

Brindle, R., Whittaker, A., Bibbey, A., Carroll, D. and Ginty, A. (2016) 'Exploring the possible mechanisms of blunted cardiac reactivity to acute psychological stress', *International Journal of Psychophysiology*, 113, pp. 1-7

DOI: <https://doi.org/10.1016/j.ijpsycho.2016.12.011>

This document is the authors' Accepted Manuscript.

License: <https://creativecommons.org/licenses/by-nc-nd/4.0>

Available from RADAR: <https://radar.brookes.ac.uk/radar/items/41820703-a6c6-450a-b8ca-983129008465/1/>

Copyright © and Moral Rights are retained by the author(s) and/ or other copyright owners unless otherwise waved in a license stated or linked to above. A copy can be downloaded for personal non-commercial research or study, without prior permission or charge. This item cannot be reproduced or quoted extensively from without first obtaining permission in writing from the copyright holder(s). The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the copyright holders.

Exploring the possible mechanisms of blunted cardiac reactivity to acute psychological stress

RUNNING HEAD: ORIGIN OF BLUNTED STRESS REACTIVITY

Ryan C. Brindle¹, Anna C. Phillips², Adam Bibbey³, Douglas Carroll², Annie T. Ginty⁴

¹Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

²School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, United Kingdom

³Department of Sport and Health Sciences, Oxford Brookes University, Oxford, United Kingdom

⁴Department of Psychology and Neuroscience, Baylor University, Waco, Texas, USA

Address correspondence to:

Ryan C. Brindle, Department of Psychiatry, University of Pittsburgh School of Medicine

3811 O'Hara Street, Pittsburgh, Pennsylvania, USA 15213

Email: BrindleRC@upmc.edu

Word Count: 4222

Abstract

Blunted cardiovascular reactivity to acute psychological stress has been linked to a range of adverse health and behavioral outcomes. However, the origins of blunted reactivity remain unclear. The current study aimed to explore the following possibilities: different appraisals of task stressfulness and/or difficulty, diminished task effort, or reduced physiological capacity to respond. Individuals characterized, via pre-screening, as blunted ($n = 17$) or exaggerated ($n = 16$) heart rate (HR) reactors to acute psychological stress (socially evaluative mental arithmetic) were exposed to a psychological stress, cold pressor and exercise tasks during a follow-up testing session while HR and blood pressure (BP) were measured. At follow-up, groups again mounted significantly different HR reactions to psychological stress, despite reporting similar levels of subjective stress and difficulty, and achieving similar tasks scores (measure of task effort) at both testing sessions. In response to the cold pressor and exercise blunted and exaggerated reactors displayed similar HR and BP responses. Results indicated that blunted reactors do not differ from exaggerated reactors on appraisals of task stressfulness or difficulty, or objective task effort, and do possess the physiological capacity to respond to other laboratory challenges. Other sources of blunted stress reactivity remain to be explored.

Keywords: Stress, Cardiovascular Reactivity, Perceptions, Blunted, Exaggerated

1. Introduction

Blunted cardiovascular stress reactivity refers to an objectively measured cardiovascular response to acute laboratory stress that is comparatively lower than typically observed. This reaction profile has received increasing research attention over the last decade as it has been shown to relate to a range of adverse health and behavioural outcomes. For example, blunted stress reactivity has been linked cross-sectionally and prospectively to increased depressive symptomatology (Carroll, Phillips, Hunt, & Der, 2007; de Rooij, Schene, Phillips, & Roseboom, 2010a; Phillips, Hunt, Der, & Carroll, 2011; Phillips, 2011; Salomon, Clift, Karlsdóttir, & Rottenberg, 2009; Salomon, Bylsma, White, Panaite, & Rottenberg, 2013; York, Hassan, Li, Li, Fillingim, & Sheps, 2007), obesity (Carroll, Phillips, & Der, 2008; Phillips, Roseboom, Carroll, & de Rooij, 2012), poor cognition, (Gao, Borlam, & Zhang, 2015; Ginty, Phillips, Der, Deary, & Carroll, 2011a,b; Ginty, Phillips, Roseboom, Carroll, & de Rooij, 2012a; Yano et al., 2016) and poor self-reported health (de Rooij & Roseboom, 2010b; Phillips, Der, & Carroll, 2009). Also, individuals characterized by disordered eating (Ginty, Phillips, Higgs, Heaney, & Carroll, 2012b; Koo-Loeb, Pedersen, & Girdler, 1998), exercise dependence (Heaney, Ginty, Carroll, & Phillips, 2011), and substance abuse (al'Absi, Hatsukami, & Davis, 2005; Lovallo, Dickensheets, Myers, Thomas, & Nixon, 2000; Panknin, Dickensheets, Nixon, & Lovallo, 2002; Sorocco, Lovallo, Vincent, & Collins, 2006) have also been shown to display blunted stress reactions. Consequently, blunted reactivity has, to some extent, taken on an identity as a biomarker for these conditions and behaviors. However, although the correlates of blunted stress reactivity have been extensively reported, the mechanisms underlying blunted cardiovascular stress reactions remain unexplored (Phillips, Ginty, & Hughes, 2013).

One possibility relates to task appraisal; blunted reactivity could potentially be the result of different subjective perceptions of stress or a reduced appraisal of task difficulty. Studies of life stress have reported that perceptions regarding the stressfulness of life events relate more strongly to cardiovascular reactivity than do actual number of life events (Carroll, Phillips, Ring, Der, & Hunt, 2005; Ginty & Conklin, 2011). Also, by biasing attention away from negative stimuli attenuated cardiovascular reactions have been achieved on subsequent stress exposures, suggesting an important role for stress perceptions in cardiovascular stress reactivity (Higgins & Hughes, 2012). Likewise, attenuated or exaggerated perceptions of task difficulty may serve to alter cardiovascular stress responses. In most, but not all studies (Willemsen, Ring, McKeever, & Carroll, 2000), an association between task difficulty and cardiovascular reactivity has been reported such that easy or overly challenging tasks result in diminished responses (Carroll, Turner, & Prasad, 1986a; Carroll, Turner, & Hellowell, 1986b; Richter, Friedrich, & Gendolla, 2008). However, some studies with tasks that were deemed neither too easy nor too challenging have failed to show significant differences in task difficulty ratings between groups characterized by different physiological responses (Ginty, et al., 2012b; Heaney et al., 2011). Consequently, it remains possible that individuals exhibiting blunted reactivity perceive less stress or perceive the acute laboratory stress tasks as too easy or overly burdening compared to exaggerated responders.

Another possibility is that blunted stress responses result from reduced participant effort (e.g., participants do not exhibit a robust cardiovascular response because they are not engaging with the stress task). A key behavioral corollary of depression is a lack of motivation (Smith, 2013). In fact, the Met variant of the Val158Met COMT gene has been shown to relate to increased depression and decreased motivation (Åberg, Fandiño-Losada, Sjöholm, Forsell, &

Lavebratt, 2011), as well as blunted cardiac stress reactivity (Mueller, Strahler, Armbruster, Lesch, Brocke, & Kirschbaum, 2012), perhaps establishing a potential genetic origin for such behavior. However, studies that have attempted to control for individual differences in task effort using subjective engagement and objective performance scores have found that blunted stress reactions remain after controlling for these factors (Ginty, et al., 2012b; Heaney et al., 2011). Similarly, recent studies using objective markers of task effort (e.g., words/minute in a speech task, pupil diameter) have found reactivity to operate independently of task effort (Salomon et al., 2013; Salomon et al., 2015). Thus, it remains less likely that blunted reactivity results from low participant effort.

