Psychoneuroendocrinology 75 (2017) 222–227

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Trait hostility and cortisol sensitivity following a stressor: The moderating role of stress-induced heart rate variability

Kyle W. Murdock[a], Angie S. LeRoy[a,b], Christopher P. Fagundes[a,c,d,*]

[a] Department of Psychology, Rice University, Bioscience Research Collaborative Room 773, 6100 Main Street, Houston, TX 77005, USA
[b] Department of Psychology, University of Houston, 3695 Cullen Boulevard Room 126, Houston, TX 77204, USA
[c] Department of Symptom Research, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 1450, Houston, TX 77030, USA
[d] Department of Psychiatry, Baylor College of Medicine, One Baylor Plaza – BCM350, Houston, TX 77030, USA

ARTICLE INFO

Article history:
Received 24 June 2016
Received in revised form 18 October 2016
Accepted 19 October 2016

Keywords:
Hostility
Heart rate variability
Cortisol
Coronary heart disease

ABSTRACT

Hostility and adverse health outcomes are inconsistently associated in the literature. Self-regulation and cortisol secretion may play important roles in differentiating those hostile individuals who are at greater risk of negative health outcomes from those who are not. In the present study, we sought to examine if having high self-regulatory strength, as indexed by high stress-induced high-frequency heart rate variability (HF-HRV), buffered the effects of hostility on cortisol secretion. Participants ($N = 213$) completed a self-report measure of hostility and measurement of HF-HRV at rest and during a social stress task. Saliva samples were collected immediately before (one sample), and over a 50 min period after (six samples), the stress task to evaluate cortisol secretion over time. Hostile individuals were less likely to demonstrate cortisol sensitivity (i.e., high change in cortisol over time) when they had high stress-induced HF-HRV. Such findings are important given that cortisol sensitivity increases risk of metabolic and inflammatory disorders via glucocorticoid resistance and inflammation. Therefore, interventions that increase stress-induced HF-HRV may reduce the impact of hostility on health outcomes.

1. Introduction

There is wealth of evidence in the health psychology and behavioral medicine literatures indicating that chronic anger and hostility contributes to the etiology of coronary heart disease (CHD) and other life-threatening illnesses. Indeed, episodes of anger and hostility precipitate coronary events (Dembroski et al., 1983). Hostility is a personality trait that includes cynicism/mistrust of others, anger, and overt and repressed aggression (Cook and Medley, 1954). Importantly, hostility is an independent risk factor for coronary heart disease and all-cause mortality after accounting for traditional health behaviors (Chida and Steptoe, 2009; Miller et al., 1996). Exaggerated stress reactivity partially explains these findings (Kiecolt-Glaser et al., 2005). Although hostility is a significant independent predictor of cardiac events, the findings relating hostility with adverse clinical outcomes are inconsistent (Hemingway, 1999). For example, hostility was not associated with CHD among large samples of patients undergoing angiography (Dembroski et al., 1985; Helmer et al., 1991). Moreover, a non-significant association between hostility and CHD was identified in a 30-year longitudinal study (Leon et al., 1988). Accordingly there are likely third variables that influence the association between hostility and health. In the present study, we sought to examine under what conditions hostility is associated with negative physiological outcomes.

Hostility is associated with substantial physiological repercussions for some hostile individuals, but importantly, not for others (e.g., Weidner et al., 1989). The mechanisms driving this finding are not fully understood. One possibility is that there are alterations in physiological systems that regulate hormonal activity, such as the hypothalamic– pituitary–adrenal (HPA) axis, for some hostile individuals. Widely referred to as the "stress hormone," cortisol is a glucocorticoid that is released by the adrenal glands when the hypothalamic pituitary adrenal (HPA) axis is activated by stress. Cortisol is important for establishing homeostasis after exposure to a stressor. In two studies, cortisol production was high among hostile individuals who developed coronary heart disease and type 2 diabetes (Brydon et al., 2010; Hacket et al., 2015). Such findings suggest that cortisol is important for distinguishing between hostile individuals who experience negative health outcomes and

* Corresponding author at: Bioscience Research Collaborative, Rm 773 MS-142, 6100 Main Street, Houston, USA.
E-mail addresses: christopher.fagundes@rice.edu, cpfagundes@mdanderson.org (C.P. Fagundes).

http://dx.doi.org/10.1016/j.psyneuen.2016.10.014
0306-4530/

those who do not. Importantly, recent work suggests that cortisol sensitivity (i.e., change in cortisol concentrations over time), as opposed to total cortisol output, is associated with glucocorticoid resistance and negative health outcomes such as inflammatory and metabolic diseases (e.g., coronary heart disease, rheumatoid arthritis, sepsis, type 2 diabetes, metabolic syndrome; for a review, see Quax et al., 2013). Cortisol sensitivity is determined by multiple factors including functional polymorphisms of the gene that encodes glucocorticoid receptors, chronic stress, and waking hours (Quax et al., 2013). It is unclear why some hostile individuals would demonstrate more cortisol sensitivity than others; however, self-regulation likely plays an important role given the association between stress and cortisol sensitivity.

1.1. Self-regulation, heart rate variability, and health

Individuals with poor self-regulatory skills (i.e., the ability to regulate behavior, emotion, and cognition; Gross, 2013) are at risk of poor physical health. Indeed, poor self-regulation is associated with increased risk of cardiovascular disease (Thayer et al., 2010) and mortality in comparison with better self-regulation (Mauss and Gross, 2004). Given that hostility is characterized as the experience of cynicism, anger, and either overt or repressed aggression, hostile individuals may need to regulate internally generated thoughts, behaviors, and emotions in order to avoid negative mental and physical health outcomes (Andrews-Hanna et al., 2014).

According to the neurovisceral integration model (Thayer and Lane, 2009), high frequency heart rate variability (HF-HRV) reflects people's ability to flexibly respond their environment, including the regulation of stressful thoughts. Stress-induced HF-HRV has been described as representing one's regulatory strength, or the ability to exert enough self-regulatory effort to overcome demanding circumstances (e.g., Beauchaine, 2001; Segerstrom and Nes, 2007). Hostile individuals may benefit from high HF-HRV when confronted with hostile thoughts and feelings. Indeed, hostile individuals who were exposed to a biofeedback training program that improved HF-HRV demonstrated lower hostility one month after the treatment (Lin et al., 2015). However, it is unclear whether stress-induced HF-HRV changes the association between hostility and biological outcomes such as cortisol output. Given that stress-induced HF-HRV represents regulatory strength, high stress-induced HF-HRV may buffer the negative physiological effects of hostility. That is, when confronted with hostile thoughts or feelings, those with high stress-induced HF-HRV may have the regulatory strength necessary to adaptively regulate their thoughts or feelings so they do not lead to maladaptive physiological stress responses such as cortisol sensitivity. Those with low stress-induced HF-HRV may be more likely to act on, or ineffectively repress, hostile thoughts or feelings, and experience poor physiological outcomes as a result.

In the present study, we sought to examine the potential interactive effects between hostility and stress-induced HF-HRV in predicting cortisol output following a stressor. Consistent with the available literature, it was hypothesized that higher hostility would be associated with greater cortisol sensitivity (i.e., change in cortisol concentration over time following a stressor); however, we hypothesized that individual's stress-induced HF-HRV would change the association between hostility and cortisol sensitivity such that the association would be significant among those with low stress-induced HF-HRV, but not among those with high stress-induced HF-HRV.

2. Materials and methods

Data from the Pittsburgh Cold Study 3 were utilized in the present study. The data are publicly available and have been described previously (e.g., Cohen et al., 2013; Janicki-Deverts et al., 2014). Briefly, healthy individuals from the Pittsburgh, Pennsylvania area were recruited to participate between 2008 and 2011. The study was approved by the Carnegie Mellon University and University of Pittsburgh institutional review boards. All participants provided informed consent and were compensated with $1000 for completing the full study protocol.

For the present study, participants ($N = 213$) completed a self-report measure of trait hostility and HF-HRV was measured at rest and during the well validated Trier Social Stress Test (TSST; Kirschbaum et al., 1993). In the present study, participants were told that they would be delivering a five-minute speech. The speech involved defending against an alleged transgression (i.e., shoplifting or a traffic violation which were counterbalanced). Following a five minute preparation period, participants delivered the video recorded speech during which HF-HRV was recorded. After the speech, participants completed a mental arithmetic task, which is standard for the TSST. Participant saliva was collected before and after the TSST as described below.

2.1. Measures

2.1.1. Trait hostility

Trait hostility was measured with a modified version of the Cook-Medley Hostility Scale (Cook and Medley, 1954) in which the 20 items comprising the cynicism, hostile affect, and aggressive responding subscales were utilized as recommended by Barefoot et al. (1989). For each item, participants were asked to indicate whether a statement about how an individual may view others was true or false for them. The number of responses that were consistent with hostility (two items were reverse coded) for each participant were summed to form an overall score in which higher scores represent greater hostility. Internal consistency for the 20 item scale in the present was acceptable ($\alpha = 0.71$).

2.1.2. Heart rate variability

HF-HRV was recorded using a respiration band and three electrocardiogram leads (Vernier Software & Technology, Beaverton, OR). The baseline period lasted 20 min. Participants were instructed to sit upright in a chair and rest quietly. Interbeat interval (IBI) sequences were recorded using an automated algorithm (Mindware Version 2.51, Mindware Technologies, LTD) and a 250 Hz sampling frequency (Malik, 1996). Measurement of HF-HRV during baseline was separated into five minute epochs. IBIs were inspected for abnormalities and edited manually. Spectral analysis of IBIs was conducting using a Fast Fourier transformation algorithm (Duhamel and Vetterli, 1990). High frequency (HF) band power was calculated as the sum of the powers associated with any peaks in the range of 0.12 Hz–0.40 Hz. The four baseline epochs were averaged to form an overall indicator of baseline HF-HRV. The same procedure was utilized to measure stress-induced HF-HRV during the TSST, which consisted of a single five minute epoch.

2.1.3. Cortisol

Saliva samples were collected with Salivette® devices (Sarstedt, Rommelsdorft, Germany), which include a roll of cotton contained within a collection tube. At each collection point, participants were instructed to place the cotton roll in their mouths and chew it until it became saturated before placing the cotton role into the inner vial of the Salivette and capping the outer tube. Saliva was collected immediately before engaging in the TSST, immediately following the TSST, and every ten minutes during a 50-min period there-

after (7 samples total). Cortisol samples were sent to Dr. Clemens Kirschbaum's laboratory in Dresden, Germany where they were assayed. Time-resolved fluorescence immunoassay, with a cortisol-biotin conjugate as a tracer1, was utilized to determine cortisol levels in saliva (Dressendörfer et al., 1992).

2.1.4. Covariates

Self-reports of participant age, sex, race, and smoking status were provided. Moreover, participant height and weight were measured to calculate a body mass index (BMI). The Macarthur Scale of Subjective Social Status USA ladder version (Adler et al., 2000) was utilized to measure adult socioeconomic status (SES). Participants were asked to indicate their own social status on an illustration of a nine step ladder in which the top represents those with the most education, money, and respected jobs. Conversely, the bottom step of the ladder represents those with the least education, money, and respected jobs. Participants were asked to place an "X" on the ladder that best represented their current position. Scores range from 1 (lowest status) to 9 (highest status).

2.2. Analytic strategy

Full information maximum likelihood (FIML) was utilized to handle random missing data, which is superior to listwise deletion or mean imputation (e.g., Akaike, 1998). Data were obtained from all participants for trait hostility, age, sex, race, BMI, smoking status, and SES. Valid HF-HRV data was obtained from 199 participants at baseline and 190 participants during the stressor. Furthermore, valid cortisol measurements across all seven time points were obtained from 202 participants. Baseline HF-HRV was included as a covariate in order for our results to reflect stress-induced HF-HRV relative to baseline. As expected when examining HF-HRV, baseline and stress-induced HF-HRV demonstrated high skewness and kurtosis (all values greater than 3.25). Accordingly, a natural log transformation was utilized to normalize the distributions of the variables. Linear regression analyses were utilized to test for moderation (Hayes, 2013). Predictors were mean centered prior to the analyses. Further, the Johnson-Neyman technique was utilized to identify regions of significance in moderation analyses (Johnson and Fay, 1950). We included the area under the curve (AUC) as our dependent variable given that stress-induced cortisol secretions change over time (e.g., Earle et al., 1999; Elzinga et al., 2005). Specifically, we calculated AUC with respect to sensitivity over time to test our primary hypotheses (AUC_I; see Fekedulegn et al., 2007). We also utilized AUC with respect to baseline (AUC_B), which reflects total cortisol output (Fekedulegn et al., 2007), in ancillary analyses.

3. Results

Descriptive statistics for study variables are presented in Table 1. Zero-order correlations revealed that participant sex ($r = -0.16$, $p = 0.02$) and race ($r = -0.16$, $p = 0.02$) were significantly associated with trait hostility such that males and non-White participants reported greater hostility. Participant age ($r = -0.47$, $p < 0.01$), baseline HF-HRV ($r = 0.72$, $p < 0.01$), and body mass index ($r = -0.34$, $p < 0.01$) were associated with stress-induced HF-HRV. Furthermore, participant age ($r = -0.18$, $p = 0.01$) and sex ($r = -0.26$, $p < 0.001$) were associated with cortisol AUC_I, with greater AUC_I among males. Using a linear regression analysis (see Table 2), trait hostility and stress-induced HF-HRV were not significantly associated with cortisol AUC_I; however, there was an interaction effect such that trait hostility was statistically significantly associated with cortisol AUC_I when stress-induced HF-HRV was low, but not high (see Fig. 1). Specifically, trait hostility and cortisol AUC_I were significantly associated when the natural log transformation of stress-induced HF-HRV was less than 5.66, which represented 27.23% of the sample. Fig. 2 depicts cortisol levels at high (+1 *SD*) and low (−1 *SD*) hostility and stress-induced HF-HRV.

Table 1
Participant characteristics ($N = 213$).

Variable	Mean (SD) or number (%)
Age	30.13 (10.85)
Sex	
Male	123 (57.75)
Female	90 (42.35)
Ethnicity	
White	71 (33.33)
Non-white	142 (66.67)
Body mass index	27.46 (6.50)
Smoking status	
Smoker	72 (33.80)
Non-smoker	141 (66.20)
Socioeconomic status ladder score	4.23 (1.87)
Trait hostility	10.03 (3.68)
Ln transformed baseline HF-HRV	6.22 (1.19)
Ln transformed stress-induced HF-HRV	6.16 (1.14)
Stress-induced cortisol AUC_I	259.08 (213.06)
Stress-induced cortisol AUC_B	56.18 (3.88)

Note. HF-HRV = high frequency heart rate variability; AUC_I = area under the curve with respect to increase/decrease; AUC_B = area under the curve with respect to baseline. The unit of cortisol measurement was nmol/l.

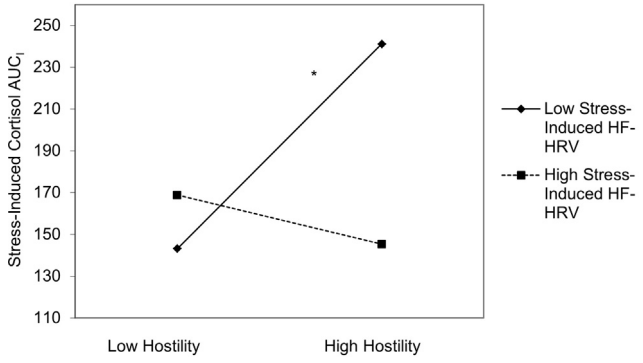

Fig. 1. Stress-induced cortisol area under the curve with respect to increase/decrease (AUC_I) at high (+1 SD) and low (-1 SD) levels of trait hostility and stress-induced high frequency hear rate variability (HF-HRV). * = significant slope.

The experimental hypotheses tested above involved cortisol sensitivity. We wanted to compare this with the baseline hypothesis involving total cortisol output (as we argued that sensitivity mattered more than output). To this end, we examined cortisol AUC_B as a dependent variable in an analysis that was analogous to the linear regression described above in order to examine if the interaction between hostility and stress-induced HF-HRV was associated with total cortisol output. Results indicated that hostility, stress-induced HF-HRV, and the interaction between hostility and stress-induced HF-HRV were not statistically significantly associated with cortisol AUC_B (see Table 2). All primary findings were significant in unadjusted models (see Table 3).

4. Discussion

Hostility is associated with increased risk of CHD and all-cause mortality (Chida and Steptoe, 2009; Miller et al., 1996). Cortisol sensitivity is a mechanism that may link hostility with inflammatory and metabolic diseases (Quax et al., 2013). However, some hostile individuals do not experience negative health outcomes (e.g., Newman et al., 2011), which may be explained by findings indicating that there was a synergistic relationship between hostility and one's capacity for self-regulation. In the current study,

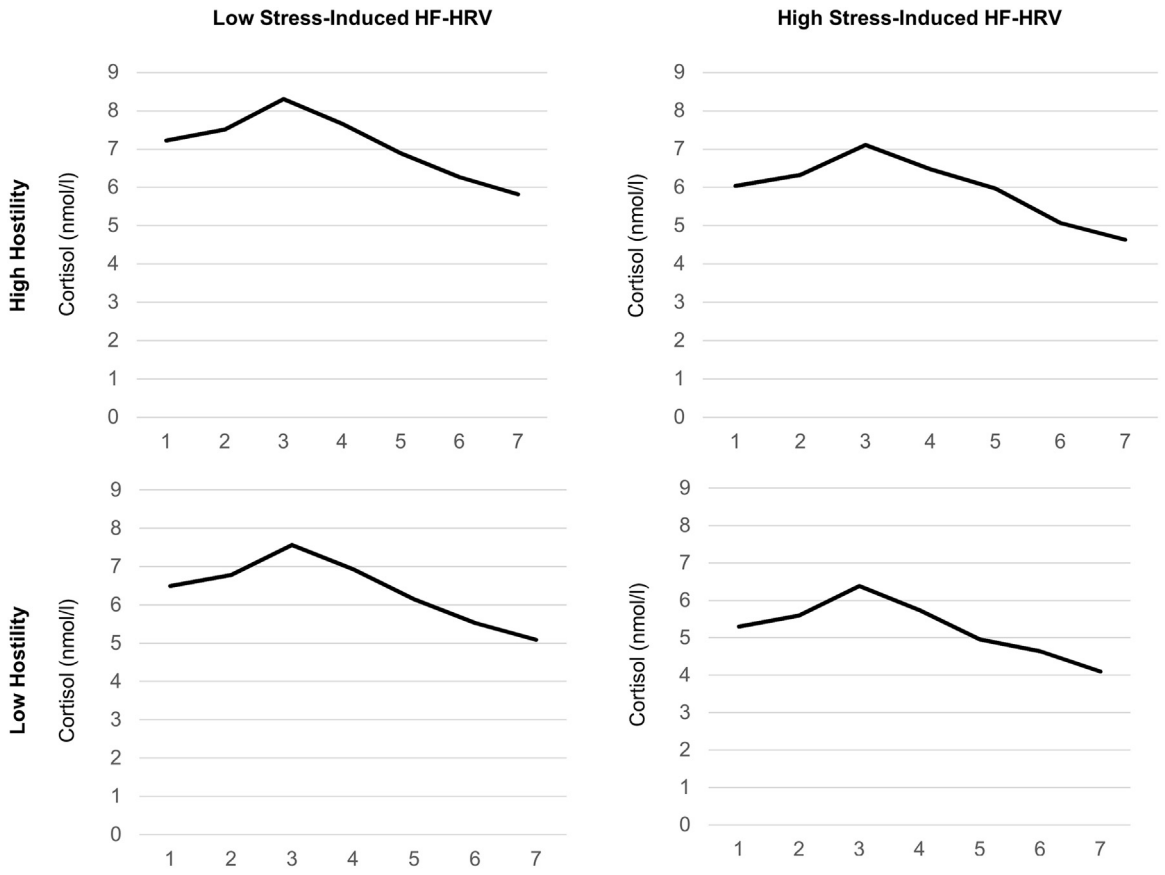

Fig. 2. Cortisol slopes associated with high (+1 *SD*) and low (-1 *SD*) hostility and stress-induced high frequency heart rate variability. 1 = Immediately before the stressor; 2 = Immediately after the stressor; 3 = 10 min after the stressor; 4 = 20 min after the stressor; 5 = 30 min after the stressor; 6 = 40 min after the stressor; and 7 = 50 min after the stressor.

we demonstrated that hostility was unrelated to cortisol sensitivity if stress-induced HF-HRV was high. When stress-induced HF-HRV was low, higher trait hostility was associated with greater cortisol sensitivity. Accordingly, stress-induced HF-HRV may be important for understanding why some hostile individuals experience negative health outcomes, while others do not.

HF-HRV is associated with one's ability to react flexibly to their environment and utilize effective self-regulation strategies (Thayer and Lane, 2009). Accordingly, present study data may suggest that those with frequent hostile thoughts may be able to successfully regulate such thoughts if they have the regulatory strength to do so. If successfully regulated over time, hostility may not lead to cortisol sensitivity; however, unsuccessful regulation of hostility may lead to cortisol sensitivity. Such findings may explain why individuals with mood disorders are more likely to demonstrate cortisol sensitivity than those without a mood disorder (Quax et al., 2013; Young et al., 2001), given that successful self-regulation is associated with decreased risk of mental health problems (Gross and Muñoz, 1995).

As mentioned previously, HF-HRV can be improved via biofeedback, and is effective at reducing hostility among some hostile individuals (Lin et al., 2015). Exercise (Iellamo et al., 2000) and mindfulness meditation (Krygier et al., 2013) are also associated with improvements in HF-HRV. Therefore, hostile individuals may benefit from a number of non-invasive treatments by which the strength of the association between hostility and cortisol sensitivity may be reduced. There are a number of other pathophysiological mechanisms (e.g., macrophage migration inhibitory factor, mitogen-activated protein kinases) that may lead to improved cortisol sensitivity if targeted in treatment; however, the clinical effectiveness of these pathways remains unclear and costly side effects can occur (e.g., restricted capacity for bone marrow to generate progenitor cells; Quax et al., 2013).

Cortisol has robust effects on immune cell development, maturation, trafficking, and cytokine production, including production of proinflammatory cytokines (McEwen et al., 1997). For those hostile individuals who are physiologically reactive to stress, inflammation may be one important mechanism underlying the association between hostility and poor health. Indeed, individuals who demonstrated hostile behaviors in a marital conflict discussion had larger increases in plasma IL-6 and TNF-alpha values the morning after the conflict compared with couples who displayed less hostility (Kiecolt-Glaser et al., 2005). Moreover, cortisol sensitivity promotes glucocorticoid resistance (Quax et al., 2013), which further enhances inflammation (e.g., Miller and Raison, 2016) and increases risk of cardiovascular disease, type 2 diabetes, some cancers, and morbidity and mortality (Kiecolt-Glaser et al., 2010). Therefore, future work would benefit from including measurement of both cortisol sensitivity and proinflammatory cytokines to extend the literature.

The present study is limited by the predominantly white sample. It will be important to investigate whether primary findings exist among diverse groups in future work given ethnic variations in HF-HRV (e.g., Hill et al., 2015). In the present study, the TSST was modified such that participants were asked to defend an alleged transgression as opposed to providing a speech as if they were a job applicant (Kirschbaum et al., 1993). Although both situations are arguably stressful, the similarities and/or differences in stress promotion are unclear. The study is also limited by the lack of inclusion of disease outcomes; however, given consistent findings link-

Table 2
Linear regression analyses of trait hostility, stress-induced heart rate variability, and their interaction in predicting cortisol area under the curve with respect to increase and baseline.

DV	Predictors	b	SE	p	95% CI
AUC_I					
	Trait hostility	5.06	3.94	0.20	−2.71, 12.84
	Stress-induced HF-HRV	−15.44	18.65	0.41	−52.21, 21.33
	Trait hostility x stress-induced HF-HRV	−7.27	3.39	0.03	−13.94, −0.59
	Age	−4.24	1.59	0.01	−7.38, −1.10
	Sex	−111.85	29.46	>0.001	−169.95, −53.76
	Race	31.21	31.22	0.32	−30.36, 92.77
	Body mass index	4.19	2.44	0.09	−0.63, 9.00
	Socioeconomic status	4.79	7.70	0.54	−10.39, 19.96
	Smoking status	3.27	31.44	0.92	−58.73, 65.27
	F	4.61			
	df	(1, 202)			
	R^2	0.15			
	ΔR^2	0.02			
AUC_B					
	Trait hostility	0.03	0.36	0.64	−0.87, 0.54
	Stress-induced HF-HRV	−0.17	0.36	0.65	−0.11, 0.18
	Trait hostility x stress-induced HF-HRV	−0.04	0.07	0.50	−0.17, 0.08
	Age	−0.06	0.03	0.07	−0.12, 0.01
	Sex	−1.03	0.56	0.07	−2.14, 0.08
	Race	0.83	0.60	0.17	−0.35, 2.00
	Body mass index	0.02	0.05	0.74	−0.08, 0.11
	Socioeconomic status	−0.12	0.15	0.41	−0.41, 0.17
	Smoking status	0.40	0.60	0.51	−0.79, 1.58
	F	0.45			
	df	(1, 202)			
	R^2	0.06			
	ΔR^2	<0.01			

Note. DV = dependent variable; SE = standard error, HF-HRV = high frequency heart rate variability; AUCI = area under the curve with respect to increase; AUCB = area under the curve with respect to baseline. Sex coded as 0 = male, 1 = female; Race coded as 0 = non-White, 1 = White; Smoking status coded as 0 = non-smoker, 1 = smoker.

Table 3
Unadjusted linear regression analyses predicting cortisol area under the curve with respect to increase and baseline.

DV	Predictors	b	SE	p	95% CI
AUC_I					
	Trait hostility	52.54	22.27	0.02	8.64, 96.44
	Stress-induced HF-HRV	64.01	40.34	0.11	−15.52, 143.54
	Trait hostility x stress-induced HF-HRV	−7.26	3.51	0.04	−14.18, −0.34
	F	4.28			
	df	(1, 208)			
	R^2	0.04			
	ΔR^2	0.02			
AUC_B					
	Trait hostility	0.36	0.41	0.39	−0.46, 1.17
	Stress-induced HF-HRV	0.55	0.75	0.47	−0.93, 2.02
	Trait hostility x stress-induced HF-HRV	−0.05	0.07	0.45	−0.18, 0.08
	F	0.57			
	df	(1, 208)			
	R^2	0.01			
	ΔR^2	<0.01			

Note. DV = dependent variable; SE = standard error, HF-HRV = high frequency heart rate variability; AUCI = area under the curve with respect to increase; AUCB = area under the curve with respect to baseline.

ing cortisol sensitivity with inflammatory and metabolic diseases (Quax et al., 2013), we can be confident that present study findings have important implications for health. Moreover, overt hostile behaviors were not examined in the present study. It would be interesting to examine if high stress-induced HF-HRV reduces the likelihood that hostile individuals engage in overt hostile behaviors in future work. Furthermore, although there is a large literature linking HF-HRV with self-regulation, caution is warranted when inferring associations between psychophysiological markers, such as HF-HRV, and a psychological construct such as self-regulatory strength (Cacioppo and Tassinary, 1990). We cannot say for certain that stress-induced HF-HRV represents self-regulatory strength as physiological responses are multiply determined and sensitive in a number of ways; however, our findings are consistent with the available literature.

5. Conclusions

In the present study, hostility was associated with cortisol sensitivity when stress-induced HF-HRV was low; however, high stress-induced HF-HRV buffered the negative physiological effects of high hostility. Such findings suggest that hostile thoughts may be appropriately regulated if one has the self-regulatory strength to do so, thereby reducing the physiological costs of hostility.

Contributors

K.W.M was involved in data analysis and manuscript writing for the present study. A.S.L and C.P.F. provided critical feedback and edited the manuscript.

Role of the funding source

The data used for this article were collected by the Laboratory for the Study of Stress, Immunity, and Disease at Carnegie Mellon University under the directorship of Sheldon Cohen, PhD; and were accessed via the Common Cold Project (CCP) website (www.commoncoldproject.com). CCP data are made publically available through a grant from the National Center for Complementary and Integrative Health (AT006694); the conduct of the study was supported by a grant from the National Institute of Allergy and Infectious Diseases (R01 AI066367); secondary support was provided by a grant from the National Institutes of Health to the University of Pittsburgh Clinical and Translational Science Institute (UL1 RR024153); and supplemental support was provided by John D. and Catherine T. MacArthur Foundation Research Network on Socioeconomic Status & Health. Preparation of the manuscript was supported by grants from the National Heart, Lung, and Blood Institute (1R01HL127260-01; 1F32HL131353).

Conflicts of interest

None.

Acknowledgement

The statistical assistance and critical feedback provided by Dr. Fred Oswald on an earlier draft of this manuscript is much appreciated.

References

Adler, N.E., Epel, E., Castellazzo, G., Ickovics, J., 2000. Relationship of subjective and objective social status with psychological and physical health: preliminary data in healthy white women. Health Psychol. 19, 586–592, http://dx.doi.org/10.1037/0278-6133.19.6.586.

Akaike, H., 1998. Information theory and an extension of the maximum likelihood principle. In: Selected Papers of Hirotugu Akaike. Springer, New York, pp. 199–213.

Andrews-Hanna, J.R., Smallwood, J., Spreng, R.N., 2014. The default network and self-generated thought: component processes, dynamic control, and clinical relevance. Ann. N. Y. Acad. Sci. 1316, 29–52, http://dx.doi.org/10.1111/nyas.12360.

Barefoot, J.C., Dodge, K.A., Peterson, B.L., Dahlstrom, W.G., Williams, R.B., 1989. The Cook-Medley hostility scale: item content and ability to predict survival. Psychosom. Med. 51 (1), 46–57.

Beauchaine, T.P.1, 2001. Vagal tone, development, and Gray's motivational theory: toward an integrated model of autonomic nervous system functioning in psychopathology. Dev. Psychopathol. 13, 183–214, http://dx.doi.org/10.1017/S0954579401002012.

Brydon, L., Strike, P.C., Bhattacharyya, M.R., Whitehead, D.L., McEwan, J., Zachary, I., Steptoe, A., 2010. Hostile and physiological responses to laboratory stress in acute coronary syndrome patients. J. Psychosom. Res. 68 (2), 109–116, http://dx.doi.org/10.1016/j.jpsychores.2009.06.007.

Cacioppo, J.T., Tassinary, L.G.1, 1990. Inferring psychological significance from physiological signals. Am. Psychol. 45 (1), 16–28, http://dx.doi.org/10.1037/0003-066X.45.1.16.

Chida, Y., Steptoe, A.1, 2009. The association of anger and hostility with future coronary heart disease: a meta-analytic review of prospective evidence. J. Am. Coll. Cardiol. 53 (11), 936–946, http://dx.doi.org/10.1016/j.jacc.2008.11.044.

Cohen, S., Janicki-Deverts, D., Turner, R.B., Casselbrant, M.L., Li-Korotky, H.S., Epel, E.S., Doyle, W.J., 2013. Association between telomere length and experimentally induced upper respiratory viral infection in healthy adults. JAMA 309 (7), 699–705, http://dx.doi.org/10.1001/jama.2013.613.

Cook, W.W., Medley, D.M., 1954. Proposed hostility and pharisaic-virtue scales for the MMPI. J. Appl. Psychol. 38, 414–418, http://dx.doi.org/10.1037/h0060667.

Dembroski, T.M., MacDougall, J.M., Herd, J.A., Shields, J.L., 1983. Perspectives on coronary-prone behavior. In: Krantz, D.S., Baum, A., Singer, J.E. (Eds.), Handbook of Psychology and Health: Vol. 3. Lawrence Erlbaum Associates, Inc, Hillsdale, NJ, pp. 57–83.

Dembroski, T.M., MacDougall, J.M., Williams, R.B., Haney, T.L., Blumenthal, J.A., 1985. Components of Type A, hostility, and anger-in: relationship to angiographic findings. Psychomat. Med. 47 (3), 219–233.

Dressendörfer, R.A., Kirschbaum, C., Rohde, W., Stahl, F., Strasburger, C.J., 1992. Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. J. Steroid Biochem. Mol. Biol. 43 (7), 683–692.

Duhamel, P., Vetterli, M., 1990. Fast Fourier transforms: a tutorial review and a state of the art. Signal Process. 19, 259–299, http://dx.doi.org/10.1016/0165-1684(90)90158-U.

Earle, T.L., Linden, W., Weinberg, J., 1999. Differential effects of harassment on cardiovascular and salivary cortisol stress reactivity and recovery in women and men. J. Psychosom. Res. 46 (2), 125–141, http://dx.doi.org/10.1016/S0022-3999(98)00075-0.

Elzinga, B.M., Bakker, A., Bremner, J.D.1, 2005. Stress-induced cortisol elevations are associated with impaired delayed, but not immediate recall. Psychiatry Res. 134 (3), 211–223, http://dx.doi.org/10.1016/j.psychres.2004.11.007.

Fekedulegn, D.B., Andrew, M.E., Burchfiel, C.M., Violanti, J.M., Hartley, T.A., Charles, L.E., Miller, D.B., 2007. Area under the curve and other summary indicators of repeated waking cortisol measurements. Psychosom. Med. 69, 651–659, http://dx.doi.org/10.1097/PSY.0b013e31814c405c.

Gross, J.J., Muñoz, R.F., 1995. Emotion regulation and mental health. Clin. Psychol. Sci. Pract. 2 (2), 151–164, http://dx.doi.org/10.1111/j.1468-2850.1995.tb00036.x.

Gross, J.J., 2013. Emotion regulation: taking stock and moving forward. Emotion 13 (3), 359–365, http://dx.doi.org/10.1037/a0032135.

Hacket, R.A., Lazzarino, A.I., Carvalho, L.A., Hamer, M., Steptoe, A., 2015. Hostility and physiological responses to acute stress in people with type 2 diabetes. Psychosom. Med. 77 (4), 458–466, http://dx.doi.org/10.1097/PSY.0000000000000172.

Hayes, A.F., 2013. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-based Approach. NY: Guilford Press, New York.

Helmer, D.C., Ragland, D.R., Syme, S.L., 1991. Hostility and coronary artery disease. Am. J. Epidemiol. 133 (2), 112–122.

Hemingway, H., 1999. Psychosocial factors in the aetiology and prognosis of coronary heart disease: systematic review of prospective cohort studies? Br. J. Med. 318 (7196), 1460–1467.

Hill, L.K., Hu, D.D., Koenig, J., Sollers, J.J., Kapuku, G., Wang, X., Snieder, H., Thayer, J.F., 2015. Ethnic differences in resting heart rate variability: a systematic review and meta-analysis. Psychosom. Med. 77 (1), 16–25, http://dx.doi.org/10.1097/PSY.0000000000000133.

Iellamo, F., Legramante, J.M., Massaro, M., Raimondi, G., Galante, A., 2000. Effects of a residential exercise training on baroreflex sensitivity and heart rate variability in patients with coronary artery disease: a randomized, controlled study. Circulation 102, 2588–2592, http://dx.doi.org/10.1161/01.CIR.102.21.2588.

Janicki-Deverts, D., Cohen, S., Doyle, W.J., Marsland, A.L., Bosch, J., 2014. Childhood environments and cytomegalovirus serostatus and reactivation in adults. Brain Behav. Immun. 40, 174–181, http://dx.doi.org/10.1016/j.bbi.2014.03.010.

Johnson, P.O., Fay, L.C., 1950. The Johnson-Neyman Technique, its theory and application. Psychometrika 15 (4), 349–367, http://dx.doi.org/10.1007/BF02288864.

Kiecolt-Glaser, J.K., Loving, T.J., Stowell, J.R., Malarkey, W.B., Lemeshow, S., Dickinson, S.L., Glaser, R., 2005. Hostile marital interactions, proinflammatory cytokine production, and wound healing. Arch. Gen. Psychiatry 62, 1377–1384, http://dx.doi.org/10.1001/archpsyc.62.12.1377.

Kiecolt-Glaser, J.K., Gouin, J.P., Hantsoo, L., 2010. Close relationships, inflammation, and health. Neurosci. Biobehav. Rev. 35 (1), 33–38, http://dx.doi.org/10.1016/j.neubiorev.2009.09.003.

Kirschbaum, C., Pirke, K.M., Hellhammer, D.H., 1993. The 'Trier Social Stress Test'–a tool for investigating psychobiological stress responses in a laboratory setting. Neuropsychobiology 28 (1–2), 76–81, 119004.

Krygier, J.R., Heathers, J.A.J., Shahrestani, S., Abbott, M., Gross, J.J., Kemp, A.H.1, 2013. Mindfulness meditation, well-being, and heart rate variability: a preliminary investigation into the impact of intensive Vipassana meditation. Int. J. Psychophysiol. 89, 305–313, http://dx.doi.org/10.1016/j.ijpsycho.2013.06.017.

Leon, G.R., Finn, S.E., Murray, D., Bailey, J.M., 1988. Inability to predict cardiovascular disease from hostility scores or MMPI items related to Type A behavior. J. Consult. Clin. Psychol. 56 (4), 597–600, http://dx.doi.org/10.1037/0022-006X.56.4.597.

Lin, I.M., Fan, S.Y., Lu, H.C., Lin, T.H., Chu, C.S., Kuo, H., Lee, F., C.S, Lu, Y.H., 2015. Randomized controlled trial of heart rate variability biofeedback in cardiac autonomic and hostility among patients with coronary artery disease. Behav. Res. Ther. 70, 38–46, http://dx.doi.org/10.1016/j.brat.2015.05.001.

Malik, M., 1996. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation 93 (5), 1043–1065, http://dx.doi.org/10.1161/01.CIR.93.5.1043.

Mauss, I.B., Gross, J.J., 2004. Emotion suppression and cardiovascular disease: is hiding feelings bad for your heart? In: Nyklicek, I., Vingerhoets, A., Temoshok, L. (Eds.), The Expression of Emotion and Health: Advances in Theory, Assessment, and Clinical Applications. New York: Brunner-Routledge, New York, pp. 62–81.

McEwen, B.S., Biron, C.A., Brunson, K.W., Bulloch, K., Chambers, W.H., Dhabhar, F.S., Goldfarb, R.H., Kitson, R.P., Miller, A.H., Spencer, R.L., Weiss, J.M., 1997. The role of adrenocorticoids as modulators of immune function in health and disease: neural, endocrine, and immune interaction. Brain Res. Rev. 23 (1–2), 79–133, http://dx.doi.org/10.1016/S0165-0173(96)00012-4.

Miller, A.H., Raison, C.L.1, 2016. The role of inflammation in depression: from evolutionary imperative to modern treatment target. Nat. Rev. Immunol. 16, 22–34, http://dx.doi.org/10.1038/nri.2015.5.

Miller, T.Q., Smith, T.W., Turner, C.W., Guijarro, M.L., Hallett, A.J., 1996. A meta-analytic review of research on hostility and physical health. Psychol. Bull. 119 (2), 322–348, http://dx.doi.org/10.1037/0033-2909.119.2.322.

Newman, J.D., Davidson, K.W., Shaffer, J.A., Schwartz, J.E., Chaplin, W., Kirkland, S., Shimbo, D., 2011. Observed hostility and the risk of incident ischemic heart disease: a prospective population study from the 1995 Canadian Nova Scotia Health Study. J. Am. Coll. Cardiol. 58 (12), 1222–1228, http://dx.doi.org/10.1016/j.jacc.2011.04.044.

Quax, R.A., Manenschijn, L., Koper, J.W., Hazes, J.M., Lamberts, S.W.J., van Rossum, E.F.C., Feelders, R.A., 2013. Glucocorticoid sensitivity in health and disease. Nat. Rev. Endocrinol. 9, 670–686, http://dx.doi.org/10.1038/nrendo.2013.183.

Segerstrom, S.C., Nes, L.S., 2007. Heart rate variability reflects self-regulatory strength, effort, and fatigue. Psychol. Sci. 18 (3), 275–281, http://dx.doi.org/10.1111/j.1467-9280.2007.01888.x.

Thayer, J.F., Lane, R.D., 2009. Claude Bernard and the heart-brain connection: further elaboration of a model of neurovisceral integration. Neurosci. Biobehav. Rev. 33 (2), 81–88, http://dx.doi.org/10.1016/j.neubiorev.2008.08.004.

Thayer, J.F., Yamamoto, S.S., Brosschot, J.F., 2010. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. Int. J. Cardiol. 141 (2), 122–131, http://dx.doi.org/10.1016/j.ijcard.2009.09.543.

Weidner, G., Friend, R., Ficarrotto, T.J., Mendell, N.R., 1989. Hostility and cardiovascular reactivity to stress in women and men. Psychosom. Med. 51 (1), 36–45.

Young, E.A., Carlson, N.E., Brown, M.B., 2001. Twenty-four-hour ACTH and cortisol pulsatility in depressed women. Neuropsychopharmacology 25 (2), 264–276, http://dx.doi.org/10.1016/S0893-133X(00)00236-0.