Blunted cardiac stress reactors exhibit relatively high levels of behavioural impulsivity

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Abstract

Blunted physiological reactions to acute psychological stress are associated with a range of adverse health and behavioural outcomes. This study examined whether extreme stress reactors differ in their behavioural impulsivity. Individuals showing blunted ($N = 23$) and exaggerated ($N = 23$) cardiovascular reactions to stress were selected by screening a healthy student population ($N = 276$). Behavioural impulsivity was measured via inhibitory control and motor impulsivity tasks. Blunted reactors exhibited greater impulsivity than exaggerated reactors on both stop-signal, $F(1,41) = 4.99, p = .03, \eta^2 = .108$, and circle drawing, $F(1,43) = 4.00, p = .05, \eta^2 = .085$, tasks. Individuals showing blunted cardiovascular stress reactions are characterized by greater impulsivity which may contribute to their increased susceptibility to outcomes such as obesity and addiction.

Keywords: Cardiovascular activity; Impulsivity; Psychological stress; Stress reactivity
1. Introduction

Individuals differ markedly in their biological reactions to standard psychological stress exposures (Carroll, 1992). In addition to long-standing and comprehensive evidence to show that those who exhibit exaggerated cardiovascular reactions to acute psychological stress are at increased risk of developing various manifestations of cardiovascular disease (Carroll et al., 2012a), there is accumulating support to suggest that attenuated cardiovascular stress reactions are associated with a range of adverse health and behavioural outcomes (Phillips et al., 2013). These adverse outcomes include obesity (Carroll et al., 2008; Phillips et al., 2012; Singh & Shen, 2013) and substance abuse addictions, such as tobacco (Evans et al., 2012; Ginty et al., 2014; Girdler et al., 1997; Roy et al., 1994; Sheffield et al., 1997; Straneva et al., 2000), alcohol (Bernardy et al., 1996; Dai et al., 2007; Errico et al., 1993; Lovallo et al., 2000; Panknin et al., 2002; Sinha et al., 2011) and/or other non-prescription drugs (Lovallo et al., 2000; Panknin et al., 2002; van Leeuwen et al., 2011). Attenuated biological reactions to stress also appear to be a feature of those who meet the criteria for exercise dependence (Heaney et al., 2011), gambling addiction (Paris et al., 2010), and disordered eating (Ginty et al., 2012; Koo-Loeb et al., 1998).

A conceptual model has been proposed whereby modified frontolimbic function of the brain leads to reduced physiological stress reactivity, altered cognition, and unstable affect regulation which then leads to impulsive behaviours, with consequences for adverse health behaviours and addiction risk (Lovallo, 2013). The association between impulsivity and cardiovascular stress reactivity in non-clinical populations is somewhat unclear. Two studies reported a negative association, higher impulsivity was related to lower cardiac reactivity (Allen et al., 2009; Munoz & Anastassiou-Hadjicharalambous, 2011). Of these studies, one study used a self-reported impulsivity measure (Allen et al., 2009), while the other examined the relationship in young children and measured pre-ejection period (PEP), a less commonly
reported cardiovascular index, as opposed to the more common measure of heart rate, making comparability difficult (HR; Munoz & Anastassiou-Hadjicharalambous, 2011). One study reported a positive association between cardiovascular reactivity and an aspect of impulsivity, temporal discounting (Diller et al., 2011). Finally, no clear association was observed by others (Mathias & Stanford, 2003), however, selection of groups was made from extreme impulsivity questionnaire scores rather than cardiovascular reactivity. In one of the few studies to have included behavioural as well as self-report measures of impulsivity, pre-adolescent children high in impulsivity had diminished cardiac responses to a mental arithmetic task (Bennett et al., 2014). To our knowledge, no study in a young adult population has examined the relationship between cardiovascular stress reactivity and impulsivity using behavioural measures of impulsivity.