Finally, it may be that individuals who display blunted stress reactions simply do not have the physiological capacity to respond. Obese and depressed individuals, two populations that display blunted stress reactions, have been shown to exhibit autonomic dysfunction. For example, several reviews concerning obesity and sympathetic nervous system activity have consistently suggested that obesity is related to basal sympathetic nervous system upregulation and decreased sympathetic nervous system reactivity to pharmacological challenges (Davy & Orr, 2009; van Baak, 2001; Young & Macdonald, 1992). Further, experimentally induced weight gain and loss has been shown to lead to decreased and increased cardiac vagal tone, respectively (Aronne, Mackintosh, Rosenbaum, Liebel, & Hirsch, 1995, 1997), suggesting a relationship between weight and cardiac parasympathetic nervous system function. Similarly, depressed individuals also display upregulated sympathetic activity, indexed by circulating catecholamines (Carney, Freedland, & Veith, 2005), and downregulated cardiac vagal tone, indexed by decreased heart rate variability (Carney, et al., 2001). Consequently, these autonomic phenotypes coupled with a recent meta-analysis that showed heart rate and blood pressure

reactions to acute psychological stress are, to a large extent, driven by relatively equal amounts of cardiac vagal withdrawal and sympathetic activation (Brindle, Ginty, Phillips, & Carroll, 2014) might suggest that autonomic dysfunction in these populations precludes the ability of the cardiovascular system to respond when faced with a range of challenges.

The current study aimed to explore these three possible reasons for blunted stress reactivity: differential appraisals of stress or task difficulty, diminished participant effort, and reduced physiological capacity to respond. The first was examined by recording subjective appraisals of stressfulness and difficulty in response to an acute psychological stress task. Next, to probe participant mental effort during psychological stress, task score was recorded and used as an objective measure of task effort. Finally, to determine whether blunted reactors possess the physiological capacity to respond to a range of challenging tasks, cardiovascular responses of blunted and exaggerated mental stress reactors were also assessed during cold exposure and exercise-stress tasks. Based on previous evidence, it was hypothesized that, compared to exaggerated mental stress reactors, blunted reactors would report less subjective stress and either low or overly high ratings of task difficulty, achieve similar task scores, and mount a blunted cardiovascular response to cold exposure and exercise-stress tasks.

2. Method

2.1 Participants

Thirty-three healthy young adults were recruited from a larger screening study (see below for further details of the screening study). All participants were free from infection and refrained from alcohol and exercise for 12 hours, smoking and caffeine for 2 hours, and eating for 1 hour prior to testing. Several participants were taking medication (SSRIs ($n = 2$), daily asthma inhalers ($n = 1$), anti-epileptics ($n = 1$), and oral contraceptives ($n = 2$)). Results of sensitivity

analyses revealed that medication status had no effect on any of the study results so these participants were included in all analyses. All participants gave informed written consent, received £20 for participating, and ethical approval was granted from the University of Birmingham Research Ethics Committee.

2.2 Screening, Selection of Participants, and Mental Stress Task

Screening participants (N = 276) completed the Paced Auditory Serial Addition Test (PASAT; Gronwall, 1977), a socially evaluative mental arithmetic task that has been shown to reliably elicit significant cardiovascular responses (Mathias, Stanford, & Houston, 2004; Ring, Burns, & Carroll, 2002). After a standard 10-minute adaptation phase, the session consisted of three 10-minute phases during which participants were instructed to sit quietly for the baseline and recovery phases. During the stress phase, participants remained seated but were required to mentally sum consecutive single digit numbers, delivered via compact disk recording, and answer verbally while retaining the most recent number in memory in order to add it to the next integer presented. Prior to commencement, participants were told that they were being videotaped for body language analysis and that they needed to look at their face live on the television screen throughout the task. They were also told that their answers would be scored for accuracy. A researcher present in the participant's field of view actively scored performance and delivered brief bursts of aversive noise in response to incorrect answers, hesitation, or gazes not focused on the television screen. In reality, participants were not videotaped and a predetermined number of noise bursts was delivered on a standardized schedule coinciding with errors or pauses where possible. These manipulations served to enhance the stress task by adding a socially evaluative component. Participants started with 1000 points and lost 5 points for every wrong answer and unattempted question. The final score was calculated as an objective index of task

effort. Finally, a 6-point Likert-style scale anchored by *not at all* and *extremely*, was used to assess subjective ratings of task stressfulness and difficulty.

Throughout all phases, HR and BP were measured discontinuously every 2 minutes using a semi-automatic sphygmomanometer (Omron, Milton Keynes, UK) with the blood pressure cuff placed over the left brachial artery. Phase means were calculated and task reactivity was defined as the difference between the arithmetic means of the stress and baseline phases.

Overall, the screening PASAT was rated as stressful ($M (SD) = 4.17 (1.11)$) and there was an overall significant increase in HR, $F(1, 275) = 602.35, p < .001, \eta^2 = .687$, systolic blood pressure (SBP), $F(1, 275) = 1245.47, p < .001, \eta^2 = .819$, and diastolic blood pressure (DBP), $F(1, 275) = 1197.78, p < .001, \eta^2 = .813$. In the whole sample, $N = 276$, reactivity (mean, standard deviation) for HR, SBP, and DBP were 17.08 (11.56) bpm, 18.25 (8.59) mmHg, and 12.16 (5.84) mmHg, respectively. Extreme cardiac reactors for the current study were recruited from the highest and lowest 15% of the HR reactivity spectrum. Consequently, the average HR reactivity of the blunted reactor group ($n = 17$) was 2.27 (3.83) bpm, while average reactivity of the exaggerated reactors ($n = 16$) was 33.70 (10.32) bpm.

2.3 Follow-up Testing Procedure

The participants identified from screening as exaggerated or blunted HR reactors attended an additional laboratory session, on average 18.88 (range: 22.43) weeks, after screening. Similar to the screening procedure, participants were required to abstain from alcohol, exercise, smoking, caffeine, and eating prior to testing, and all self-reported that they did not have a current acute illness. After instrumentation, participants experienced a 10-minute adaptation period before task commencement. Participants then completed the same PASAT as in screening followed by a cold pressor task, sub-maximal exercise, and a sub-maximal VO_2

estimation task. The PASAT and cold pressor were counterbalanced while the submaximal exercise and sub-maximal VO_2 task remained in fixed order after the PASAT and cold pressor. Each task had individual baseline, tasks, and recovery phases. For the cold pressor task each phase was 4min whereas for the exercise task each phase lasted 5min.

2.4 Cold Pressor Task

Participants were required to sit quietly during baseline and recovery phases. During the stress phase, participants submerged their left foot in a water bath (10°C) for 4 minutes. These conditions were chosen so that an adequate amount of physiological data could be collected.

