Special Interest Group on Pain in Childhood
INTERNATIONAL ASSOCIATION FOR THE STUDY OF PAIN

Pediatric Pain Letter
Commentaries on pain in infants, children, and adolescents

February 2018 **Vol. 20 No. 1** **www.childpain.org/ppl**
Editor: Deirdre E. Logan, PhD, deirdre.logan@childrens.harvard.edu

Commentary

Measuring caregiver HRV in the acute pain context: Methodological considerations

Kaytlin Constantin, Heidi N. Bailey, and C. Meghan McMurtry

In pediatric pain contexts, caregivers often experience distress and increases in physiological response when viewing their child in pain (Smith et al., 2007; Goubert et al., 2008). Caregivers must regulate their own emotional experience to accurately interpret and effectively respond to their child's needs (Vervoort & Trost, 2017). Increasingly, researchers have utilized heart rate variability (HRV) or the variation in time between consecutive heartbeats, as an objective index of emotion regulation (Appelhans & Luecken, 2006; Balzarotti et al., 2017). Numerous physiological measures, including heart rate and electrodermal activity, are available to assess general autonomic arousal associated with the experience of emotions. In contrast, HRV can inform an individual's regulation of emotions given neural connections between the heart and the brain (Balzarotti et al., 2017). HRV at the high or respiratory frequency (i.e. respiratory sinus arrhythmia) is a noninvasive index of autonomic flexibility or the body's ability to rapidly adjust physiological states via the vagus nerve by increasing or decreasing heart rate (Porges, 2007). HRV is also posited to distally index cortical systems that support regulated emotional responses (e.g. captures the activity between the prefrontal cortex and the vagus nerve; Thayer & Lane, 2000).

Physiological research in the field of pediatric pain has focused on the child in pain; recently, it has been recognized that examining HRV in individuals beyond those experiencing pain (e.g. caregivers) is also relevant to understanding the child's pain-related experience (Vervoort et al., 2014; Constantin et al., 2016). Examining caregiver HRV can provide complementary information regarding their emotional response in the context of their child's pain. Such information may be useful in determining whether caregivers may benefit from interventions focused on emotion regulation strategies. Nevertheless, only two investigations to date have explored parent HRV in the context of acute pediatric pain (Vervoort et al., 2014; Constantin et al., 2017).

Laborde and colleagues (2017) provide an in depth review of HRV methodology and recommendations; however, it is not specific to the pain context and may be less accessible to readers who are new to HRV methodology. In contrast, the aim of our paper is to provide succinct and explicit guidance for professionals who are less familiar with HRV methodology. Specifically, we provide a brief overview of the methodological considerations when examining caregiver high frequency HRV in the pediatric pain context, with regard to: (1) study design, (2) selecting an HRV parameter, (3) apparatus and subject preparation, and (4) data cleaning and analysis. Table 1 presents general methodological recommendations. In the text, we explore general and pain-specific (when applicable) methodological considerations.

Study design: pain stimulus and time blocks

Prospective studies should include at least three time blocks, allowing for comparison of HRV during: *baseline*, *event*, and *post-event* blocks (see

