



Distinct trajectories of caregiver–toddler physiological attunement during routine vaccinations

Miranda G. Di Lorenzo-Klas^a, Jordana A. Waxman^a, David B. Flora^a, Louis A. Schmidt^b, Hartley Garfield^{c,d}, Dan Flanders^d, Eitan Weinberg^d, Deena Savlov^d, Rebecca R. Pillai Riddell^{a,c,d,*}

Abstract

Introduction: Toddlers rely on their caregivers for regulatory support when faced with pain-related distress. The caregiver's ability to support their toddler relies on their capacity to regulate their own distress and respond effectively to the child's need for support. The aim of the current study was to describe patterns of caregiver–toddler physiological co-regulatory patterns, also known as attunement, during routine vaccinations across the second year of life.

Methods: Caregiver–toddler dyads (N = 189) were part of a longitudinal cohort observed at either 12-, 18-, or 24-month well-baby vaccinations. Parallel-process growth-mixture modeling was used to examine patterns of dyadic physiological co-regulatory responses, indexed by high-frequency heart rate variability (HF-HRV).

Results: Three groups of dyads were discerned. The largest group (approximately 80%) demonstrated physiological attunement, with a stable and parallel regulatory pattern of HF-HRV from baseline to postneedle. The second group (7.9%) had parallel regulatory trajectories but with notably lower (ie, less regulated) HF-HRV values, which indicates independent regulatory responses (ie, a lack of attunement among dyad members). The third group (11.1%) showed diverging regulatory trajectories: Caregivers showed a stable regulatory trajectory, but toddlers demonstrated a steep decrease followed by an increase in HF-HRV values that surpassed their baseline levels by the third minute postneedle. Post hoc analyses with the HF-HRV groupings explored heart rate patterns and potential predictors.

Conclusions: These findings elucidate potential adaptive and maladaptive co-regulatory parasympathetic patterns in an acute pain context.

Keywords: Caregiver–child, Co-regulation, Acute pain, Heart rate variability

1. Introduction

Research has increasingly elucidated the fundamental role of the caregiver in the acute pediatric pain context, particularly early in life.^{21,47} The “development of the infant acute pain response—revised model” (DIAPR-R) is grounded in attachment theory¹⁰ and conceptualizes the impact of biopsychosocial factors on the development of early pain experiences.²¹ The model asserts the primacy of the caregiver–child relationship, particularly how dyad

members respond to and adjust to one another, as the toddler regulates their pain-related distress (eg, a child signals distress to their caregiver, and the caregiver responds sensitively to the child's needs). The dynamic and reciprocal responding between caregivers and their toddler is known as attunement.^{5,20} Much of the research examining the influence between caregivers and their toddlers in the pain context has focused on the links between caregiver behaviours (eg, caregiver sensitivity) and infant and toddler pain-related distress

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

^a York University, Toronto, ON, Canada, ^b McMaster University, Hamilton, ON, Canada, ^c The Hospital for Sick Children, Toronto, ON, Canada, ^d University of Toronto, Toronto, ON, Canada

*Corresponding author. Address: Department of Psychology, York University, 4700 Keele St, OUCH Laboratory, 2004/6 Sherman Health Sciences Building, Toronto, ON M3J 1P3, Canada. Tel.: 416-736-2100; fax: 416-736-5772. E-mail address: rpr@yorku.ca (R.R. Pillai Riddell).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.painreports.com).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The International Association for the Study of Pain. This is an open access article distributed under the Creative Commons Attribution-NoDerivatives License 4.0 (CC BY-ND) which allows for redistribution, commercial and non-commercial, as long as it is passed along unchanged and in whole, with credit to the author.

PR9 8 (2023) e1077

<http://dx.doi.org/10.1097/PR9.0000000000001077>

behaviours.^{4,17,18,38} To our knowledge, no research has examined young child and caregiver attunement during an acute pain experience using cardiac physiology.

Caregiver physiology, through its influence on caregiver behaviours in response to their child's distress (eg, sensitive or insensitive behaviours) and the sensory experience of the child (eg, the child hearing caregiver's calm heart rate during skin-to-skin contact), operates as a co-regulator of young children's physiological response to stress.^{11,24} Thus, gaining an understanding of caregiver-child co-occurring physiological responses in the pain context is important, as sustained dysregulation in the caregiver or child may indicate a dyad that is struggling to adaptively respond to and regulate distress, which may in turn then influence future pain experiences for the child.^{17,31,38}

Extensive research examining physiological responses to distress has demonstrated that the response of the parasympathetic system, commonly indexed with high-frequency heart rate variability (HF-HRV), reflects a regulatory response to distress,^{3,7,16} including pain-related distress.^{36,49} Within the broader developmental literature, many studies have examined caregiver-child HF-HRV attunement within an experimental distress context.¹⁹ However, no studies have examined the attunement patterns of caregiver and toddler HF-HRV during an acute pain procedure in early life.

1.1. Present study

The current study examines the co-regulatory patterns of caregiver and toddler HF-HRV during vaccination. Attunement in this context reflects whether the patterns of cardiac responding are similar in caregivers and children, as they regulate from pain-related distress. Parallel-process growth-mixture modeling (GMM) was used to describe variability in caregiver-toddler attunement patterns over the course of the vaccination. Because previous work has demonstrated variable pain responses in young children,^{37,48} we hypothesized that there would be distinct groupings of co-occurring caregiver and child HF-HRV trajectory patterns. Furthermore, we aimed to further contextualize the attunement patterns by examining the heart rate outcomes of dyads in each group derived from the GMM. Heart rate reflects both sympathetic and parasympathetic activity, and thus provides indication of sympathetically mediated arousal in response to a stressor.⁸ Finally, post hoc analyses were used to examine predictors of the attunement trajectory patterns.

2. Method

2.1. Participants

Caregiver-toddler dyads were recruited from 2 pediatric clinics in the greater Toronto area. Dyads were observed at routine vaccination appointments at the age of 12, 18, or 24 months. This study used a subsample of 189 dyads (Fig. 1) with both caregiver and toddler cardiac data available at the 12- (n = 81), 18- (n = 66), or 24-month (n = 42) vaccination appointments (if a dyad had data from multiple appointments, data from only the most recent appointment was included), with a mean age of 17.04 months (SD = 4.80). Table 1 contains demographic and other characteristics of the dyads included. Exclusion criteria were Neonatal Intensive Care Unit (NICU) stay during infancy, prematurity (<37 weeks' gestation), suspected or confirmed developmental delay, chronic illness, or lack of caregiver fluency in English. Toddlers were 55% male, generally healthy, came from middle-class families, and had well-educated caregivers.

