Adverse childhood experiences and autonomic regulation in response to acute stress: the role of the sympathetic and parasympathetic nervous systems

Katja Winzeler[a,b], Annette Voellmin[a,b], Evelin Hug[a,b], Ursula Kirmse[c], Simone Helmig[a], Mary Princip[d], Christian Cajochen[e], Klaus Bader[a] and Frank H. Wilhelm[f]

[a]Center for Specific Psychotherapy, CBT Unit, Psychiatric Hospital of the University of Basel, Basel, Switzerland; [b]Department of Psychology, Division of Clinical Psychology and Psychotherapy, University of Basel, Basel, Switzerland; [c]Department of Psychology, Division of General and Biological Psychology, University of Konstanz, Konstanz, Germany; [d]Department of Medicine, Division of Clinical Science, University of Bern, Inselspital, Bern, Switzerland; [e]Center for Chronobiology, Psychiatric Hospital of the University of Basel, Basel, Switzerland; [f]Department of Psychology, Division of Clinical Psychology, Psychotherapy, & Health Psychology, University of Salzburg, Salzburg, Austria

ABSTRACT

Background and objectives: After a previous report demonstrated blunted heart rate (HR) reactivity in association with adverse childhood experiences (ACEs) [Voellmin, A., Winzeler, K., Hug, E., Wilhelm, F. H., Schaefer, V., Gaab, J., … Bader, K. (2015). Blunted endocrine and cardiovascular reactivity in young healthy women reporting a history of childhood adversity. *Psychoneuroendocrinology*, 51, 58–67. doi:10.1016/j.psyneuen.2014.09.008], the present analysis aimed at clarifying the role of the sympathetic and parasympathetic branches of the autonomic nervous system in this relationship.

Design and Methods: One hundred eighteen healthy young women provided data on ACEs and underwent psychosocial stress testing. Systolic blood pressure (SBP) and respiratory sinus arrhythmia (RSA, quantified by high-frequency HR variability) were assessed as measures of sympathetic and parasympathetic cardiovascular activity, respectively. A mediation model was calculated to test the indirect effects of ACEs on HR via SBP and RSA.

Results: The effect of ACEs on HR reactivity was mediated by SBP reactivity but not by RSA reactivity. ACEs were associated with reduced SBP at rest.

Conclusions: ACEs were associated with down-regulation in a measure of sympathetic but no alteration in a measure of parasympathetic cardiovascular stress reactivity in adulthood. Future research will need to clarify whether this indicates risk or resilience.

Early adversity has been associated with alterations of psychobiological stress systems and various adverse health outcomes (e.g., Gilbert et al., 2009; Miller, Chen, & Parker, 2011). In a recent study we found blunted endocrine (cortisol) and heart rate (HR) reactivity to a psychosocial stress task in association with adverse childhood experiences (ACEs) in healthy young women (Voellmin et al., 2015). Since HR is regulated by both sympathetic (increase) and parasympathetic (decrease) efferent activity of the autonomic nervous system (ANS), it remains unclear whether this blunted HR reactivity is caused by sympathetic hyporeactivity or deficient vagal withdrawal, or a combination of both (Berntson, Cacioppo, & Quigley, 1991). Thus, the present secondary, follow-up analysis aimed at

clarifying the role of sympathetic (indexed by systolic blood pressure, SBP) and parasympathetic (indexed by respiratory sinus arrhythmia, RSA) branches of the ANS in mediating the effect of ACEs on blunted HR reactivity to psychosocial stress.

Changes in the functioning of stress response systems due to repeated or long-lasting ACEs or trauma have been suggested to be the cause for higher vulnerability to stress-related disorders (e.g., Felitti et al., 1998; Wegman & Stetler, 2009). Current models assume that ACEs have the potential to alter patterns of endocrine and autonomic discharge in the long-term by disturbing efficient central nervous system regulation and adaptation in response to stress, thereby creating a state of allostatic load (cf. reviews by Chrousos & Gold, 1992; Lovallo, 2011; McEwen, 1998; McEwen, 2016). Theoretical considerations and initial evidence suggest that allostatic load can take either the direction of failure to shut off the stress response and a resulting chronic hyperactivity but also the direction of failure to mobilize a full response and a resulting blunted pattern (Lovallo, 2011; McEwen, 1998).

Since a stress response in HR and other peripheral organismic functions is often comprised of both, sympathetic activation and parasympathetic withdrawal, both branches of the ANS may play a role in regulating stress-induced arousal (Berntson et al., 1991). Sufficient blood supply to muscles and other organs during stress responding is assured by up-regulation of blood pressure. Particularly SBP is known to be regulated almost exclusively by the sympatho-adrenal axis via beta-adrenergic receptors and thus constitutes a putative index of sympathetic cardiovascular activity (Obrist, 1976, 1981; Silvestrini & Gendolla, 2011). On the other hand, RSA, referring to the rhythmic oscillation of HR linked to the phases of the respiratory cycle, indicates efferent activity of the parasympathetic nervous system (PNS) innervating the heart, or cardiac vagal control (Berntson et al., 1997; Grossman, Stemmler, & Meinhardt, 1990).

