kopp, L., Zhang, X., Creavey, K. L., & Skowron, E. A. (2022). An event-based analysis of maternal physiological reactivity following aversive child behaviors. *Psychophysiology*, *59*(11), e14093.	2022	Wrong age (mean or range > 48 months)
52	Reindl, V., Wass, S., Leong, V., Scharke, W., Wistuba, S., Wirth, C. L., ... & Gerloff, C. (2022). Multimodal hyperscanning reveals that synchrony of body and mind are distinct in mother-child dyads. *NeuroImage*, *251*, 118982.	2022	Wrong age (mean or range > 48 months)
53	Thomas, S. R., Woods, K. E., Mazursky-Horowitz, H., Novick, D. R., Dougherty, L. R., Glasper, E. R., & Chronis-Tuscano, A. (2022). Cortisol Reactivity and Observed Parenting among Mothers of Children with and without ADHD. *Journal of Attention Disorders*, *26*(12), 1605-1621.	2022	Wrong age (mean or range > 48 months)
54	Zhang, X., Gatzke-Kopp, L. M., Cole, P. M., & Ram, N. (2022). The role of strategy-use and parasympathetic functioning in maternal emotion regulation. *Journal of Family Psychology*.	2022	Wrong age (mean or range > 48 months)
55	Atzaba-Poria, N., Deater-Deckard, K., & Bell, M. A. (2017). Mother–child interaction: Links between mother and child frontal electroencephalograph asymmetry and negative behavior. *Child development*, *88*(2), 544-554.	2017	No distress paradigm (task intended or expected to elicit child distress)
56	Rheinheimer, N., Beijers, R., Cooijmans, K. H., Brett, B. E., & de Weerth, C. (2022). Effects of skin-to-skin contact on full-term infants' stress reactivity and quality of mother–infant interactions. *Developmental Psychobiology*, 64(7), e22308.	2022	No distress paradigm (task intended or expected to elicit child distress)
57	Brand, S. R., Brennan, P. A., Newport, D. J., Smith, A. K., Weiss, T., & Stowe, Z. N. (2010). The impact of maternal childhood abuse on maternal and infant HPA axis function in the postpartum period. *Psychoneuroendocrinology*, *35*(5), 686-693.	2010	No distress paradigm (task intended or expected to elicit child distress)
58	Smith, E. S., Crawford, T. J., Thomas, M., & Reid, V. M. (2020). The influence of maternal schizotypy on the perception of facial emotional expressions during infancy: an event-related potential study. *Infant Behavior and Development*, *58*, 101390.	2020	No distress paradigm (task intended or expected to elicit child distress)
59	Waters, S. F., West, T. V., & Mendes, W. B. (2014). Stress contagion: Physiological covariation between mothers and infants. *Psychological science*, *25*(4), 934-942.	2014	No distress paradigm (task intended or expected to elicit child distress)

60	Manini, B., Cardone, D., Ebisch, S. J., Bafunno, D., Aureli, T., & Merla, A. (2013). Mom feels what her child feels: thermal signatures of vicarious autonomic response while watching children in a stressful situation. *Frontiers in human neuroscience*, *7*, 299.	2013	No distress paradigm (task intended or expected to elicit child distress)
61	Ebisch, S. J., Aureli, T., Bafunno, D., Cardone, D., Romani, G. L., & Merla, A. (2012). Mother and child in synchrony: thermal facial imprints of autonomic contagion. *Biological psychology*, *89*(1), 123-129.	2012	No distress paradigm (task intended or expected to elicit child distress)
62	Thompson, L. A., & Trevathan, W. R. (2008). Cortisol reactivity, maternal sensitivity, and learning in 3-month-old infants. *Infant Behavior and Development*, *31*(1), 92-106.	2008	No distress paradigm (task intended or expected to elicit child distress)
63	Susman, E. J., Schmeelk, K. H., Ponirakis, A., & Gariepy, J. L. (2001). Maternal prenatal, postpartum, and concurrent stressors and temperament in 3-year-olds: a person and variable analysis. *Development and Psychopathology*, *13*(3), 629-652.	2001	No distress paradigm (task intended or expected to elicit child distress)
64	Tirosh, E., Kessel, A., Jaffe, M., & Cohen, A. (1999). Outcome of idiopathic apparent life-threatening events: Infant and mother perspectives. *Pediatric pulmonology*, *28*(1), 47-52.	1999	No distress paradigm (task intended or expected to elicit child distress)
65	Clauss, N. J., Byrd-Craven, J., Kennison, S. M., & Chua, K. J. (2018). The roles of mothers' partner satisfaction and mother-infant communication duration in mother-infant adrenocortical attunement. *Adaptive Human Behavior and Physiology*, *4*, 91-107.	2018	No distress paradigm (task intended or expected to elicit child distress)
66	Thompson, L. A., Morgan, G., Jurado, K. A., Gunnar, M. R., & Bauer, P. J. (2015). A longitudinal study of infant cortisol response during learning events. *Monographs of the society for research in child development*, i-143.	2015	No distress paradigm (task intended or expected to elicit child distress)
67	Thompson, L. A., Morgan, G., Jurado, K. A., Gunnar, M. R., & Bauer, P. J. (2015). A longitudinal study of infant cortisol response during learning events. *Monographs of the society for research in child development*, i-143.	2015	No distress paradigm (task intended or expected to elicit child distress)
68	Blandon, A. Y. (2015). Mothers' and fathers' responses to children's negative emotions: Family and physiological correlates. *Family Relations*, *64*(3), 431-445.	2015	No distress paradigm (task intended or expected to elicit child distress)
69	Lunkenheimer, E., Tiberio, S. S., Skoranski, A. M., Buss, K. A., & Cole, P. M. (2018). Parent-child coregulation of parasympathetic processes varies by social context and risk for psychopathology. Psychophysiology, 55(2), e12985.	2015	No distress paradigm (task intended or expected to elicit child distress)
70	Thompson, L. A., Liberty, R., & Corr, A. (2022). "Does your baby watch TV?": The associations between at-home TV watching and laboratory challenge cortisol are different for young infants and their mothers. *Developmental Psychobiology*, *64*(2), e22236.	2022	No distress paradigm (task intended or expected to elicit child distress)
71	Thompson, L. A., & White, B. L. (2022). Social network and behavioral synchrony influences on maternal and infant cortisol response. *Journal of Human Behavior in the Social Environment*, *32*(5), 574-590.	2022	No distress paradigm (task intended or expected to elicit child distress)
72	Schechter, D. S., Moser, D. A., Paoloni-Giacobino, A., Stenz, L., Gex-Fabry, M., Aue, T., ... & Rusconi Serpa, S. (2015). Methylation of NR3C1 is related to maternal PTSD, parenting stress and maternal medial prefrontal cortical activity in response to child separation	2015	No parent biological stress measured concurrently or in response to child distress