Primary caregivers had a mean age of 36 years (SD = 5.54). They reported diverse cultural backgrounds. The majority reported

being born in Canada (57.6%), with a large proportion of caregivers born outside of Canada, including Asia (18.3%), South America (5.8%), Europe (5.2%), Africa (2.1%), Russia (2.1%), United States/Mexico (2.1%), or Australia (1.6%). On average, caregiver ratings of acculturation indicated a strong identification with both their heritage cultural (ie, a culture inherited across generations of their family) and mainstream North American culture (ie, the culture within which they reside), suggesting the sample reflected the integrated categorization of acculturation.⁹

2.2. Procedure and apparatus

Ethics approval was obtained for this study through the research ethics review board at the participating university. Caregivers were made aware of the study upon entering the pediatric clinic for their child's vaccination appointment. If they agreed to speak to a researcher, caregivers were approached by a research assistant who explained the study. Informed consent was obtained from all caregivers included in the study. Caregivers were asked to fill out a short demographic questionnaire immediately before the vaccination appointment. During the appointment, caregiver-toddler dyads were videotaped and both members of the dyad were connected to mobile monitoring devices to measure their HF-HRV and heart rate (HR) before and after the needle. Cardiac data were collected using Mindware wireless monitors (MW 1000 A) with a sampling rate of 500 Hz. Mindware software (BioLab 3.3) was used to acquire electrocardiogram (ECG) data continuously, and Noldus technologies were used to synchronize video and cardiac data capture. Based on the methodology from a previous longitudinal infant cohort,³⁷ dyads were examined for 1 minute before the needle and up to 3 minutes after the needle. All caregivers held their toddler during the vaccination. Once monitoring equipment was in place, dyads were observed with minimal interference from the research team. Caregivers who participated in the study were given an information sheet on evidenced-based pain management strategies.⁴⁴

2.3. Measures

2.3.1. Demographic information

The short demographic questionnaire included questions about caregiver age, education, self-reported heritage culture, relation to the child, and toddler age and sex. Caregivers were also asked to report on child factors that are known to affect biological indicators,^{35,46} including time since last feeding and since last nap, and number of needles the toddler received during the vaccination appointment.

2.3.2. Cardiac indicators: high-frequency heart rate variability and heart rate

Cardiac data were processed using Mindware HRV 3.1.5. Heart rate was derived from the identification of R-waves, and HF-HRV was calculated from spectral analysis of the R-R intervals (ie, the intervals between successive heart beats)¹³ using the Mindware HRV algorithm to identify each R wave. We used frequency bands within the range of spontaneous respiration (0.24–1.04 Hz for toddlers and 0.12–0.40 for adults).^{6,13}

All coders were trained to edit artifact by an experienced primary coder. A total of 20% of the sample was double-coded for reliability. Overall, interrater reliability was high (intraclass correlations between 0.96 and 0.99). Data were edited for artifacts because of software misidentification or equipment failure (eg, device malfunction). Decisions to exclude data because of artifact were made in

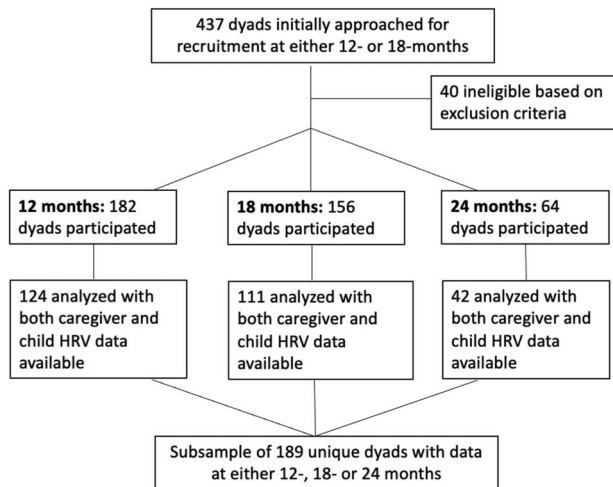


Figure 1. Participant flow diagram.

consultation with the primary coder and decided on an epoch-by-epoch basis. Editing of artifacts was below 5% for all participants.

Cardiac values (HF-HRV and HR) were calculated for eight 30-second epochs: 60 to 31 seconds before the first needle, 30 seconds to 1 second before the first needle, 1 to 30 seconds after the last needle, 31 to 60 seconds after the last needle, 61 to 90 seconds after the last needle, 91 to 120 seconds after the last needle, 121 to 150 seconds after the last needle, and 151 to 180 seconds after the last needle. Our methods are consistent with official guidelines on HRV standards of measurement that suggest approximately 1 minute of data is needed to identify the high-frequency components of HRV.⁴⁵

2.4. Analysis plan

Growth-mixture modeling (GMM) was used to describe variation in patterns of cardiac outcomes over time (ie, trajectories) using a small number of latent classes or groups.³³ Specifically, our goal was to identify distinct regulatory trajectory groups to represent heterogeneity in how caregivers and their toddlers respond and recover simultaneously (ie, parallel processes) in a stressful context. With GMM, each dyad receives a score representing the probability of membership in each discerned group. We then classified each dyad into the group for which it had the highest probability of membership. These models were estimated using the robust maximum likelihood estimator (MLR) in Mplus version 8.0³² to account for nonnormality in the data, which also handles incomplete data using full-information maximum likelihood.

Separate univariate latent growth curve models were first estimated for caregiver and toddler HF-HRV individually to examine the form of the HF-HRV trajectories (ie, linear or nonlinear).²⁹ For the sake of estimating a smoother trajectory pattern, we averaged the 30-second HF-HRV epochs of the caregiver and toddler for every minute preneedle and postneedle (ie, our timepoints became baseline [60–1 second before the needle], post 1 [1–60 seconds postneedle], post 2 [61–120 seconds postneedle], and post 3 [121–180 seconds postneedle]). Model fit was examined using the root mean square error of approximation (RMSEA), the comparative fit index (CFI), and the Tucker–Lewis index (TLI). As approximate guidelines, RMSEA values of 0.06 or lower indicate good fit as well as CFI and TLI values of 0.95 or higher.²⁶

Next, we estimated a single-group parallel-process GMM. This model was then compared to a set of GMM models specified by

Table 1

Demographic and personal characteristics.