Elevated tonic sympathetic activity during resting baselines has been found in non-clinical samples in association with adversity in some studies (Paulus, Argo, & Egge, 2013; Su et al., 2014) while others have found no such differences (Leitzke, Hilt, & Pollak, 2015; Lovallo, Farag, Sorocco, Cohoon, & Vincent, 2012). Regarding stress reactivity in healthy populations in association with various psychosocial factors (including life events and childhood maltreatment), Chida and Hamer (2008) provide an extensive review. Regarding sympathetic nervous system (SNS) reactivity and ACEs in particular, there is support for both, heightened reactivity (Oosterman, de Schipper, Fisher, Dozier, & Schuengel, 2010; Otte et al., 2005) and blunted reactivity (e.g., Ginty, Masters, Nelson, Kaye, & Conklin, 2016; Leitzke et al., 2015; Lovallo et al., 2012; Murali & Chen, 2005; see also review by Lovallo, 2013). Blunted SBP was found in association with maltreatment and violence exposure (Leitzke et al., 2015; Murali & Chen, 2005). A large study by Lovallo et al. (2012) showed diminished HR reactivity with increasing ACEs; however, the study did not include more direct measures of SNS and PNS reactivity.

Concerning adversity and PNS there is evidence for lower tonic RSA in non-clinical samples in association with ACEs (Dale et al., 2009; Miskovic, Schmidt, Georgiades, Boyle, & MacMillan, 2009). Concerning RSA withdrawal in response to psychosocial stress, blunted RSA stress reactivity or reduced recovery in the context of adversity has been found in non-clinical samples (Arditi-Babchuk, Feldman, & Gilboa-Schechtman, 2009; Dale et al., 2009). Still, others found no differences in RSA baseline or reactivity in association with ACEs (Shenk, Putnam, Rausch, Peugh, & Noll, 2014; van Ockenburg et al., 2015).

Some of the divergent findings may be due to the fact that studies differ regarding sample characteristics, age groups, type of adversity, and stress tasks used. Further, some of the inconsistencies might be the result of inadequate adjustment for confounding factors such as respiratory rate (RR), known to influence vagal measures (Grossman & Taylor, 2007). To our knowledge, no study has examined the association between both, sympathetic and parasympathetic cardiovascular stress responsivity, HR, and ACEs in otherwise healthy young adults in the same analysis.

In accordance with the study by Lovallo et al. (2012), a recent study from our research group found blunted HR stress response in association with ACEs in healthy young women (Voellmin et al., 2015).

However, these two studies do not allow drawing conclusions about relative contributions of the SNS and PNS in blunting HR response during stress. Therefore, the present follow-up analysis aimed at exploring the role of the SNS and PNS in our previous findings using a mediation model and additional measures. We expected that participants with higher number of ACEs would show either blunted sympathetic (in terms of SBP) response or less parasympathetic (in terms of RSA) withdrawal, or both, in response to a psychosocial stress task and that either SBP or RSA reactivity, or both, would mediate the relationship between ACEs and HR reactivity. Additionally, we examined the relationship of ACEs with resting baseline levels of SBP, RSA, and HR in a similar mediational model.

Method

Participants

Data for the present analysis were collected in the context of a larger study investigating acute stress, emotion regulation, and sleep. The sample included 146 young and physically as well as mentally healthy women (mean age 21.7 ± 1.7 years) who were recruited at three schools for health care professions and social work in Basel, Switzerland. Exclusion criteria for all participants included current physical or psychiatric illness, pregnancy, regular heavy tobacco use (> 5 cigarettes a day), consumption of illegal drugs, and the use of any medication interfering with the ANS or the adrenocorticoid system. Participants provided written informed consent prior to participation and received monetary compensation of 150 CHF for their participation. The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee Basel. While all of the 146 participants completed the study, acute respiratory illness during the laboratory session as well as technical difficulties with the data acquisition system and technical failure of the respiration sensors (i.e., data missing completely at random) resulted in a final sample of 118 participants for whom all relevant physiological data for the current analysis were available.

Procedure

All appointments took place in the laboratory of the cognitive-behavioural therapy outpatient clinic of the Psychiatric Hospital of the University of Basel, Switzerland. Exclusion criteria and information on ACEs were assessed during a first appointment while at the second appointment, participants reported to the laboratory for the stress examination. They were told that the laboratory assessment would include a test on cognitive performance.