	among mothers with histories of violence exposure. *Frontiers in psychology*, *6*, 690.		
73	Perone, S., Gartstein, M. A., & Anderson, A. J. (2020). Dynamics of frontal alpha asymmetry in mother-infant dyads: Insights from the Still Face Paradigm. *Infant Behavior and Development*, *61*, 101500.	2020	No parent biological stress measured concurrently or in response to child distress
74	Musser, E. D., Ablow, J. C., & Measelle, J. R. (2012). Predicting maternal sensitivity: The roles of postnatal depressive symptoms and parasympathetic dysregulation. *Infant Mental Health Journal*, *33*(4), 350-359.	2012	No parent biological stress measured concurrently or in response to child distress
75	Luijk, M. P., Saridjan, N., Tharner, A., Van Ijzendoorn, M. H., Bakermans-Kranenburg, M. J., Jaddoe, V. W., ... & Tiemeier, H. (2010). Attachment, depression, and cortisol: Deviant patterns in insecure-resistant and disorganized infants. *Developmental psychobiology*, *52*(5), 441-452.	2010	No parent biological stress measured concurrently or in response to child distress
76	Rudd, K. L., Caron, Z., Jones-Mason, K., Coccia, M., Conradt, E., Alkon, A., & Bush, N. R. (2022). The prism of reactivity: Concordance between biobehavioral domains of infant stress reactivity. *Infant Behavior and Development*, *67*, 101704.	2022	No parent biological stress measured concurrently or in response to child distress
77	Underwood, J. J., & Gartstein, M. A. (2022). Investigating the links between parent–child interactions and context-specific electroencephalography asymmetry: Neurophysiology behind a frustrating task. *Journal of Experimental Child Psychology*, *218*, 105375.	2022	No parent biological stress measured concurrently or in response to child distress
78	Krzeczkowski, J. E., Van Lieshout, R. J., & Schmidt, L. A. (2022). Transacting brains: testing an actor–partner model of frontal EEG activity in mother–infant dyads. *Development and Psychopathology*, *34*(3), 969-980.	2022	No parent biological stress measured concurrently or in response to child distress
79	Mueller, I., Snidman, N., DiCorcia, J. A., & Tronick, E. (2021). Acute maternal stress disrupts infant regulation of the autonomic nervous system and behavior: A CASP study. *Frontiers in Psychiatry*, *12*, 714664.	2021	No parent biological stress measured concurrently or in response to child distress
80	Rudd, K. L., Roubinov, D. S., Jones-Mason, K., Alkon, A., & Bush, N. R. (2021). Developmental consequences of early life stress on risk for psychopathology: Longitudinal associations with children's multisystem physiological regulation and executive functioning. *Development and psychopathology*, *33*(5), 1759-1773.	2021	No parent biological stress measured concurrently or in response to child distress
81	Ablow, J. C., Marks, A. K., Shirley Feldman, S., & Huffman, L. C. (2013). Associations between first-time expectant women's representations of attachment and their physiological reactivity to infant cry. *Child Development*, *84*(4), 1373-1391.	2013	No parent biological stress measured concurrently or in response to child distress
82	ARAI, Y. C., Kandatsu, N., Ito, H., Sato, Y., Satake, Y., Mizutani, M., ... & Komatsu, T. (2008). Induction and emergence behavior of children undergoing general anesthesia correlates with maternal salivary amylase activity before the anesthesia. *Acta anaesthesiologica scandinavica*, *52*(2), 285-288.	2008	No parent biological stress measured concurrently or in response to child distress
83	Li, Z., Sturge-Apple, M. L., & Davies, P. T. (2022). Family instability, parenting, and child externalizing problems: Moderation by maternal sympathetic stress reactivity. *Development and Psychopathology*, 1-13.	2022	No parent biological stress measured concurrently or in response to child distress

84	Jewell, S. L., Luecken, L. J., Gress-Smith, J., Crnic, K. A., & Gonzales, N. A. (2015). Economic stress and cortisol among postpartum low-income Mexican American women: Buffering influence of family support. *Behavioral Medicine*, *41*(3), 138-144.	2015	No data on parents' biological stress response or associations with parent behaviour
85	Castral, T. C., Warnock, F. F., Ribeiro, L. M., Vasconcelos, M. G. L. D., Leite, A. M., & Scochi, C. G. S. (2012). Maternal factors regulating preterm infants' responses to pain and stress while in maternal kangaroo care. *Revista latino-americana de enfermagem*, *20*, 435-443.	2012	No data on parents' biological stress response or associations with parent behaviour
86	Tronick, E., Mueller, I., DiCorcia, J., Hunter, R., & Snidman, N. (2021). A Caretaker Acute Stress Paradigm: Effects on behavior and physiology of caretaker and infant. *Developmental psychobiology*, *63*(2), 237-246.	2021	No data on parents' biological stress response or associations with parent behaviour
87	Braren, S. H., Perry, R. E., Ursache, A., & Blair, C. (2019). Socioeconomic risk moderates the association between caregiver cortisol levels and infant cortisol reactivity to emotion induction at 24 months. *Developmental psychobiology*, *61*(4), 573-591.	2019	No data on parents' biological stress response or associations with parent behaviour
88	Skoranski, A. M., Lunkenheimer, E., & Lucas-Thompson, R. G. (2017). The effects of maternal respiratory sinus arrhythmia and behavioral engagement on mother-child physiological coregulation. *Developmental Psychobiology*, *59*(7), 888-898.	2017	No data on parents' biological stress response or associations with parent behaviour
89	Waters, S. F., West, T. V., Karnilowicz, H. R., & Mendes, W. B. (2017). Affect contagion between mothers and infants: Examining valence and touch. *Journal of Experimental Psychology: General*, *146*(7), 1043.	2017	No data on parents' biological stress response or associations with parent behaviour
90	Pratt, M., Singer, M., Kanat-Maymon, Y., & Feldman, R. (2015). Infant negative reactivity defines the effects of parent–child synchrony on physiological and behavioral regulation of social stress. *Development and psychopathology*, *27*(4pt1), 1191-1204.	2015	No data on parents' biological stress response or associations with parent behaviour
91	Martorell, G. A., & Bugental, D. B. (2006). Maternal variations in stress reactivity: implications for harsh parenting practices with very young children. *Journal of Family Psychology*, *20*(4), 641.	2006	No data on parents' biological stress response or associations with parent behaviour
92	Ludmer, J. A., Gonzalez, A., Kennedy, J., Masellis, M., Meinz, P., & Atkinson, L. (2018). Association between maternal childhood maltreatment and mother-infant attachment disorganization: Moderation by maternal oxytocin receptor gene and cortisol secretion. *Hormones and behavior*, *102*, 23-33.	2018	No data on parents' biological stress response or associations with parent behaviour
93	Juul, S. H., Hendrix, C., Robinson, B., Stowe, Z. N., Newport, D. J., Brennan, P. A., & Johnson, K. C. (2016). Maternal early-life trauma and affective parenting style: the mediating role of HPA-axis function. *Archives of women's mental health*, *19*, 17-23.	2016	No data on parents' biological stress response or associations with parent behaviour
94	Abney, D. H., daSilva, E. B., & Bertenthal, B. I. (2021). Associations between infant–mother physiological synchrony and 4-and 6-month-old infants' emotion regulation. *Developmental Psychobiology*, *63*(6), e22161.	2021	No data on parents' biological stress response or associations with parent behaviour
95	Fuchs, A., Lunkenheimer, E., & Brown, K. (2021). Parental history of childhood maltreatment and child average RSA shape parent–child RSA synchrony. *Developmental psychobiology*, *63*(6), e22171.	2021	No data on parents' biological stress response or associations with parent behaviour

96	Lunkenheimer, E., Brown, K. M., & Fuchs, A. (2021). Differences in mother–child and father–child RSA synchrony: Moderation by child self-regulation and dyadic affect. *Developmental psychobiology*, *63*(5), 1210-1224.	2021	No data on parents' biological stress response or associations with parent behaviour
97	Krzeczkowski, J. E., Schmidt, L. A., Ferro, M. A., & Van Lieshout, R. J. (2022). Follow the leader: Maternal transmission of physiological regulatory support to distressed infants in real-time. *Journal of Psychopathology and Clinical Science*, *131*(5), 524.	2022	No data on parents' biological stress response or associations with parent behaviour
98	Laurent, H. K., Sbrilli, M., Dawson, D., Finnegan, M., & Ramdas-Neal, D. (2021). Disentangling levels of mother–infant neuroendocrine attunement and longitudinal relations with maternal risk and protective factors. *Developmental psychobiology*, *63*(1), 88-97.	2021	No data on parents' biological stress response or associations with parent behaviour
99	Feldman, R., Granat, A. D. I., Pariente, C., Kanety, H., Kuint, J., & Gilboa-Schechtman, E. (2009). Maternal depression and anxiety across the postpartum year and infant social engagement, fear regulation, and stress reactivity. *Journal of the American Academy of Child & Adolescent Psychiatry*, *48*(9), 919-927.	2009	No data on parents' biological stress response or associations with parent behaviour

APPENDIX E

Risk of Bias Assessment Tool

Item 1: Is there a risk of bias related to the definition, validity, and reliability of physiological outcome measures?

