

RZ Interval as an Impedance Cardiography Indicator of Effort-Related Cardiac Sympathetic Activity

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Silvia, P.J., McHone, A.N., Mironovová, Z., Eddington, K.M., Harper, K.L., Sperry, S.H., & Kwapil, T.R. RZ Interval as an Impedance Cardiography Indicator of Effort-Related Cardiac Sympathetic Activity. *Applied Psychophysiology and Biofeedback* **46**, 83–90 (2021).

<https://doi.org/10.1007/s10484-020-09493-w>

This is a post-peer-review, pre-copyedit version of an article published in *Applied Psychophysiology and Biofeedback*. The final authenticated version is available online at: <http://dx.doi.org/10.1007/s10484-020-09493-w>

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Abstract:

Research on effort and motivation commonly assesses how the sympathetic branch of the autonomic nervous system affects the cardiovascular system. The cardiac pre-ejection period (PEP), assessed via impedance cardiography, is a common outcome, but assessing PEP requires identifying subtle points on cardiac waveforms. The present research examined the psychometric value of the RZ interval (RZ), which has recently been proposed as an indicator of sympathetic activity, for effort research. Also known as the initial systolic time interval (ISTI), RZ is the time (in ms) between the ECG R peak and the dZ/dt Z peak. Unlike PEP, RZ involves salient waveform points that are easily and reliably identified. Data from two experiments evaluated the suitability of RZ for effort paradigms and compared it to a popular automated PEP method. In Studies 1 ($n = 89$) and 2 ($n = 71$), participants completed a standard appetitive task in which each correct response earned a small amount of cash. As expected, incentives significantly affected PEP and RZ in both experiments. PEP and RZ were highly correlated (all $r_s \geq 0.89$), and RZ consistently yielded a larger effect size than PEP. In Study 3, a quantitative synthesis of the experiments indicated that the effect size of RZ's response to incentives (Hedges's $g = 0.432$ [0.310, 0.554]) was roughly 15% larger than PEP's effect size ($g = 0.376$ [0.256, 0.496]). RZ thus appears promising for future research on sympathetic aspects of effort-related cardiac activity.

Keywords: Effort | Pre-ejection period | RZ | Initial systolic time interval | Impedance cardiography | Motivation

Article:

Influenced by Obrist's (1981) active coping model, research on the psychophysiology of effort has traditionally emphasized autonomic outcomes that reflect the sympathetic branch's beta-adrenergic impact on the heart (Gendolla et al. 2019). Early work consistently found that systolic blood pressure (SBP) was sensitive to factors important to effort, such as the difficulty of a task and the value of goals and incentives (Wright 1996), and SBP continues to be prominent (e.g., Barreto et al. 2015; Hess et al. 2016; Silvia 2012). Recent work has emphasized the cardiac pre-ejection period (PEP; Kelsey 2012), a systolic time interval typically assessed via impedance cardiography. PEP is the time in ms between the onset of depolarization (the ECG Q point) and the onset of ejection, defined as the opening of the aortic valve (the dZ/dt B point; see Fig. 1).