2.5 Sub-maximal Exercise Task

Participants sat quietly during baseline and recovery phases. During the stress phase, participants engaged in 5 minutes of steady state cycling at a workload of 50W (Ring, Harrison, Winzer, Carroll, Drayson, & Kendall, 2000).

2.6 Sub-maximal VO_2 Estimation Task.

The standardised bicycle YMCA protocol (Golding, Myers, & Sinning, 1989) was used to estimate maximal aerobic capacity, VO_2 . Briefly, starting at 50W, participants complete consecutive 3 min stages of increasing workload according to a standardised algorithm until 75% maximum HR is reached, defined as $220\text{bpm} - \text{age}$. Following completion, sex, age, weight, and the workload (in Watts) and HR associated with the final two stages undertaken by the participant were used to derive an estimated VO_2 max score. This protocol has been validated against various VO_2 max tests and been shown to accurately estimate aerobic capacity (Beekley, et al., 2004).

2.7 Cardiovascular Measures and Data Reduction

Heart rate was measured continuously during all task phases via three-lead electrocardiogram (ECG). Beat-to-beat SBP and DBP was measured during all tasks from the middle finger of the supported non-dominant hand using a Finapres system (Ohmeda 2300, Louisville, CO, USA). Finapres measures were corrected with absolute measurements taken using a semi-automatic sphygmomanometer and BP cuff placed over the brachial artery of the dominant arm. As the screening session used a brachial cuff to measure BP, correcting Finapres measures with brachial arm BP measures also served to facilitate comparison of reactivity across testing sessions. Measures of HR, SBP, and DBP were averaged for each task phase, and task reactivity for each task was defined as the arithmetic difference between stress and baseline phase means for each respective task.

2.8 Statistical Analyses

Differences in group characteristics were assessed using one-way analysis of variance (ANOVA) and chi-square. First, mixed (2: testing session x 2: group) ANOVAs were used to assess whether groups remained significantly different on HR reactivity at follow-up and if groups differed on performance or self-reported stress at either time point. Next, to compare blunted and exaggerated reactors on reactivity scores from the cold pressor and exercise tasks, to determine whether blunted reactors have the capacity to respond to stress tasks other than mental stress, multivariate ANOVAs (MANOVA) were used for each task grouping HR, SBP, and DBP reactivity scores. Significant effects of group were followed-up with one-way ANOVAs for each reactivity variable. Removal of one multivariate outlier from the blunted reactor group during analysis of exercise reactivity failed to change the results and was thus kept in the reported analyses; no multivariate outliers were emerged from cold pressor analyses. Finally, group differences in VO_2 max were analysed with one-way ANOVA. Small discrepancies in

degrees of freedom reflect occasional missing data due to technical error. Partial η^2 values are presented as measures of effect size, data are presented as mean (standard deviation) unless otherwise stated, and significance was operationalized as $p < .05$.

3. Results

3.1 Validation of Blunted and Exaggerated Responder Groups

Sixteen exaggerated cardiac reactors and 17 blunted cardiac reactors returned for follow-up testing. Blunted and exaggerated cardiac reactors did not differ in age, BMI, gender, or waist-hip ratio (Table 1). Analysis with mixed ANOVA revealed a significant main effects of testing session, $F(1, 31) = 29.53, p < .001, \eta^2 = .488$, and group, $F(1, 31) = 143.84, p < .001, \eta^2 = .823$, for HR reactivity. On average, HR reactivity was higher during the screening session and in the exaggerated group. A significant testing session x group interaction emerged, $F(1, 31) = 62.48, p < .001, \eta^2 = .668$. As expected, post-hoc analysis showed that exaggerated reactors, in both testing sessions, registered significantly higher HR reactivity scores compared to blunted reactors, despite HR reactivity significantly declining across sessions in the exaggerated group (Figure 1A). Critically, in neither testing session did baseline HR significantly differ across groups, $F(1, 31) = .446, p = .509, \eta^2 = .014$. For blood pressure, a main effect of time was found for both SBP, $F(1, 29) = 9.77, p = .004, \eta^2 = .252$, and DBP, $F(1, 29) = 12.35, p = .001, \eta^2 = .299$; reactivity during screening was higher than at follow-up. A significant main effect of group was found for SBP, $F(1, 29) = 14.74, p = .001, \eta^2 = .337$, while a marginally significant effect of group was found for DBP, $F(1, 29) = 3.44, p = .074, \eta^2 = .106$. In both cases exaggerated reactors displayed greater reactivity. No significant testing session x group interaction was found for either SBP or DBP (Figure 1B & C).

RUNNING HEAD: ORIGIN OF BLUNTED STRESS REACTIVITY

Table 1. Group Characteristics and PASAT Score and Appraisals

| | Blunted Reactors M(SD) N = 17 | Exaggerated Reactors M(SD) N = 16 | <i>p</i> | |
|----------------------------------|----------------------------------|--------------------------------------|-------------------------------|------------------|
| Age (years) | 20.35 (2.60) | 19.81 (1.05) | .44 | |
| BMI (kg/m ²) | 22.39 (2.74) | 23.46 (2.21) | .23 | |
| Waist to Hip Ratio | 0.79 (0.04) | 0.79 (0.05) | .83 | |
| Gender (% male) | 52.94 | 68.75 | .35 | |
| | Blunted Reactors M (SD) | | Exaggerated Reactors M(SD) | |
| | <u>Screening</u> | <u>Follow-up</u> | <u>Screening</u> | <u>Follow-up</u> |
| Subjective Stress, 0-10 scale | 6.74 (2.33) | 6.64 (1.1) | 7.54 (1.11) | 6.36 (1.60) |
| Subjective Difficulty, 0-6 scale | 4.12 (0.99) | 4.18 (0.81) | 4.06 (0.93) | 3.94 (0.83) |
| PASAT Score, max 1000 | 693.82 (167.80) | 718.82 (142.93) | 746.56 (147.54) | 770.31 (135.41) |

Note: No significant difference between groups on score, stress, or difficulty in either screening or follow-up testing sessions.