To determine the response to this item, studies will be evaluated based on the four criteria below.

1. **Collection of baseline physiological data**
   - ☐ **Low risk of bias:** Baseline data collection is clearly described (i.e., when during the study visit the sample was collected, what participants were doing during the baseline [for outcomes that involve continuous monitoring instead of a single sample]) and the data collected likely reflect a valid baseline measurement.
   - ☐ **High risk of bias:** Data collected during baseline task likely reflect cognitive, physical, or emotional stress and therefore may confound results **OR** no baseline sample collected.
   - ☐ **Unclear risk of bias:** Baseline task is included but not clearly defined.

   Note: If authors indicate that the first phase of the distress task was used as the baseline recording, use your judgment to determine if it likely reflects a true baseline (i.e., a low-demand situation that is unlikely to elicit parent stress or reactivity). If baseline is an interactive episode (e.g., free play between parent and child), it should not be considered as a baseline.
2. **Definition of physiological outcome**
   - ☐ **Low risk of bias:** Outcome is named (e.g., heart rate variability) and is clearly defined (e.g., high-frequency heart rate variability). Specific requirements by outcome include:

     Cardiac outcomes:
     - Outcome name: heart rate variability, respiratory sinus arrhythmia, heart rate, heart period, sympathovagal balance, pre-ejection period
     - Required details: frequency bands used (e.g., low-frequency, high-frequency) or cites study that clearly defines outcome parameters (e.g., peak-to-valley technique; Grossman et al., 1990)

     Electrodermal activity:
     - Outcome name: skin conductance level, skin conductance response
     - Required details: recording sites

     Cortisol
     - Outcome name: salivary cortisol
     - Required details: units of measurement (e.g., nmol/L, µg/dL, ng/mL)

     Alpha Amylase
     - Outcome name: salivary alpha amylase
     - Required details: units of measurement (e.g., U/mL)
   - ☐ **High risk of bias:** The outcome is not clearly named and/or the authors' have incorrectly defined the outcome (i.e., outcome description does not match the methodology used).
   - ☐ **Unclear risk of bias:** Outcome is named, but definition is missing some required details that support interpretation of the outcome.
3. **Validity/reliability of physiological data collection methods**
   - ☐ **Low risk of bias:** Specific requirements by outcome include:

     Cardiac outcomes:
     1. Participants received instructions to avoid food/caffeine/exercise/alcohol prior to study visit
     2. A sampling rate of at least 250 Hz was used
     3. Epoch lengths are at least 1 minute in duration or are averaged over adjacent epochs that add up to at least 1 minute, **and**
     4. Authors report that participants maintained a consistent posture during data collection (or posture was tracked and statistically controlled for).

        Note: When evaluating whether studies controlled for/standardized parent posture, here is some guidance for determining whether the risk of bias is Low, High, or Unclear:
        - **Low:** study used a task that requires parents to maintain same position for the whole task (e.g., Still Face Procedure)

- **High:** study used a task that involves change in posture throughout the task (e.g., Strange Situation Procedure), but posture wasn't explicitly controlled for
- **Unclear:** not enough information about the task to conclude whether parent posture would change during the task

Electrodermal activity:

1. Participants received instructions to avoid food/caffeine/exercise/alcohol prior to study visit, **and**
2. A sampling rate of at least 200 Hz was used.

Cortisol:

1. Participants received instructions to avoid food/caffeine/exercise/alcohol prior to study visit, **and**
2. At least 2 samples collected (including baseline sample), with "reactivity" sample being collected 20-40 minutes post-stressor (recovery sample, if applicable, was collected 40+ minutes post-stressor)

Alpha amylase:

1. Participants received instructions to avoid food/caffeine/exercise/alcohol prior to study visit, **and**
2. At least 2 samples collected, with "reactivity" sample being collected 5-10 minutes post-stressor

☐ **High risk of bias:** There is evidence that one or more of the requirements was not met.

☐ **Unclear risk of bias:** The study is missing detail on one or more of the requirements, but there is no evidence that requirements were not met.

4. **Validity/reliability of physiological data processing methods**

☐ **Low risk of bias:** The following data processing considerations are discussed:

1. General data processing procedures were described (i.e., software for processing cardiac/electrodermal data, assay methods for salivary measures),
2. Strategy for handling artifacts (i.e., manual or automatic editing; for cardiac outcomes only) and/or outliers were described, **and**
3. Distribution of outcome variable and associated transformation (if applicable) were described.

☐ **High risk of bias:** No information on data processing is provided.

☐ **Unclear risk of bias:** Data processing procedures are missing details related to one or more areas described above.

Item 2: Is there a risk of bias due to the exclusion of key potential confounding variables?

It is expected that studies would have addressed the key potentially confounding variables listed below. This could be done by either:

1. Statistically controlling for the variable
2. Providing an appropriate justification for why the variable was not included as a covariate (e.g., preliminary analyses showed no association with the outcome, authors listed the covariate as an exclusion criterion, all participants' data would be equally impacted by the covariate)

Key potentially confounding variables:

- Sex (not applicable if all participants are same sex)
- Food intake within last 2 hours
- Medication use
- Time of day

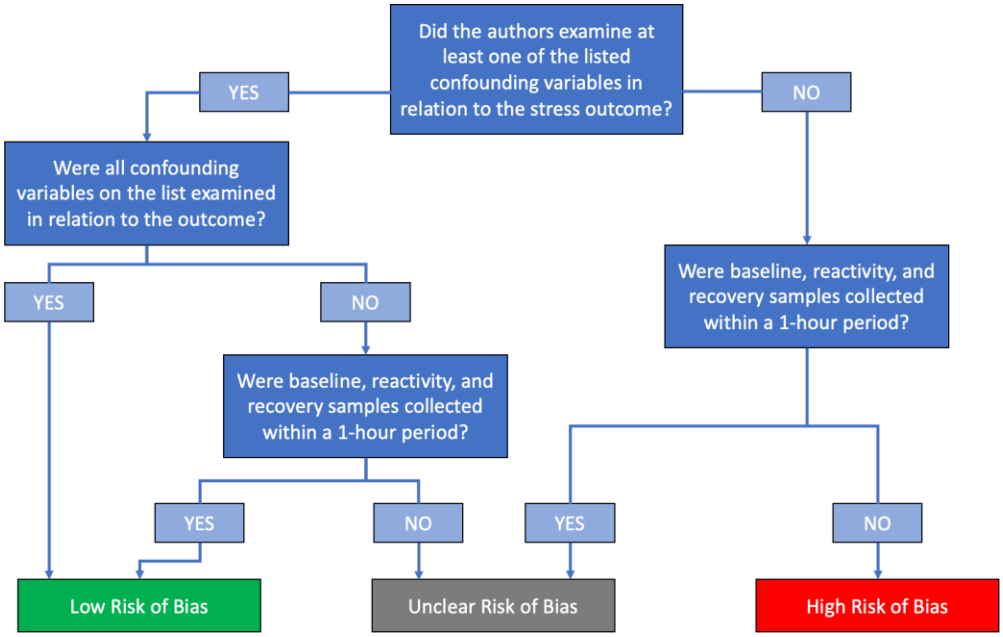
The influence of confounding variables on study outcomes depends partly on study design. In studies where the outcomes are collected within a short time (< 1 hour) frame, confounding variables can contribute to between-person differences in the outcome. However, in studies where the outcomes are collected over a longer time frame (> 1 hour), confounding variables can contribute to between-person and within-person differences in the study outcome. Accordingly, the risk of bias due to confounding variables will depend on the study design. Criteria for Low, High, and Unclear risk of bias are