Table 1
General methodological recommendations

Methodological Consideration	Recommendations	Example Citations
Study Design	Three time blocks: 1. Baseline: passive resting, neutral video, or "Vanilla" baseline (resting HRV). 2. Event: immediately before or during child pain (HRV reactivity). 3. Post-event: following child pain (HRV recovery).	(1) Kogan et al. (2013) (2) Nahman-Averbuch et al. (2016)* (3) Werner et al. (2015)
	Blocks should be designed similarly to minimize differences in HRV due to body position and speaking.	Peltola et al. (2012); Laborde et al. (2017)
Choosing a Parameter	Select parameter(s) that reflect(s) vagal tone. Commonly used parameters: 1. Root mean square of successive differences between interbeat intervals (RMSSD); time-domain method. 2. High-frequency HRV (HF-HRV; reflects 0.15 to 0.40 Hz); frequency-domain method. 3. Peak-valley; utilizes time properties and respiration signal.	(1, 2) Vervoort et al. (2014)* (2) Park et al. (2014) (3) Stellar et al. (2015)
	Report both time- and frequency-domain parameters.	Laborde et al. (2017)
Preparation of Apparatus & Skin	Electrode application site preparation to lower skin impedance: a. Clean and dry the area. b. Remove non-conductive skin cells.	Kligfield et al. (2007)
	Latex-free and hypoallergenic electrodes minimize adverse skin reactions to electrode adhesive.	
	Respiration: thoracic and/or abdominal band. Can also be measured post-hoc (e.g., ECG-derived respiration), although this is less accurate.	Al-Khalidi et al. (2011); Laborde et al. (2017)
Data Cleaning and Analysis	Inspect data manually for artifacts prior to utilizing software correction methods. Artifacts: 1. Technical artifacts: missing or distorted beat resulting from poorly fastened electrodes, sweating, movement. 2. Physiological artifacts: abnormal heart rhythm resulting from disturbed electrical activity in the heart (e.g., ectopic beats).	Peltola (2012)
	Commonly used software: 1. AcqKnowledge: acquire, edit, analyze ECG data. 2. Kubios HRV: HRV analysis. 3. ARTiiFACT: HRV analysis.	(1) Appelhans & Luecken (2008)* (2) Park et al. (2014) (3) Vervoort et al. (2014)*

*Indicates pain-specific citation.

Table 1). This provides three indicators of HRV: resting, reactivity (i.e. change score between baseline and event), and recovery (change score between event and post-event; Laborde et al., 2017). Depending on the research question, an additional index may be calculated by examining the changes between baseline and post-event. Optimally, each block must be the same length, which will vary by the metric used (see Shaffer & Ginsberg, 2017 for an overview of HRV metrics), with a minimum of one-minute and preferably at least two-minute time windows (European Society of Cardiology, 1996; Grant et al., 2011).

In the pediatric pain context, further delineation regarding the experience captured within each time block is needed; research could benefit from more sensitive temporal measurement of HRV as seen in existing behavioral observations of infant and child acute pain responses (e.g. Waxman et al., 2017)[1]. For example, two types of baseline blocks are possible: a resting and immediate pre-pain baseline. Pure resting baseline measures of HRV are typically obtained while an individual is relaxed and sitting comfortably, and acclimatized to the environment with nothing specifically happening (Laborde et al., 2017). This leads to the question of whether it is possible to acquire a true resting baseline measure if caregivers arrive to the study anticipating child pain, which may be accompanied by a heightened state of arousal (Smith et al., 2007). A pre-pain baseline occurs in preparation for the event. In the case of a needle, this may include the health care provider entering the room, swabbing, and handling the materials. HRV during the painful procedure (i.e. event block) requires the use of a pain anchor, or the exact timing of the beginning and ending of the painful procedure to ensure each time block captures the same experience for each individual. Acquiring HRV during child pain may prove difficult logistically in clinical settings and the researcher must decide whether it is possible to consistently obtain a minimum recording of one minute during the child's experience of pain, or whether measuring caregiver HRV immediately before child pain (e.g. anticipation) is more feasible. Longer time blocks are more reliable; therefore, feasibility concerns must be balanced with reliability. However, longer time blocks may compromise validity and the specificity of the emotional experience being captured. Ultimately, the ability to capture caregiver HRV during child pain will depend on the pain stimulus or the type of painful procedure. Caregiver HRV during child pain could be examined during longer painful procedures, such as lumbar punctures and bone marrow aspirations, as well as laboratory pain, heel lances, and venipunctures that are typically longer in duration compared to a vaccination. For shorter procedures, examining HRV immediately before (pain anticipation) and/or after (pain reactivity) the procedure may be more likely. The age of the child is relevant to consider when examining pain reactivity, with infants having longer peak distress responses than preschool and school-aged children (Pillai Riddell et al., 2013; Waxman et al., 2017). Post-event recordings should be acquired following child pain to provide a recovery measure of HRV. Moreover, ideally, multiple post-event recordings could be applied to track the progression of HRV recovery; specifically, to examine early regulation immediately after the procedure, later regulation two or three minutes after the procedure, and determine when caregiver HRV returns to resting levels. A final consideration is that movement should be minimized during each recording as it complicates the interpretation of HRV (European Society of Cardiology, 1996). Parents can be instructed to minimize their movement to reduce potential artifacts, although this may interfere with their typical behaviors and interactions with their child.

Choosing a parameter

HRV parameters can be categorized under time-domain (i.e. statistical calculation), frequency-domain (i.e. filtering ECG signal into different frequency bands), and non-linear indices (Smith et al., 2013). HRV in the high (vs. low) frequency band, between 0.15 to 0.40 Hz, is of most interest as it is posited to index vagal influence on the heart (Porges, 2007). The most common parameters are reported in Table 1. All measures are highly

[1] We thank a reviewer for raising this important issue and his/her helpful discussion points.

correlated and thought to be comparable indices of vagal tone when respiration frequency is within 9 and 24 cycles per minute, equivalent to between 0.15 and 0.40 Hz (Grossman et al., 1990; Berntson et al., 1997). Therefore, it is recommended that respiration rate be measured to ensure breathing is within this normal range; these data can be acquired online during the experiment or offline utilizing post hoc analyses (e.g. Kubios HRV; see Laborde et al., 2017). HRV may also be affected by other extraneous variables (e.g. caffeine and nicotine consumption; Quintana & Heathers, 2014); Laborde and colleagues (2017) provide a demographic form that may be used to consider potential sources of variability.

Apparatus and skin preparation

In the clinical setting, which may involve either small rooms (e.g. for venipuncture) or transitioning from room to room (perioperative), a wireless ECG system will offer the most flexibility for both patients and health care providers (e.g. less equipment is attached to the caregiver). Numerous ECG configurations with varying numbers of leads (e.g. three, five, twelve) are available to acquire HRV data, and the placement of the electrodes is dependent on the number of leads (see Kligfield et al., 2007, for details). However, as described in Table 1, a consistent approach to preparing the skin for HRV recording is recommended. Dry electrodes, caregiver perspiration, and hair may prevent the electrodes from sticking well. Gel may be applied if electrodes are dry, and storing electrodes in an airtight package will prevent drying. Respiration rate can be acquired by respiratory inductance plethysmography, which utilizes a thoracic and/or abdominal band to monitor chest and abdominal movement (see Al-Khalidi et al., 2011, for a review).

Data cleaning and analysis

An electrocardiogram (ECG) is commonly used to acquire HRV data as it allows precise inspection and cleaning of the data (Shaffer et al., 2014). The data should first be visually inspected for technical and physiological artifacts before using software correction programs (see Peltola, 2012, for a review). The data can be manually edited by using the deletion correction method (i.e. removing abnormal interbeat intervals and shifting subsequent intervals to replace the deleted ones), although the absolute number of samples in the segment is decreased; thus, a time-block of longer duration is desirable (e.g. record for an additional 15 seconds for a 1-minute time block). Alternately, other correction methods involving interpolation preserve the continuous HRV sample.

Software programs are available to acquire and edit the ECG signal (e.g. AcqKnowledge 5.0 [Biopac Systems Inc.]), and existing specialized HRV programs are user-friendly and freely available (e.g. ARTiiFACT; Kaufmann et al., 2011; Kubios HRV Standard; Tarvainen et al., 2017) or can be purchased (e.g. Kubios HRV Premium; Tarvainen et al., 2017[2]) to edit and analyze the ECG recording (see Table 1). Specialized programs compute HRV parameters using both time-domain methods (reported in units of milliseconds [ms]) and frequency-domain methods (reported in units of squared milliseconds [ms^2]). It is a widely held standard among physiological researchers to report the natural logarithm of an HRV parameter (e.g. Goedhart et al., 2007).

Conclusions

This commentary sought to provide clinician-scientists with concrete introductory knowledge on measuring caregiver HRV in the pediatric pain context. The ultimate goal is to foster research examining caregiver physiology to clarify the associations between caregiver physiological, subjective, and behavioral responses, and child pain experience. Incorporating HRV measures into pediatric pain research has theoretical implications (e.g. contributes to existing biopsychosocial models of pain) and may lead to downstream clinical implications (e.g. applying interventions that target HRV).

Kaytlin Constantin, MA
Department of Psychology, University of Guelph, Guelph, ON, Canada
email: kaytlin@uoguelph.ca

---

[2] Of relevance, Kubios HRV Standard only reads data files based on RR intervals; Kubios HRV Premium is required to read ECG files.

Heidi N. Bailey, PhD
Department of Psychology, University of Guelph, Guelph, ON, Canada

C. Meghan McMurtry, PhD
Department of Psychology, University of Guelph, Guelph, ON; Pediatric Chronic Pain Program, McMaster Children's Hospital, Hamilton, ON; Children's Health Research Institute, London, ON; Department of Paediatrics, Schulich School of Medicine & Dentistry, Western University, London, ON, Canada

Acknowledgement

The authors gratefully acknowledge funding by the Ontario Graduate Scholarship to K Constantin.

References

Al-Khalidi FQ, Saatchi R, Burke D, Elphick H, Tan S. Respiration rate monitoring methods: a review. Pediatr Pulmonol 2011;46:523-529. www.pubmed.gov/21560260

Appelhans BM, Luecken LJ. Heart rate variability as an index of regulated emotional responding. Rev Gen Psychol 2006;10;229-240.

Appelhans BM, Luecken LJ. Heart rate variability and pain: associations of two interrelated homeostatic processes. Biol Psychol 2008;77:174-182. www.pubmed.gov/18023960

Balzarotti S, Biassoni F, Colombo B, Ciceri MR. Cardiac vagal control as a marker of emotion regulation in healthy adults: a review. Biol Psychol 2017;130:54-66. www.pubmed.gov/29079304

Berntson GG, Bigger JT Jr, Eckberg DL, Grossman P, Kaufmann PG, Malik M, et al. Heart rate variability: origins, methods, and interpretive caveats. Psychophysiology 1997;34:623-648. www.pubmed.gov/9401419

Biopac Systems Inc. AcqKnowledge 5 Software Guide. www.biopac.com/wp-content/uploads/AcqKnowledge-5-Software-Guide.pdf

Constantin K, McMurtry CM, Bailey HN. Parental cardiac response in the context of pediatric acute pain: current knowledge and future directions. Pain Manag 2017;7:81-87. www.pubmed.gov/27882803

Constantin K, Moline RL, McMurtry CM, Bailey HN. Parent cardiac response in the context of their child's completion of the cold pressor task: a pilot study. Children 2017;4:100. www.pubmed.gov/29160828

European Society of Cardiology and the North American Society of Pacing and Electrophysiology Task Force. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 1996;93:1043-1065. www.pubmed.gov/8598068

Goedhart AD, van der Sluis S, Houtveen, JH, Willemsen G, de Geus EJ. Comparison of time and frequency domain measures of RSA in ambulatory recordings. Psychophysiology 2007;44:203-215. www.pubmed.gov/17343704

Goubert L, Vervoort T, Sullivan MJ, Verhoeven K, Crombez G. Parental emotional responses to their child's pain: the role of dispositional empathy and catastrophizing about their child's pain. J Pain 2008;9:272-279. www.pubmed.gov/18206424

Grant CC, van Rensburg DC, Strydom N, Viljoen M. Importance of tachogram length and period of recording during noninvasive investigation of the autonomic nervous system. Ann Noninvasive Electrocardiol 2011;16:131-139. www.pubmed.gov/21496163

Grossman P, van Beek J, Wientjes C. A comparison of three quantification methods for estimation of respiratory sinus arrhythmia. Psychophysiology 1990;27:702-714. www.pubmed.gov/2100356

Kaufmann T, Sütterlin S, Schulz S, Vögele C. ARTiiFACT: a tool for heart rate artifact processing and heart rate variability analysis. Behav Res Methods 2011;43:1161-1170. www.pubmed.gov/21573720