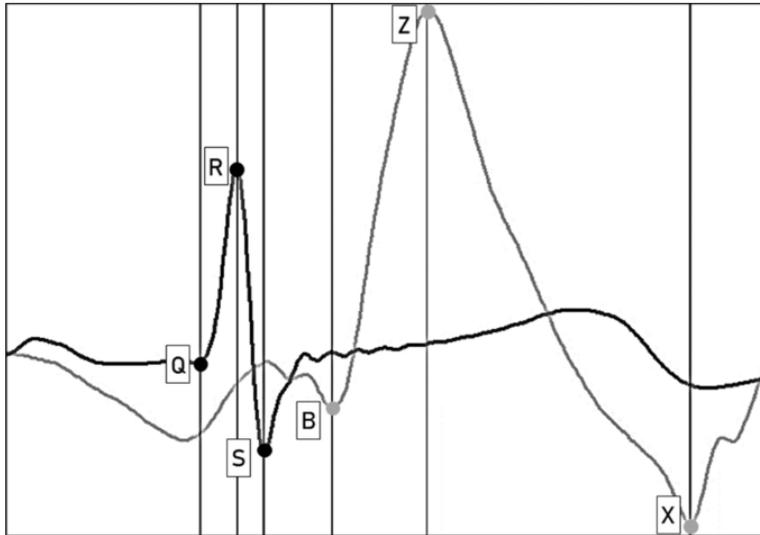


Fig. 1. An illustration of PEP and RZ. *Note* This figure illustrates the two waveforms used in impedance cardiography: (1) an electrocardiogram (ECG), shown in black; and (2) an impedance cardiogram (dZ/dt), shown in grey, obtained from measuring thoracic electrical impedance over the course of the cardiac cycle. The time intervals between points on these waveforms are used to measure PEP and RZ. PEP is the time (in ms) between the ECG Q point (the onset of ventricular depolarization) and the dZ/dt B point (the opening of the aortic valve). RZ is the time (in ms) between the ECG R point (apex of the R wave) and the dZ/dt Z point. The Z point is the peak of the dZ/dt waveform, and it corresponds to the point of the aortic arch's maximal diameter during ventricular ejection. The RZ interval can thus be viewed as the period between the heart's peak electrical and peak mechanical activity (Meijer et al. 2008). Note that R and Z are salient points defined by distinctive peaks of their respective waveforms. The figure comes from a 60-s ensemble average, and the points were identified by the Mindware IMP 3.1 software according to the description in Study 1

Impedance-based assessment of PEP has been a fruitful addition to mental effort research. Nevertheless, PEP has some longstanding assessment issues that remain unresolved (Mendes 2009; Sherwood et al. 1990). The Q and B points that define PEP can be subtle and hard to pinpoint because of individual-differences in cardiac waveforms and the many factors that can degrade cardiac signals assessed non-invasively with skin electrodes (Berntson et al. 2004; Cybulski 2011). In response, researchers have developed alternative methods for approximating and estimating the points' locations. These approximations facilitate scoring for large-sample projects and avoid the need to exclude large portions of otherwise unscorable data.

For the ECG Q point, for example, researchers have suggested using the onset of the Q wave, the peak of the Q wave, the onset of the R wave, or a fixed constant (e.g., 40 or 48 ms before R) to identify Q (Berntson et al. 2004; Sherwood et al. 1990; van Lien et al. 2013). Others have

suggested abandoning the Q point entirely and using the peak of the R wave instead (Seery et al. 2016). For the B point, many identification methods have been proposed, such as using the second and third derivatives of the dZ/dt signal, the dZ/dt zero-crossing point, or the primary rapid-rise in dZ/dt (Árbol et al. 2017; Ermishkin et al. 2014; Forouzanfar et al. 2018; Lozano et al. 2007; Sherwood et al. 1990).

One prominent method, developed by Lozano et al. (2007), estimates the likely B point as a regression function of the distance between the ECG R point and the dZ/dt Z point. Their research found that 93% of the between-person variance in the distance between R and B could be captured by a simple linear model ($RB = RZ * 0.55 + 4.45$), which in practice (e.g., Mindware's IMP software) is commonly implemented as 55% of the RZ interval plus 4 ms. This slope/intercept method is probably the most widely used B-point approximation method in contemporary research.

PEP is the most prominent impedance indicator of sympathetic activity, but additional ones have been developed. The complexity of identifying PEP's points suggests that the validity of these other indicators deserves a closer look. The RZ interval—also known as the initial systolic time interval (ISTI) and as RZ—is an old outcome (e.g., Wilde et al. 1981) that has increasingly attracted attention as a promising indicator of contractility (Cybulski 2011; Meijer et al. 2008, 2010; Van Eijnatten et al. 2014). RZ is the time in ms between the ECG R peak and the dZ/dt Z peak (see Fig. 1). Z is the point during ejection in which the aortic arch has its maximal diameter (Van Eijnatten et al. 2014), so RZ can be viewed as the time between the heart's peak electrical activity and its peak mechanical activity (Meijer et al. 2008).