described below, and the flowchart that follows can be used to determine the risk of bias due to the exclusion of key potential confounding variables.

☐ **Low risk of bias (must meet at least one of the following criteria):**
- Within-person differences in outcome are unlikely to be caused by time-based effects of confounding variable (i.e., baseline, reactivity, and recovery samples were collected within a short [<1 hour] time frame) **and** at least one confounding variable listed above was mentioned/examined in relation to outcome (includes sex).
- Within-person differences in outcome may be caused by time-based effects of confounding variables (i.e., baseline, reactivity, and recovery samples were collected within a longer [>1 hour] time frame) **and** all of the above confounding variables were mentioned/examined in relation to the outcome.

☐ **High risk of bias:**
- Within-person differences in outcome may be caused by time-based effects of confounding variables (i.e., baseline, reactivity, and recovery samples were collected within a longer [>1 hour] time frame) **and** none of the above confounding variables were mentioned/examined in relation to the outcome.

☐ **Unclear risk of bias (must meet at least one of the following criteria):**
- Within-person differences in outcome are unlikely to be caused by time-based effects of confounding variable (i.e., baseline, reactivity, and recovery samples were collected within a short [<1 hour] time frame) **and** none of the confounding variables listed above was mentioned/examined in relation to outcome.
- Within-person differences in outcome may be caused by time-based effects of confounding variables (i.e., baseline, reactivity, and recovery samples were collected within a longer [>1 hour] time frame) **and** at least one confounding variable listed above was mentioned/examined in relation to the outcome.



Item 3: Is there a risk of bias related to the definition, validity, and reliability of behavioural outcome measures?

☐ **Low risk of bias (must meet all criteria):**
- An established measure of parent behaviour was used (e.g., AMBIANCE, Ainsworth Sensitivity Scales) **OR** the authors clearly described how behaviour was coded (i.e., the definition and interpretation of a low score vs. high score are clear)
- There is evidence for adequate inter-rater reliability (i.e., minimum of 80% agreement between coders, kappa equal to or greater than 0.6, and intra-class correlation of 0.7)[1]

[1] Based on minimum criterion level recommendations from Horner et al., 2005 and Mitchell, 1979, as cited in Yoder & Symons, 2010.

- There is evidence suggesting that coders were blinded to study hypotheses and/or participant data on other variables

☐ **High risk of bias (one criterion required):**
- A novel measure of parent behaviour was used (i.e., no previous reference cited) and insufficient information is provided to interpret the meaning of a low vs. high score
- There is evidence for inadequate inter-rater reliability (i.e., less than 80% agreement between coders, kappa < 0.6, intra-class correlation < 0.7) **OR** there is evidence that a single coder completed all coding and no reliability estimates are provided
- There is evidence suggesting that coding was biased by coders' knowledge of study hypotheses and/or participant data on other variables

☐ **Unclear risk of bias (one criterion required):**
- No information is provided on inter-rater reliability
- No information provided on coder blinding, but no evidence to suggest bias related to unblinded coding

☐ **Not applicable (no behavioural outcome measure)**

Note: If a study meets some "high risk of bias" criteria and some "unclear risk of bias" criteria, it should receive a decision of "high risk of bias".

Item 4: Is there a risk of bias due to missing data?

This item allows us to determine whether missing data biased the results of the study and whether the results of the study are reflective of the population they are intended to reflect. Risks of bias due to missing data can be introduced when some participants are missing data on select measures or when participants drop out from longitudinal studies. This criterion can be verified by comparing the # of participants recruited and the # for whom data is reported.

☐ **Low risk of bias (must meet all relevant criteria):**
- There is a low level of missing data (5% or less)[2] on the physiological and behavioural (if applicable) measures **OR** the authors examined the relationship between missingness and (at minimum) demographic variables.
- [For studies using longitudinal datasets]: Participant loss to follow-up was equal to or less than 20%[3] **OR** participant drop-out was unrelated to demographic variables.

☐ **High risk of bias (one criterion required):**
- There is a high level of missing data (i.e., 20% or more) **AND** the authors did not examine the relationship between missingness and demographic factors.
- [For studies using longitudinal datasets]: Participant loss to follow-up was more than 20% **AND** authors did not examine relationship between dropout and demographic factors.

☐ **Unclear risk of bias (one criterion required):**
- The proportions of missing data on physiological or behavioural outcomes were not reported or could not be determined **OR** there is a moderate level of missing data (between 5% and 20%) and authors did not examine relationship between missingness and demographic factors.
- [For studies using longitudinal datasets]: The rate of participant loss to follow-up was not reported or could not be determined.

Note: If a study meets some "high risk of bias" criteria and some "unclear risk of bias" criteria, it should receive a decision of "high risk of bias".

Item 5: Is there a risk of bias due to poorly defined or poorly applied inclusion and exclusion criteria?

[2] Cochrane risk of bias tool defines low risk of bias as "all or nearly all data points available". We defined this as 95%.

[3] Criterion from the NIH Quality Assessment Tool.

☐ **Low risk of bias:**
- Inclusion and/or exclusion criteria were clearly defined by the authors and used to screen participants during recruitment (note: can assume that inclusion/exclusion criteria were applied during recruitment unless evidence suggests otherwise).

☐ **High risk of bias:**
- There is evidence that inclusion and/or exclusion criteria were used inconsistently (i.e., different criteria used for different participants) or were used to exclude participants who had already been recruited.

☐ **Unclear risk of bias:**
- The authors do not provide information on inclusion or exclusion criteria **OR** inclusion/exclusion criteria had to be inferred.

Note: In addition to confirming that inclusion/exclusion criteria were specified for the study, it is also necessary to confirm that the criteria were applied consistently. Review the "Methods" and "Results" sections to confirm that there is no evidence that some participants' data were excluded after their participation. Information on this can also be gathered by comparing the # of participants recruited and the # for whom data is reported.

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APPENDIX F

Description of distress paradigms.