Caregiver age in years, mean (SD)	36 (5.54)
Toddler age in months, mean (SD)	17.04 (4.80)
Toddler age by appointment, n (%)	
12 mo	81 (42.9)
18 mo	66 (34.9)
24 mo	42 (22.2)
Sex of toddler, n (%)	
Male	104 (55.0)
Female	85 (45.0)
Relationship to toddler, n (%)	
Mother	163 (86.2)
Father	24 (12.7)
Other	2 (1.1)
Caregiver education, n (%)	
Graduate school/professional training	92 (48.7)
University graduate	60 (31.7)
Partial university (at least 1 y)	5 (2.6)
Trade school/community college	26 (13.8)
High school graduate	2 (1.1)
Missing	4 (2.1)
Acculturation status, mean (SD)	
Way of life reflects heritage culture	7.78 (2.13)
Way of life reflects mainstream North American/Canadian culture	6.33 (2.83)
At vaccination appointment	
Minutes since last feed for toddler, mean (SD)	102.22 (71.46)
Minutes since last nap for toddler, mean (SD)	137.38 (101.53)
No. of needles toddler received, mode (range)	1 (1–3)

increasing the number of groups. Model fit was compared using Akaike's information criterion (AIC)² and the Bayesian information criterion (BIC).⁴² Smaller values of AIC and BIC are associated with better model fit, while accounting for model complexity. The number of groups specified increased until AIC and BIC no longer decreased. The optimal number of groups was determined with consideration of the information criteria and interpretability of the model.²⁹

Once the optimal model was determined, dyad group membership (ie, the group for which they had the highest probability of belonging) was exported to SPSS (Version 26).²⁷ Mean heart rate across epochs was calculated and trajectories were plotted for groups 1 to 3 to further contextualize findings with another biological indicator. Post hoc multinomial logistic regression was used to examine whether dyadic or contextual factors (ie, toddler sex, toddler age, relation to child, baseline caregiver and toddler HF-HRV, time of last nap, time of last feed, and number of needles toddler received) predicted group membership. Predictors were examined in separate models to maximize the sample size for each analysis.

3. Results

Table 2 presents the overall sample mean values and SDs of caregiver and toddler HF-HRV. **Table 3** presents the correlations among caregiver and toddler HF-HRV variables.

3.1. Concurrent changes in caregiver and toddler high-frequency heart rate variability during vaccination

3.1.1. Unconditional growth curve models

Table S1 (available as supplemental digital content at <http://links.lww.com/PR9/A190>) provides the intercept and linear slope factor mean values, SE estimates, and model fit for the

Table 2
Mean values and SDs of caregiver and toddler high-frequency heart rate variability from the overall sample and the 3 groups discerned from the parallel-process growth-mixture model.

	Baseline Mean (SD)	Post 1 Mean (SD)	Post 2 Mean (SD)	Post 3 Mean (SD)
Overall				
Caregiver HF-HRV	4.78 (1.20)	4.84 (1.22)	4.74 (1.23)	4.73 (1.15)
Toddler HF-HRV	3.90 (1.26)	3.81 (1.47)	3.78 (1.22)	3.96 (1.19)
Group 1				
Caregiver HF-HRV	4.93 (1.11)	5.01 (1.13)	4.89 (1.16)	4.89 (1.02)
Toddler HF-HRV	4.05 (1.13)	4.18 (1.31)	4.03 (1.06)	4.03 (1.01)
Group 2				
Caregiver HF-HRV	3.29 (1.19)	3.28 (0.88)	3.26 (0.88)	2.86 (0.75)
Toddler HF-HRV	2.43 (1.00)	2.13 (1.10)	1.75 (0.88)	1.81 (0.78)
Group 3				
Caregiver HF-HRV	4.80 (1.06)	4.78 (1.23)	4.78 (1.24)	4.85 (1.18)
Toddler HF-HRV	3.92 (1.55)	2.35 (0.91)	3.55 (1.09)	4.93 (0.82)

Group 1 represents 80.9% of dyads, group 2 represents 7.9% of dyads, and group 3 represents 11.1% of dyads.
 HF-HRV, high-frequency heart rate variability.

unconditional latent growth curve models of caregiver and toddler HF-HRV. Among toddlers, mean HF-HRV was 3.81 at post 1 and 3.96 at post 3, suggesting a small average change from the reactivity to regulatory phases. The SD of the toddler HF-HRV slope was 0.40, indicating that most data points clustered around the average slope. There was a small average decrease in caregiver mean HF-HRV scores from 4.84 at post 1 to 4.73 at post 3. The SD of the caregiver slope factor was 0.26, suggesting low heterogeneity in caregiver HF-HRV outcomes. Fit indices for the caregiver and toddler growth curve models indicated good fit to the data (see Table S1, available as supplemental digital content at <http://links.lww.com/PR9/A190>), supporting the estimation of linear growth models using a growth mixture modeling approach.

3.1.2. Parallel-process growth-mixture model

Table S2 (available as supplemental digital content at <http://links.lww.com/PR9/A190>) displays the fit indices of 1- to 4-group GMM models. The toddler slope factor variances were fixed to 0 to obtain proper model solutions. Based on the fit indices and interpretability of the model solution, we considered the 3-group model optimal. Table S3 (available as supplemental digital content at <http://links.lww.com/PR9/A190>) presents the intercept and linear slope factor mean values and SE estimates

for groups 1 to 3. Table S4 (available as supplemental digital content at <http://links.lww.com/PR9/A190>) includes the inter-factor correlations between groups. Figure 2 depicts the trajectories for the 3-group model. See Table 2, available as supplemental digital content at <http://links.lww.com/PR9/A190>, for model-estimated mean values for caregiver and toddler HF-HRV prevaccination and postvaccination across groups.