RUNNING HEAD: ORIGIN OF BLUNTED STRESS REACTIVITY

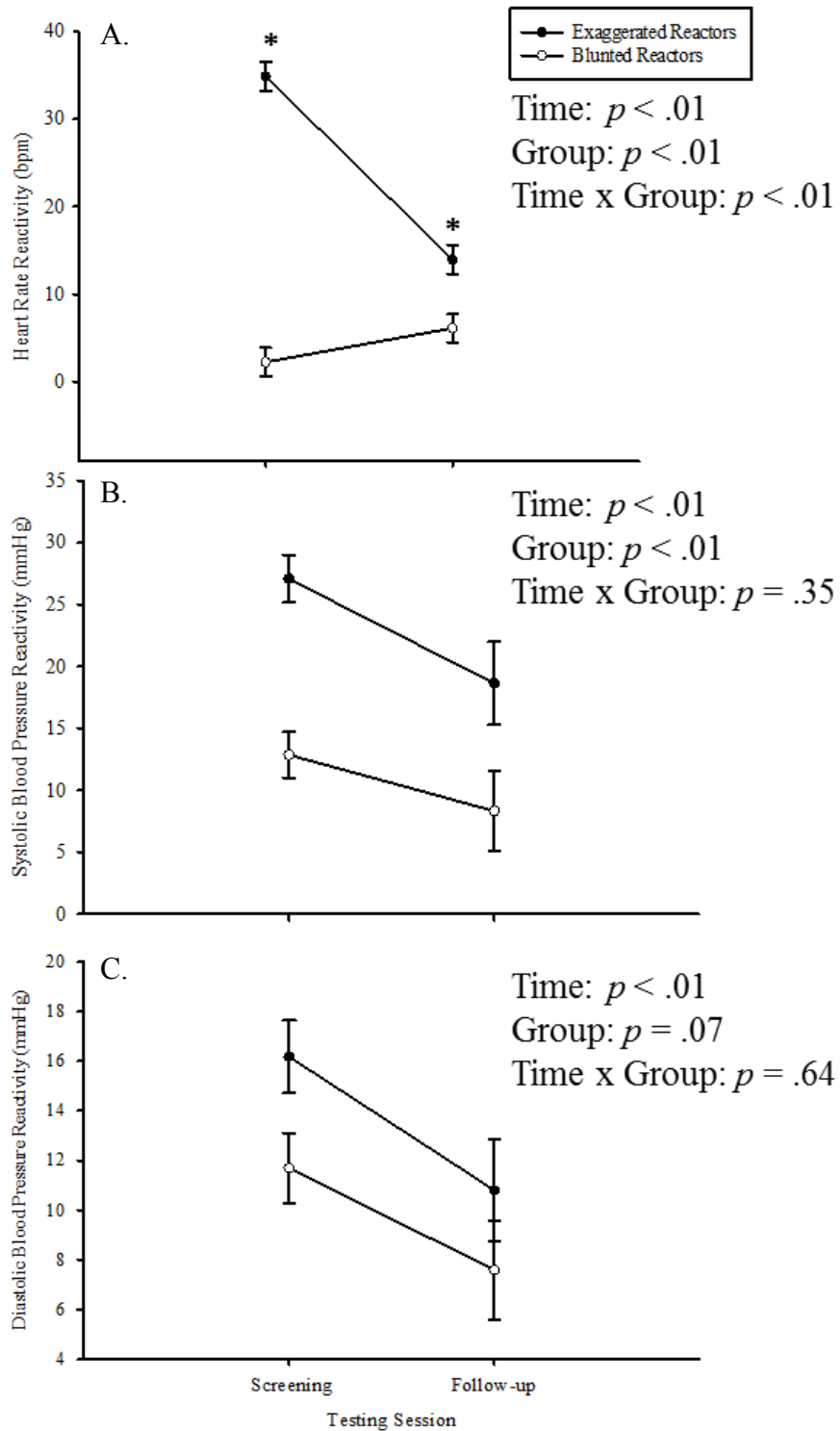


Figure 1. A. Heart rate, B. Systolic, and C. Diastolic blood pressure reactivity to mental stress across testing two consecutive sessions in blunted ($n = 17$) and exaggerated ($n = 16$) cardiac reactors. *indicates significant group difference, $p < .05$

3.2 Source 1: Different Appraisal of Stress Task

Mixed (2: testing session x 2: group) ANOVAs did not reveal any significant main effects of testing session or group, or testing session x group interaction for measures of subjective PASAT stressfulness (p range: 0.09-0.59) or difficulty (p range: 0.58-0.85; Table 1).

3.3 Source 2: Diminished Effort

No significant main effect of testing session or group was observed for PASAT score (p range: 0.09-0.31). Similarly, no significant testing session x group interaction emerged ($p = 0.96$); in both testing sessions no significant difference of PASAT score between groups was present (Table 1).

3.4 Source 3: Reduced Physiological Capacity to Respond

For illustrative purposes, reactivity change scores for each group to the cold pressor and exercise tasks are plotted in Figure 2. MANOVA failed to reveal a significant main effect of group for cold pressor, $F(3, 28) = .080, p = .970, \eta^2 = .009$, or exercise, $F(3, 28) = .547, p = .655, \eta^2 = .055$, reactivity; groups did not differ on HR, SBP, or DBP reactivity in either task. No significant group difference emerged for estimated VO2 max, $F(1, 28) = .012, p = .915, \eta^2 < .001$, (Figure 2).

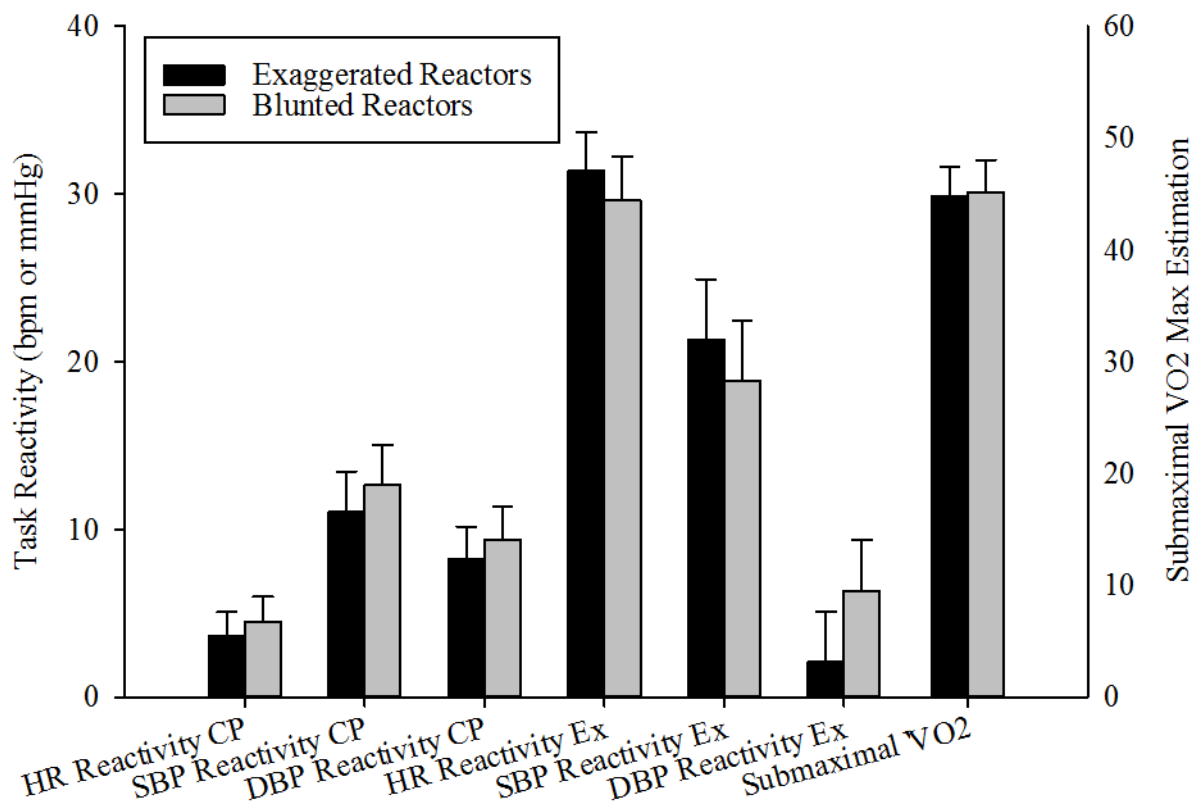


Figure 2. Cardiovascular reactivity values and submaximal VO₂ max in blunted (n = 17) and exaggerated (n = 16) cardiac reactors. No significant group differences emerged. CP = Cold Pressor Task, Ex = Exercise Task