Task and Citation	Studies using task	Task description	Parent behaviour constraints
Fear – Attachment threat			
Still Face Procedure (SFP; Tronick et al., 1978)	(Brown et al., 2021) (Busuito et al., 2019) (Crockett et al., 2013) (Feldman et al., 2010) (Gao et al., 2022) (Ham & Tronick, 2006) (Ham & Tronick, 2009) (Lan et al., 2022) (Laurent et al., 2017) (Leerkes et al., 2016) (Leerkes et al., 2017) (Mills-Koonce et al., 2007) (Mills-Koonce et al., 2009) (Moore et al., 2009) (Morelius et al., 2015) (Oppenheimer et al., 2013) (Ostlund et al., 2017) (Ramdas et al., 2021) (Volpe et al., 2020) (Weisman et al., 2013) (Xu & Groh, 2021)	After two minutes of parent-child play, parent transitioned to staring at child with completely neutral affect (Still Face episode) for two minutes, followed by two minutes of normal interaction.	Completely constrained behaviour during Still Face episode
SFP + Emotion Exposure	(Moore, 2009)	Prior to the Still Face Procedure, infants watched while experimenter spoke to parent using either an excited, angry, or neutral tone of voice.	Parent instructed not to respond to experimenter; completely constrained behaviour during Still Face episode.
SFP + Maternal Touch (Stack & Muir, 1992)	(Feldman et al., 2010)	During the Still Face episode, parents instructed to maintain tactile contact with child in any way they chose while maintaining a neutral face.	Same as standard procedure.

SFP + Gentle Touch Stimulation (adapted from Feldman et al., 2010; Stack & Muir, 1992)	(Van Puyvelde et al., 2021)	Instead of normal play, procedure began with a series of three baseline episodes during which parents provided varying degrees of physical contact to infant ranging from no touch to gentle touch.	During baseline episodes, parents instructed to sit quietly and not initiate interaction (apart from gentle touch stimulation).
Double SFP (Provenzi et al., 2016)	(Provenzi et al., 2019)	Includes a second Still Face episode and a second reunion episode.	Same as standard procedure.
Strange Situation Procedure (Ainsworth et al., 1978)	(Atkinson et al., 2013) (Bader et al., 2021) (Hill-Soderlund et al., 2008) (Kern & Laurent, 2019) (Khoury et al., 2016) (Khoury et al., 2021) (Laurent, Ablow, et al., 2011) (Laurent, Stevens, et al., 2011) (Laurent et al., 2012) (Ludmer et al., 2017) (Ramdas et al., 2021) (Sturge-Apple et al., 2011) (Volpe et al., 2020)	Series of parent-child separations and reunion episodes incorporating exposure to an unfamiliar stranger.	During separations, parent was able to view child through monitor but not intervene. Parent instructed to avoid initiating play with child once child was settled.
Separation-reunion procedure	(Schechter et al., 2014)	In addition to separations and reunions, included clean-up and play activity.	Not indicated.
Lab-TAB Maternal separation (Goldsmith & Rothbart, 1993)	(Laurent et al., 2018) (Ramdas et al., 2021) (Volpe et al., 2020)	Parent separated and left child alone in room for up to 30 seconds.	Parent was able to view child through monitor but not intervene.
Fear - Distress to novelty			
Lab-TAB Mask Task (Goldsmith & Rothbart, 1993)	(Hibel et al., 2009) (Hibel et al., 2015)	Experimenter addressed child while wearing a series of unusual masks.	Parent instructed not to intervene.
Lab-TAB - Stranger approach (Goldsmith & Rothbart, 1993)	(Laurent et al., 2018) (Ramdas et al., 2021) (Volpe et al., 2020)	Adult stranger approached, engaged, and picked up child.	Parent typically instructed not to intervene.
Stranger in costume	(Augustine et al., 2019)	Child was approached by an experimenter dressed in an ogre costume who made repeated requests for child engagement over 4 minutes.	Parent asked to remain neutral and uninvolved for first minute and could then respond freely to child without addressing the experimenter.

Clown Task (adapted from Buss & Goldsmith, 2000; Buss, 2011; Nachmias et al., 1996)	(Kiel et al., 2021)	Child was approached by an experimenter dressed in a clown costume who made repeated requests for child engagement.	No constraints; parent instructed to behave naturally.
Novel toy approach	(Leerkes et al., 2016) (Leerkes et al., 2017)	Child was repeatedly approached by toy with flashing lights, motion, and sound while confined in high chair.	Parent asked to remain neutral and uninvolved for first minute and could then interact freely.
Stranger/Robot Procedure (adapted from Mullen, Snidman, and Kagnan, 1993)	(van Bakel et al., 2008)	14-minute procedure involving approach by adult stranger, confrontation with moving toy, and normal play.	Parent was completing questionnaires in the same room and instructed not to actively engage child.
Frustration - Child			
Lab-TAB Arm Restraint (Goldsmith & Rothbart, 1993)	(Bernard et al., 2017) (Hibel et al., 2009) (Hibel et al., 2015) (Luecken et al., 2019) (Mills-Koonce et al., 2007)	Parent or examiner gently restrained child's arms at their sides, typically after the child had begun engaging with a toy.	Parent typically instructed not to intervene.
Prolonged arm restraint	(Leerkes et al., 2016) (Leerkes et al., 2017)	Examiner restrained child's arms for 4 minutes.	Parent asked to remain neutral and uninvolved for first minute and could then interact freely.
Lab-TAB Barrier Task (Goldsmith & Rothbart, 1993)	(Hibel et al., 2009) (Hibel et al., 2015)	Child was presented with an attractive toy which was then repeatedly removed by examiner and placed behind a clear barrier.	Parent typically instructed not to intervene.
Toy Removal Task (Braungart-Rieker & Stifter, 1996)	(Atkinson et al., 2013) (Khoury et al., 2016)	Parent engaged child with an attractive toy and then proceeded to repeatedly remove the toy and place it out of reach before returning it to the child.	Parent typically instructed to remain neutral and non-interactive.
Toy Removal Variation	(Augustine et al., 2019)	After child was presented with an attractive toy, examiner removed the toy, placed it in a jar that the child was unable to open, and repeatedly requested that child retrieve toy.	Parent asked to remain neutral and uninvolved for first minute and could then interact freely without removing toy from jar.
Frustration - Dyadic			

Discipline Encounter Phone Task (Arnold & O'Leary, 1995; Slep & O'Leary 1998)	(Franz et al., 2021) (Lorber & O'Leary, 2005)	Parent was asked to keep child away from attractive toys for 10 minutes while parent was being kept on the phone with the examiner.	Parent required to split attention between phone conversation and managing child.
Parent-Child Challenge Task (Lunkenheimer et al., 2017)	(Fuchs et al., 2021) (Lunkenheimer et al., 2017) (Skoranski & Lunkenheimer, 2021)	Dyads worked collaboratively on developmentally advanced puzzles under time constraint.	Parent instructed to use their words and not physically assist their child.
Puzzle Task	(Miller et al., 2015)	Dyad worked collaboratively on a developmentally advanced puzzle that child could not complete alone.	No constraints; parent instructed to behave naturally.
Origami Task (Hane et al., 2008; Hastings et al., 2008)	(Miller et al., 2015)	Dyads worked collaboratively on developmentally advanced puzzle under a time constraint.	Parent instructed to use their words and not physically assist their child.
Additive fear and frustation			
Arm restraint and noise burst	(Hendrix et al., 2018)	Child underwent arm restraint followed by noise burst stressor.	Parent viewed all procedures from a monitor outside the room.
Modified Cromwell Procedure (Zeanah et al., 2000)	(Cordero et al., 2017)	30-minute procedure involving elements of separation-reunion, novelty, frustration, and normal interaction.	Not indicated.
Emotion Regulation Paradigm (Diener & Mangelsdorf, 1999)	(Roque et al., 2012)	Series of brief exposures to toy removal, distress to novelty (i.e., unpredictable toy), and play.	Parent instructed to remain uninvolved unless child experienced sustained distress.
Naturalistic stressor			
Needle Pain (Heel Stick)	(Spratt et al., 2016)	Infant underwent a heel stick blood draw for a research study.	No constraints, parent permitted to leave room.
Needle Pain (Routine Vaccination)	(Braarud & Stormark, 2006)	Infant underwent routine vaccination while seated on parent's lap.	No constraints.