Upon arrival, participants were seated in a comfortable chair, approximately 1 m in front of a 22-inch computer screen. After attachment of all sensors for psychophysiological measures and a 10-minute accommodation period, a resting baseline measurement was conducted for five minutes. Participants then engaged in the stress task, which was followed by a recovery period. At the end of the laboratory testing, participants were debriefed and the nature and goals of the preceding stress induction task were fully disclosed.

Stress induction

The Montreal Imaging Stress Task (MIST; Dedovic et al., 2005) is a standardized computer-supported psychosocial stress task and consists of a series of arithmetic challenges, combined with social-evaluative threat (for a detailed description, see Dedovic et al., 2005 and Voellmin et al., 2015). The task consists of three 4-minute stress periods with feedback of 2–3 minutes in between. In contrast to other often used psychosocial stress tasks, the MIST does not require vocalization during stress assessment. This ensures that respiratory pattern change due to speaking (steep, short inspiration, and long expiration, Wilhelm, Handke, & Roth, 2003) cannot interfere with RSA assessment.

Physiological measures

SBP was assessed using an automatic cuff inflation blood pressure device (Aponorm Basis Control, Germany) that was activated to provide discrete measurements during the last minute of baseline and about 30 seconds after the start of each stress period.

ECG and respiratory data were sampled continuously at 1024 Hz using Vitaport 3 (TEMEC Instruments B.V., The Netherlands). Data reduction and artifact editing were performed using ANSLAB (Blechert, Peyk, Liedlgruber, and Wilhelm, 2015). ECG was acquired in a standard Lead II configuration using three Ag/AgCl electrodes (two active, one ground). R-waves were detected and converted to instantaneous interbeat interval (IBI) time series, which were resampled to 4 Hz using cubic-spline interpolation. All calculations are based on IBI rather than HR metrics due to its relative linearity in analyses of autonomic control (cf. Quigley & Berntson, 1996). To compute RSA, edited 4-Hz IBI time series were linearly detrended and power-spectral densities for each experimental period were computed within the 0.15–0.5 Hz frequency band using the Welch algorithm (Welch, 1967), which creates ensemble averages of successive periodograms (for details, see Blechert, Peyk, Liedlgruber, and Wilhelm, 2015). Resulting estimates were transformed by natural logarithm.

RR was assessed to account for its potential confounding influence on PNS change estimation by RSA in within-subject reactivity analyses (Grossman & Taylor, 2007). Respiration pattern was recorded using inductive plethysmography (Respiband, Ambulatory Monitoring Inc., Ardsley, NY) at the rib cage. Onsets of respiratory cycles were identified and instantaneous RR (in cycles per minute, cpm) was calculated as 60/cycle duration (in seconds).

For all variables, averages for baseline and the three stress periods were computed. Baseline-to-stress reactivity (Δ) scores were computed by subtracting baseline values from the mean of all three stress periods. Note that for ΔRSA, higher values represent less RSA withdrawal.

Psychological measures

ACEs before the age of 18 years were assessed with a German translation of the Early Trauma Inventory Self-Report questionnaire (ETI-SR, Bremner, Bolus, & Mayer, 2007), which includes 31 items on general trauma (e.g., natural disasters and death of close person), 9 items on physical abuse, 7 items on emotional abuse, and 15 items on sexual abuse. Events were summed up to a total score of occurred events (ACE total score). The ETI-SR has shown good internal consistency (Cronbach α = 0.78–0.90; 0.74 in the present sample) as well as validity in all trauma domains (Bremner et al., 2007).

Symptoms of depression were assessed with the German version of the Center for Epidemiological Studies Depression Scale (CES-D; German version: ADS-K, Hautzinger & Bailer, 1993), which is well-established and has shown high internal consistency (Cronbach α = 0.90) and test–retest reliability (r = 0.81). In order to obtain an index of physical fitness participants were asked to rate their degree of physical activity during a typical week.

Data analysis

Analyses were performed using IBM SPSS (version 23.0; SPSS, Chicago, IL). Prior to analysis, data were checked for outliers and ACE total score as well as RSA measures were transformed by natural logarithm to meet distributional assumptions.

Two mediation models were calculated using PROCESS Model 4 (Hayes, 2013) to test the indirect effects of ACEs on (1) baseline IBI via baseline SBP and baseline RSA and (2) ΔIBI via ΔSBP and ΔRSA. Unstandardized effects are reported. To qualify indirect effects, bias-corrected bootstrap confidence intervals based on 10,000 bootstrap samples are reported. Kappa^2 is reported as a measure of effect size with 0.01, 0.09, and 0.25 representing small, medium, and large effects, respectively (Preacher & Kelley, 2011).

Since PROCESS did not allow entering ΔRR as covariate specifically for ΔRSA, an adjusted ΔRSA measure (ΔRSA$_{adj}$) was obtained by calculating residuals from a linear regression relating ΔRR to ΔRSA ($r = -.275$, $p < .01$). Baseline RSA was not adjusted, as this is less useful for individual difference analyses (see Grossman & Kollai, 1993; Grossman & Taylor, 2007). There were no significant relationships between baseline or Δ scores of SBP, RSA, IBI, or ACEs and two other potentially confounding variables, depressive symptoms and physical fitness, and therefore they were not controlled for in the analyses.