4. Discussion

The present study aimed to empirically test three possible sources of blunted cardiac reactivity to acute psychological stress: deficient appraisals of task stressfulness and difficulty, diminished task effort, and a reduced physiological capacity to respond. Participants displaying extreme (i.e., blunted or exaggerated) HR responses to a standardized acute mental stress test were re-exposed to acute psychological stress, and also to cold pressor, and exercise tasks. At both testing sessions, groups did not differ on subjective appraisals of task stressfulness or difficulty. Similarly, groups appeared to exert the same amount of task effort at both testing sessions, indicated by similar psychological stress task scores. Finally, groups did not significantly differ on cardiovascular reactivity to either the cold pressor or exercise tasks. These data are consistent with the hypothesis that individuals displaying blunted cardiac stress reactivity do not differ from exaggerated reactors in task appraisals or effort and do have the physiological capacity to respond to challenging conditions.

From a psychological perspective it has been suggested that blunted stress reactions may originate from a differential task appraisal in favor of reduced awareness of stress. However, results of the current study do not support this source of blunted responding as groups did not differ on subjective measures of PASAT stressfulness or difficulty in either of the two testing sessions, yet in both sessions registered significantly differed cardiac responses. These results resonate with other studies that have failed to consistently demonstrate an association between perceived stress and reactivity (Allen, Batty, Dodd, & Young, 1985; Schwerdtfeger, 2004). Further, it has been reported that individuals with high levels of anxiety or depression appraise stress tasks as highly stressful yet exhibit blunted reactivity (de Rooij et al., 2010a; Duncko, Makatsori, Fickova, Selko, & Jezova, 2006; Salomon et al., 2009). Also, individuals high in

neuroticism or low on openness showed blunted cardiovascular and cortisol reactions to a battery of stress tasks despite rating them as more stressful (Bibbey, Carroll, Roseboom, Phillips, & de Rooij, 2013). Finally, a meta-analysis concluded that the influence of task-induced negative emotion on physiological reactivity was limited (e.g., small effects; Feldman, Cohen, Lepore, Matthews, Kamarck, & Marsland, 1999). Thus, given that blunted reactivity is observed alongside relatively normal or increased appraisals of stress, it would appear, then, that cardiovascular reactivity and stress appraisal operate, to some extent, independently (de Rooij et al., 2010a).

Diminished task effort has been suggested as a candidate source of blunted stress reactivity (Wright, Martin, & Bland, 2003). However, results from the current study do not support this notion as groups did not differ on objective PASAT score, a proxy measure of task effort, in either testing session. These results bolster initial reports that found that blunted reactions were independent of subjective effort and task score (Ginty et al., 2012b; Heaney et al., 2011). What is more, these results resonate with more recent studies that have objectively measured participant effort and found stress reactivity to be unrelated to measures of effort. For example, a study employing a speech task reported that, relative to controls, individuals with major depression exhibit blunted stress reactivity but failed to differ from control subjects on number of words used in the speech, number of prompts from the experimenter to continue speaking, or number of words signaling dysfluency (Salomon et al., 2013). In another study, pupil diameter reactivity, an accepted index of cognitive effort, and cardiovascular reactivity were measured in response to a digit span test and were found to be unrelated suggesting that task effort does not drive cardiovascular stress reactions (Salomon et al., 2015).

Finally, that blunted cardiac stress reactors responded no differently than exaggerated cardiac reactors to the cold pressor and exercise tasks and registered similar scores on the submaximal VO_2 test strongly suggest that blunted stress reactors do possess the capacity to respond physiologically to other challenging conditions and do not differ from exaggerated reactors in aerobic capacity. In other words, blunted stress reactivity is not the result of generally compromised physiological regulation. These data accord with those from other studies that appear to suggest that blunted stress reactivity manifests only in response to psychological stress tasks that require active coping. For example, in a study of individuals with varying levels of depressive symptomatology, symptom level predicted blunted stress reactivity in response to active (a speech task and viewing of the speech task performance) stressors, but not a passive (cold pressor) stressor (Schwerdtfeger & Rosenkaimer, 2011). In two other independent samples of clinically depressed participants, blunted stress responses were recorded in response to a speech task but effects pertaining to mirror tracing and cold pressor tasks were small to nonexistent (Salomon et al., 2009; Salomon et al., 2013).

In light of the present results the question still stands though: what is the origin of blunted stress reactivity? Several possibilities still exist. First, blunted stress reactivity may result from central motivational dysregulation; suboptimal functioning of the central nervous system substrates that support motivation and motivated behavior (Carroll, Lovallo, & Phillips, 2009; Carroll, Phillips, & Lovallo, 2011; Lovallo, 2011). Emerging evidence is supportive of this view as two studies comparing extreme blood pressure (Gianaros, May, Siegle, & Jennings, 2005) and cardiac reactors (Ginty, Gianaros, Derbyshire, Phillips, & Carroll, 2013) found that extreme reactors display disparate activation patterns in sub-regions of the cingulate cortex, insula, and amygdala while under mental stress. Second, titration of the cardiovascular response by some

other physiological system may manifest in a blunted response profile. For example, increases in cardiac output are can be accommodated, to a large extent, by inverse changes in vascular resistance (James, Gregg, Matyas, & Hughes, 2012). Thus, blunted reactors may simply be exhibiting a greater degree of compensation compared to other reactors. Similarly, Berntson and colleagues (1991, 1994) pointed out that the parasympathetic and sympathetic nervous systems do not lie on a continuous spectrum but are orthogonal. This makes possible a scenario whereby blunted reactors have dual activation of the parasympathetic and sympathetic nervous systems, which through antagonist action on each other produce a weak net reaction. In other words, from the perspective of the peripheral nervous system, blunted reactors may not be producing a blunted response *per se*. Nonetheless, these possibilities require empirical support and emphasize the need to assess reactivity using multivariate approaches across multiple physiological systems. Finally, emerging research concerning early childhood adversity is beginning to bring to light the possibility that blunted stress responses are a product of naturally selected adaptation processes. Although not all reports are consistent (Heim, et al., 2000; Leucken, 2000), both laboratory (Carpenter et al., 2007; MacMillan et al., 2009) and epidemiological (Lovallo, Farag, Sorocco, Cohoon, & Vincent, 2012) studies have demonstrated that individuals who report having experienced adverse childhood trauma display blunted cardiovascular and cortisol responses later in life. This is also consistent with cross-sectional evidence indirectly linking negative life events with blunted stress reactivity (Ginty, Masters, Nelson, Kaye, & Conklin, in press; Phillips, Carroll, Ring, Sweeting, West, 2005).