Note: SFP = Still Face Procedure.

APPENDIX G

OUCHIE-RV Coding Scheme

Toddler behaviour coding

Behaviour	0	1	2	3
Toddler distress	Baby **does not exhibit any distress** during the epoch (i.e., calm, no complaints).	Baby is in **low distress** throughout the epoch. Baby makes some complaints, but no signs of moderate to high distress. Examples: yells, moans (closed mouth), whimpers	Baby shows signs of **moderate to high distress** throughout the epoch. Periods of moderate to high distress makes up **less than 50% of the epoch**.	Baby is in **moderate to high distress** for **50% of the epoch or more**.

Caregiver behaviour coding

Behaviour	0	1	2
Caregiver affect incongruence *(Is caregiver's emotional response [i.e., facial expressions and/or vocalizations] matched to baby's distress?)*	**Parent exhibits an absence of affect incongruence in reaction to baby distress.** Parent's emotional response is consistently appropriately matched to baby's (i.e., sympathetic, concerned, calm **or** is not overtly incongruent (e.g., generally neutral affect with no moments of marked incongruence) for the entire duration of baby's distress.	**Parent exhibits some affect incongruence in reaction to baby distress,** but no marked or pervasive incongruence. Examples of **minor incongruence** include: • Brief displays of mild positive affect (e.g., smiling while trying to distract baby, moments of amused expression). • Brief grimace in reaction to needle while facing away from baby. • Brief expression of positive affect, fear, anger, or sadness that is clearly directed to or in reaction to someone else in the room.	**Parent exhibits marked or pervasive affect incongruence in reaction to baby distress.** **Pervasive affect incongruence** describes parents whose affect is repeatedly incongruent throughout the epoch (i.e., prolonged instances of the examples described under "1"). **Marked affect incongruence** includes: • Overt and unambiguous expressions of parent fear, anger, sadness, or inappropriate positive affect (i.e., positive affect that is in reaction to distress, different from positive affect in distraction attempt). This incongruence is directed toward the distressed baby (e.g., anger/frustration towards baby, overt fearfulness, overt denial of baby distress, laughing at baby).

		Repeated verbal reassurance (e.g., "it's ok") that does not have a negative (i.e., frustrated, angry, scared) tone.	Parent exhibits no contingent emotional response to overt infant signals. For example, parent shows flat or neutral affect in reaction to baby's increases in distress.
Caregiver attention diversion *(Is caregiver's attention focused on their distressed baby?)*	**Complete absence of attention diversion.** Parent regularly directs eye contact, vocalizations, and/or physical comforting toward baby and does not clearly shift attention away from baby throughout baby's distress. Note: briefly glancing away from baby (i.e., 1 or 2 seconds) is not counted as diversion.	**Parent exhibits partial attention diversion.** Some lapses in attention occur, but diversion is neither marked nor pervasive. Parent may shift their attention away from baby (e.g., talking to someone else in the room), but show **clear evidence of splitting their attention** (i.e., "checking in" with baby approximately every 5 seconds by directing eye contact, vocal contact, and/or responsive physical contact to baby) and show **no evidence of marked diversion** (otherwise, score as a 2)	**Parent exhibits marked and/or pervasive attention diversion from their distressed baby.** **Pervasive attention diversion:** parent's attention is directed elsewhere (away from baby) throughout majority of baby's distress (i.e., no eye contact, talking to infant, providing physical comfort) for majority of distress. **Marked attention diversion:** • Parent shifts attention away from baby without maintaining split attention (i.e., 5+ seconds with no attention to infant) A clear bid for attention from baby (e.g., low/no → moderate/high distress) is *unacknowledged* by parent (e.g., by making eye contact, vocal contact, and/or physical contact with infant)
Caregiver physical distance *(Is caregiver providing sufficient physical proximity as a strategy to soothe baby?)*	**Complete absence of prolonged physical distance from distressed baby.** There are few or no lapses in parent's efforts to promote proximity throughout baby's distress and no lapses are marked/pervasive. This typically involves facilitating chest-to-chest contact with baby, but can also involve keeping a hand on baby's back, leaning head towards baby, and other forms of close physical contact, depending on baby's size and signaling.	**Some instances of prolonged physical distance from distressed baby.** The parent inconsistently promotes close physical proximity with distressed baby. Parent shows some evidence of using physical proximity as a soothing strategy (e.g., positioning baby closer), but there are missed opportunities to initiate closer physical contact. Lapses in physical proximity are not marked and/or pervasive.	**Instances of physical distance from distressed baby are marked and/or pervasive.** **Pervasive physical distance:** Proximity is sub-optimal (i.e., no chest-to-chest) and parent shows minimal evidence of increasing physical proximity as a strategy to soothe baby. There is an absence of close physical contact and/or an absence of parent efforts to achieve proximity throughout baby's distress. **Marked physical distance:** Parent prevents or denies distressed baby's request for proximity, for example, by separating from distressed baby or denying baby's bid for closer contact.

APPENDIX H

Research Consent Form (12-month example)

Title of Research Project:
Physiological and Behavioural Regulatory Processes in Recovering from Distress: Developmental and Contextual Dimensions in Infancy

Investigators:
Primary Investigator: Dr. Rebecca Pillai Riddell, CPsych, PhD
Room 2038 Sherman Health Sciences Research Centre, York University, (416) 736-2100 x20177

Project Co-Investigators:
Dr. Louis Schmidt, PhD, McMaster University
Dr. Karen Mathewson, PhD, McMaster University

Dr. Hartley Garfield

Dr. Dan Flanders, MD

Dr. Eitan Weinberg, MD

Purpose of the Research:
Infants undergo immunization injections, or 'shots' as part of routine medical care. Immunizations are given with a needle, which can be painful. We are doing this study to understand ways that we can help infants when they are experiencing pain. We are interested in how this pain behaviour and physical reaction to pain develops over the second year of life (12, 18, and 24 months), and how it relates to developmental outcomes (cognitive, communication, physical, social/emotional, adaptive) at the end of the second year of life (24 months). We are also interested in how moms' well-being impacts the development of these outcomes. We have already videotaped 2000 immunizations over the first year of life and look forward to learning more about the second year of life.

Description of the Research:
You will be asked to participate at 3 appointments over the course of the year. At your child's 12-month, 18-month, and 24-month appointment:

1. We will be videotaping you and your child during their immunizations.
2. Parents will be asked to fill out questionnaires to help us better understand the parent and their child (10-15 minutes) over the phone within one week that is convenient for the parent.
3. We will be connecting your child to equipment that measures their heart rate and stress. Heart rate will be monitored using baby-friendly stickers put on their shoulder blade and lower ribs.
4. Parents will be connected to equipment that measures their heart rate and stress. Heart rate will be monitored using the same baby-friendly stickers put on below their shoulder blade and lower ribs.
5. We will conduct a chart review of your child's health record at your pediatrician's clinic
6. After you child's 24-month immunization, we will ask you if you want to participate in a developmental assessment of your infant. We will assess your child's cognitive (thinking) and

motor (physical milestones like holding a ball) development. You will get a tailored report that will help you learn about your child and how to optimize his/her development. You do not have to agree to participate in this assessment. You will be asked separately to consent to this portion, after you speak to the project coordinator on the phone.