Given that impulsivity is associated with the unhealthy outcomes linked to attenuated biological stress reactivity, we re-examined its relationship with cardiovascular stress reactivity. However, instead of the predominantly used self-report measures, we administered two behavioural tests of impulsivity to our participants, selected as unambiguously exaggerated or blunted cardiac reactors following the stress testing of a substantial young adult sample. We considered that pre-selecting on the basis of stress reactivity and using behavioural measures would afford a more powerful test of the hypothesis that blunted stress reactors would be characterized by greater impulsivity. The examination of a young adult sample is particularly important given that impulsivity during this stage provides exaggerated risks to health development and may signify deficits in brain maturation (Romer, 2010).

2. Materials and Methods
2.1. Participants

Two hundred and seventy six healthy University of Birmingham students (147 women) attended an initial laboratory stress-testing session during which cardiovascular stress reactivity was determined. Using cut-offs of the 15% highest and 15% lowest HR reactions, 23 exaggerated reactors and 23 blunted reactors were selected and returned to complete the impulsivity tasks. The mean (SD) age of the selected sample was 22.6 (8.09) years and their mean (SD) body mass index (BMI) was 22.9 (2.91) kg/m². The majority of the selected participants indicated they were “white” (89%). None of the participants had a history of cardiovascular disease, a current illness or infection, or were taking medication. All participants provided written informed consent, and the study was approved by the University of Birmingham ethics committee.

2.2. Cardiovascular Reactivity Screening Procedure

Individuals were required to refrain from eating for 1 hour, drinking caffeine or smoking for 2 hours, and from physical exercise and drinking alcohol for 12 hours, prior to laboratory stress testing. Systolic (SBP) and diastolic (DBP) blood pressure and HR were measured at minutes 2, 4, 6 and 8 during a 10-minute baseline and paced auditory serial addition stress test (PASAT) using a semi-automatic arm sphygmomanometer (Omron, IL). A single measure was also taken during a 10 minute adaptation period for familiarity, although this measure was disregarded. The PASAT (Gronwall, 1977) reliably perturbs cardiovascular activity (Ginty et al., 2013; Ring et al., 2002) and has good test-retest reliability (Willemsen et al., 1998). Participants were presented with a series of single digits and were required to add the present number to the previously presented number, and report their answer aloud. To increase potential stress, participants were filmed, received brief bursts of loud aversive noise, and were placed on a leader board: the protocol has been described in detail elsewhere.
Immediately following the PASAT, participants rated their perceived level of task engagement and stressfulness using a 7-point Likert-type scale ranging from 0, not at all to 6, extremely.

Participants’ cardiovascular reactivity was calculated as the mean PASAT level minus mean baseline level. Individuals scoring within the top and bottom 15% of HR reactions were invited back to complete the behavioural tasks. HR reactivity, rather than SBP or DBP, was the chosen selection criteria as blunted HR reactivity is more consistently associated with adverse health and behavioural outcomes (Bibbey et al., 2013; Ginty et al., 2012; Phillips et al., 2011), and the deactivation in anterior cingulate cortex is related to HR reactivity (Critchley et al., 2000; Critchley et al., 2003; Ginty et al., 2013), as well as being implicated in impulsivity (Fineberg et al., 2014).

2.3. Impulsivity Tasks

The stop-signal task (Inquisit by Millisecond, Seattle) measures the inhibitory control aspect of impulsivity and has been detailed elsewhere (Logan et al., 1997). Participants were required to respond as fast and accurately as possible to a left or right arrow in the centre of the computer screen: the go task. On 25% of the go task trials, an auditory beep (stop signal) is presented and participants are required to inhibit their response to the go task on that trial; the stop task. Consequently, failing to inhibit when presented with a stop signal indicates poor impulse control and greater impulsivity (Logan et al., 1997). Following a tracking procedure (Logan et al., 1997), the delay between the stop signal and the go signal (stop-signal delay), originally set to 250ms, is adjusted to ensure the participant inhibits their response approximately 50% of the time. Therefore, the main outcome in the present study is the mean stop signal reaction time (SSRT); longer times indicate greater impulsivity and less inhibitory control. The current study consisted of 32 practice trials, then three experimental
blocks of 64 trials which were used for data analysis. The stop-signal task has a respectable pedigree as a measure of impulse control (Kwon & Kwon, 2013; Logan et al., 1997; Verbruggen & Logan, 2009).