The current study is not without limitations. First, these data concern young healthy participants and although males and females were included in the study, generalizability to older adults remains to be determined. Second, it could be argued that the small sample size of each

group detracts from the results. However, extreme groups were obtained from an initially large sample (N = 276) and recruited for additional testing using a strict 15th percentile rule. Also, at follow-up, group differences in HR reactivity still remained suggesting that the sample size was large enough to detect group differences in cardiovascular reactions. Finally, recruiting extreme groups is not an uncommon research strategy (Gianaros et al., 2005; Ginty et al., 2013). Third it could be argued that individual differences in cardiac reactivity are not temporally stable.

However, results from the present study showed that groups remained significantly different on HR reactivity at follow-up, bolstering previous research that has shown individual differences in cardiovascular reactivity to be stable over years (Ginty et al., 2013; Hassellund, Flaa, Sandvik, Kjeldsen, & Rostrup, 2010; Kasprovicz, Manuck, Malkoff, & Krantz, 1990; Sherwood, Turner, Light, & Blumenthal, 1990)

In summary, this study examined possible sources of blunted cardiovascular reactions to acute psychological stress. Results indicated that individuals who exhibit blunted cardiac reactivity to psychological stress do indeed have the capacity to respond to other cardiovascular challenges, as evidenced by their normative responses to other non-mental stress tasks. In addition, blunted stress reactions did not appear to result from a lower level of perceived stress, decreased task effort, or deficient appraisal of task difficulty.

Acknowledgements

Annie Ginty was funded by an AXA Research Fund Postdoctoral Fellowship and HL07560 during data collection and write-up of this manuscript. Adam Bibbey was funded by a Doctoral Award from the Economic and Social Research Council, UK. Ryan Brindle was funded by a Doctoral Elite Scholarship from the University of Birmingham and is now supported by HL082610. The authors would like to thank all the undergraduate research assistants whom contributed to the screening study recruitment and testing.

References

- Åberg, E., Fandiño-Losada, A., Sjöholm, L.K., Forsell, Y, & Lavebratt, C. (2011). The functional Val¹⁵⁸Met polymorphism in catechol-O-methyltransferase (COMT) is associated with depression and motivation in men from a Swedish population-based study. *Journal of Affective Disorders, 129*, 158-166. doi: 10.1016/j.jad.2010.08.009
- al'Absi, M., Hatsukami, D., & Davis, G.L. (2005). Attenuated adrenocorticotrophic responses to psychological stress are associated with early smoking relapse. *Psychopharmacology, 181*, 107-117. doi: 10.1007/s/00213-005-2225-3
- Allen, P.I.M., Batty, K.A., Dodd, C.A.S., & Young, S.K. (1985). Dissociation between emotional and endocrine responses preceding an academic examination in male medical students. *Journal of Endocrinology, 107*, 163-170. doi: 10.1677/joe.0.1070163
- Aronne, L.J., Mackintosh, R., Rosenbaum, M., Leibel, R.L., & Hirsch, J. (1997). Cardiac autonomic nervous system activity in obese and never-obese young men. *Obesity Research, 5*, 354-359. doi: 10.1002/j.1550-8528.1997.tb00564.x
- Aronne, L.J., Mackintosh, R., Rosenbaum, M., Leibel, R.L., & Hirsch, J. (1995). Autonomic nervous system activity in weight gain and weight loss. *American Journal of Physiology, 269*, R222-R225.
- Beekley, M.D., Brechue, W.F., Dehoyos, D.V., Garzarella, L., Werber-Zion, G., Pollock, M.L. (2004). Cross-validation of the YMCA submaximal cycle ergometer test to predict VO₂max. *Research Quarterly for Exercise and Sport, 75*, 337-342. doi: 10.1080/02701367.2004.10609165. doi: 10.1080/02701367.2004.10609165
- Berntson, G.G., Cacioppo, J.T., Quigley, K.S., & Fabro, V.T. (1994). Autonomic space and psychophysiological response. *Psychophysiology, 31*, 44-61. doi: 10.1111/j.1469-8986.1994.tb01024.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
- Bibbey, A., Carroll, D., Roseboom, T.J., Phillips, A.C., & de Rooij, S.R. (2013). Personality and physiological reactions to acute psychological stress. *International Journal of Psychophysiology*, *90*, 28-36. doi: 10.1016/j.ijpsycho.2012.10.018.
- Brindle, R.C., Ginty, A.T., Phillips, A.C., & Carroll, D. (2014). A tale of two mechanisms: A meta-analytic approach toward understanding the autonomic basis of cardiovascular reactivity to acute psychological stress. *Psychophysiology*, *51*, 964-976. doi: 10.1111/psyp.12248
- Carpenter, L.L., Carvalho, J.P., Tyrka, A.R., Wier, L.M., Mello, A.F., Mello, M.F., et al. (2007). Decreased ACTH and cortisol responses to stress in healthy adults reporting significant childhood maltreatment. *Biological Psychiatry*, *15*, 1080-1087. doi: 10.1016/j.biopsych.2007.05.002
- Carney, R.M., Freedland, K.E., & Veith, R.C. (2005). Depression, the autonomic nervous system, and coronary heart disease. *Psychosomatic Medicine*, *67*, S29-S33. doi: 10.1097/01.psy.0000162254.61556.d5
- Carney, R.M., Blumenthal, J.A., Stein, P.K., Watkins, L., Catellier, D., Berkman, L.F., et al. (2001). Depression, heart rate variability, and acute myocardial infarction. *Circulation*, *104*, 2024-2028. doi: 10.1161/hc4201.097834
- Carroll, D., Phillips, A.C., & Lovallo, W.R. (2011). The behavioural and health corollaries of blunted physiological reactions to acute psychological stress: revising the reactivity hypothesis, in: Wright, R.A., Gendolla, G.H.E. (Eds.). *Motivation Perspectives of*

Cardiovascular Response. APA Press, Washington, DC, pp. 243-263. doi:

10.1037/13090-012

Carroll, D., Lovallo, W.R., & Phillips, A.C. (2009). Are large physiological reactions to acute psychological stress always bad for health? *Social Personality and Psychology*

Compass, 3, 725-743. doi: 10.1111/j.1751-9004.2009.00205.x

Carroll, D., Phillips, A.C., & Der, G. (2008). Body mass index, abdominal adiposity, obesity, and cardiovascular reactions to psychological stress in a large community sample.

Psychosomatic Medicine, 20, 653-660. doi: 10.1097/psy.0b013e31817b9382

Carroll, D., Phillips, A.C., Hunt, K., & Der, G. (2007). Symptoms of depression and cardiovascular reactions to acute psychological stress: Evidence from a population study.

Biological Psychology, 75, 68-74. doi: 10.1016/j.biopsycho.2006.12.002

Carroll, D., Phillips, A.C., Ring, C., Der, G., & Hunt, K. (2005). Life events and hemodynamic stress reactivity in the middle-aged and elderly. *Psychophysiology*, 42, 269-276. doi:

10.1111/j.1469-8986.2005.00252.x

Carroll, D., Turner, J.R., & Prasad, R. (1986a). The effects of level of difficulty of mental arithmetic challenge on heart rate and oxygen consumption. *International Journal of*

Psychophysiology, 4, 167-173. doi: 10.1016/0167-8760(86)90012-7

Carroll, D., Turner, J.R., & Hellawell, J.C. (1986b). Heart rate and oxygen consumption during active psychological challenge: The effects of level of difficulty. *Psychophysiology*, 23,

174-181. doi: 10.1111/j.1469-8986.1986.tb00613.x

Davy, K.P., & Orr, J.S. (2009). Sympathetic nervous system behavior in human obesity.