RZ has been used for decades in impedance cardiography research. Many studies have shown that RZ behaves similarly to PEP, which isn't unsurprising in light of their overlap in the cardiac cycle (see Fig. 1). For example, both PEP and RZ respond similarly to exercise (Meijer et al. 2008; Wilde et al. 1981), stress (Kelsey and Guethlein 1990), dobutamine infusion (van der Meer et al. 1999), and changes in posture and activity levels (van Lien et al. 2013). In their analysis of RZ/ISTI and the slope/intercept approximation, van Lien et al. (2013, p. 68) noted:

Changes in cardiac contractility are reflected not only in the time it takes the left ventricle to build up sufficient force to open the aortic valve (reflected in the B-point) but also in the time it takes to reach peak ventricular ejection (dZ/dt -min peak), which is reflected by the ISTI. Hence the information between PEP and ISTI strongly overlaps empirically and theoretically, and ISTI might itself be considered as a measure of cardiac sympathetic control based on physiological grounds.

One psychometric virtue of RZ is that it probably contains less measurement error. PEP and RZ are difference scores—the difference, in ms, between two points in the cardiac cycle—and the reliability of a difference score stems in part from the reliability of the two primary scores (Rogosa and Willett 1983). Errors in measuring single waveform landmarks—such as Q, B, R, and Z—will thus result in increased error in the resulting difference scores. The identification of the subtle Q and B points for PEP probably involves more error than RZ, which is defined by two salient peaks that are easily identified with automated methods (Meijer et al. 2008). It thus

seems likely that RZ could be advantageous solely for reliability reasons—its points can be more precisely identified—rather than for strictly physiological or theoretical reasons.

The present research, in the spirit of calls for additional validity testing (van Lien et al. 2013), evaluated the suitability of RZ as an indicator of effort-related sympathetic activity in contexts calling for mental effort. As noted earlier, SBP and PEP are popular outcomes in this area. An additional, complementary indicator would be valuable, particularly for ambulatory impedance methods (Sperry et al. 2018). Ambulatory assessment is becoming increasingly popular, but it yields noisier signals (Cybulski 2011) in which Q and B are typically less apparent (van Lien et al. 2013). We used a prototypical incentive paradigm: exerting effort to attain an appealing reward (Silvia et al. in press). Effects of incentives on PEP in appetitive effort paradigms are well-established (e.g., Richter 2012; Richter et al. 2008; Richter and Gendolla 2009), so these classic, touchstone paradigms are useful for evaluating RZ relative to PEP. We assessed PEP using the Lozano et al. (2007) slope/intercept approach, both because it is ubiquitous in modern research and because a conceptual replication of van Lien et al.'s (2013) findings would contribute to the growth of knowledge about RZ/ISTI.

In two experiments, participants completed a reward-seeking task that allowed them to work at their own pace and accumulate cash rewards for each correct response. Baseline-to-task change in PEP and RZ was assessed, and the relative influence of incentives on each cardiac outcome was evaluated. Study 1 is a re-analysis of a recent effort study that did not initially evaluate RZ (Harper et al. 2016); the data from Study 2 are novel and reported here for the first time.¹ Study 3 concludes with a meta-analytic synthesis of the incentive experiments to summarize the relative effects of PEP and RZ in response to incentives.

Study 1

In Study 1, we used a standard paradigm from the mental effort literature to evaluate the effects of incentives on effort-related cardiac activity. Participants worked on a self-paced task in which each correct response earned a small amount of money. In such circumstances (Brehm and Self 1989; Wright 2008), the intensity of effort is a function of the value of the incentive, and many studies find that indicators of beta-adrenergic sympathetic influences on the heart increase when incentives are provided in such tasks (Richter 2012). Both RZ and PEP, assessed via the Lozano et al. (2007) method, were scored so that we could evaluate how highly they correlate and whether one has a larger effect size.