Group 1 (80.9% of the sample) caregivers and toddlers demonstrated generally stable levels of HF-HRV from baseline to post 3 epochs and mirrored one another in their responses. Specifically, both caregivers and toddlers in group 1 demonstrated a small increase in HF-HRV immediately after the needle and returned to baseline levels by the third minute postneedle. Group 2 (7.9% of sample) dyads showed lower HF-HRV at baseline relative to group 1. The caregivers and their toddlers demonstrated a parallel response pattern whereby their HF-HRV levels continued to decrease postneedle and did not return to baseline levels by the third minute. Group 3 (11.1% of sample) displayed similar but slightly lower baseline HF-HRV levels compared with group 1 caregivers and toddlers. The dyads in group 3 showed diverging response patterns such that caregivers maintained stable levels of HF-HRV postneedle, comparable with the caregivers in group 1, and toddlers' HF-HRV decreased immediately after the needle and then increased steeply during the second and third postneedle minutes, surpassing their baseline levels.

3.1.3. Heart rate patterns of groups

The mean heart rate of caregivers and toddlers across 1-minute epochs were calculated post hoc according to group membership from the GMM of HF-HRV and are plotted in Figure 3. Group 1 toddlers experienced an increased heart rate immediately postneedle and a return to baseline levels by the third minute postneedle. Caregivers in group 1 maintained a stable heart rate across epochs. The low baseline and decreasing HF-HRV pattern of group 2 dyads is also reflected in their heart rate responses. Both caregivers and toddlers display a high baseline heart rate, with caregivers maintaining that level of high heart rate across epochs. Toddlers showed an increase in heart rate from baseline right after the needle and maintained a high heart rate (ie, no return to baseline) throughout all postneedle epochs. Group 3 caregivers maintained a stable heart rate level, similar to caregivers in group 1, with slight fluctuations. In contrast, group 3 toddlers demonstrated a steep increase in heart rate

Table 3
Correlations between caregiver and toddler high-frequency heart rate variability (1-minute epochs included in growth-mixture modelings).

	1.	2.	3.	4.	5.	6.	7.	8.
1. Caregiver HF-HRV baseline	—	0.54*	0.52*	0.57*	0.07	0.15	0.16*	0.17*
2. Caregiver HF-HRV post 1		—	0.73*	0.73*	0.12	0.03	0.17*	0.16*
3. Caregiver HF-HRV post 2			—	0.79*	0.15	0.06	0.22*	0.20*
4. Caregiver HF-HRV post 3				—	0.20*	0.08	0.27*	0.27*
5. Toddler HF-HRV baseline					—	0.53*	0.63*	0.63*
6. Toddler HF-HRV post 1						—	0.60*	0.52*
7. Toddler HF-HRV post 2							—	0.74*
8. Toddler HF-HRV post 3								—

* $P < 0.05$.
 HF-HRV, high-frequency heart rate variability.

Downloaded from <http://journals.lww.com/painreports> by BhDMf5ePHkav1zEoum1tQInN4akLlNEZgbsIH0o4XMI0h0CycwC X1AWnYop/IIQHd3i3D000Ry/TVSF14C3V/C4/OA/PDda8K2+Y6H5r15KE= on 08/04/2023

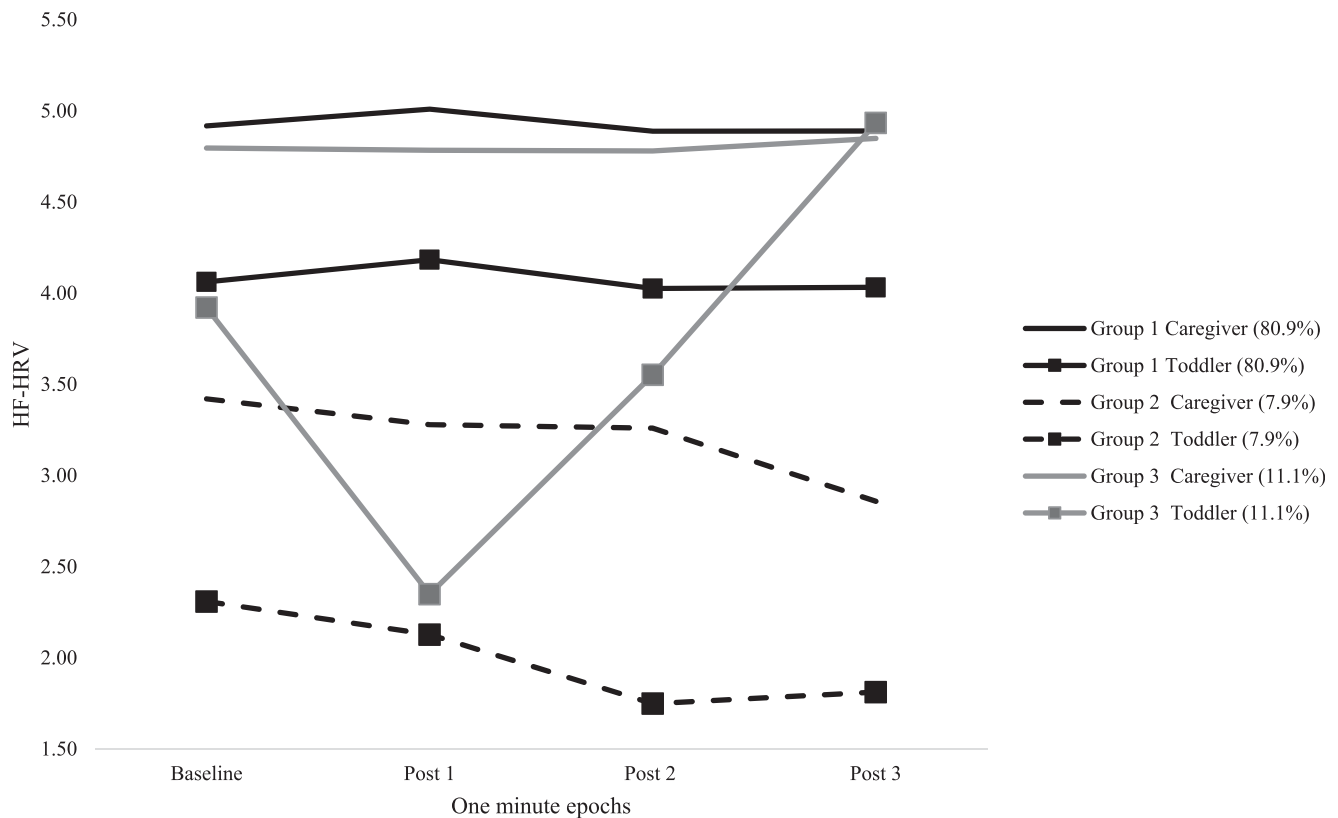


Figure 2. Three-group parallel-process growth-mixture model of caregiver and toddler concurrent high-frequency heart rate variability (HF-HRV) across averaged 1-minute epochs. Baseline values were calculated post hoc using the exported class membership variable.

immediately after the needle and decreased to baseline levels by the third minute postneedle.