The Circle Drawing Task (Bachorowski & Newman, 1990) is a measure of motor impulsivity. Participants were asked to trace the outline of a large printed circle (50.80 cm ø), using their index finger from a starting point at the top of the circle. In condition 1 (neutral), participants traced around the circle. In condition 2 (inhibition), they were instructed to trace the circle as slowly as possible without stopping. Circle Time Difference was then calculated by subtracting the inhibition condition time from the neutral condition time; smaller time differences indicate greater impulsivity (Avila et al., 2004).

2.4. Behavioral Task Laboratory Procedure

The behavioural tasks were undertaken in a laboratory specifically designed to minimize external or environmental distractions likely to affect performance. Task order was counterbalanced and the study employed a double-blind testing procedure, such that neither participant nor experimenter was made aware of the stress reactivity status of the participant.

2.5. Data analysis

Group differences in participant characteristics, stress task performance and engagement, and cardiovascular baseline and reactivity variables were tested using univariate ANOVA for continuous variables, and chi-square for categorical variables. Repeated measures ANOVAs were used to confirm that the stress task perturbed cardiovascular activity. Univariate ANOVAs were used to compare reactivity group differences in impulsivity, with partial η² reported as effect size. Three participants for the stop-signal task and one participant for the circle drawing task were not included in the analysis due to technical failures.
3. Results

3.1. Socio-demographics and cardiovascular stress reactivity

The summary socio-demographic and anthropometric data, PASAT ratings, and cardiovascular baseline and stress reactivity measures are presented in Table 1. There were no significant group differences in sex, age, PASAT total score or self-reported stress task impact (all \( p's > .05 \)).

From the overall screening procedure of 276 participants, the respective ranges for HR (\( M=17.08, SD=11.56 \)), SBP (\( M=18.25, SD=8.59 \)), and DBP (\( M=12.16, SD=5.84 \)) reactivity were as follows: -7.75 to 75.00 bpm; -2.25 to 46.50 mmHg; -1.25 to 28.50 mmHg. Repeated measures ANOVA indicated that the stress task significantly perturbed HR, \( F(1,275)=602.35, p < .001, \eta^2_p = .678 \), SBP, \( F(1,275)=1245.47, p < .001, \eta^2_p = .819 \), and DBP, \( F(1,275)=1197.78, p < .001, \eta^2_p = .813 \).

There were no significant differences between the exaggerated and blunted reactor groups in baseline HR, SBP and DBP. In contrast, and as would be expected, the selected groups differed substantially in cardiovascular reactivity: HR, \( F(1,44)=199.92, p < .001, \eta^2_p = .820 \); SBP \( F(1,44)=53.29, p < .001, \eta^2_p = .548 \); and DBP, \( F(1,44)=12.24, p = .001, \eta^2_p = .218 \).
Table 1: Socio-demographics, stress task performance and ratings, and cardiovascular reactivity measures for the blunted and exaggerated stress reactivity groups.

<table>
<thead>
<tr>
<th></th>
<th>Blunted</th>
<th>Exaggerated</th>
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<tbody>
<tr>
<td>N (%)/ Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (females)</td>
<td>11 (48)</td>
<td>12 (52)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>24.63 (10.75)</td>
<td>20.50 (2.66)</td>
</tr>
<tr>
<td>PASAT total score</td>
<td>695.43 (130.80)</td>
<td>715.65 (151.58)</td>
</tr>
<tr>
<td>Engagement</td>
<td>4.04 (1.15)</td>
<td>4.52 (1.12)</td>
</tr>
<tr>
<td>Stressfulness</td>
<td>3.91 (1.47)</td>
<td>4.48 (1.08)</td>
</tr>
<tr>
<td>Baseline HR (bpm)</td>
<td>71.51 (12.75)</td>
<td>71.14 (14.37)</td>
</tr>
<tr>
<td>Baseline SBP (mmHg)</td>
<td>120.10 (16.53)</td>
<td>118.48 (10.43)</td>
</tr>
<tr>
<td>Baseline DBP (mmHg)</td>
<td>74.60 (10.11)</td>
<td>72.32 (6.64)</td>
</tr>
<tr>
<td>HR reactivity (bpm)*</td>
<td>2.00 (3.17)</td>
<td>39.28 (12.24)</td>
</tr>
<tr>
<td>SBP reactivity (mmHg)*</td>
<td>12.05 (6.97)</td>
<td>28.11 (7.92)</td>
</tr>
<tr>
<td>DBP reactivity (mmHg)*</td>
<td>9.67 (7.18)</td>
<td>16.02 (4.92)</td>
</tr>
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Note: * p ≤ .001