Method

Participants and Design

A final sample of 89 women (age $M = 18.53$ years, $SD = 1.08$, range from 18 to 23) took part and received credit toward a voluntary research option in a psychology class. Approximately 43% of

¹ Specifically, in Study 1, the PEP data were reported as part of a study on perfectionism and mental effort (Harper et al. 2016). RZ was not reported or discussed. For this re-analysis, the degrees of freedom may vary slightly because of differences in missing data associated with the different variables of interest. In Study 2, the parity task data have not been previously reported.

the sample identified as African American, 45% as European American, and 8% as Hispanic or Latinx (people could select more than one category).

Procedure

The data were from a larger study of perfectionism and effort (Harper et al. 2016). People participated individually, and a researcher of the same gender (but not necessarily of the same race or ethnicity) conducted the experiment. After the participant provided informed consent, the experimenter explained that the purpose of the study was to assess physiological responses during mental effort, concentration, and attention. The participant expected to work on a computer task that required some effort, such as making quick decisions and judgments. The electrodes were then placed for the physiological assessments. After the signals stabilized, people completed a baseline period in which they completed demographic items and individual-differences surveys. The last 5 min of the baseline period were used for the baseline physiological values.

The Parity Task. After the baseline, participants completed a *parity task*, a popular mental-effort task in modern work (e.g., Chatelain and Gendolla 2015; Framorando and Gendolla 2018; Silvia et al. 2014a, b, 2018, in press). Each trial of this task involved seeing a word in the center of the screen. The word is flanked by two numbers, and participants must ignore the word and judge whether the numbers have the same parity (both are odd or both are even) or different parity (one is odd and the other is even). Responses were collected using a high-speed keyboard. Each trial began with a fixation cross, shown for 350 ms, followed by the parity item (e.g., 4 HOME 6). The item stayed on the screen until the person responded, so the participants were able to work at their own pace (Wright et al. 2002). After the response, there was a 750 ms inter-trial interval before the next item appeared. All items were presented in black using 28-point Tahoma font on a white background. The task lasted for 3 min and was controlled using MediaLab and DirectRT research software.

To ensure the parity task was approach-oriented and appetitive, we offered an incentive. People would receive 3 cents, paid in cash after the session, for each correct response. All correct responses were rewarded, and there were no penalties for mistakes. Because people could work at their own pace, expending more effort to complete more trials within the three-minute task period would yield a higher reward.

Physiological Assessment. PEP and RZ were assessed using impedance cardiography. A Mindware Bionex chassis collected the signals at a 1000 Hz sampling rate. The signals were filtered offline (0.5–45 Hz for both EKG and dZ/dt , a low cutoff of 10 Hz for Z_0 , and a 60 Hz notch filter). Using spot electrodes, we used a modified Lead-II configuration to obtain an electrocardiogram (ECG) and a standard tetrapolar configuration to obtain the impedance cardiogram (ICG). The ECG electrodes were placed on the right clavicle and on both sides of the participant's body at the lowest rib. The receiving pair of ICG electrodes was placed on the xiphoid process and the left clavicle. The sending pair of ICG electrodes was placed on the back (one 4 cm below the horizontal plane of the xiphoid process, and the other one 4 cm above the left clavicle).

The impedance data were scored using IMP 3.1 (Mindware, Gahanna, OH). Ensemble averages (Kelsey et al. 1998) were formed for each 60-s period, yielding 8 periods (5 baseline, 3 task). The first physiological outcome was the RZ interval: the difference in ms between the R point on the ECG wave and the Z point on the dZ/dt wave. The second physiological outcome was the pre-ejection period (PEP): the difference in ms between the Q point on the EKG wave and the R point on the dZ/dt wave. The Q point was identified as the lowest point within 35 ms window before the R point of the ECG (Berntson et al. 2004). The B point was calculated using the Lozano et al. (2007) formula ($RB = 55\%$ of the RZ interval plus 4 ms).