3.1.4. Post hoc analyses

Eight multinomial logistic regression models were estimated to determine how well individual and contextual characteristics predict group membership; these characteristics included toddler sex, toddler age, caregiver relation to child, time since last nap, time since last feed, number of needle toddlers received, and baseline HF-HRV of caregivers and toddlers. Results are presented in **Table 4**. Group 1 was the reference category because it is the largest and is considered the normative-stable group. Lower caregiver and toddler baseline HF-HRV values were significantly associated with an increased likelihood of being in group 3 compared with group 1, odds ratio (OR) = 0.29, $P < 0.001$, and OR = 0.29, $P < 0.001$, respectively. None of the other characteristics significantly predicted group membership.

4. Discussion

To our knowledge, this is the first study to examine the co-occurring physiological response patterns of caregivers and their toddlers, measured with HF-HRV, in a pain context. Correlations indicated that caregiver HF-HRV across baseline and postneedle epochs are positively related, albeit small relations, with toddlers' postneedle HF-HRV (post 2 and post 3). Based on correlations alone, it cannot be interpreted whether caregivers and their toddlers are regulated or dysregulated together. Thus, further analyses were conducted to discern distinct trajectory groupings that indicated meaningful differences in dyadic responses within

an acute pain context. In addition, individual and contextual factors were examined as predictors of the groups. Our discussion focuses on the caregiver and toddler co-regulatory patterns for each group. Considering the importance of early attachment relationships in serving as the primary context in which young children regulate distress,^{1,10} we speculate about the attunement patterns for each group according to differences in attachment (ie, secure vs insecure relationships) patterns that have been shown to be associated with physiological responses to non-pain-related distress in children.^{22,40}

4.1. Caregiver-toddler co-regulatory trajectories

Parallel-process growth-mixture modeling was used to characterize heterogeneity in caregiver-toddler physiological co-regulatory responses during routine vaccination. Specifically, 3 groups sufficiently characterized the variation in dyad HF-HRV outcomes. Group 1 represented most dyads (80.9%) and was characterized by parallel caregiver and toddler regulatory trajectories that were stable from preneedle to postneedle. The initial arousal of toddlers in group 1, as indexed by heart rate, demonstrated a normative peak distress response (ie, activation of the sympathetic branch of the autonomic system) followed by a steady decline in heart rate to baseline levels by the third minute postneedle. Caregivers in group 1 maintained a stable and normative heart rate pattern, indicating low levels of arousal in response to their child's vaccination. When confronted with a distressing situation, it is common for individuals to initially experience decreases in HF-HRV from baseline levels, reflecting withdrawal of parasympathetic control of the heart (ie, leading to increases in heart rate), which mobilizes the individual to engage in active coping to return to homeostasis.³⁹ However, the

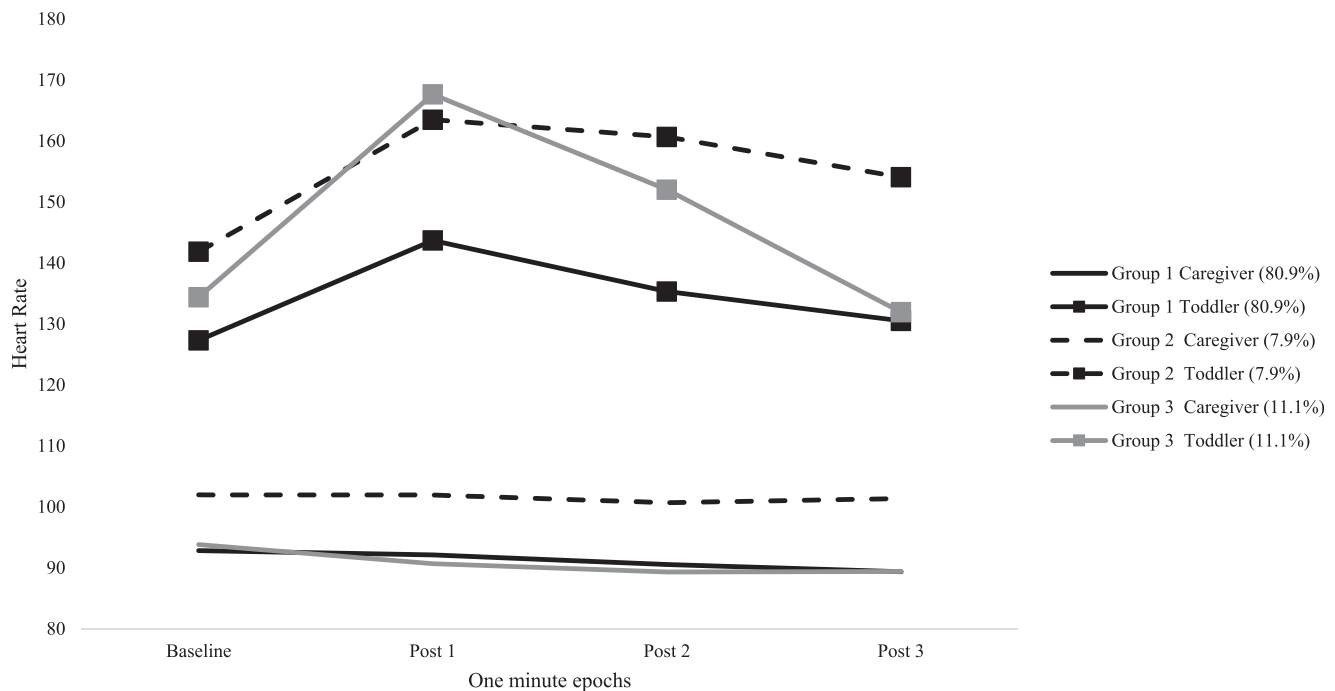


Figure 3. Distinct trajectories of caregiver and child concurrent heart rate based on groupings derived from the parallel-process growth-mixture model of HF-HRV outcomes. Heart rate values were calculated post hoc using the exported class membership variable. HF-HRV, high-frequency heart rate variability.