3.2. Behavioral task outcomes

For the stop-signal task, ANOVA revealed a significant group difference in the SSRT, \( F(1,41) = 4.99, p = .03, \eta^2_p = .108 \), with the blunted group registering a larger SSRT, indicating lower inhibitory control and greater impulsivity. This effect is illustrated in Fig. 1a. For the circle drawing task, there was also a significant group difference in Circle Time Difference, \( F(1,43) = 4.00, p = .05, \eta^2_p = .085 \), with the blunted group producing a shorter Circle Time Difference reflecting greater impulsivity. This effect is illustrated in Fig. 1b.
Fig. 1 Mean (SE) (a) Stop signal reaction time, and (b) Circle time difference for the blunted and exaggerated stress reactivity groups. * $p \leq .05$
4. Discussion

The present study is the first we are aware of to both screen a substantial sample to select extreme cardiovascular stress reactors and to use behavioural measures to determine whether young adults with blunted or exaggerated reactions differ in terms of impulsivity. As hypothesized, individuals with blunted reactivity were more impulsive. This emerged for both measures of impulsivity.

The present results are in line with those from a recent study examining the association between impulsivity and cardiovascular reactivity in pre-adolescent children (Bennett et al., 2014). Bennett et al. (2014) found diminished cardiac stress reactions to be related to two behavioral measures of impulsivity as well as by parental ratings of impulsivity (Bennett et al., 2014). Our findings also resonate with those from a study of pre-school children, where diminished sympathetic stress reactivity, indexed by PEP, was associated with greater impulsivity on response inhibition tasks (Munoz & Anastassiou-Hadjicharalambous, 2011). A further study of university students also reported greater impulsivity in those with diminished cardiovascular stress responses, using self-report measures of impulsivity (Allen et al., 2009). One study reported an association in the opposite direction (Diller et al., 2011); however, this study employed a temporal discounting task to assess impulsivity, and not a response inhibition or motor impulsivity task as used in the present study. Notably, the two previous behaviourally-based studies which are in agreement with our current findings also measured response inhibition (Bennett et al., 2014; Munoz & Anastassiou-Hadjicharalambous, 2011) or motor impulsivity tasks (Bennett et al., 2014). It is possible that the type of impulsivity tapped in the present study is more closely related to the elements of behavioural disinhibition which has been associated with less activation the brain areas related to addictive behaviours and to blunted cardiovascular reactivity (Wilbertz et al., 2014); this is an area that warrants further investigation. Overall, although counter evidence
does exist (Diller et al., 2011), our results contribute to what might reasonably be regarded as an emerging consensus linking blunted stress reactivity and impulsivity (Allen et al., 2009; Bennett et al., 2014; Munoz & Anastassiou-Hadjicharalambous, 2011).