Results and Discussion

PEP and RZ correlated very highly in both the baseline ($r = 0.92$) and task ($r = 0.94$) periods. Repeated-measures ANOVAs examined change in RZ and PEP from baseline to task.² Table 1 displays the descriptive statistics. Both RZ ($F(1, 88) = 4.57, p = 0.035$, partial $\eta^2 = 0.049$) and PEP ($F(1, 88) = 2.95, p = 0.089$, partial $\eta^2 = 0.032$) declined from baseline to task, reflecting increased sympathetic influence during the task. Notably, RZ had a larger effect size than PEP (partial $\eta^2 = 0.049$ vs 0.032).

Table 1. Descriptive Statistics: Studies 1 and 2

	Study 1		Study 2	
	Baseline	3 cents	Baseline	3 cents
PEP	119.96 (1.13)	119.14 (1.17)	130.37 (.97)	128.80 (1.08)
RZ	159.24 (1.74)	157.45 (1.81)	173.11 (1.66)	169.83 (1.92)

Study 1 $n = 89$; Study 2 $n = 71$. Standard errors are in parentheses. PEP = pre-ejection period (in ms); RZ = RZ interval (in ms)

Study 2

In Study 2, we sought to replicate the effects from Study 1 using essentially the same methods.

Method

Participants and Design

A sample of 71 women (age $M = 19.13$ years, $SD = 1.32$, range from 18 to 25) took part and received credit toward a voluntary research option in a psychology class. Approximately 48% of the sample identified as African American, 44% as European American, and 8% as Hispanic or Latinx (people could select more than one category).

Procedure

² As an aside, PEP and RZ had similar correlations between the baseline values and baseline-to-task difference scores. These correlations were small in both Study 1 (PEP: $r = -.13, p = .221$; RZ: $r = -.16, p = .134$) and Study 2 (PEP: $r = .00, p = .992$; RZ: $r = .08, p = .535$). Likewise, PEP and RZ at baseline had similar correlations with other physiological scores at baseline, such as with respiration rates in Study 1 (PEP: $r = -.02, p = .857$; RZ: $r = -.01, p = .908$) and Study 2 (PEP: $r = -.14, p = .250$; RZ: $r = -.14, p = .252$) and with interbeat intervals in Study 1 (PEP: $r = -.06, p = .608$; RZ: $r = .06, p = .551$) and Study 2 (PEP: $r = .32, p = .007$; RZ: $r = .27, p = .026$).

The procedure and physiological assessment were essentially identical to Study 1. After a 5-min baseline period, people completed a 3-min block of the parity task and were told they would receive 3 cents for each correct response. The physiological assessment and scoring were the same.

Results and Discussion

As before, PEP and RZ correlated highly in both the baseline ($r = 0.89$) and task ($r = 0.92$) periods. Repeated-measures ANOVAs examined change in RZ and PEP from baseline to task. Table 1 displays the descriptive statistics. Both RZ ($F(1, 70) = 15.40, p < 0.001$, partial $\eta^2 = 0.180$) and PEP ($F(1, 70) = 10.52, p = 0.002$, partial $\eta^2 = 0.131$) declined significantly from baseline to task. Notably, as in Study 1, RZ had a larger effect size than PEP (partial $\eta^2 = 0.180$ vs 0.131).

Study 3: Synthesis of Parity Studies with Cash Incentives

Studies 1 and 2 found slightly larger effects for RZ than for PEP. To estimate an overall summary, in Study 3 we conducted a quantitative synthesis of the effect sizes from the two experiments. The effect sizes were based on the change in PEP and RZ from baseline to task, using paired-sample t -values as the input statistic.

To expand the synthesis, we added effect sizes from all experiments our research group has conducted that used the parity incentive task and assessed PEP and RZ. This yielded two additional studies. The first study published PEP and RZ effects for a procedure that offered 1 cent or 5 cents (within-person) as an incentive in a sample of 51 young college-aged adults (Harper et al. 2018). The second study published PEP effects, with RZ in its online supplemental material, for a procedure that offered 3 cents or 15 cents (within-person) as an incentive in a sample of 71 adults (Silvia et al. 2020), some of whom met clinical criteria for major depressive disorder according to structured clinical interviews.