toddlers in group 1 did not seem to activate their internal regulatory system (ie, the parasympathetic system) to return to homeostasis. Instead, we postulate that the toddler's caregiver provided "external" coping resources, including remaining calm and responding to the child's needs with close-contact soothing, which allowed the toddler to adequately recover from pain-related distress.⁴⁷ The attuned physiological response patterns of dyads in group 1 are consistent with what would be expected from a secure attachment relationship. Young children with a secure attachment rely on their caregiver as an external source of regulation.^{1,22} Engaging with one's caregiver via physical proximity—behaviour often exhibited by secure infants—has been shown to reduce pain-related distress in the vaccination context.^{23,25}

Group 2 characterized 7.9% of dyads in the current study. Both members of the dyad demonstrated lower HF-HRV values across baseline and postneedle epochs compared with the normative and stable responses of group 1. Caregivers and toddlers in group 2 mirrored each other in their regulatory responses, with continual decreases in HF-HRV until the third minute postneedle. It is important to highlight that the dyad did not demonstrate a HF-HRV withdrawal response (ie, a clear lowering of HF-HRV values) followed by augmentation (ie, increase in HF-HRV values), which indicates an internal regulatory response. According to their heart rate responses, the toddlers and caregivers also demonstrated higher peak arousal compared with group 1 dyads and sustained distress that did not return to baseline levels by 3 minutes postneedle. These findings suggest that these toddlers were suboptimally regulating, leaving them less able to return to baseline. The poorer regulatory coping resources likely results in prolonged activation of the parasympathetic system (ie, stable, low HF-HRV scores across time). We speculate that the caregiver in group 2 did not have the capacity to respond to their child's needs and soothe their child's pain-related distress given their own internal dysregulation (ie, consistent low HF-HRV and high heart rate). Although the regulatory trajectories of the dyad look synchronous, each dyad

member likely responds to their distress independently, indicating a lack of attunement.³⁰ Further, this pattern of underregulation in group 2 toddlers has been linked to resistant attachment style in young children,^{12,40} whereby children both seek and resist contact with their primary caregiver, which leads to difficulty calming down and responding to their caregiver's attempts to soothe distress.

Lastly, group 3 dyads represented 11.1% of the sample. Unlike the other 2 groups, the caregivers and toddlers within this group demonstrated very different arousal and regulatory responses. Specifically, caregivers in group 3 exhibited normative HF-HRV and heart rate trajectory responses comparable with the caregivers in group 1. However, the toddlers demonstrated a large withdrawal response (ie, steep decrease in HF-HRV) followed by large increase in HF-HRV that surpassed their baseline levels. When the initial arousal is very high, which was evident based on toddler peak heart rate, the parasympathetic system can overcompensate in attempt to regulate the extreme arousal.⁷ This exaggerated regulatory response seen in group 3 toddlers suggests that they overly rely on their own internal physiological resources to cope with distress despite their caregiver's physical presence. The struggle to adjust one's responses appropriately among dyad members in a distress context (eg, caregiver does not offer support to their child in distress) indicates potential misattunement.³⁰ Furthermore, this pattern of overregulation in the toddler has been associated with an avoidant attachment style between caregivers and young children, whereby the caregiver does not provide adequate regulatory support to the child and the child does not rely on their caregiver for external regulatory support.^{1,40}

4.2. Predictors of co-regulatory groups

Several individual and contextual factors were examined as potential predictors of group membership (ie, the caregiver-toddler co-regulatory trajectories). Only caregiver and

Table 4

Post hoc logistic regressions analyses predicting caregiver–toddler high-frequency heart rate variability trajectory groups.

Predictor	B	SE B	OR	95% CI	P
Toddler sex					
Group 2	0.68	0.55	1.98	0.67–3.83	0.82
Group 3	0.18	0.47	1.20	0.48–3.00	0.86
Toddler age					
Group 2	0.21	0.34	1.23	0.63–2.40	0.86
Group 3	−0.32	0.32	0.73	0.39–1.35	0.83
Caregiver relation to toddler					
Group 2	−0.25	0.81	0.78	0.16–3.79	0.86
Group 3	−0.16	0.67	0.85	0.23–3.16	0.86
Time since last nap					
Group 2	−0.001	0.003	1.00	0.99–1.01	0.86
Group 3	0.002	0.002	1.00	0.99–1.01	0.85
Time since last feed					
Group 2	0.004	0.003	1.00	0.99–1.01	0.83
Group 3	0.002	0.003	1.00	0.99–1.01	0.86
No. of needles					
Group 2	−0.66	0.44	0.51	0.22–1.21	0.69
Group 3	0.04	0.32	1.04	0.55–1.97	0.90
Caregiver baseline HF-HRV					
Group 2	−1.25	0.29	0.29	0.16–0.51	0.00
Group 3	−0.11	0.22	0.90	0.58–1.38	0.86
Toddler baseline HF-HRV					
Group 2	−1.26	0.29	0.29	0.16–0.51	0.00
Group 3	−0.10	0.20	0.91	0.61–1.35	0.86

95% CI, 95% confidence interval of odds ratio; B, unstandardized estimate; OR, odds ratio; SE B, SE of unstandardized estimate.

HF-HRV, high-frequency heart rate variability.

child baseline values of HF-HRV significantly predicted group membership. Specifically, lower caregiver and toddler baseline HF-HRV values predicted membership in group 2 (the group with consistently low HF-HRV levels) compared with group 1 dyads, suggesting that both caregivers and toddlers had lower regulatory functioning from baseline. These results parallel previous work that suggests young children with lower baseline HF-HRV values have less potential to engage their internal physiological regulatory system (ie, demonstrate HRV withdrawal) and thus have reduced regulatory resources to cope with distress.¹⁵ Further, previous research has shown that children who are distressed before a needle procedure experience more pain-related behavioural distress after receiving the needle.¹⁸ This finding highlights the need for caregivers to provide support to their toddlers in regulating distress beginning before a vaccination procedure.

4.3. Limitations

As discussed in previous published papers using the same sample,^{49,50} our study sample includes healthy toddlers and caregivers with high education levels that may affect the generalizability of our findings. Furthermore, the sample sizes of dyads in groups 2 and 3 ($n = 15$ and 21 , respectively) were smaller than the number of dyads in group 1 ($n = 153$), which may have limited the ability to detect associations in our post hoc analyses. Future work will benefit from collecting more detailed information about factors that may modify HRV (eg, chronic illness, mental health, medications, medical conditions⁴¹) or pain-related distress (eg, vaccine choice²⁸) and examine the role of these variables.

5. Conclusions: research and clinical implications

This study presents a novel examination of distinct caregiver–child attunement profiles based on HF-HRV outcomes during toddler vaccinations. Most dyads in the sample displayed a stable and unchanging HF-HRV trajectory, indicating that toddlers relied on their caregivers as an external source of regulation to soothe their pain-related distress. In groups where dyads experienced a lack of attunement or were misattuned, toddlers were either under-regulated (ie, less able to use internal or external resources to regulate pain-related distress) or overregulated (ie, the toddler appears to be overly reliant on internal regulatory systems instead of their caregiver). Similar patterns of physiological responses have been found in previous research with young children in experimental distress context.⁴⁰ Moreover, our findings are consistent with caregiver–child attachment relationship styles that have provided an important understanding of a caregiver's ability to respond effectively to their child and a child's ability to regulate their distress in the vaccination context.^{23,25,34}

The ability to regulate from distress within pain contexts and beyond develops over the course of early childhood and plays an important role in a variety of developmental and psychosocial outcomes.^{14,15,43} This study highlights patterns of caregiver–toddler distress responding that reflect a lowered capacity to cope with pain-related distress, which ultimately may undermine a child's ability to cope with future pain-related distress. Researchers should continue to study potentially maladaptive attunement patterns by further exploring caregiver and child factors that predict these groups, as well as examine whether different attunement patterns predict behavioural pain-related distress in the vaccination context. It is also critical for health care providers to help caregivers support their children during vaccination procedures (eg, inform caregivers about evidence-based strategies to support their child in distress) and encourage caregivers to seek their own individual or parenting support if needed.

Disclosures

The authors have no conflict of interest to declare.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PR9/A190>.

Article history:

Received 31 May 2022

Received in revised form 19 January 2023

Accepted 28 February 2023

References

- [1] Ainsworth MS. Infant–mother attachment. *Am Psychol* 1979;34:932–7.
- [2] Akaike H. Likelihood of a model and information criteria. *J Econom* 1981; 16:3–14.
- [3] Appelhans BM, Luecken LJ. Heart rate variability as an index of regulated emotional responding. *Rev Gen Psychol* 2006;10:229–40.
- [4] Atkinson NH, Gennis H, Racine NM, Pillai Riddell R. Caregiver emotional availability, caregiver soothing behaviors, and infant pain during immunization. *J Pediatr Psychol* 2015;40:1105–14.
- [5] Atkinson L, Jamieson B, Khoury J, Ludmer J, Gonzalez A. Stress physiology in infancy and early childhood: cortisol flexibility, attunement and coordination. *J Neuroendocrinol* 2016;28. doi: 10.1111/jne.12408.
- [6] Bar-Haim Y, Marshall PJ, Fox NA. Developmental changes in heart period and high-frequency heart period variability from 4 months to 4 years of age. *Dev Psychobiol* 2000;37:44–56.