Videotapes will be viewed later by research assistants that do not know the identity of the children or parents to score their behaviours. Videotaping infants is not part of standard care, however, it does not interfere with the procedures being conducted, and is the usual way we measure pain in research studies.

I agree for my child and myself to be videotaped by research team: □ AGREE □ DISAGREE
I agree for my child's medical chart to be reviewed by research team: □ AGREE □ DISAGREE

In addition, I agree or consent for this immunization tape(s)/photograph(s) to be used for:
□ Other studies on the same topic
□ Teaching and demonstration at York University
□ Teaching and demonstration at meetings outside York University
□ Not to be used for anything else.

Risks and Potential Discomforts or Inconvenience:
The baby-friendly stickers used to measure heart rate and emotional arousal may cause minor discomfort to you or your child's skin. In pilot testing, no children were distressed by removal of the baby-friendly stickers. Additionally, filling out the well-being questionnaires will take about 20 minutes of your time outside of the clinic appointment.

Physiological data will be analyzed later by research assistants that do not know the identity of the parents or children. Putting baby friendly stickers on parents and infants to measure their physical reaction is not part of standard care, however, it does not interfere with the procedures being conducted, and is a common way we measure pain in research studies.

Potential Benefits:
You will receive an electronic copy of your child's immunization, a $10 gift certificate after each immunization, and a $5 gift certificate after each phone interview. Participating in the immunization phase will allow you access to the second phase of the study. In the assessment phase, families will receive a valuable report about their child's development based on gold standard assessment tools.

Potential Benefits to Society:
In the future, society may benefit from the results of this study because it will teach us about how regulating from distress during infancy relates to later child development.

Alternatives to Participation:
Participation in research is voluntary. You can choose not to participate or you may withdraw at any time without affecting your child's medical care.

Confidentiality:
We will respect your privacy. No information about who you are will be given to anyone or be published without your permission, unless the law requires us to do this. For example, the law requires Dr. Pillai Riddell to give information about you if a child has been abused, if you have an illness that could spread to others, if you or someone else talks seriously about suicide (killing themselves), or if the court orders us to give them the study papers. You will be contacted if any of these issues have arisen. York University Research Monitors may see your health record to check on the study to ensure we are being compliant. By signing this consent

form, you agree to let these people look at your records. We will give you a copy of this research consent form for your files.

The data produced from this study will be stored in a secure, locked location. Only members of the research team (and maybe those individuals described above) will have access to the data. This could include external research team members. Following completion of the research study, the data will be kept as long as required and then destroyed as required by York University policy. Published study results will not reveal your identity. The supervisors of this project are located at York University.

Participation:
It is your choice to take part in this study. You can stop at any time. The care you get at your doctor's office will not be affected in any way whether or not you take part in this study.
New information that we get while we are doing this study may affect your decision to take part in this study. If this happens, we will tell you about this new information. And we will ask you again if you still want to be in the study.
During this study we may create new tests, new medicines, or other things that may be worth some money. Although we may make money from these findings, we cannot give you any of this money now or in the future because you took part in this study.

Sponsorship:
This study is paid for through funds allocated to Dr. Pillai Riddell from the Natural Sciences and Engineering Research Council.

Conflict of Interest:
The research team members have no conflict of interest to declare.

Consent:
By signing this form, I agree that:
1) You have explained this study to me. You have answered all my questions.
2) You have explained the possible harms and benefits (if any) of this study.
3) I know what I could do instead of taking part in this study. I understand that I have the right not to take part in the study and the right to stop at any time. My decision about taking part in the study will not affect my health care.
4) I am free now, and in the future, to ask questions about the study.
5) I have been told that my medical records will be kept private except as described to me.
6) I understand that no information about who I am will be given to anyone or be published without first asking my permission.
7) I have read and understood pages 1-4 of this form. I agree, or consent, to take part in this study.

If you have any questions about this study, please call Dr. Rebecca Pillai Riddell at the number on the first page of the consent form. You can also contact the Project Coordinator, Stefano Costa at cohort@yorku.ca. This research has been reviewed by the Human Participants Review Committee in accordance with York's Senate Policy on Research Ethics (York University). This study conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. If you have any questions about this process or about your rights as a participant in the study, please contact Ms. Alison Collins-Mrakas, Manager, Research Ethics, Office of Research Ethics, 5th Floor, York Research Tower, York University (telephone 416-736-5914 or e-mail at acollins@yorku.ca).

Contact Information (RA must check legibility):

Parent Name: _____
Child's Name: _____

Preferred Telephone Number for scheduling appointments (with parent who spends most time with child): _____
Alternative Telephone Number: _____

Best Days and Time to Contact Parent (Please give an approximate 1-2 hour window e.g. 3 to 7pm)?

Monday to Friday_____
Saturday and Sunday_____

Home Mailing Address (To mail Tim Card after phone interview):

_____

_____

_____

_____

Email Address:

_____
Please print clearly!

<u>Future Contact Specifications</u>:

The OUCH lab is often conducting new studies where parents and their children can get involved. We would like to ask you to participate but you can <u>always</u> choose not to participate and ask us to stop contacting you. We would never contact you more than once or twice a year for a new study.

I consent for researchers to contact me via mail, email or phone regarding *(check which statement applies)*:

- ☐ No further contact (aside from contact directly related to participation in this current study).
- ☐ Further contact for results of this study.
- ☐ Further contact for results of this study and opportunities for participation in new future studies.

<u>Video Use in the Media:</u>

- ☐ I consent for my videos to be used for media coverage of the study, which may include print articles, news videos, or publications on websites. We will never release you or your child's identity and will notify you in advance if your video is chosen to be used and which media outlet the video will be using your video. You will always be given the opportunity to withdraw consent.

APPENDIX I

Participant Information Sheet (12-month example)

PART 1: PARENT QUESTIONS – *These questions refer to the parent who will be most responsible for **soothing** child during needle.* (*If possible, all questions to be asked by Clinic RA)*

1. **Your birth date** (dd/mm/yyyy)_____

2. **Your relationship to Infant:** Mother Father Other _____

3. **Who is currently the primary caregiver of your infant?**
   Mother Father Equally between Mother & Father Other _____

4. **Time since last fed**: _____Hours _____Minutes

5. **Time since last napped**: _____Hours _____Minutes

6. **Number of Family Members living in your household**: Adults _____ Children_____

7. **For each child in your family please list their age and sex**.
   Age of infant brought in today: _____(months) **Male** **Female**
   Birth date of infant (dd/mm/yyyy): _____

   Ages/genders of your other children:
   Age: _____ Male Female
   Age: _____ Male Female
   Age: _____ Male Female
   Age: _____ Male Female

8. **Which caregivers are present at this immunization?** (circle one number):
   1. Mom only
   2. Dad only
   3. Mom and Dad
   4. Nanny
   5. Grandparents
   6. Parent(s) and Nanny
   7. Parent(s) and Grandparent(s)
   8. Other _____
   9. Parent(s) and Other _____

b) How many other children are present, if any? (do not include child getting the needle) ____

9. Since your child's birth, have you taken any infant parenting classes/workshops? **Yes No**
   If <u>yes</u>, how many? _____

10. Since your child's birth, have you read any infant parenting books/watched videos? **Yes No**
    If <u>yes</u>, how many?_____

11. Since your child's birth, approximately how often do you visit parenting websites?

Never	**Once a day**	**Once a week**	**Once every few weeks**	**Once a month**	**Once a year**

12. Since your child's birth, have you received any guidance from an organization or professional to help with parenting your children (e.g. health unit nurse, midwife, Early Years Centre, Healthy Babies Healthy Children, Hincks-Dellcrest, Jessie's Place)? **Yes No**
    If <u>yes</u>, from how many organizations/professionals? _____

13. Has your child been given EMLA or TYLENOL prior to the appointment?:
    EMLA TYLENOL NONE

14. A) Since your child's birth, has your infant been separated from his/her primary caregiver for longer than 24 hours (e.g. infant hospitalization, parent hospitalization, Children's Aid involvement, parent travel, family emergency)?
    Circle: **YES NO**

    ***If you circled YES*:**
    Approximately, how many separations longer than 24 hours have occurred? _____
    How long was the longest period of separation _____(days)

15. **Child's Medical History**

Please check next to any illness or condition that your child has had since birth. When you check an item, also note the approximate date of the illness or your child's age at illness.