We restricted the synthesis to studies using the same conceptual framework and paradigm to remain circumspect about the breadth of claims we can draw from this research. For studies that included within-subjects incentive conditions, we computed the effect sizes using the larger incentive in each study (i.e., 5 cents and 15 cents) for independent effects and to provide a “best case” estimate of PEP and RZ effects for researchers conducting power analyses.

The analysis was conducted with the Comprehensive Meta-Analysis 2.2 software using a fixed-effects model, given that all the experiments used the same equipment, methods, and paradigm, and inverse-variance weighting. Table 2 reports the effect sizes in Hedges’s g metric for each study along with the overall summary effect size synthesized across the 4 studies. Conventional guidelines view g values of 0.20, 0.50, and 0.80 as small, medium, and large effect sizes, respectively (Cumming 2012).

For PEP, the overall effect size was $g = 0.376$ [95% CI 0.256, 0.496], $Z = 6.12, p < 0.001$. For RZ, the overall effect size was $g = 0.432$ [95% CI 0.310 0.554], $Z = 6.96, p < 0.001$. RZ’s effect

size was thus roughly 15% larger than PEP’s effect size. These summary effect sizes are good guides for researchers planning future research, and they suggest that RZ had a notable effect-size advantage over PEP in the present set of experiments.

Table 2. Synthesis of Effect Sizes for Parity Incentive Experiments

	PEP	RZ	<i>n</i>	Incentive (cents)
Study 1	0.181 [-0.027, 0.388]	0.225 [0.016, 0.433]	89	3
Study 2	0.381 [0.142, 0.619]	0.461 [0.218, 0.703]	71	3
Harper et al. (2018)	0.516 [0.225, 0.807]	0.608 [0.310, 0.905]	51	5
Silvia et al. (2020)	0.547 [0.299, 0.794]	0.574 [0.326, 0.826]	71	15
Summary Effect	0.376 [0.256, 0.496]	0.432 [0.310, 0.554]		

Effect sizes are Hedges’s *g* coefficients; 95% confidence intervals around *g* are in brackets. The summary effects and confidence intervals are from a fixed-effects meta-analysis. The results from a random-effects model yield the same conclusions (PEP: $g = 0.392$ [0.218, 0.566]; RZ: $g = 0.451$ [0.270, 0.632])

Discussion

Research on mental effort emphasizes indicators of sympathetic activity on the heart (Gendolla et al. 2019; Richter 2012, 2013), and systolic blood pressure (SBP) and the pre-ejection period (PEP) have historically been the most popular ones. The present research explored the psychometric utility of the RZ interval, also known as the initial systolic time interval (ISTI; Meijer et al. 2008, 2010), for assessing effort-related sympathetic activity. Like PEP, RZ reflects changes in sympathetically mediated contractility. Unlike PEP, however, it is defined by two easily identified points.

Both experiments used a standard incentive paradigm to examine changes in PEP and RZ. As expected, they found significant declines in PEP due to task incentives (Richter 2012). RZ showed essentially similar patterns—like PEP, it declined significantly from baseline to task, reflecting greater contractility during the incentive task. Notably, the effect sizes were higher for RZ than for PEP. When pooled quantitatively, RZ’s weighted average effect size was around 15% larger than PEP’s. This is consistent with the higher reliability associated with identifying the R and Z points. As noted earlier, impedance cardiography has a long history of developing methods for identifying and approximating Q and B (Árbol et al. 2017; Berntson et al. 2004; Lozano et al. 2007; Sherwood et al. 1990), which can be subtle waveform points that are not always apparent. Any errors associated with assessing these points feed into subsequent difference scores involving them, so the increased reliability of assessing RZ (rather than a fundamental physiological reason) is probably why it results in larger effect sizes.