Impulsivity, particularly during young adult life, has been implicated in an increase in the risk of unhealthy behaviours and developments due to structural brain deficits and lack of experience with novel adult behaviours (Romer, 2010). This study goes some way to indicate a potential biological mechanism associated with impulsivity. Greater understanding of the underlying mechanisms may have prognostic value in aiding the screening and development of appropriate interventions, ultimately preventing the adverse impulsivity outcomes in later life. Central motivational dysregulation has been proposed to underpin the link between blunted stress reactivity and outcomes such as obesity, depression, a range of substance and behavioural dependencies, and bulimia (Carroll et al., 2009; Carroll et al., 2011; Lovallo, 2011). Thus, blunted stress reactivity can be considered a peripheral marker of dysregulation of the neural systems that support motivation, emotional regulation, and goal-directed behaviour. Evidence in support of this comes from functional Magnetic Resonance Imaging studies; individuals characterized by blunted cardiovascular stress reactivity showed diminished activation/de-activation in the anterior and posterior cingulate cortex, and the amygdala during stress exposure (Gianaros et al., 2005; Ginty et al., 2013). These brain areas are involved in motivational processes and goal-directed behaviour as well as in autonomic nervous system regulation (Bush et al., 2000; Hagemann et al., 2003; Lovallo, 2005). They have also been implicated in impulsivity; individuals with greater impulsivity show similar deficiencies in the frontolimbic areas of the brain (Horn et al., 2003; Inuggi et al., 2014). Further, impulsivity has been shown to be higher in individuals with addiction to alcohol (Aragues et al., 2011), tobacco (Balevich et al., 2013), other non-prescription substances (Perry & Carroll, 2008), gambling (Leeman & Potenza, 2012), and exercise dependence...
(Freimuth et al., 2011), as well as in those who are obese or have eating disorders (Schag et al., 2013). Recent evidence also indicates that individuals with blunted stress reactions have higher levels of criminality and re-offending (De Vries-Bouw et al., 2011), are more likely to drive under the influence of alcohol (Couture et al., 2008), and engage in general disruptive behaviour (De Vries-Bouw et al., 2011). Again, impulsivity has been shown to be associated with each of these behavioural outcomes (Patton et al., 1995; Treloar et al., 2012).

The idea of central motivational dysregulation has recently been incorporated into a conceptual model of stress and health which proposes dysfunction in the frontolimbic areas of the brain leads to both diminished stress reactivity and compromised regulation of motivation and emotion (Lovallo, 2013). The latter is manifest as poorer impulse control and, consequently, increased risk for adverse health behaviours, anti-social behaviour, and addiction (Lovallo, 2013). By further demonstrating an association between impulsivity, as reflected in poorer inhibitory control, greater motor impulsivity, and blunted stress reactivity, our present findings lend further support to this model. Interestingly, the exaggerated stress responders in our study did not show this pattern of poor impulse control, but rather showed low behavioural impulsivity. Consequently, it could be concluded that exaggerated responders might be protected against the range of negative health outcomes associated with high impulsivity and blunted stress reactivity such as addictions. However, it should be noted that strong impulse control alone does not protect exaggerated responders from other negative health outcomes; the high cardiovascular drive exemplified by exaggerated stress responders has been amply demonstrated by ourselves and others to be associated with prospective risk of hypertension and CVD mortality, e.g., (Carroll et al., 2012a; Carroll et al., 2012b; Carroll et al., 2003; Chida & Steptoe, 2010; Treiber et al., 2003)

The present study is not without limitations. It may be argued that the sample size of 23 individuals in each group was modest. However, the current study screened a substantial
number of participants ($N = 276$) and selected extreme reactors from a strict $15^{th}$ percentile cut-off to ensure substantial reactivity differentiation between groups. Results indicated there were significant differences in cardiovascular reactivity between the selected exaggerated and blunted groups. Although, with hindsight, it may have been preferable to examine the association between reactivity and impulsivity continuously and, accordingly, include ‘normal’ reactivity, screening participants based on cardiovascular reactions and selecting extreme groups for further investigation is not uncommon (Gianaros et al., 2005; Ginty, 2013). Second, it is always possible that individuals, as a result of demand characteristics (Damaser et al., 2010), behaved differently in a laboratory than they would in a real world environment. However, performance on both the stop-signal task (Logan et al., 1997) and the circle-tracing task (Bachorowski & Newman, 1990) have been related to self-reported and everyday occurrences of impulsive behaviours. In terms of strengths, the present study employed a double-blind testing procedure whereby neither experimenter nor participant were aware of the participant’s reactivity status, and the use of behavioural rather than self-report measures of impulsivity provides a more comprehensive investigation.

In summary, blunted stress reactors were characterized by high levels of behavioural impulsivity compared to exaggerated reactors. Over a period of years this increased impulsivity could potentially contribute to the development of addictions and the adverse health outcomes associated with blunted stress reactivity.
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Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic and