STRESS
The International Journal on the Biology of Stress

Taylor & Francis
Taylor & Francis Group

Stress
The International Journal on the Biology of Stress

ISSN: 1025-3890 (Print) 1607-8888 (Online) Journal homepage: https://www.tandfonline.com/loi/ists20

Heart rate increase predicts challenging behavior episodes in preschoolers with autism

Heather J. Nuske, Emma Finkel, Darren Hedley, Valentina Parma, Liza Tomczuk, Melanie Pellecchia, John Herrington, Steven C. Marcus, David S. Mandell & Cheryl Dissanayake

To cite this article: Heather J. Nuske, Emma Finkel, Darren Hedley, Valentina Parma, Liza Tomczuk, Melanie Pellecchia, John Herrington, Steven C. Marcus, David S. Mandell & Cheryl Dissanayake (2019): Heart rate increase predicts challenging behavior episodes in preschoolers with autism, Stress, DOI: 10.1080/10253890.2019.1572744

To link to this article: https://doi.org/10.1080/10253890.2019.1572744

STRESS
https://doi.org/10.1080/10253890.2019.1572744

Taylor & Francis
Taylor & Francis Group

Check for updates

ORIGINAL RESEARCH REPORT

Heart rate increase predicts challenging behavior episodes in preschoolers with autism

Heather J. Nuske[a], Emma Finkel[c], Darren Hedley[d], Valentina Parma[e], Liza Tomczuk[f], Melanie Pellecchia[a], John Herrington[b], Steven C. Marcus[a], David S. Mandell[a] and Cheryl Dissanayake[d]

[a]Center for Mental Health, University of Pennsylvania, Philadelphia, PA, USA;[b]Center for Autism Research, Children's Hospital of Philadelphia, Philadelphia, PA, USA;[c]Psychology Department, School of Arts and Sciences, University of Pennsylvania, Philadelphia, PA, USA;[d]School of Psychology and Public Health, Olga Tennison Autism Research Centre, La Trobe University, Melbourne, Australia;[e]Scuola Internazionale Superiore di Studi Avanzati, Trieste, Italy;[f]Neuroscience Program, Dickinson College, Carlisle, PA, USA

ABSTRACT
Identifying triggers for challenging behavior is difficult in some children with autism because of their limited communication abilities. Physiological indicators of stress may provide important insights. This study examined whether heart rate (HR) predicts challenging behavior in children with autism. While wearing an electrocardiograph monitor, 41 children with autism aged 2- to 4-years participated in tasks designed to induce low-level stress (e.g. waiting for a snack). Coders identified 106 time periods during which challenging behaviors occurred and also coded 106 randomly selected time samples that did not include challenging behaviors. Thirteen (32%) participants exhibited challenging behaviors and were included in the study. Baseline-corrected HR was computed for each behavior/time sample. On average, children with autism showed a $22 \pm 16\%$ HR increase from baseline 58 ± 22 seconds before the onset of a challenging behavior episode. Peak HR change had moderate predictive utility (area under the curve = .72, $p < .001$). The increase in HR before challenging behaviors was similar for children of different characteristics (age, autism severity, expressive language ability, overall developmental ability). Results highlight the promise of using physiological stress to predict challenging behavior in preschoolers with autism; although, they need to be replicated in larger samples. Given recent advances in wearable biosensing, it may be useful to incorporate HR monitoring in autism intervention.

LAY SUMMARY
In children with autism, changes in heart rate (HR) may help us predict when challenging behavior is about to occur – but this hypothesis has not been well studied. In this study, HR increase moderately predicted challenging behavior in preschoolers with autism. Given recent advances in wearable sensors, it may be useful to incorporate HR monitoring in autism intervention.

ARTICLE HISTORY
Received 7 July 2018
Accepted 13 January 2019

KEYWORDS
Autism spectrum disorder; challenging behavior; heart rate; biosensing; preschoolers; Laboratory Temperament Assessment Battery

Many children with autism spectrum disorder, a disorder of social communication impairments and behavioral rigidity (American Psychiatric Association [APA], 2013) exhibit challenging behaviors (e.g. Matson, Wilkins, & Macken, 2008; McTiernan, Leader, Healy, & Mannion, 2011), which can have a devastating impact on family well-being (Lecavalier, Leone, & Wiltz, 2006), predict teacher burnout (Hastings & Brown, 2002), and are the most frequent cause of hospitalizations (Siegel & Gabriels, 2014). Children with autism often have difficulty communicating their emotions (Hedman et al., 2012; Nuske, Vivanti, & Dissanayake, 2013); therefore, it can be difficult to infer when they are experiencing stress. Our research has shown less concordance between internal physiological arousal and external emotional communication in preschoolers with autism than in typically developing children (Nuske et al., 2018). As a result, it may be difficult for parents and teachers to know when to intervene to reduce oncoming challenging behaviors. Indeed, evidence-based approaches to managing challenging behaviors emphasize the importance of understanding triggers (Doehring, Reichow, Palka, Phillips, & Hagopian, 2014; Machalicek, O'Reilly, Beretvas, Sigafoos, & Lancioni, 2007; Otten & Tuttle, 2010), but parents and teachers report that challenging behaviors surface without warning.

Many challenging behaviors may be a reaction to stress that can be detected through physiological signals. When stressed, one's HR increases, pupils dilate, skin sweats, the face heats up and heart rate variability (HRV) decreases (Bradley, Miccoli, Escrig, & Lang, 2008; Ioannou, Gallese, & Merla, 2014; Kreibig, 2010; Stern, Ray, & Quigley, 2001; Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). HRV is an established measure of regulated emotional responding in typically developing children, adolescents and adults (Appelhans & Luecken, 2006; Beauchaine, 2015; Berna, Ott, & Nandrino, 2014; Williams et al., 2015). In typically developing infants and preschoolers, HR and HRV have been found to be

CONTACT Heather J. Nuske hjnuske@upenn.edu Center for Mental Health, University of Pennsylvania, Philadelphia, PA, USA
Supplemental data for this article can be accessed here.

associated with emotional reactivity and social skills, as well as behavior problems (Calkins & Keane, 2004; Cole, Zahn-Waxler, Fox, Usher, & Welsh, 1996; Eisenberg et al., 1988; Fox, 1989). Porges, Doussard-Roosevelt, Portales, and Greenspan (1996) first described that physiological dysregulation may have a causal relation to child behavior problems; this model has been supported in children at-risk for externalizing disorders (Calkins, Graziano, & Keane, 2007), children with conduct problems (e.g. Beauchaine, Gatzke-Kopp, & Mead, 2007), and children with reactive aggression (Scarpa, Haden, & Tanaka, 2010). In children with autism, one study found associations between lower HRV and behavioral problems (Van Hecke et al., 2009). Therefore, HR and HRV not only reflect objective measurement of emotional dysregulation, but may also be used to better understand, and even predict behavioral problems in children with autism and other disorders.

Preliminary findings also suggest the potential use of *in vivo* recording of HR and HRV to better understand behavioral problems as they occur in individuals with autism. Two single-case studies have shown elevated HR prior to challenging behavior episodes in autism and/or intellectual disability. HR was examined in the 5-second (Barrera, Violo, & Graver, 2007) or 15-second interval preceding the onset of challenging behaviors (Freeman, Horner, & Reichle, 1999; see also reanalysis of data using a 30-second window; Freeman, Grzymala-Busse, Riffel, & Schroeder, 2001). Although informative, if physiological arousal is to inform in-the-moment treatment planning, analysis of a longer time window is needed, to allow time to intervene. In their research on nine hospitalized youth with autism, Cumpanasoiu et al. (2017) found a longer time window predicted aggression. It is not yet clear at which time point, before the onset of a challenging behavior episode, HR signals are most predictive of the oncoming behavior. Moreover, as these studies were conducted with youth or adults, it is unclear whether these HR predictors apply to young children with autism. HR signals may predict challenging behaviors in some children with autism with certain characteristics, rather than in all children with autism. Based on existing literature, we hypothesized that increase in HR and decrease in HRV would be associated with the onset of challenging behavior episodes in preschoolers with autism. We also explored whether this association varied by gender, age, autism severity, cognitive ability and expressive language ability.

Methods

Participants

Forty-one children with autism aged 2- to 4-years were recruited as part of a larger study on emotional reactivity and regulation (Nuske, Hedley, Tseng, Begeer, & Dissanayake, 2017; Nuske, Hedley, Woollacott, et al., 2017), and participated in tasks from the Laboratory Temperament Assessment Battery (Goldsmith, Reilly, Lemery, Longley, & Prescott, 1999; Goldsmith & Rothbart, 1999). Our previous studies focused on emotion regulation strategies and did not present any HR or HRV data. The tasks in the current study mimicked everyday life experiences requiring emotional regulation in low-level stress situations (e.g. interacting with a stranger, waiting for a snack) as well as two situations during which children usually experience positive emotion (e.g. bubbles, peek-a-boo task; see Nuske, Hedley, Woollacott, et al., 2017 for a description of tasks). Thirteen (32%; 10 males, three females) children were included as participants in this study (see Table 1 for participant characteristics) as they presented with significant challenging behaviors (see Table 2 for coding scheme) during the 1–1.5 h long testing sessions. An additional child also exhibited these behaviors, but due to technical problems with the electrocardiogram (ECG), HR data were not recorded.

Table 1. Participant characteristics.

	M/ratio	*SD*	Min	Max
Age (months)	37.46	4.612	29	44
Males:females	10:3	–	–	–
Autism symptoms				
ADOS CS[a]	7.69	2.689	3	10
SCQ[b]	14.85	8.345	4	27
Cognitive development (MSEL[c])				
Standard score	66.23	20.41	49	117
Verbal developmental quotient	54.87	29.14	24	119
Receptive language (months)	20.62	12.80	8	49
Expressive language (months)	20.23	9.65	9	39
Nonverbal developmental quotient	62.07	24.46	20	108

[a]Autism Diagnostic Observation Schedule Comparison Score.
[b]Social Communication Questionnaire.
[c]Mullen Scales of Early Learning. Age equivalents in months are reported for Receptive Language and Expressive Language.

Two participants were taking medication at the time of testing; one participant was taking Risperidone and Lovan, and another was taking Akatinol Memantine, Pantogam Active, Cerebrolysin, and Encefabol (Piritinol). The first of these children also had Fragile X full mutation; no other parent participant reported a genetic condition in their child. Analyses were conducted with and without these participants, to ensure that they alone did not drive observed effects. As the pattern of results were unaffected, and due to the small sample size, data from these participants were retained.

Procedure

Upon arrival for the testing session, parents were shown a picture book detailing each of the tasks the child would be involved with by the first author, while their child engaged in 5–10 min of warm-up play with a second experimenter. Informed consent from parents was taken before entering the testing room. Parents were seated in a comfortable chair and provided with a laptop to complete the study questionnaires during the session and were instructed to “act as they normally would” if their child approached them. Parents (or a familiar caregiver) were present in the room throughout the testing session. Tasks were administered in a fixed sequence (see Nuske, Hedley, Tseng, et al., 2017; Nuske, Hedley, Woollacott, et al., 2017) to maintain any carryover emotion effects between the tasks constant across participants. Start time varied across participants (9:15 am–1:30 pm, median = 10 am). The research was approved by the La Trobe University Human Ethics Committee (approval number 11-052),

Table 2. Challenging behavior categories and examples taken from the literature.

Category	*M* (*SD*), across children	Example behaviors
Aggression towards others *n* = 4	.46 (1.13)	• Hitting others • Pushing others • Aggravates others physically • Pulling others hair • Kicking/hitting others • Grabbing from others
Property destruction (aggression towards objects) *n* = 24	1.77 (1.69)	• Throwing/kicking/pushing objects • Banging on objects • Ripping paper
Self-injury (aggression towards self) *n* = 2	N/A	• Head banging • Poking self in eye • Pinching/scratching self • Pulling own hair • Swallowing objects
Loud noises *n* = 52	4.38 (3.5)	• Screaming/yelling • Crying • Whining loudly
Noncompliance *n* = 24	2.08 (1.89)	• Stubborn/uncooperative • Transition difficulties • Out of seat behavior • Leaving caregiver's supervision without permission
All challenging behaviors *n* = 106	8.69 (4.82)	

and consent from the children's parents was obtained according to the Declaration of Helsinki (BMJ 1991; 302: 1194).

Measures

Autism symptoms. Clinic-based diagnoses of the children with autism were confirmed using the Autism Diagnostic Observation Schedule (ADOS-2; Lord et al., 2012), a semi-standardized play-based assessment of autism symptoms administered by research-reliable clinicians. Modules are selected based on the age/language level of children (10 × Toddler Module, 2 × Module 1, 1 × Module 2). ADOS-2 calibrated Comparison Scores (CS) are on a 10-point scale with scores anchored to ADOS-2 classifications (higher scores indicating higher autism symptoms), based on the raw overall scores, module used, and age of the child. Severity scores are provided by the publisher for Modules 1–3 (Lord et al., 2012). For the present study, CS for the toddler module were based on algorithms provided by Esler et al. (2015; see also Hedley, Nevill, Uljarević, Butter, & Mulick, 2016). Additionally, parents completed the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003). The SCQ is a 40-item, parent-report measure of symptomatology associated with autism, with total possible scores ranging from 0 to 39 (higher scores signify higher autism symptoms), and with a recommended cutoff of 12 for children younger than 8 years (Corsello et al., 2007).

Overall developmental ability/expressive language ability. Overall developmental ability was assessed using the Mullen Scales of Early Learning (Mullen, 1995), a standardized assessment for children up to 68 months of age. This assessment includes four sub-scales for the age range in the study: Visual Reception (a child's ability to process visual information, e.g. matching shapes), Fine Motor (a child's motor co-ordination in tasks related to writing readiness and the manipulation of objects, e.g. drawing lines), Receptive Language (a child's understanding of language, including attention to speech, and knowledge of vocabulary and concepts, e.g. following directions) and Expressive Language (a child's ability to use actions and spoken language, including grammar, to express meaning and logical reasoning, e.g. naming objects). Items follow a developmental trajectory, hence are different for children of different ages. These four scales are included in the Early Learning Composite, the standard score ($M = 100$; $SD = \pm 15$), and each scale produces a separate age equivalent score (in months, e.g. 24 months equals skills equivalent to a typical 24-month-old). The age equivalent scores of the Expressive Language sub-scale was used as a measure of expressive language in the children. Following the recommendations of Dykens and Lense (2011), the sample included children with autism across functioning levels, with 69.2% low-functioning (standard score <70), 15.4% moderately functioning (standard score 70–84) and 15.4% high-functioning (standard score ≥ 85).

Physiological measurement. Children wore vests with sewn-in pockets to house the Biopac BioNomadix ECG and accelerometer module transmitters. ECG electrodes which connected to the transmitters were placed on children's back (instead of chest) to avoid children pulling at them. Transmitters connected wirelessly to the Biopac MP150 receiver, allowing children free movement around the testing room. HR and HRV were measured during three time periods: resting state, before challenging behaviors and before random times periods where no challenging behaviors occurred.

Resting state period. To establish a baseline HR/HRV for each child, date were collected during a 3-min resting period data, when the child was calm (i.e. no negative emotion or high intensity positive emotion), not moving too much (three-coordinate accelerometer data were checked and referenced to ECG data to ensure data did not have movement artifacts) and not interacting with others (for eight children this was during watching a relaxing, developmentally appropriate video (the last 3 min of *Sweet Dreams Spot*; Cooper-Vince et al., 2017), for five children, this was when they were engaged in free play while sitting). A 3-min resting state period was selected given the age of children, and used previously as an alternative to 5-min epochs in younger samples (Cooper-Vince et al., 2017), and in autism samples (Matsushima et al., 2016).

Challenging behaviors. After establishing reliability (80% agreement on two consecutive videos), coders blind to study hypotheses coded the following challenging behaviors from the session videos: aggression, self-injury, property destruction, loud noises and noncompliance after children were fitted with ECG equipment (see below for details on ECG recording). Additionally, 15% of videos were double-coded, with 87.56% agreement between coders. Consensus coding was conducted on discrepancies between codes. The selection of challenging behaviors to code was based on those included in Machalicek et al. (2007), Matson and Rivet (2008), and Rojahn, Matson, Lott, Esbensen, and Smalls (2001). See Table 2 for examples of each challenging behavior category and frequency of challenging behavior categories. In order to code discrete challenging behavior episodes (as behaviors sometimes overlapped), after coding a challenging behavior, a new challenging behavior episode was only coded if there was at least a 2-min break since the last time the child exhibited a challenging behavior.

Random time sampling. Based on previous work in the area, in order to compare HR/HRV before challenging behaviors (n= 106) to a "non-event" (i.e. a time in which no challenging behavior occurred), we computed the same number of randomly selected points from the same session per participant in which no challenging behaviors occurred (e.g. Barrera et al., 2007); videos were checked at these time points to verify this. The locations of random nonoccurrence points were selected by a random number generator (*StatTrek: Statistics Random Number Generator*), corresponding to time during the session. No duplications were allowed. Where a period of challenging behavior was found, another random number was computed until a true nonevent was found. If random events overlapped with one another, the number that appeared first in the sequence was moved earlier to create a 2-min time difference between events.

Electrocardiogram event marking and cleaning. First, resting state periods and challenging behaviors were labeled on the software using the synced video stream, and random time samples were marked on the software corresponding to the randomly generated numbers. ECG data were processed in Biopac AcqKnowledge version 4.4.2. Second, a band-pass (finite impulse response) filter was applied to de-noise the ECG signal, with low frequency fixed at 1 Hz and high frequency at 35 Hz (e.g. Khaing & Naing, 2011; Ruha, Sallinen, & Nissila, 1997). Third, QRS complexes were labeled and visually inspected for artifacts in the marked data sections (Task Force of the ESC and NASPE, 1996). In patches of data artifacts, due to movement (accelerometer data were referenced), data were either linearly interpolated in-between R peaks and/or R signals were amplified, so that extracted data metrics were unaffected by artifacts (Task Force of the ESC and NASPE, 1996). For eight challenging behaviors (in data from three participants), the previous 2-min period of ECG data contained artifacts in the majority of the period, so those challenging behaviors were excluded from the analysis (eight loud noises and four noncompliance; final numbers are reported in Table 2).

Heart rate (HR) and heart rate variability extraction. For each challenging behavior and random time sample, baseline-corrected peak HR (beats per minute (BPM)) and HRV (root mean square of the successive differences (RMSSD)) were extracted from the cleaned ECG signal from the 2-min period before the challenging behavior onset. Increase in BPM from baseline reflects majority sympathetic activity, whereas increase in RMSSD, a commonly reported measure of HRV, from baseline reflects majority parasympathetic activity (Kleiger, Stein, Bosner, & Rottman, 1992; Kreibig, 2010; Stern et al., 2001; Task Force of the ESC and NASPE, 1996). RMSSD is recommended as the measurement of short term components of the HRV, and is preferred to other HRV metrics such as pNN50 and NN50 as it has better statistical properties (Task Force of the ESC and NASPE, 1996).

Statistical analysis

All data analyses were completed in SPSS. Normality was assessed in all continuous variables using the methods outlined in Tabachnick and Fidell (2007), with a critical value set at ±3.29. As RMSSD data were positive skewed, they were log-transformed. Baseline BPM and RMSSD were significantly correlated with change in BPM ($r = .56$, $p < .001$) and RMSSD ($r = .53$, $p < .001$), respectively, so all analyses of change in BPM and RMSSD included baseline BPM and RMSSD, respectively, as a covariate. Two ANOVAs were computed to test whether percentage change in HR (baseline-corrected BPM) and HRV (baseline-corrected RMSSD) were higher before challenging behavior episodes relative to random time samples. All challenging behaviors were analyzed together as there were no significant differences in BPM or RMSSD before different challenging behaviors (all $ps > .24$). To test the hypothesis that baseline-corrected BPM and baseline-corrected RMSSD would be associated with onset of challenging behavior episodes, conditional logistic regression analyses were run, nested by child, with challenging behavior vs. random time sample as the dependent variable. Random time sample was entered as the reference category so that odds ratios reflected the odds of a challenging behavior episode. Conditional logistic regression was chosen as the statistical technique to avoid bias arising from the unconditional analysis of matched data (Sun, Sinha, Wang, & Maiti, 2011). To explore whether the association between HR/HRV and challenging behavior was moderated by child characteristics, main effects and interaction effects between HR/HRV and age, gender, autism severity, and cognitive ability were added to the model. Models were run separately per interaction to avoid collinearity between independent variables. The predictive utility of HR increase and HRV decrease for challenging behaviors (vs. random time samples) was also examined via a receiver operating curve (ROC) analysis. Area under the curve coefficients from the ROC area designated as follows: .90–1 = excellent, .80–.90 = good, .70–.80 = fair, .60–.70 = poor and .50–.60 = fail.

Table 3. Conditional logistic regression on the effect of peak heart rate (bpm) increase and child characteristics on challenging behavior.

	Model Summary		Change Summary		Individual Predictors		
	p	χ^2	p	χ^2	p	Exp(B)	B
Step 1	.003	8.97	–	–	.003	0.977**	–.02
Baseline heart rate (BPM)							
Step 2	<.000	32.51	<.000	23.26	<.000	1.037***	.04
BPM increase (% change[a]) before:							
• Random time sample: $M = 8.18$, $SD = 14.59$							
• Challenging behavior: $M = 21.96$, $SD = 16.10$							
Step 3	<.001	48.14	.02	8.33	.02	0.207*	–1.57
Gender (0 = female, 1 = male)							
Gender (0 = female, 1 = male) × BPM increase					.29	1.017	.02
Age (months)	<.001	50.51	<.001	20.42	<.001	0.768***	–.26
Age (months) × BPM increase					.14	1.004	.004
Autism severity (SCQ[b])	<.001	92.53	<.001	61.83	<.001	.872***	–.14
Autism severity (SCQ[b]) × BPM increase					.968	1.000	<.001
Overall developmental ability[c]	<.001	97.02	<.001	44.30	<.001	1.072***	.07
Overall developmental ability[c] × BPM increase					.568	1.000	<.001
Expressive language[d]	<.001	83.94	<.001	29.59	<.001	1.094***	.09
Expressive language[d] × BPM increase					.958	1.000	<.001

*$p < .05$.
**$p < .01$.
***$p < .001$.
[a]From baseline BPM.
[b]Social communication questionnaire total score.
[c]Mullen scales of early learning standard score (early learning composite).
[d]Expressive language age equivalent.

Results

Heart rate

Mean baseline-corrected BPM before challenging behavior was significantly higher (M= 21.96, SD= 16.10) than before random time samples (M= 8.18, SD= 14.59), $F(1, 212)$= 51.20, $p < .001$, ηp^2= .20 (controlling for baseline BPM), with the peak at M= 57.96 s, SD= 21.60. The conditional regression results, determining whether peak HR increase from baseline predicts challenging behavior episodes, relative to a random time sample, are presented in Table 3. Heart rate increase was significantly associated with challenging behavior, with each 1% increase in HR from baseline associated with four times higher likelihood of a challenging behavior (vs. random time sample). Though all of the main effects of child characteristics were significant (gender, age, autism severity, overall developmental ability and expressive language), none of the interactions of BPM increase with child characteristics were significant at $p < .05$. In the ROC analysis, the area under the curve was .72, $p < .001$, 95% CI= .65 to .79, see Figure 1.

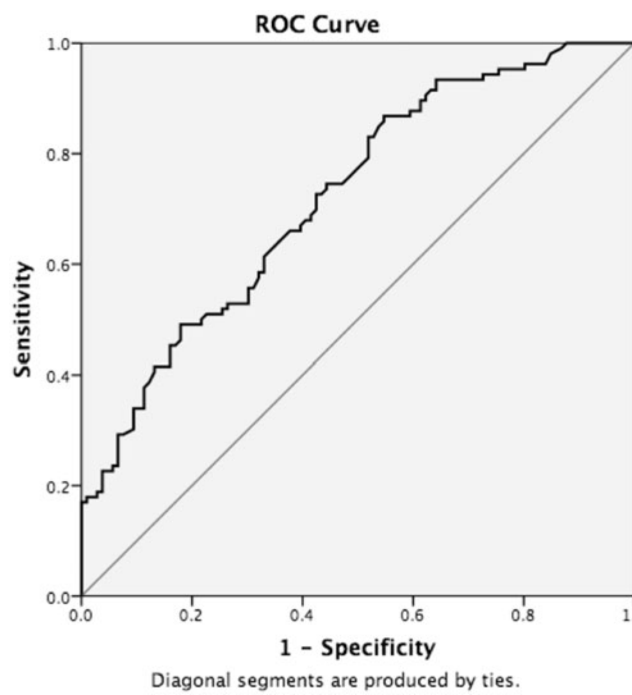

Figure 1. Receiver operating curve statistics (sensitivity and specificity) on the predictive utility of baseline-corrected heart rate (% increase).

Heart rate variability

Mean baseline-corrected RMSSD (% change) before challenging behavior (M= –26.08, SD= 71.06) was not significantly different than before random time samples (M= 2.85, SD= 87.17), $F(1, 212)$= 0.14, p= .71, $\eta p^2 < .01$ (controlling for baseline RMSSD). The conditional regression results, determining whether % RMSSD change from baseline predicts challenging behavior episodes, relative to a random time sample, are presented in Table 4. Heart rate variability change was not a significant predictor. The ROC analysis (sensitivity and specificity) also indicated that as a solitary predictor, HRV change is not significant; area under the curve= .52, p= .58, 95% CI= .44 to .61, see Supplementary Material. Though the main effects of age, overall developmental ability and expressive language were significant, none of the interactions of RMSSD increase with child characteristics were significant at $p < .05$.