The present research suggests that RZ is a promising indicator for future research on the psychophysiology of mental effort in response to incentives. Obviously, much more research is needed to evaluate it across a wider range of contexts. But the present findings, taken together with past work, suggest that RZ deserves attention as an additional outcome in future work. It’s worth noting that two prior studies from our lab using different paradigms and tasks found similar effects. One study found larger effects for RZ during an open-ended creative thinking task (Silvia et al. 2014a), and another found a larger effect for RZ when people were asked to “do their best” on a task (Silvia et al. 2014b). Neither study had anything at stake or offered incentives, but they provide additional indirect support for exploring RZ further.

We should emphasize that our aims in this project were essentially psychometric. We sought to examine the value of RZ relative to PEP based on statistical criteria—relative effect sizes in a standard mental effort paradigm—rather than on underlying physiological processes. RZ might be preferred for cases in which researchers are more interested in general sympathetic effects than in separating specific alpha and beta-adrenergic effects. Because PEP measures the period of the cardiac cycle in which the ventricle is isolated from both the aorta and atria, it may be less sensitive to afterload than RZ and could thus be a more precise measure of beta-adrenergic influence (Kelsey 2012). Although PEP and RZ seem similar in the relative contributions of sympathetic activation, preload, and afterload (Meijer et al. 2008, 2010; van Eijnatten et al. 2014), their relative physiological dynamics have not been intensively studied thus far.

Likewise, our conclusions regarding the relative effect sizes of RZ and PEP apply only for the PEP scoring method that was examined: the slope/intercept method developed by Lozano et al. (2007). Their method overlaps considerably with the RZ interval and has the virtue of approximating the B-point. As noted earlier, many approaches to identifying and approximating PEP's points have been developed (Árbol et al. 2017; Forouzanfar et al. 2018). These methods serve as more efficient alternatives to the laborious hand-scoring of individual cardiac cycles, but as in all psychological measurement, there are usually trade-offs between cost (in time, training, and personnel) and precision. The RZ interval may be better or worse than other ways of identifying Q and B points. Comparing RZ to a range of alternate scoring methods—from other point-identification methods to hand-scored signals—to determine its relative efficiency is an important direction for future research.

Finally, the present experiments are limited to a particular population and paradigm: seated young women in good cardiac health working on a mental effort task for cash rewards. It would be valuable to compare PEP and RZ in other contexts where sympathetic cardiac activity is commonly assessed, such as paradigms using physical exercise, pharmacological blockades, and mental and physical stressors (e.g., Lackner et al. 2015; Meyer et al. 2016; Mitchell et al. 2017). To date, there's some evidence that RZ's similarity to PEP is general beyond mental effort, such as physical exertion (van Eijnatten et al. 2014; Wilde et al. 1981), Valsalva maneuvers (Meijer et al. 2010), and dobutamine infusion (van der Meer et al. 1999). Understanding the relative scope and generality of the RZ-PEP relationship across paradigms and populations is an important task for future work.

We strongly encourage researchers using other PEP scoring methods and other paradigms to explore RZ in their own data files, which probably already contain the information needed to compute RZ. Aside from the virtue of expanding one's toolbox, RZ holds promise for research in applied and field contexts, which often has noisier signals due to diminished control over the environment and participant movement. Ambulatory impedance methods, for example, yield much noisier signals, so RZ, as a relatively more robust method, may prove to be especially useful for exploring autonomic processes outside the laboratory (Cybulski 2011; Sperry et al. 2018).

Data Availability

Research materials have been archived at Open Science Framework: <https://osf.io/3kwmr/>.

Acknowledgements

This research was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R15MH079374. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. An earlier version of this research was presented at the annual meetings of the Southeastern Psychological Association and Society of Southeastern Social Psychologists. Materials are available at Open Science Framework: <https://osf.io/3kwmr/>.

Funding

This research was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R15MH079374. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Ethics declarations

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical Approval

All procedures involving human participants were approved and monitored by the Institutional Review Board of the University of North Carolina at Greensboro.

Informed Consent

Informed consent was obtained from all participants included in these studies.

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