Neuroscience and Biobehavioral Reviews, 33, 116-124. doi:

10.1016/j.neubiorev.2008.05.024

- de Rooij, S.R., Schene, A.H., Phillips, D.I., & Roseboom, T.J. (2010a). Depression and anxiety: Associations with biological and perceived stress reactivity to psychological stress protocol in a middle-aged population. *Psychoneuroendocrinology*, *35*, 866-877. doi: 10.1016/j.psyneuen.2009.11.011
- de Rooij S.R. & Roseboom, T.J. (2010b). Further evidence for an association between self-reported health and cardiovascular as well as cortisol reactions to acute psychological stress. *Psychophysiology*, *47*, 1172-1175. doi: 10.1111/j.1469-8986.2010.01023.x
- Duncko, R., Makatsori, A., Fickova, E., Selko, D., & Jezova, D. (2006). Altered coordination of the neuroendocrine response during psychosocial stress in subjects with high trait anxiety. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *30*, 1058-1066. doi: 10.1016/j.pnpbp.2006.04.002.
- Feldman, P.J., Cohen, S., Lepore, S.J., Matthews, K.A., Kamarck, T.W., & Marsland, A.L. (1999). Negative emotions and acute psychological responses to stress. *Annals of Behavioral Medicine*, *21*, 216-222. doi: 10.1007/BF02884836
- Gao, Y., Borlam, D., & Zhang, W. (2015). The association between heart rate reactivity and fluid intelligence in children. *Biological Psychology*, *107*, 69-75. doi: 10.1016/j.biopsycho.2015.03.006
- Gianaros, P.J., May, C.J., Siegle, G.J., & Jennings, J.R. (2005). Is there a functional neural correlate of individual differences in cardiovascular reactivity? *Psychosomatic Medicine*, *67*, 31-39. doi: 10.1097/01.psy.0000151487.05506.dc
- Ginty, A.T., Masters, N.M., Nelson, E.B., Kaye, K., & Conklin, S.M. (in press). Cardiovascular reactions to psychological stress and abuse history: the role of occurrence, frequency, and type of abuse. *Anxiety, Stress, & Coping*.

- Ginty, A.T., Gianaros, P.J., Derbyshire, S.W., Phillips, A.C., & Carroll, D. (2013). Blunted cardiac stress reactivity relates to neural hypoactivation. *Psychophysiology*, *50*, 219-229. doi: 10.1111/psyp.12017
- Ginty, A.T., Phillips, A.C., Roseboom, T.J., Carroll, D., and de Rooij, S.R. (2012a). Cardiovascular and cortisol reactions to acute psychological stress and cognitive ability in Dutch Famine Birth Cohort Study. *Psychophysiology*, *49*, 391-400. doi: 10.1111/j.1469-8986.2011.01316.x
- Ginty, A.T., Phillips, A.C., Higgs, S., Heaney, J.L.J., & Carroll, D. (2012b). Disordered eating behavior is associated with blunted cortisol and cardiovascular reactions to acute psychological stress. *Psychoneuroendocrinology*, *37*, 715-724. doi: 10.1016/j.psyneuen.2011.09.004
- Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., and Carroll, D. (2011a). Cognitive ability and simple reaction time predict cardiac reactivity in the West of Scotland Twenty-08 Study. *Psychophysiology*, *48*, 1022-1027. doi: 10.1111/psyp.12617
- Ginty, A.T., Phillips, A.C., Der, G., Deary, I.J., Carroll, D. (2011b). Heart rate reactivity is associated with future cognitive ability and cognitive change in a large community sample. *International Journal of Psychophysiology*, *82*, 167-174.
- Ginty, A.T., & Conklin, S.M. (2011). High perceived stress in relation to life events is associated with blunted cardiac reactivity. *Biological Psychology*, *86*, 383-385. doi: 10.1016/j.ijpsycho.2011.08.004
- Golding, L.A., Myers, C.R., & Sinning, W.E. (1989). Y's ways to physical fitness. Champaign, IL. Human Kinetics Publishers, Inc.

- Gronwall, D.M.A. (1977). Paced auditory serial-addition task: A measure of recovery from concussion. *Perceptual and Motor Skills*, *44*, 367-373. doi: 10.2466/pms.1977.44.367
- Hassellund, S.S., Flaa, A., Sandvik, L., Kjeldsen, S.E., & Rostrup, M. (2010). Long-term stability of cardiovascular and catecholamine responses to stress tests: An 18-year follow-up study. *Hypertension*, *55*, 131-136.
- Heaney, J.L.J., Ginty, A.T., Carroll, D., & Phillips, A.C. (2011). Preliminary evidence that exercise dependence is associated with blunted cardiac and cortisol reactions to acute psychological stress. *International Journal of Psychophysiology*, *79*, 323-329. doi: 10.1016/j.ijpsycho.2010.11.010
- Heim, C., Newport, D.J., Heit, S., Graham, Y.P., Wilcox, M.M., Bonsall, R., et al. (2000). Pituitary-adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. *JAMA*, *284*, 592-597. doi: 10.1001/jama.284.5.592
- Higgins, N.M., & Hughes, B.M. (2012). Individual differences in the impact of attentional bias training on cardiovascular responses to stress in women. *Anxiety, Stress and Coping: An International Journal*, *25*, 381-395. doi: 10.1080/10615806.2011.616956
- James, J.E., Gregg, M.E., Matyas, T.A., & Hughes, B.M. (2012). Stress reactivity and the hemodynamic profile-compensation deficit (HP-CD) model of blood pressure regulation. *Biological Psychology*, *90*, 161-170. doi: 10.1016/j.biopsycho.2012.02.021
- Kasprowicz, A.L., Manuck, S.B., Malkoff, S.B., & Krantz, D.S. (1990). Individual differences in behaviourally evoked cardiovascular response: Temporal stability and hemodynamic patterning. *Psychophysiology*, *27*, 605-619.

RUNNING HEAD: ORIGIN OF BLUNTED STRESS REACTIVITY

- Koo-Loeb, J.H., Pedersen, C., & Girdler, S.S. (1998). Blunted cardiovascular and catecholamine stress response reactivity in women with bulimia nervosa. *Psychiatry Research, 80*, 13-27. doi: 10.1016/S0165-1781(98)00057-2
- 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
- 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., Dickensheets, S.L., Myers, D., Thomas, T.L., & Nixon, S.J. (2000). Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. *Alcoholism: Clinical and Experimental Research, 24*, 651-658. doi: 10.1111/j.1530-0277.2000.tb02036.x
- Luecken, L.J. (2000). Parental caring and loss during childhood and adult cortisol responses to stress. *Psychology and Health, 15*, 841-851. doi: 10.1080/08870440008405586
- Mathias, C.W., Stanford, M.S., & Houston, R.J. (2004). The psychological experience of the paced auditory serial addition task (PASAT): Does the PASAT induce autonomic arousal? *Archives of Clinical Neuropsychology 19*, 543-554. doi: 10.1016/j.acn.2003.08.001
- MacMillan, H.L., Georgiades, K., Duku, E.K., Shea, A., Steiner, M., Niec, A., et al. (2009). Cortisol response to stress in female youths exposed to childhood maltreatment: Results of the Youth Mood Project. *Biological Psychiatry, 66*, 62-68. doi: 10.1016/j.biopsycho.2008.12.014

Mueller, A., Strahler, J., Armbruster, D., Lesch, K.P., Brocke, B., & Kirschbaum, C. (2012).