- [7] Bertson GG, Bigger JT, Eckberg DL, Grossman P, Kaufmann PG, Malik M, Nagaraja HN, Porges SW, Saul JP, Stone PH, Molen MW. Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology* 1997;34:623–48.
- [8] Bertson GG, Quigley KS, Lozano D. *Cardiovascular psychophysiology. Handbook of psychophysiology*. 3rd ed. New York, NY: Cambridge University Press, 2007. p. 182–210.
- [9] Berry JW. *Conceptual approaches to acculturation. Acculturation: advances in theory, measurement, and applied research*. Washington, DC: American Psychological Association, 2003. p. 17–37.
- [10] Bowlby J. Attachment and loss: retrospect and prospect. *Am J Orthopsychiatry* 1982;52:664–78.
- [11] Braren SH, Pery RE, Ursache A, Blair C. Socioeconomic risk moderates the association between caregiver cortisol levels and infant cortisol reactivity to emotion induction at 24 months. *Dev Psychobiol* 2019;61: 573–91.
- [12] Braungart-Rieker JM, Garwood MM, Powers BP, Wang X. Parental sensitivity, infant affect, and affect regulation: predictors of later attachment. *Child Dev* 2001;72:252–70.
- [13] Cacioppo JT, Tassinary LG, Bertson GG, editors. *Handbook of psychophysiology*. 2nd ed. Cambridge, UK; New York, NY: Cambridge University Press, 2000.
- [14] Calkins SD, Dedmon SE. Physiological and behavioral regulation in two-year-old children with aggressive/destructive behavior problems. *J Abnorm Child Psychol* 2000;28:103–18.
- [15] Calkins SD. Cardiac vagal tone indices of temperamental reactivity and behavioral regulation in young children. *Dev Psychobiol* 1997;31:125–35.
- [16] Calkins SD. Caregiving as coregulation: psychobiological processes and child functioning. *Biosocial foundations of family processes*. New York, NY: Springer, 2011. p. 49–59.
- [17] Campbell L, Pillai Riddell R, Garfield H, Greenberg S. A cross-sectional examination of the relationships between caregiver proximal soothing and infant pain over the first year of life. *PAIN* 2013;154:813–23.
- [18] Campbell L, Pillai Riddell R, Cribbie R, Garfield H, Greenberg S. Preschool children's coping responses and outcomes in the vaccination context: child and caregiver transactional and longitudinal relationships. *PAIN* 2018;159:314–30.
- [19] Di Lorenzo MG, Buceasa O, Rumeo C, Waxman JA, Flora DB, Schmidt LA, Riddell RP. Caregiver and young child biological attunement in distress contexts: a systematic review and narrative synthesis. *Neurosci Biobehav Rev* 2022;132:1010–36.
- [20] Feldman R. Parent–infant synchrony and the construction of shared timing; physiological precursors, developmental outcomes, and risk conditions. *J Child Psychol Psychiatry* 2007;48:329–54.
- [21] Goubert L, Pillai Riddell R, Simons L, Borsook D. Theoretical basis of pain. In: Stevens B, Hathway G, Zempsky W, editors. *Oxford textbook of pediatric pain*. Oxford, United Kingdom: Oxford University Press, 2021.
- [22] Groh AM, Narayan AJ. Infant attachment insecurity and baseline physiological activity and physiological reactivity to interpersonal stress: a meta-analytic review. *Child Dev* 2019;90:679–93.
- [23] Hillgrove-Stuart J, Riddell RP, Flora DB, Greenberg S, Garfield H. Caregiver soothing behaviors after immunization and infant attachment: a longitudinal analysis. *J Dev Behav Pediatr* 2015;36:681–9.
- [24] Hofer M. Hidden regulators within the mother–infant interaction. In: *Nurturing Children and Families*. pp. 154–63.
- [25] Horton R, Pillai Riddell R, Moran G, Lisi D. Do infant behaviors following immunization predict attachment? An exploratory study. *Attach Hum Dev* 2016;18:90–9.
- [26] Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Model Multidiscip J* 1999;6:1–55.
- [27] IBM Corp. *IBM SPSS statistics for Mac, Version 26.0*. Armonk, NY: IBM Corp, 2019.
- [28] Ipp M, Cohen E, Goldbach M, Macarthur C. Effect of choice of measles-mumps-rubella vaccine on immediate vaccination pain in infants. *Arch Pediatr Adolesc Med* 2004;158:323–6.
- [29] Jung T, Wickrama KAS. An introduction to latent class growth analysis and growth mixture modeling. *Soc Personal Psychol Compass* 2008;2: 302–17.
- [30] Ludmer Nofech-Mozes JA, Jamieson B, Gonzalez A, Atkinson L. Mother–infant cortisol attunement: associations with mother–infant attachment disorganization. *Dev Psychopathol* 2020;32:43–55.
- [31] McMurtry CM, Pillai Riddell R, Taddio A, Racine N, Asmundson GJG, Noel M, Chambers CT, Shah V; HELPinKids&Adults Team. Far from “just a poke”: common painful needle procedures and the development of needle fear. *Clin J Pain* 2015;31:S3–11.
- [32] Muthén LK, Muthén B. *Mplus user's guide: statistical analysis with latent variables, user's guide*. 8th ed. Los Angeles, CA: Muthén & Muthén, 1998.
- [33] Muthén B, Shedden K. Finite mixture modeling with mixture outcomes using the EM algorithm. *Biometrics* 1999;55:463–9.
- [34] O'Neill MC, Pillai Riddell R, Bureau J-F, Deneault A-A, Garfield H, Greenberg S. Longitudinal and concurrent relationships between caregiver–child behaviours in the vaccination context and preschool attachment. *PAIN* 2021;162:823–34.
- [35] Oberlander T, Saul JP. Methodological considerations in heart rate variability analysis. In: Rautaharju F, Rautaharju P, editors. *Investigative electrocardiography in epidemiological studies and clinical trials*. London: Springer, 2007. p. 68–73.
- [36] Oberlander TF, Grunau RVE, Whitfield MF, Saul JP. Cardiac autonomic and behavioral responses to acute pain in 4 month old infants † 80. *Pediatr Res* 1997;41:16.
- [37] Pillai Riddell R, Flora DB, Stevens SA, Stevens B, Cohen LL, Greenberg S, Garfield H. Variability in infant acute pain responding meaningfully obscured by averaging pain responses. *PAIN* 2013;154:714–21.
- [38] Pillai Riddell R, Campbell L, Flora DB, Racine N, Din Osmun L, Garfield H, Greenberg S. The relationship between caregiver sensitivity and infant pain behaviors across the first year of life. *PAIN* 2011;152:2819–26.
- [39] Porges SW. The polyvagal perspective. *Biol Psychol* 2007;74:116–43.
- [40] Qu J, Leerkes EM. Patterns of RSA and observed distress during the still-face paradigm predict later attachment, compliance and behavior problems: a person-centered approach. *Dev Psychobiol* 2018;60:707–21.
- [41] Quintana DS, Heathers JAJ. Considerations in the assessment of heart rate variability in biobehavioral research. *Front Psychol* 2014;5:805.
- [42] Schwarz G. Estimating the dimension of a model. *Ann Stat* 1978;6: 461–4.
- [43] Stifter CA, Corey JM. Vagal regulation and observed social behavior in infancy. *Soc Dev* 2001;10:189–201.
- [44] Taddio A, Appleton M, Bortolussi R, Chambers C, Dubey V, Halperin S, Hanrahan A, Ipp M, Lockett D, MacDonald N, Midmer D, Mousmanis P, Palda V, Pielak K, Riddell RP, Rieder M, Scott J, Shah V. Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline. *CMAJ* 2010;182:E843–55.
- [45] Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology. Heart rate variability. *Circulation* 1996;93:1043–65.
- [46] Waxman JA, Pillai Riddell RR, Tablon P, Schmidt LA, Pinhasov A. Development of cardiovascular indices of acute pain responding in infants: a systematic review. *Pain Res Manag* 2016;2016:e8458696.
- [47] Waxman J, Martin J, Riddell RP. Understanding infant pain responding within a relational context. *Neonatal pain*. New York, NY: Springer, 2017. p. 89–104.
- [48] Waxman JA, DiLorenzo MG, Riddell RRP, Flora DB, Greenberg S, Garfield H. Preschool needle pain responding: establishing ‘normal’. *J Pain* 2017;18:739–45.
- [49] Waxman JA, DiLorenzo MG, Riddell RRP, Flora DB, Schmidt LA, Garfield H, Flanders D, Weinberg E, Savlov D. An examination of the reciprocal and concurrent relations between behavioral and cardiac indicators of acute pain in toddlerhood. *PAIN* 2020;161:1518–31.
- [50] Waxman JA, DiLorenzo MG, Pillai Riddell RR, Flora DB, Schmidt LA, Garfield H, Flanders D, Weinberg E, Savlov D. Investigating convergence of cardiac and behavioral indicators of distress during routine vaccinations over the second year of life. *Dev Psychobiol* 2021;63:437–51.