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

Ryan C. Brindle [a,*], Anna C. Whittaker [b,1], Adam Bibbey [c], Douglas Carroll [b], Annie T. Ginty [d]

[a] Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, USA
[b] School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, United Kingdom
[c] Department of Sport and Health Sciences, Oxford Brookes University, Oxford, United Kingdom
[d] Department of Psychology and Neuroscience, Baylor University, Waco, TX, USA

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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.

1. Introduction

Blunted cardiovascular stress reactivity refers to an objectively measured cardiovascular response to acute laboratory-based psychological stress that is comparatively lower than typically observed and may reflect an inability to effectively mobilize the stress-response system to cope with stressful situations (Phillips et al., 2013; McEwen, 1998). 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 behavioral outcomes. For example, blunted stress reactivity has been linked cross-sectionally and prospectively to increased depressive symptomatology (Carroll et al., 2007; de Rooij et al., 2010a; Phillips et al., 2011; Phillips, 2011; Salomon et al., 2009; Salomon et al., 2013; York et al., 2007), obesity (Carroll et al., 2008; Phillips et al., 2012), poor cognition, (Gao et al., 2015; Ginty et al., 2011a, 2011b; Ginty et al., 2012a; Yano et al., 2016) and poor self-reported health (de Rooij and Roseboom, 2010b; Phillips et al., 2009). Also, individuals characterized by disordered eating (Ginty et al., 2012b; Koo-Loeb et al., 1998), exercise dependence (Heaney et al., 2011), and substance abuse (al' Absi et al., 2005; Lovallo et al., 2000; Panknin et al., 2002; Sorocco et al., 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 et al., 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 et al., 2005; Ginty and 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 and Hughes, 2012). Likewise, attenuated or exaggerated perceptions of task difficulty may serve to alter cardiovascular stress responses. In most, but not all studies (Willemsen et al., 2000), an association between task difficulty and cardiovascular reactivity has been reported such that easy or overly challenging tasks result in diminished responses (Carroll et al., 1986a; Carroll et al., 1986b; Richter et al.,

* Corresponding author at: Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15213, USA.
E-mail address: BrindleRC@upmc.edu (R.C. Brindle).
[1] Previously Phillips.

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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 Val^{158}Met COMT gene has been shown to relate to increased depression and decreased motivation (Åberg et al., 2011), as well as blunted cardiac stress reactivity (Mueller et al., 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 and Orr, 2009; van Baak, 2001; Young and Macdonald, 1992). Further, experimentally induced weight gain and loss has been shown to lead to decreased and increased cardiac vagal tone, respectively (Aronne et al., 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 et al., 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 et al., 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 and the number of unattempted questions were recorded and used as objective measures 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 pressor 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 h, smoking and caffeine for 2 h, and eating for 1 h 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 et al., 2004; Ring et al., 2002). After a standard 10-minute adaptation phase, the session consisted of three 10-minutes 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 or unattempted question. The final score and number of unattempted questions were calculated as objective indices 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 min 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, $F(1, 275) = 602.35$, $p < 0.001$, $\eta^2 = 0.687$, systolic blood pressure (SBP), $F(1, 275) = 1245.47$, $p < 0.001$, $\eta^2 = 0.819$, and diastolic blood pressure (DBP), $F(1, 275) = 1197.78$, $p < 0.001$, $\eta^2 = 0.813$. 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. In total, 85 participants were re-contacted and 35 (41.18%) chose to participate in the follow-up study. Response rates for the blunted and exaggerated cardiac reactivity groups were 45.26% and 37.21%, respectively. Consequently, the average HR reactivity of the