Genetic contribution to acute autonomic stress responsiveness in children. *International Journal of Psychophysiology*, *83*, 302-308. doi: 10.1016/j.ijpsycho.2011.11.007

Panknin, T.L., Dickensheets, S.L., Nixon, S.J., & Lovallo, W.R. (2002). Attenuated heart rate

responses to public speaking in individuals with alcohol dependence. *Alcoholism,*

Clinical and Experimental Research, *26*, 841-847. doi: 10.1111/j.1530-

0277.2002.tb02613.x

Phillips, A.C., Ginty, A.T., & Hughes, B.M. (2013). The other side of the coin: Blunted

cardiovascular and cortisol reactivity are associated with negative health outcomes.

International Journal of Psychophysiology, *90*, 1-7. doi: 10.1016/j.ijpsycho.2013.02.002

Phillips, A.C., Roseboom, T.J., Carroll, D., & de Rooij, S.R. (2012). Cardiovascular and cortisol

reactions to acute psychological stress and adiposity: Cross-sectional and prospective

associations in the Dutch Famine Birth Cohort study. *Psychosomatic Medicine*, *74*, 699-

710. doi: 10.1097/psy.0b013e31823e3b91

Phillips, A.C., Hunt, K., Der, G., & Carroll, D. (2011). Blunted cardiac reactions to acute

psychological stress predict symptoms of depression five years later: Evidence from a

large community study. *Psychophysiology*, *48*, 142-148. doi: 10.1111/j.1469-

8986.2010.01045.x

Phillips, A.C. (2011). Blunted cardiovascular reactivity relates to depression, obesity, and self-

reported health. *Biological Psychology*, *86*, 106-113. doi:

10.1016/j.biopsycho.2010.03.016

- Phillips, A.C., Der, G., & Carroll, D. (2009). Self-reported health and cardiovascular reactions to psychological stress in a large community sample: Cross-sectional and prospective associations. *Psychophysiology*, *46*, 1020-1027. doi: 10.1111/j.1469-8986.2009.00843.x
- Phillips, A.C., Carroll, D., Ring, C., Sweeting, H., & West, P. (2005). Life events and acute cardiovascular reactions to mental stress: A cohort study. *Psychosomatic Medicine*, *67*, 384-392. doi: 10.1097/01.psy.0000160464.6326.5d
- Richter, M., Friedrich, A., & Gendolla, G.H.E. (2008). Task difficulty effects on cardiac activity. *Psychophysiology*, *45*, 869-875. doi: 10.1111/j.1469-8986.2008.00688.x
- Ring, C., Harrison, L.K., Winzer, A., Carroll, D., Drayson, M., & Kendall, M. (2000). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of alpha-adrenergic blockade. *Psychophysiology*, *37*, 634-643. doi: 10.1111/1469-8986.3750634
- Ring, C., Burns, V.E., & Carroll, D. (2002). Shifting hemodynamics of blood pressure control during prolonged mental stress. *Psychophysiology* *39*, 585-590. doi: 10.1017.S0048577202011320
- Salomon, K., Jin, A.B., & Webb, A.K. (2015). Cardiovascular reactivity during a cognitive task is not related to measures of effort [abstract]. *Psychosomatic Medicine*, *77*, A-15.
- Salomon, K., Bylsma, L.M., White, K.E., Panaite, V., & Rottenberg, J. (2013). Is blunted cardiovascular reactivity in depression mood-state dependent? A comparison of major depressive disorder remitted depression and health controls. *International Journal of Psychophysiology*, *90*, 50-57. doi: 10.1016/j.ijpsycho.2013.05.018

- Salomon, K., Clift, A., Karlsdóttir, M., & Rottenberg, J. (2009). Major depressive disorder is associated with attenuated cardiovascular reactivity and impaired recovery among those free of cardiovascular disease. *Health Psychology, 28*, 157-165. doi: 10.1037/a0013001
- Schwerdtfeger, A., & Rosenkaimer, A. (2011). Depressive symptoms and attenuated physiological reactivity to laboratory stressors. *Biological Psychology, 87*, 430-438. doi: 10.1016/j.biopsycho.2011.05.009
- Schwerdtfeger, A. (2004). Predicting autonomic reactivity to public speaking: Don't get fixed on self-report data! *International Journal of Psychophysiology, 52*, 217-224. doi: 10.1016/j.ijpsycho.2003.10.008.
- Sherwood, A., Turner, J.R., Light, K.C., & Blumenthal, J.A. (1990). Temporal stability of the hemodynamics of cardiovascular reactivity. *International Journal of Psychophysiology, 10*, 95-98.
- Sorocco, K. H., Lovallo, W. R., Vincent, A. S., & Collins, F. L. (2006). Blunted hypothalamic-pituitary-adrenocortical axis responsivity to stress in persons with a family history of alcoholism. *International Journal of Psychophysiology, 59*, 210-217. doi: 10.1016/j.ijpsycho.2005.10.009
- Smith, B. (2013). Depression and motivation. *Phenomenology and the Cognitive Sciences, 12*, 615-635. doi: 10.1007/s11097-012-9264-0
- van Baak, M.A. (2001). The peripheral sympathetic nervous system in human obesity. *Obesity Reviews, 2*, 3-14. doi: 10.1046/j.1467-789x.2001.00010.x
- Willemsen, G., Ring, C., McKeever, S., & Carroll, D. (2000). Secretory immunoglobulin A and cardiovascular activity during mental arithmetic: Effects of task difficulty and task order. *Biological Psychology, 52*, 127-141. doi: 10.1016/S0301-0511(99)00028-9

- Wright, R.A., Martin, R.E., & Bland, J.L. (2003). Energy resource depletion, task difficulty, and cardiovascular responses to a mental arithmetic challenge. *Psychophysiology*, *40*, 98-105. doi: 10.1111/1496-8986.00010
- Yano, Y., Ning, H., Reis, J.P., Lewis, C.E., Launer, L.J., Bryan, N., et al. (2016). Blood pressure reactivity to psychological stress in young adults and cognition in midlife: The coronary artery risk development in young adults (CARDIA) study. *Journal of the American Heart Association*, *13*, e002718. doi: 10.1161/JAHA.115002718
- York, K.M., Hassan, M., Li, Q., Li, H., Fillingam, R.B., & Sheps, D.S. (2007). Coronary artery disease and depression: Patients with more depressive symptoms have lower cardiovascular reactivity during laboratory-induced mental stress. *Psychosomatic Medicine*, *69*, 521-528. doi: 10.1097/PSY.0b013e3180cc2601
- Young, J.B., & Macdonald, I.A. (1992). Sympathoadrenal activity in human obesity: Heterogeneity of findings since 1980. *International Journal of Obesity and Related Metabolic Disorders*, *16*, 959-967.