Results

Sample characteristics for age, years of education, symptoms of depression, physical fitness, ACEs, IBI, SBP, RSA, RR, ΔIBI, ΔSBP, ΔRSA, ΔRR, are displayed in Table 1. Results from paired samples t-tests indicated that the stress task had high potency and induced significant increase in SBP ($t(117) = -22.51$, $p < .001$, $d = -2.07$) and RR ($t(117) = -2.89$, $p = .005$, $d = -0.27$) as well as decrease in IBI ($t(117) = 19.26$, $p < .001$, $d = 1.77$) and RSA ($t(117) = 9.03$, $p < .001$, $d = 0.83$).

Mediational analysis for baseline measures

In mediation analysis of the relationship between ACEs and baseline IBI via SBP and RSA (Figure 1(a)) no significant relationship of ACEs with IBI and thus no mediation was observed. Still, the analysis indicated a significant association between ACEs and SBP ($a_1 = -2.61$, $p = .025$), as well as between RSA and IBI ($b_2 = 75.17$, $p < .001$).

Mediational analysis for stress reactivity measures

As illustrated in Figure 1(b), mediation analysis confirmed that the total effect (without mediators) for ACEs on ΔIBI was highly significant ($c = 48.91$, $p = .002$) (cf. Voellmin et al.,

Table 1. Means (SD) of sample characteristics, ACE scores, and physiological measures during baseline and in response to stress (stress minus baseline reactivity scores) ($N = 118$).

	Mean	SD	Range
Age (years)	21.76	1.70	18–25
Education (years)[a]	12.53	1.43	9–17
Depressive symptoms	6.30	4.83	0–21
Physical fitness[b]	3.70	1.01	2–6
ACEs			
Total score (0–62)	3.99	3.55	0–18
General trauma (0–31)	2.14	2.07	0–10
Physical abuse (0–9)	0.89	1.02	0–5
Emotional abuse (0–7)	0.55	1.16	0–6
Sexual abuse (0–15)	0.41	0.77	0–4
IBI (ms)			
Baseline	858.69	111.06	556.14–1115.72
Reactivity	−209.05	117.92	−526.09–11.40
SBP (mmHg)			
Baseline	111.14	8.62	93.00–136.00
Reactivity	17.57	8.48	−7.67–35.00
RSA (ln ms^2)			
Baseline	7.77	1.01	4.64–10.23
Reactivity	−1.12	1.35	−5.31–0.91
RR (cpm)			
Baseline	19.44	3.21	8.72–28.27
Reactivity	0.89	3.35	−6.94–9.78

Notes: ACEs: adverse childhood experiences from ETI-SR; IBI: interbeat interval; SBP: systolic blood pressure; RSA: respiratory sinus arrhythmia; RR: respiratory rate. Depressive symptoms from the German version of the CES-D Scale.
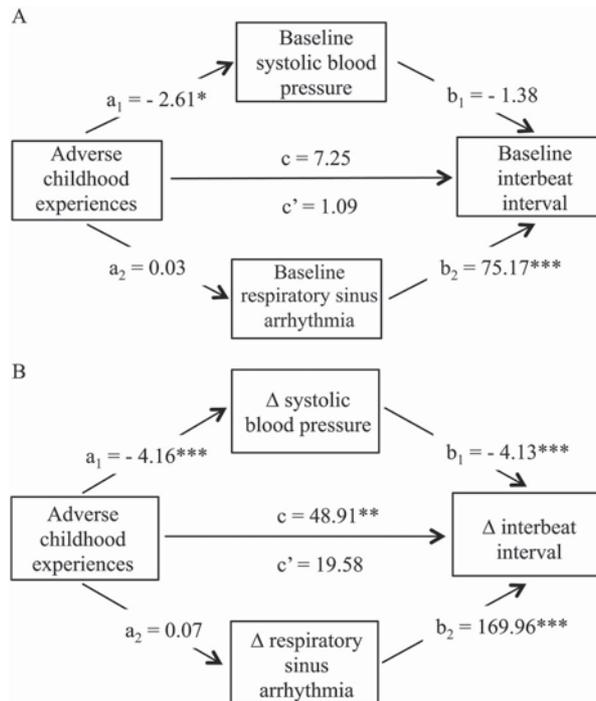[a]$n = 109$, [b]$n = 108$.

Figure 1. (a) Resting baseline model: jointly considered mediations for the relationship between ACEs and IBI by the two mediators SBP and RSA, using baseline scores. This analysis confirms no significant relationship between ACEs and IBI and thus no mediation (see text for details) and (b) stress reactivity model: jointly considered mediations for the relationship between ACEs and IBI by the two mediators SBP and RSA, using reactivity scores. This analysis confirms a significant and full mediation for SBP and no mediational role for RSA. ACEs: adverse childhood experiences from ETI-SR; IBI: interbeat interval; SBP: systolic blood pressure; RSA: respiratory sinus arrhythmia; c: total effect. $*p < .05$, $**p < .01$, $***p < .001$; $N = 118$.

2015). The indirect effect was statistically different from zero for ΔSBP ($a_1b_1 = 17.15$, 95% CI [8.27, 31.50], Sobel's $z = 2.84$, $p = .005$, $\kappa^2 = 0.155$, 95% CI [0.079, 0.257]), but not for ΔRSA$_{adj}$ ($a_2b_2 = 12.18$, 95% CI [−6.43, 33.24], Sobel's $z = 1.30$, $p = .195$, $\kappa^2 = 0.092$, 95% CI [0.005, 0.227]). The direct effect of ACEs on ΔIBI was not significant anymore when including the mediators in the model ($c' = 19.58$, $p = .085$). This indicates full mediation of the effect of ACEs on ΔIBI by ΔSBP and a lack of mediation by ΔRSA$_{adj}$. This mediation pattern was preserved when using unadjusted RSA in the analysis.

Discussion

The present study examined the relationship between ACEs, SBP, RSA, and IBI (a measure inversely related to HR) at baseline as well as in response to a psychosocial stress task using a mediation model. Results extend our previous finding of blunted HR reactivity in response to the stress task (Voellmin et al., 2015). Our results show full mediation of the effect of ACEs on IBI reactivity by SBP reactivity and no mediation by RSA reactivity. Importantly, SBP reactivity was blunted in association with higher numbers of ACEs, suggesting down-regulation of phasic sympathetic stress responses. No significant association was found between ACEs and RSA reactivity when controlling for RR changes, which indicates that blunted HR response was not appreciably influenced by alterations in parasympathetic functioning due to ACEs. A similar analysis for resting baseline did not reveal an effect of ACEs on IBI and thus no significant mediation for SBP or RSA.

The result of blunted SBP in association with ACEs is in accordance with the findings of Lovallo et al. (2012) and Leitzke et al. (2015), who reported blunted HR or SBP reactivity in their samples. Lovallo et al. (2012) explain their finding with altered functioning of stress systems towards a blunted response, and argue that deviations from the norm in either direction (exaggerated or diminished stress reactivity) might signal a system's loss of efficient allostatic regulation (see for review: Carroll, Lovallo, & Phillips, 2009; Gold & Chrousos, 2002; Lovallo, 2011). Leitzke et al. (2015) consider the possibility of useful adaptation as an explanation for their finding of blunted SBP reactivity in youth. They argue that an attenuated stress response might be adaptive in the context of repeated significant, but not overwhelming stress exposure because it reduces chronic activation, fearfulness, and psychophysiological activity to subsequent stressors (Gunnar, Frenn, Wewerka, & Van Ryzin, 2009; Leitzke et al., 2015). Similarly, the recently proposed adaptive calibration model (Del Giudice, Ellis, & Shirtcliff, 2011) postulates a nonlinear relation between exposure to adversity and stress response, with moderate stress environments leading to a buffered responsivity pattern. In our healthy sample, ACE scores were on the lower end of the continuum, which suggests that the dosage of stressful experiences in the high-ACE individuals was still low enough to promote development of stress resistance. Since such considerations are speculative without long-term health outcomes, only further research with prospective design can show whether blunted SNS stress response represents a beneficial adaptation or is a predictor of altered stress responsivity with long-term adverse health consequences. The adaptive calibration model is also in accordance with our finding of reduced baseline SBP in association with higher ACEs, since it includes both, lower basal SNS activity as well as lower SNS responsivity in a buffered stress response pattern. Still, our result is contrary to some findings of heightened SNS activity at rest in non-clinical samples (Paulus et al., 2013; Su et al., 2014).

No significant association was found between ACEs and RSA reactivity (and therefore no significant mediation effect for RSA) after controlling for the well-established confounding influence of within-individual changes in RR (Grossman & Taylor, 2007). This suggests that in our sample, change in parasympathetic functioning to stress did not appreciably depend on the number of ACEs and that the blunted HR reactivity previously found in relation to ACEs (Voellmin et al., 2015) was probably primarily due to reduced sympathetic reactivity. Also, no significant association was found between ACEs and RSA at baseline. Although there is evidence showing lower baseline RSA in association with adversity (Dale et al., 2009; Miskovic et al., 2009), our finding is in accordance with results from a representative sample of the Dutch population showing no differences in RSA measures at rest in the context of ACEs (van Ockenburg et al., 2015).

The present study has several limitations: we deliberately examined a homogenous sample of healthy young women in the context of our larger ongoing study about acute stress, emotion regulation, and sleep in young adults. This limits the ability to generalize the present results to male or higher-age populations as well as clinical samples. Nevertheless, our results are in accordance with findings of blunted blood pressure reactivity in samples with younger age, mixed gender, and mixed ethnicity (Leitzke et al., 2015; Lovallo et al., 2012). Our sample consisted of young women attending schools for health care professions, which may imply self-selection bias in the direction of more stress-resilient individuals. Participants with psychiatric diagnosis or physical pathology had been excluded and this may have restricted the range of ACEs and stress reactivity. Established measures of RSA have been criticized for being susceptible to changes in beta-adrenergic tone, thus not perfectly separating vagal from sympathetic influences (see e.g., Grossman & Taylor, 2007). Concerning the measurement of sympathetic reactivity, additional cardiovascular sympathetic indices, such as pre-ejection period would have been advantageous. Our recordings included only discrete blood pressure readings which limits information on cardiovascular dynamics (e.g., beat-to-beat cross-correlations including baroreflex sensitivity) that may be particularly important for assessing disturbance in the complex and integrated system of central and peripheral feedback loops likely affected by allostatic load (McEwen, 2016). In this respect, given that autonomic branches are not independent on a beat-by-beat level, the testing of causal pathways based on averages may have

led to over- or underestimations of autonomic effects, particularly since mediators (SBP, RSA) and outcome (HR) were estimated at the same time. Since the assessment of ACEs was based on retrospective self-report, effects of memory biases cannot be excluded. Still, retrospective recalls of sexual and physical abuse, as well as physical and emotional neglect, have been evaluated to be sufficiently valid (Hardt & Rutter, 2004).

Despite these limitations, the present study provides some incremental knowledge regarding the relationship between ACEs and the autonomic patterning of the cardiovascular stress response. Strengths of the study are its relatively large sample size and control for potentially confounding variables. The confinement of the sample to healthy young women allowed investigating the association between ACEs and stress response in a relatively homogenous non-clinical sample, free of psychiatric comorbidities and medications interfering with stress system assessment. Results extend our finding of blunted HR reactivity in response to a stress task in relation to elevated ACEs (Voellmin et al., 2015) by pointing to down-regulation of phasic sympathetic stress response in the absence of measureable alteration of parasympathetic functioning. Understanding the underlying mechanisms in alterations and partial failure of stress response systems may aid in targeting interventions for persons at risk. Future research may focus on prospective investigation of the relative contribution of sympathetic and parasympathetic regulation in the context of ACEs, which would help clarify whether blunted stress reactivity indicates a risk for negative health outcomes or might be a sign of resilience and beneficial brain adaptation (Belsky & Pluess, 2013; McEwen, 2016).

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

References

Arditi-Babchuk, H., Feldman, R., & Gilboa-Schechtman, E. (2009). Parasympathetic reactivity to recalled traumatic and pleasant events in trauma-exposed individuals. *Journal of Traumatic Stress*, *22*, 254–257. doi:10.1002/Jts.20417

Belsky, J., & Pluess, M. (2013). Beyond risk, resilience, and dysregulation: Phenotypic plasticity and human development. *Development and Psychopathology*, *25*, 1243–1261. doi:10.1017/S095457941300059X

Berntson, G. G., Bigger, J. T., Eckberg, D. L., Grossman, P., Kaufmann, P. G., Malik, M., … VanderMolen, M. W. (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology*, *34*, 623–648. doi:10.1111/j.1469-8986.1997.tb02140.x

Berntson, G. G., Cacioppo, J. T., & Quigley, K. S. (1991). Autonomic determinism – the modes of autonomic control, the doctrine of autonomic space, and the laws of autonomic constraint. *Psychological Review*, *98*, 459–487. doi:10.1037/0033-295x.98.4.459

Blechert, J., Peyk, P., Liedlgruber, M., & Wilhelm, F. H. (2015). ANSLAB: Integrated multi-channel peripheral biosignal processing in psychophysiological science. *Behavior Research Methods*. doi:10.3758/s13428-015-0665-1

Bremner, J. D., Bolus, R., & Mayer, E. A. (2007). Psychometric properties of the early trauma inventory-self report. *The Journal of Nervous and Mental Disease*, 195, 211–218. doi:10.1097/01.nmd.0000243824.84651.6c

Carroll, D., Lovallo, W. R., & Phillips, A. C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social and Personality Psychology Compass*, *3*, 725–743. doi:10.1111/j.1751-9004.2009.00205.x

Chida, Y., & Hamer, M. (2008). Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: A quantitative review of 30 years of investigations. *Psychological Bulletin*, *134*, 829–885. doi:10.1037/a0013342

Chrousos, G. P., & Gold, P. W. (1992). The concepts of stress and stress system disorders – overview of physical and behavioral homeostasis. *JAMA*, *267*, 1244–1252. doi:10.1001/jama.267.9.1244

Dale, L. P., Carroll, L. E., Galen, G., Hayes, J. A., Webb, K. W., & Porges, S. W. (2009). Abuse history is related to autonomic regulation to mild exercise and psychological wellbeing. *Applied Psychophysiology and Biofeedback*, *34*, 299–308. doi:10.1007/s10484-009-9111-4

Dedovic, K., Renwick, R., Mahani, N. K., Engert, V., Lupien, S. J., & Pruessner, J. C. (2005). The Montreal imaging stress task: Using functional imaging to investigate the effects of perceiving and processing psychosocial stress in the human brain. *Journal of Psychiatry & Neuroscience*, 30, 319–325. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1197276/

Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). The adaptive calibration model of stress responsivity. *Neuroscience and Biobehavioral Reviews*, 35, 1562–1592. doi:10.1016/j.neubiorev.2010.11.007

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., … Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults – the adverse childhood experiences (ACE) study. *American Journal of Preventive Medicine*, 14, 245–258. doi:10.1016/S0749-3797(98)00017-8

Gilbert, R., Widom, C. S., Browne, K., Fergusson, D., Webb, E., & Janson, S. (2009). Burden and consequences of child maltreatment in high-income countries. *Lancet*, 373, 68–81. doi:10.1016/S0140-6736(08)61706-7

Ginty, A. T., Masters, N. A., Nelson, E. B., Kaye, K. T., & Conklin, S. M. (2016). Cardiovascular reactions to psychological stress and abuse history: The role of occurrence, frequency, and type of abuse. *Anxiety, Stress, & Coping*. Advance online publication. doi:10.1080/10615806.2016.1210791

Gold, P. W., & Chrousos, G. P. (2002). Organization of the stress system and its dysregulation in melancholic and atypical depression: High vs low CRH/NE states. *Molecular Psychiatry*, 7, 254–275. doi:10.1038/sj/mp/4001032

Grossman, P., & Kollai, M. (1993). Respiratory sinus arrhythmia, cardiac vagal tone, and respiration – within-individual and between-individual relations. *Psychophysiology*, 30, 486–495. doi:10.1111/j.1469-8986.1993.tb02072.x

Grossman, P., Stemmler, G., & Meinhardt, E. (1990). Paced respiratory sinus arrhythmia as an index of cardiac parasympathetic tone during varying behavioral tasks. *Psychophysiology*, 27, 404–416. doi:10.1111/j.1469-8986.1990.tb02335.x

Grossman, P., & Taylor, E. W. (2007). Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and biobehavioral functions. *Biological Psychology*, 74, 263–285. doi:10.1016/j.biopsycho.2005.11.014

Gunnar, M. R., Frenn, K., Wewerka, S. S., & Van Ryzin, M. J. (2009). Moderate versus severe early life stress: Associations with stress reactivity and regulation in 10–12-year-old children. *Psychoneuroendocrinology*, 34, 62–75. doi:10.1016/j.psyneuen.2008.08.013

Hardt, J., & Rutter, M. (2004). Validity of adult retrospective reports of adverse childhood experiences: Review of the evidence. *Journal of Child Psychology and Psychiatry*, 45, 260–273. doi:10.1111/j.1469-7610.2004.00218.x

Hautzinger, M., & Bailer, M. (1993). *Allgemeine depressions-Skala (ADS): Manual*. Weinheim: Beltz Test.

Hayes, A. F. (2013). *Introduction to mediation, moderation, and conditional process analysis. A regression-based approach*. New York, NY: The Guilford Press.

Leitzke, B. T., Hilt, L. M., & Pollak, S. D. (2015). Maltreated youth display a blunted blood pressure response to an acute interpersonal stressor. *Journal of Clinical Child and Adolescent Psychology*, 44, 305–313. doi:10.1080/15374416.2013.848774

Lovallo, W. R. (2011). Do low levels of stress reactivity signal poor states of health? *Biological Psychology*, 86, 121–128. doi:10.1016/j.biopsycho.2010.01.006

Lovallo, W. R. (2013). Early life adversity reduces stress reactivity and enhances impulsive behavior: Implications for health behaviors. *International Journal of Psychophysiology*, 90, 8–16. doi:10.1016/j.ijpsycho.2012.10.006

Lovallo, W. R., Farag, N. H., Sorocco, K. H., Cohoon, A. J., & Vincent, A. S. (2012). Lifetime adversity leads to blunted stress axis reactivity: Studies from the Oklahoma family health patterns project. *Biological Psychiatry*, 71, 344–349. doi:10.1016/j.biopsych.2011.10.018

McEwen, B. S. (1998). Stress, adaptation, and disease – allostasis and allostatic load. *Neuroimmunomodulation*, 840, 33–44. doi:10.1111/j.1749-6632.1998.tb09546.x

McEwen, B. S. (2016). In pursuit of resilience: Stress, epigenetics, and brain plasticity. *Annals of the New York Academy of Sciences*, 1373, 56–64. doi:10.1111/nyas.13020

Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a model of behavioral and biological mechanisms. *Psychological Bulletin*, 137, 959–997. doi:10.1037/A0024768

Miskovic, V., Schmidt, L. A., Georgiades, K., Boyle, M., & MacMillan, H. L. (2009). Stability of resting frontal electroencephalogram (EEG) asymmetry and cardiac vagal tone in adolescent females exposed to child maltreatment. *Developmental Psychobiology*, 51, 474–487. doi:10.1002/Dev.20387

Murali, R., & Chen, E. (2005). Exposure to violence and cardiovascular and neuroendocrine measures in adolescents. *Annals of Behavioral Medicine*, 30, 155–163. doi:10.1207/s15324796abm3002_8

Obrist, P. A. (1976). The cardiovascular-behavioral interaction – as it appears today. *Psychophysiology*, 13, 95–107. doi:10.1111/j.1469-8986.1976.tb00081.x

Obrist, P. A. (1981). *Cardiovascular psychophysiology*. New York, NY: Plenum Press.

van Ockenburg, S. L., Tak, L. M., Bakker, S. J., Gans, R. O., de Jonge, P., & Rosmalen, J. G. (2015). Effects of adverse life events on heart rate variability, cortisol, and C-reactive protein. *Acta Psychiatrica Scandinavica*, 131, 40–50. doi:10.1111/acps.12286

Oosterman, M., de Schipper, J. C., Fisher, P., Dozier, M., & Schuengel, C. (2010). Autonomic reactivity in relation to attachment and early adversity among foster children. *Development and Psychopathology*, 22, 109–118. doi:10.1017/S0954579409990290

Otte, C., Neylan, T. C., Pole, N., Metzler, T., Best, S., Henn-Haase, C., … Marmar, C. R. (2005). Association between childhood trauma and catecholamine response to psychological stress in police academy recruits. *Biological Psychiatry*, *57*, 27–32. doi:10.1016/j.biopsych.2004.10.009

Paulus, E. J., Argo, T. R., & Egge, J. A. (2013). The impact of posttraumatic stress disorder on blood pressure and heart rate in a veteran population. *Journal of Traumatic Stress*, *26*, 169–172. doi:10.1002/Jts.21785

Preacher, K. J., & Kelley, K. (2011). Effect size measures for mediation models: Quantitative strategies for communicating indirect effects. *Psychological Methods*, *16*, 93–115. doi:10.1037/a0022658

Quigley, K. S., & Berntson, G. G. (1996). Autonomic interactions and chronotropic control of the heart: Heart period versus heart rate. *Psychophysiology*, *33*, 605–611. doi:10.1111/j.1469-8986.1996.tb02438.x

Shenk, C. E., Putnam, F. W., Rausch, J. R., Peugh, J. L., & Noll, J. G. (2014). A longitudinal study of several potential mediators of the relationship between child maltreatment and posttraumatic stress disorder symptoms. *Development and Psychopathology*, *26*, 81–91. doi:10.1017/S0954579413000916

Silvestrini, N., & Gendolla, G. H. (2011). Beta-adrenergic impact underlies the effect of mood and hedonic instrumentality on effort-related cardiovascular response. *Biological Psychology*, *87*, 209–217. doi:10.1016/j.biopsycho.2011.02.017

Su, S. Y., Wang, X. L., Kapuku, G. K., Treiber, F. A., Pollock, D. M., Harshfield, G. A., … Pollock, J. S. (2014). Adverse childhood experiences are associated with detrimental hemodynamics and elevated circulating endothelin-1 in adolescents and young adults. *Hypertension*, *64*, 201–207. doi:10.1161/Hypertensionaha.113.02755

Voellmin, A., Winzeler, K., Hug, E., Wilhelm, F. H., Schaefer, V., Gaab, J., … Bader, K. (2015). Blunted endocrine and cardiovascular reactivity in young healthy women reporting a history of childhood adversity. *Psychoneuroendocrinology*, *51*, 58–67. doi:10.1016/j.psyneuen.2014.09.008

Wegman, H. L., & Stetler, C. (2009). A meta-analytic review of the effects of childhood abuse on medical outcomes in adulthood. *Psychosomatic Medicine*, *71*, 805–812. doi:10.1097/Psy.0b013e3181bb2b46

Welch, P. D. (1967). Use of fast Fourier transform for estimation of power spectra – a method based on time averaging over short modified periodograms. *IEEE Transactions on Audio and Electroacoustics*, *15*(2), 70–73. doi:10.1109/Tau.1967.1161901

Wilhelm, F. H., Handke, E. M., & Roth, W. T. (2003). Detection of speaking with a new respiratory inductive plethysmography system. *Biomedical Sciences Instrumentation*, *39*, 136–141. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12724882