Kligfield P, Gettes LS, Bailey JJ, Childers R, Deal BJ, Hancock EW, et al. Recommendations for the standardization and interpretation of the electrocardiogram: part I: the electrocardiogram and its technology: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society endorsed by the International Society for Computerized Electrocardiology. Circulation 2007;115:1306-1324. www.pubmed.gov/17322457

Kogan A, Gruber J, Shallcross AJ, Ford BQ, Mauss IB. Too much of a good thing? Cardiac vagal tone's nonlinear relationship with well-being. Emotion 2013;13:599-604. www.pubmed.gov/23731433

Laborde S, Mosley E, Thayer JF. Heart rate variability and cardiac vagal tone in psychophysiological research – recommendations for experiment planning, data analysis, and data reporting. Front Psychol 2017;20:213. www.pubmed.gov/28265249

Nahman-Averbuch H, Dayan L, Sprecher E, Hochberg U, Brill S, Yarnitsky D, et al. Sex differences in the relationships between parasympathetic activity and pain modulation. Physiol Behav 2016;154:40-48. www.pubmed.gov/26556539

Park G, Vasey MW, Van Bavel, JJ, Thayer JF. When tonic cardiac vagal tone predicts changes in phasic vagal tone: the role of fear and perceptual load. Psychophysiology 2014;51: 419-426. www.pubmed.gov/24571084

Peltola MA. Role of editing of R-R intervals in the analysis of heart rate variability. Front Physiol 2012;3:148. www.pubmed.gov/22654764

Pillai Riddell R., Flora DB, Stevens SA, Stevens B, Cohen LL, Greenberg S, et al. Variability in infant acute pain responding meaningfully obscured by averaging pain responses. Pain 2013;154(5):714-721. www.pubmed.gov/23531475

Porges SW. The polyvagal perspective. Biol Psychol 2007;74:116-143. www.pubmed.gov/17049418

Quintana DS, Heathers JAJ. Considerations in the assessment of heart rate variability in biobehavioral research. Front Psychol 2014;5:805. www.pubmed.gov/25101047

Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health 2017;5:258. www.pubmed.gov/29034226

Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. Front Physiol 2014;5:1040. www.pubmed.gov/25324790

Smith AL, Owen H, Reynolds KJ. Heart rate variability indices for very short-term (30 beat) analysis. Part 1: survey and toolbox. J Clin Monit Comput 2013;27:569-576. www.pubmed.gov/23674071

Smith RW, Shah V, Goldman RD, Taddio A. Caregivers' responses to pain in their children in the emergency department. Arch Pediatr Adolesc Med 2007;161:578-582. www.pubmed.gov/17548763

Stellar JE, Cohen A, Oveis C, Keltner D. Affective and physiological responses to the suffering of others: compassion and vagal activity. J Pers Soc Psychol 2015;108:572-585. www.pubmed.gov/25621856

Tarvainen MP, Lipponen J, Niskanen J, Ranta-aho PO. Kubios HRV: user's guide. 2017. www.kubios.com/downloads/Kubios_HRV_Users_Guide.pdf

Thayer JF, Lane RD. A model of neurovisceral integration in emotion regulation and dysregulation. J Affect Disord. 2000;61:201-216. www.pubmed.gov/11163422

Vervoort T, Trost Z. Examining affective-motivational dynamics and behavioral implications within the interpersonal context of pain. J Pain 2017;18:1174-1183. www.pubmed.gov/29309272

Vervoort T, Trost Z, Sütterlin S, Caes L, Moors A. Emotion regulatory function of parent attention to child pain and associated implications for parental pain control behaviour. Pain 2014;155:1453-1463. www.pubmed.gov/24769189

Waxman JA, DiLorenzo MG, Pillai Riddell RR, Flora DB, Greenberg S, Garfield H. Preschool needle pain responding: establishing 'normal'. J Pain 2017;18:739-745. www.pubmed.gov/28196739

Werner GG, Ford BQ, Mauss IB, Schabus M, Blechert J, Wilhelm FH. High cardiac vagal control is related to better subjective and objective sleep quality. Biol Psychol 2015;106: 79-85. www.pubmed.gov/25709072