Discussion

The aim in this study was to determine the predictive utility of HR increase and HRV decrease to challenging behaviors in young children with autism. The findings indicate that HR

Table 4. Conditional logistic regression on the effect of heart rate variability (RMSSD) change and child characteristics on challenging behavior.

	Model summary		Change summary		Individual predictors		
	p	χ^2	*p*	χ^2	*p*	*Exp(B)*	*B*
Step 1	<.001	17.18	–	–	<.001	1.627***	.45
Baseline heart rate variability (RMSSD)							
Step 2	<.001	17.26	.74	0.11	.74	1.097	.09
RMSSD % change[a] before:							
• Random time sample: $M = -26.08$, $SD = 71.06$							
• Challenging behavior: $M = 2.85$, $SD = 87.17$							
Step 3	<.001	27.22	.06	5.49	.09	0.124	−2.09
Gender (0 = female, 1 = male)							
Gender (0 = female, 1 = male) × RMSSD change					.25	0.214	.76
Age (months)	<.001	51.75	<.001	30.52	.003	0.604**	−.50
Age (months) × RMSSD change					.08	1.158	.15
Autism severity (SCQ[b])	<.001	55.64	<.001	38.45	.88	1.010	.009
Autism severity (SCQ[b]) × RMSSD change					.08	0.945	−.06
Overall developmental ability[c]	<.001	121.46	<.001	75.92	<.001	1.17***	.16
Overall developmental ability[c] × RMSSD change					.445	0.989	−.01
Expressive language[d]	<.001	60.25	<.001	37.42	.04	1.136*	.127
Expressive language[d] × RMSSD change					.82	0.992	−.01

*$p < .05$.
**$p < .01$.
***$p < .001$.
[a]From baseline RMSSD.
[b]Social communication questionnaire total score.
[c]Mullen scales of early learning standard score (early learning composite).
[d]Expressive language age equivalent.

increase, but not HRV decrease, is associated with onset of challenging behaviors in preschoolers with autism. Therefore, HR may provide useful decision support during moment-to-moment treatment planning for preschoolers with autism.

Interestingly, though HRV typically decreases during stress conditions in adolescents and adults (Li et al., 2009), this was not found in our sample of preschoolers before challenging behaviors. A possible explanation for these discrepant findings is that HRV increases from 3 to 9 years (Goto et al., 1997), and by preschool age this may not be yet a stable system for emotion regulation. Indeed, some children decreased HRV before challenging behavior (as would be expected), but others increased HRV, and the variability was large, suggesting no consistency in HRV stress responses at this age. HR increase before challenging behavior was more pronounced for children with autism who were older than 37 months, which indicates that challenging behaviors were associated with higher stress levels in older preschoolers with autism. Given the discrepancy between findings on HR and HRV further research is needed to elucidate the relationship between cardiac reactivity and challenging behavior in clinical pediatric populations, including school-age children and adolescents.

Of note, baseline HR and HRV were associated with challenging behavior in the children. Results suggests that when considering how cardiac stress relates to challenging behavior in children with autism, it is important to take into account the child's resting level or baseline autonomic arousal levels. Curiously, directions of associations with baseline HR and HRV were not as expected, with lower baseline HR and higher baseline HRV relating to challenging behavior, relative to the non-challenging behavior random time sample. This is inconsistent with previous findings of associations between lower HRV with high reactive aggression in children (Scarpa et al., 2010) and high emotional instability in adults (Koval et al., 2013), along with countless reports of associations between lower HRV and difficulties with emotion regulation among child, adolescent, and adult samples (see Beauchaine, 2015; Berna et al., 2014; Williams et al., 2015). Additional research with larger, more representative samples, is needed to further explore this finding.

Advanced warning of an oncoming challenging behavior episode may be particularly important for minimally verbal children with autism who have limited means to communicate their stress to others. About a third of children with autism are minimally verbal (e.g. have less than 20 functional words) past age 5, even after early intervention (DiStefano, Shih, Kaiser, Landa, & Kasari, 2016; Hus, Pickles, Cook, Risi, & Lord, 2007). However, verbal ability was not found to interact significantly with HR increase for the prediction of challenging behavior, suggesting that HR increase is a useful biomarker regardless of children's verbal ability.

Given the recent technological advances in wearable biosensing (e.g. wireless ECG, fitness chest straps and wristbands) which allows for less invasive, less costly and less restrictive tracking of physiological stress over time (Wang et al., 2017), it may be useful, based on our results, to incorporate HR monitoring in early autism intervention (Goodwin, 2008). By signaling children's stress, such wearables may allow parents and teachers to intervene and create learning opportunities for emotional expression and regulation at critical time points. However, given the strength of the prediction and likelihood of false positives, individualized human–computer interaction and machine learning algorithms may be needed to increase the utility of including such information in moment-to-moment treatment planning. Heart rate monitoring may also help to inform intervention in children with other disorders, such as children with conduct disorder, given previous findings of an association between cardiac reactivity and conduct problems in children (e.g. Beauchaine et al., 2007). Further research is needed to investigate the predictive utility of cardiac reactions for externalizing behaviors in children with autism of different characteristics and other conditions.

Limitations

A key limitation in this study was the small sample size, which limits power to detect true effects. However, there was a large number of challenging behaviors across the 13 participants (n= 106) who were drawn from a larger sample of preschoolers with autism (n= 41). Furthermore, as the only published study in this area included two participants with autism (Barrera et al., 2007), the current findings from the sample of 13 provide an important, albeit preliminary, indication of the utility of HR data in marking the onset of challenging behaviors in young children with autism. A further limitation was that data were collected in a laboratory setting, and may not generalize to the challenging behaviors in children with autism within everyday community settings (Matson et al., 2008). However, given the recent advent of commercially available wearable biosensors, this study provides the groundwork for future studies on challenging behaviors in children with autism in settings that matter most, such as home or school.

Conclusions

The findings from the current study provide an initial indication that HR increase can predict challenging behavior episodes in preschoolers with autism. The findings suggest that ongoing HR monitoring may be useful in moment-to-moment decision support for the prevention of challenging behavior episodes in some children with autism. Future research is needed to confirm these preliminary findings.

Acknowledgements

First and foremost, the authors would like to thank the families who took part in this study. We would also like to acknowledge the hard work and dedication of all the students who worked on the testing and data processing aspects of the project (in alphabetical order): Erin Battersby, Lacey Chetcuti, Siobhan Ede, Samantha Galea, Siobhan Korbut, Alice Maier, Jacqueline Maya, Anushka Phal, Ensu Sahin, Danielle Smith, Jessica Tsoutsoulis, and Jennifer Vong.

Funding

This work is supported by Pierce Armstrong Foundation, La Trobe University, Veski Victoria Fellowships, and McMorris Family Foundation.

Notes on contributors

Dr Heather Joy Nuske is a Research Associate in Psychiatry at the University of Pennsylvania. She studies developmental and physiological indices of emotional dysregulation in children with autism, and the implementation of social and emotional learning programs to support children's positive academic, social and wellbeing outcomes.

Emma Finkel holds a Bachelor's Degree in Psychology with Honors from the University of Pennsylvania. She contributed to the project as a Research Assistant at the Center for Autism Research, Children's Hospital of Philadelphia. Her research interests include ASD, developmental disorders, learning disabilities, and early childhood trauma.

Dr Darren Hedley is a research fellow at the Olga Tennison Autism Research Centre, La Trobe University, Australia. His research examines autism across the lifespan, including early development and behavior impacts through to employment, mental health and well-being in adults.

Dr Valentina Parma is a neuroscientist, who is expert in perceptual and motor behavior in clinical populations, including autism. Since her post-doc, she has been developing her skills in human psychophysiology related to stressful events.

Liza Tomczuk holds a Bachelor of Science in Neuroscience from Dickinson College. She contributed as a Research Assistant at the Penn Center for Mental Health and is currently a Clinical Research Coordinator in Cardiac Electrophysiology, University of Pennsylvania. Her research interests include ASD, cardiovascular disease, and public health issues.

Dr Melanie Pellecchia is an Assistant Professor of Psychology in Psychiatry at the University of Pennsylvania. Dr. Pellecchia studies methods to improve the implementation of evidence-based practices for children with autism spectrum disorder and their families in schools and community settings.

Dr John Herrington is an Assistant Professor in the Department of Child Psychiatry and Behavioral Science, University of Pennsylvania and Associate Director of the Developmental Neuroimaging Program, Center for Autism Research, Children's Hospital of Philadelphia. His work focuses on the cognitive neuroscience of social and emotional information processing in autism.

Dr Steven C. Marcus is a Research Associate Professor in the School of Social Policy & Practice and Perelman School of Medicine, University of Pennsylvania. He is an epidemiologist, statistician, computer scientist, and a mental health services researcher studying the outcomes and quality of care of patients with serious mental disorders.

Dr David Mandell is professor of psychiatry and directs the Center for Mental Health at the University of Pennsylvania Perelman School of Medicine.

Professor Cheryl Dissanayake is Founding Director and Olga Tennison Chair of Autism Research at La Trobe University. She is also a Fellow of the International Society for Autism Research, and vice-President of the Australasian Society for Autism Research. Her research focus has been on understanding early developmental mechanisms in autism.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work is supported by Pierce Armstrong Foundation, La Trobe University, Veski Victoria Fellowships, and McMorris Family Foundation.

References

American Psychiatric Association [APA]. (2013). *DSM-5: Diagnostic and statistical manual of mental disorders*. Washington, DC: American Psychiatric Publishing, Inc.

Appelhans, B.M., & Luecken, L.J. (2006). Heart rate variability as an index of regulated emotional responding. *Review of General Psychology*, *10*, 229.doi:10.1037/1089-2680.10.3.229

Barrera, F.J., Violo, R.A., & Graver, E.E. (2007). On the form and function of severe self-injurious behavior. *Behavioral Interventions*, *22*, 5–33. doi: 10.1002/bin.228

Beauchaine, T.P. (2015). Future directions in emotion dysregulation and youth psychopathology. *Journal of Clinical Child and Adolescent Psychology*, *44*, 875–896. doi:10.1080/15374416.2015.1038827

Beauchaine, T.P., Gatzke-Kopp, L., & Mead, H.K. (2007). Polyvagal theory and developmental psychopathology: Emotion dysregulation and conduct problems from preschool to adolescence. *Biological Psychology*, *74*, 174–184. doi:10.1016/j.biopsycho.2005.08.008

Berna, G., Ott, L., & Nandrino, J.-L. (2014). Effects of emotion regulation difficulties on the tonic and phasic cardiac autonomic response. *PLoS One*, *9*, e102971. doi:10.1371/journal.pone.0102971

Bradley, M.M., Miccoli, L., Escrig, M.A., & Lang, P.J. (2008). The pupil as a measure of emotional arousal and autonomic activation. *Psychophysiology*, *45*, 602–607. doi:10.1111/j.1469-8986.2008.00654.x

Calkins, S.D., & Keane, S.P. (2004). Cardiac vagal regulation across the preschool period: Stability, continuity, and implications for childhood adjustment. *Developmental Psychobiology*, *45*, 101–112. doi:10.1002/dev.20020

Calkins, S.D., Graziano, P.A., & Keane, S.P. (2007). Cardiac vagal regulation differentiates among children at risk for behavior problems. *Biological Psychology*, *74*, 144–153. doi:10.1016/j.biopsycho.2006.09.005

Cole, P.M., Zahn-Waxler, C., Fox, N.A., Usher, B.A., & Welsh, J.D. (1996). Individual differences in emotion regulation and behavior problems in preschool children. *Journal of Abnormal Psychology*, *105*, 518–529. doi:10.1037/0021-843X.105.4.518

Cooper-Vince, C.E., DeSerisy, M., Cornacchio, D., Sanchez, A., McLaughlin, K.A., & Comer, J.S. (2017). Parasympathetic reactivity and disruptive behavior problems in young children during interactions with their mothers and other adults: A preliminary investigation. *Developmental Psychobiology*, *59*, 543–550. doi:10.1002/dev.21511

Corsello, C., Hus, V., Pickles, A., Risi, S., Cook, E.H., Leventhal, B.L., & Lord, C. (2007). Between a ROC and a hard place: Decision making and making decisions about using the SCQ. *Journal of Child Psychology and Psychiatry*, *48*, 932–940. doi:10.1111/j.1469-7610.2007.01762.x

Cumpanasoiu, D., Mazefsky, C., Stedman, A., Peura, C., Tian, P., Guo, Y., … Goodwin, M.S. (2017). 5.12 physiological biomarkers for prediction of imminent aggression in minimally verbal children with autism spectrum disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *56*, S256–S257. doi:10.1016/j.jaac.2017.09.295

DiStefano, C., Shih, W., Kaiser, A., Landa, R., & Kasari, C. (2016). Communication growth in minimally verbal children with ASD: The importance of interaction. *Autism Research*, 9, 1093–1102. doi:10.1002/aur.1594

Doehring, P., Reichow, B., Palka, T., Phillips, C., & Hagopian, L. (2014). Behavioral approaches to managing severe problem behaviors in children with autism spectrum and related developmental disorders: A descriptive analysis. *Child and Adolescent Psychiatric Clinics*, *23*, 25–40. doi:10.1016/j.chc.2013.08.001

Dykens, E.M., & Lense, M. (2011). Intellectual disabilities and autism spectrum disorder: A cautionary note. In D. Amaral, G. Dawson, & D.H. Geschwind (Eds.), *Autism spectrum disorders*. Oxford, UK: Oxford University Press.