Illness or condition	Date(s) or age(s)	Illness or condition	Date(s) or age(s)
□Measles	_____	□Visual problems	_____
□German Measles	_____	□Fainting spells	_____
□Mumps	_____	□Loss of consciousness *(please specify cause)*	_____
□Chicken Pox	_____	□Lead Poisoning	_____
□Whooping Cough	_____	□Ear Problems	_____
□Diphtheria	_____	□TB	_____
□Scarlet Fever	_____	□Bone or joint disease	_____
□Meningitis	_____	□Anemia	_____
□Pneumonia	_____	□Jaundice/Hepatitis	_____
□Encephalitis	_____	□Cancer	_____

□High fever (>41°C or 105.8°F) _____
□Seizure _____
□Allergy _____
□Hay Fever _____
□Injuries to head _____
□Broken bones _____
□Hospitalization _____
(please specify reason)
□Operations _____
(please specify)
□Otitis media _____
□Heart disease _____
□Asthma _____
□Bleeding problems_____
□Eczema or hives _____
□Paralysis _____
□Stomach pumped_____
□Thrush _____
□Circumcision _____
□Other _____

16. Since birth, has your child been diagnosed with any other chronic illnesses not listed above?
Yes No
If yes, which chronic illness and at what age were they diagnosed? _____
_____

17. Since birth, has your child taken any medication long-term (i.e. longer than 2 weeks)?
Yes No
If yes, please list: _____
_____

PART 2: PREGNANCY HISTORY – If child is adopted please check box: ☐

(If so, please fill as much of the following information as you are aware of, which regards to the child's birth mother, her pregnancy, and delivery.)

1. During pregnancy, were you on medication? **Yes□ No□**
   If yes, what kind? _____
2. During pregnancy, did you smoke? **Yes□ No□**
   If yes, how many cigarettes each day? _____
3. During pregnancy, did you drink alcoholic beverages? **Yes□ No□**
   If yes, what did you drink? _____
   Approximately how much alcohol was consumed each day? _____
4. During pregnancy, did you use drugs? **Yes□ No□**
   a. If yes, what kind?_____
5. Were there any complications during pregnancy (excessive vomiting, excessive staining/blood loss, threatened miscarriage, infections, toxemia, fainting, dizziness, etc.)
   _____
   _____
6. Duration of pregnancy (weeks):_____
7. Duration of labour (total hours):_____
8. Were there indications of fetal distress during labour or during birth? **Yes□ No□**
9. Were forceps used during delivery? **Yes□ No□**
10. Was delivery normal? **Yes□ No□**
11. Was a Caesarean section performed? **Yes□ No□**

12. Was delivery breach? **Yes□ No□**
13. Was delivery induced? **Yes□ No□**
    If yes on any of the above, for what reason? _____
14. Was your child premature? **Yes□ No□**
    a. If so, by how many weeks?_____
15. What was your child's birth weight? (in pounds)_____
16. Were there any birth defects or complications? **Yes□ No□**
    a. If yes, please describe: _____
    _____

PART 3: PRIMARY CAREGIVER AND SPOUSE BACKGROUNDS – *(If possible, all questions to be asked by Clinic RA)*

1. **Your Highest Education (circle one number):**
    1. Graduate School/Professional Training
    2. University graduate (4 years college)
    3. Partial university (at least 1 year)
    4. Trade School/Community College
    5. High School Graduate
    6. Some high school
    7. Junior high school graduate
    8. Less than 7th grade

    a) **Your Current Occupation _____**

2. **If applicable, your Spouse's Highest Education (circle one number):**
    1. Graduate School/Professional Training
    2. University graduate (4 years college)
    3. Partial university (at least 1 year)
    4. Trade School/Community College
    5. High School Graduate
    6. Some high school
    7. Junior high school graduate
    8. Less than 7th grade

    a) **If applicable, Your Spouse's Current Occupation _____**

3. **What language is spoken most in your home (only put two languages if they are equally spoken)** _____

4. **What country was the primary caregiver born in:_____**

    a) If applicable, what country was your spouse born in:_____

5. **What country was the primary caregiver's parents born in:_____**

    a) If applicable, what country were your spouse's parents born in: _____

6. **How long has the primary caregiver lived in Canada: _____**

    a) If applicable, how long has your spouse lived in Canada: _____

7. **On a scale of 0 to 10, where 0 is "Not at All" and 10 is "Completely", how much do you feel your way of life reflects mainstream North American/Canadian culture? _____**

a) If applicable, how much do you feel your spouse's way of life reflects mainstream North American/Canadian culture: _____

8. **What is your heritage culture (**It may be the culture of your birth, the culture in which you have been raised, or another culture that forms part of your background. Pick the culture that has influenced you *most*. If you do not feel that you have been influenced by any other culture, please try to identify a culture that may have had an impact on previous generations of your family.**): _____**

   a) If applicable, what is your spouse's heritage culture: _____

9. **On a scale of 0 to 10, where 0 is "Not at All" and 10 is "Completely", how much do you feel your way of life reflects your heritage culture? _____**

   a) If applicable, how much do you feel your spouse's way of life reflects his/her heritage culture: _____

PART 4: PARENT RATINGS (PRE-IMMUNIZATION)

Pre-Immunization **Self-Worry** Rating
*On a scale from 0 to 10, how worried about the needle pain are **YOU**, right now, before the needle, where 0 is "no worry at all" and 10 is "the most worry possible"?*

_____

PART 5: PARENT RATINGS (POST-IMMUNIZATION)

To be done approximately 5 minutes after last needle!

Post-Immunization **Self-Worry** Rating
*On a scale from 0 to 10, how worried about the needle pain are **YOU**, right now, after the needle, where 0 is "no worry at all" and 10 is "the most worry possible"?*

_____

Post-Immunization **Child Pain** Rating
On a scale from 0 to 10, how much pain do you think your child experienced from the needles they just received, where 0 is "no pain at all" and 10 is "the worst pain possible"?

_____

PART 6: VACCINES GIVEN BY IMMUNIZATION NEEDLE

RA to fill out (ask nurse or doctor for vaccine name and trade name)

Disease it Protects Against

- ☐ Prevnar _____
- ☐ Twinrix _____
- ☐ Bexsero _____
- ☐ Menjugate _____
- ☐ Pediacel _____
- ☐ Menveo _____
- ☐ Nimenrix _____
- ☐ Other (list name) _____

How many needles total: _____

1. Vaccines in needle #1:_____

2. Vaccines in needle #2:_____

Name(s) of physician or resident who gave needle(s): _____