Eisenberg, N., Fabes, R.A., Bustamante, D., Mathy, R.M., Miller, P.A., & Lindholm, E. (1988). Differentiation of vicariously induced emotional reactions in children. *Developmental Psychology*, *24*, 237.doi:10.1037/0012-1649.24.2.237

Esler, A.N., Bal, V.H., Guthrie, W., Wetherby, A., Weismer, S.E., & Lord, C. (2015). The autism diagnostic observation schedule, toddler module: Standardized severity scores. *Journal of Autism and Developmental Disorders*, *45*, 2704–2720. doi:10.1007/s10803-015-2432-7

Fox, N.A. (1989). Psychophysiological correlates of emotional reactivity during the first year of life. *Developmental Psychology*, *25*, 364.doi:10.1037/0012-1649.25.3.364

Freeman, R., Grzymala-Busse, J., Riffel, L., & Schroeder, S. (2001). Analysis of self-injurious behavior by the LERS data mining system. In *Annual Conference of the Japanese Society for Artificial Intelligence* (pp. 395-399). Berlin, Heidelberg: Springer.

Freeman, R.L., Horner, R.H., & Reichle, J. (1999). Relation between heart rate and problem behaviors. *American Journal on Mental Retardation*, *104*, 330–345. doi:10.1352/0895-8017(1999)104 < 0330:RBHRAP>2.0.CO;2

Goldsmith, H.H., & Rothbart, M.K. (1999). *Laboratory temperament assessment battery Lab-Tab. Locomotor Version 3.1*. Madison, WI: H. Hill Goldsmith, Ph. D., Personality Development Laboratory, Department of Psychology, University of Wisconsin.

Goldsmith, H.H., Reilly, J., Lemery, K.S., Longley, S., & Prescott, A. (1999). *Laboratory temperament assessment battery: preschool version (version 1.0, Technical Report)*. Madison, WI: Department of Psychology, University of Wisconsin.

Goodwin, M.S. (2008). Enhancing and accelerating the pace of autism research and treatment: The promise of developing innovative technology. *Focus on Autism and Other Developmental Disabilities*, *23*, 125.doi:10.1177/1088357608316678

Goto, M., Nagashima, M., Baba, R., Nagano, Y., Yokota, M., Nishibata, K., & Tsuji, A. (1997). Analysis of heart rate variability demonstrates effects of development on vagal modulation of heart rate in healthy children. *The Journal of Pediatrics*, *130*, 725–729. doi:10.1016/S0022-3476(97)80013-3

Hastings, R.P., & Brown, T. (2002). Coping strategies and the impact of challenging behaviors on special educators' burnout. *Mental Retardation*, *40*, 148–156. doi:10.1352/0047-6765(2002)040 < 0148:CSATIO>2.0.CO;2

Hedley, D., Nevill, R., Uljarević, M., Butter, E., & Mulick, J.A. (2016). ADOS-2 Toddler and Module 1 standardized severity scores as used by community practitioners. *Research in Autism Spectrum Disorders*, *32*, 84–95. doi:10.1016/j.rasd.2016.09.005

Hedman, E., Miller, L., Schoen, S., Nielsen, D., Goodwin, M., & Picard, R.W. (2012). Measuring autonomic arousal during therapy. In *Proceedings of the Design and Emotion* (pp. 11–14). Citeseer. Retrieved from http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.666.3372&rep=rep1&type=pdf

Hus, V., Pickles, A., Cook, E.H., Risi, S., & Lord, C. (2007). Using the autism diagnostic interview—Revised to increase phenotypic homogeneity in genetic studies of autism. *Biological Psychiatry*, *61*, 438–448. doi:10.1016/j.biopsych.2006.08.044

Ioannou, S., Gallese, V., & Merla, A. (2014). Thermal infrared imaging in psychophysiology: Potentialities and limits. *Psychophysiology*, *51*, 951–963. doi:10.1111/psyp.12243

Khaing, A.S., & Naing, Z.M. (2011). Quantitative investigation of digital filters in electrocardiogram with simulated noises. *International Journal of Information and Electronics Engineering*, *1*, 210. doi:10.7763/IJIEE.2011.V1.33

Kleiger, R.E., Stein, P.K., Bosner, M.S., & Rottman, J.N. (1992). Time domain measurements of heart rate variability. *Cardiology Clinics*, *10*, 487–498. doi:10.1016/S0733-8651(18)30230-3

Koval, P., Ogrinz, B., Kuppens, P., Bergh, O.V., den, Tuerlinckx, F., & Sütterlin, S. (2013). Affective instability in daily life is predicted by resting heart rate variability. *PLoS One*, *8*, e81536. doi:10.1371/journal.pone.0081536

Kreibig, S.D. (2010). Autonomic nervous system activity in emotion: A review. *Biological Psychology*, *84*, 394–421. doi:10.1016/j.biopsycho.2010.03.010

Lecavalier, L., Leone, S., & Wiltz, J. (2006). The impact of behaviour problems on caregiver stress in young people with autism spectrum disorders. *Journal of Intellectual Disability Research*, *50*, 172–183. doi:10.1111/j.1365-2788.2005.00732.x

Li, Z., Snieder, H., Su, S., Ding, X., Thayer, J.F., Treiber, F.A., & Wang, X. (2009). A longitudinal study in youth of heart rate variability at rest and in response to stress. *International Journal of Psychophysiology*, *73*, 212–217. doi:10.1016/j.ijpsycho.2009.03.002

Lord, C., Rutter, M., DiLavore, P.C., Risi, S., Gotham, K., & Bishop, S. (2012). *Autism diagnostic observation schedule: ADOS-2*. Torrance: Western Psychological Services.

Machalicek, W., O'Reilly, M.F., Beretvas, N., Sigafoos, J., & Lancioni, G.E. (2007). A review of interventions to reduce challenging behavior in school settings for students with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *1*, 229–246. doi:10.1016/j.rasd.2006.10.005

Matson, J.L., & Rivet, T.T. (2008). Characteristics of challenging behaviours in adults with autistic disorder, PDD-NOS, and intellectual disability.

Journal of Intellectual and Developmental Disability, *33*, 323–329. doi:10.1080/13668250802492600

Matson, J.L., Wilkins, J., & Macken, J. (2008). The relationship of challenging behaviors to severity and symptoms of autism spectrum disorders. *Journal of Mental Health Research in Intellectual Disabilities*, *2*, 29–44. doi:10.1080/19315860802611415

Matsushima, K., Matsubayashi, J., Toichi, M., Funabiki, Y., Kato, T., Awaya, T., & Kato, T. (2016). Unusual sensory features are related to resting-state cardiac vagus nerve activity in autism spectrum disorders. *Research in Autism Spectrum Disorders*, *25*, 37–46. doi:10.1016/j.rasd.2015.12.006

McTiernan, A., Leader, G., Healy, O., & Mannion, A. (2011). Analysis of risk factors and early predictors of challenging behavior for children with autism spectrum disorder. *Research in Autism Spectrum Disorders*, *5*, 1215–1222. doi:10.1016/j.rasd.2011.01.009

Mullen, E.M. (1995). *Mullen scales of early learning*. Circle Pines, MN: American Guidance Service.

Nuske, H.J., Hedley, D., Tomczuk, L., Finkel, E., Thomson, P., & Dissanayake, C. (2018). Emotional coherence difficulties in preschoolers with autism: Evidence from internal physiological and external communicative discoordination. In *International Society for Autism Research*.

Nuske, H.J., Hedley, D., Tseng, C.H., Begeer, S., & Dissanayake, C. (2017). Emotion regulation strategies in preschoolers with autism: Associations with parent quality of life and family functioning. *Journal of Autism and Developmental Disorders, 48*, 1287–1300. doi:10.1007/s10803-017-3391-y

Nuske, H.J., Hedley, D., Woollacott, A., Thomson, P., Macari, S., & Dissanayake, C. (2017). Developmental delays in emotion regulation strategies in preschoolers with autism. *Autism Research, 10*, 1808–1822. doi:10.1002/aur.1827

Nuske, H.J., Vivanti, G., & Dissanayake, C. (2013). Are emotion impairments unique to, universal, or specific in autism spectrum disorder? A comprehensive review. *Cognition and Emotion*, *27*, 1042–1061. doi:10.1080/02699931.2012.762900

Otten, K., & Tuttle, J. (2010). *How to reach and teach children with challenging behavior (K-8): Practical, ready-to-use interventions that work* (Vol. *7*). San Francisco: John Wiley & Sons.

Porges, S.W., Doussard-Roosevelt, J.A., Portales, A.L., & Greenspan, S.I. (1996). Infant regulation of the vagal "brake" predicts child behavior problems: A psychobiological model of social behavior. *Developmental Psychobiology*, *29*, 697–712. doi:10.1002/(SICI)1098-2302(199612)29:8 < 697::AID-DEV5 > 3.0.CO;2-O

Rojahn, J., Matson, J.L., Lott, D., Esbensen, A.J., & Smalls, Y. (2001). The Behavior Problems Inventory: An instrument for the assessment of self-injury, stereotyped behavior, and aggression/destruction in individuals with developmental disabilities. *Journal of Autism and Developmental Disorders*, *31*, 577–588. doi:10.1023/A:1013299028321

Ruha, A., Sallinen, S., & Nissila, S. (1997). A real-time microprocessor QRS detector system with a 1-ms timing accuracy for the measurement of ambulatory HRV. *IEEE Transactions on Bio-Medical Engineering*, *44*, 159–167. doi:10.1109/10.554762

Rutter, M., Bailey, A., & Lord, C. (2003). *The Social Communication Questionnaire: Manual*. Los Angeles: Western Psychological Services.

Scarpa, A., Haden, S.C., & Tanaka, A. (2010). Being hot-tempered: Autonomic, emotional, and behavioral distinctions between childhood reactive and proactive aggression. *Biological Psychology*, *84*, 488–496. doi:10.1016/j.biopsycho.2009.11.006

Siegel, M., & Gabriels, R.L. (2014). Psychiatric hospital treatment of children with autism and serious behavioral disturbance. *Child and Adolescent Psychiatric Clinics of North America*, *23*, 125–142. doi:10.1016/j.chc.2013.07.004

Stern, R.M., Ray, W.J., & Quigley, K.S. (2001). *Psychophysiological recording*. New York, NY: Oxford University Press.

Sun, J.X., Sinha, S., Wang, S., & Maiti, T. (2011). Bias reduction in conditional logistic regression. *Statistics in Medicine*, *30*, 348–355. doi:10.1002/sim.4105

Tabachnick, B.G., & Fidell, L.S. (2007). Using multivariate statistics. Boston: Allyn & Bacon/Pearson Education.

Task Force of the ESC and NASPE. (1996). Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology (ESC) and the North American Society of Pacing and Electrophysiology (NASPE). *Circulation*, *93*, 1043–1065. doi:10.1161/01.CIR.93.5.1043

Thayer, J.F., Ahs, F., Fredrikson, M., Sollers, J.J., & Wager, T.D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience and Biobehavioral Reviews*, *36*, 747–756. doi:10.1016/j.neubiorev.2011.11.009

Van Hecke, A.V., Lebow, J., Bal, E., Lamb, D., Harden, E., Kramer, A., … Porges, S.W. (2009). Electroencephalogram and heart rate regulation to familiar and unfamiliar people in children with autism spectrum disorders. *Child Development*, *80*, 1118–1133. doi:10.1111/j.1467-8624.2009.01320.x

Wang, R., Blackburn, G., Desai, M., Phelan, D., Gillinov, L., Houghtaling, P., & Gillinov, M. (2017). Accuracy of wrist-worn heart rate monitors. *JAMA Cardiology*, *2*, 104–106. doi:10.1001/jamacardio.2016.3340

Williams, D.P., Cash, C., Rankin, C., Bernardi, A., Koenig, J., & Thayer, J.F. (2015). Resting heart rate variability predicts self-reported difficulties in emotion regulation: A focus on different facets of emotion regulation. *Frontiers in Psychology*, *6*, 261. doi:10.3389/fpsyg.2015.00261