Is blunted cardiovascular reactivity in depression mood-state dependent? A comparison of major depressive disorder remitted depression and healthy controls

Kristen Salomon *, Lauren M. Bylsma, Kristi E. White, Vanessa Panaite, Jonathan Rottenberg

University of South Florida, United States

**ARTICLE INFO**

Article history:
Received 4 December 2012
Received in revised form 21 May 2013
Accepted 31 May 2013
Available online xxxx

Keywords:
Cardiovascular
Depression
Reactivity
Blood pressure
Heart rate
Impedance cardiography

**ABSTRACT**

Prior work has repeatedly demonstrated that people who have current major depression exhibit blunted cardiovascular reactivity to acute stressors (e.g., Salomon et al., 2009). A key question regards the psychological basis for these deficits, including whether such deficits are depressed mood-state dependent or whether these effects are trait-like and are observed outside of depression episodes in vulnerable individuals. To examine this issue, we assessed cardiovascular reactivity to a speech stressor task and a forehead cold pressor in 50 individuals with current major depressive disorder (MDD), 25 with remitted major depression (RMD), and 45 healthy controls. Heart rate (HR), blood pressure and impedance cardiography were assessed and analyses controlled for BMI and sex. Significant group effects were found for SBP, HR, and PEP for the speech preparation period and HR, CO, and PEP during the speech. For each of these parameters, only the MDD group exhibited attenuated reactivity as well as impaired SBP recovery. Reactivity and recovery in the RMD group more closely resembled the healthy controls. Speeches given by the MDD group were rated as less persuasive than the RMD or healthy controls’ speeches. No significant differences were found for the cold pressor. Blunted cardiovascular reactivity and impaired recovery in current major depression may be mood-state dependent phenomena and may be more reflective of motivational deficits than deficits in the physiological integrity of the cardiovascular system.

© 2013 Elsevier B.V. All rights reserved.

**1. Introduction**

Depression has emerged as an important psychological predictor of risk for cardiovascular disease. Prospective evidence links depression among otherwise healthy individuals with future incidence of cardiovascular disease (Kuper et al., 2002; Penninx et al., 2001; Rugulies, 2002; Wuslin and Singal, 2003). Recently, evidence has pointed to a relationship between depression and blunted cardiovascular reactivity. For example, our research group reported that individuals meeting DSM-IV criteria for major depressive disorder (MDD) demonstrated less reactivity but impaired recovery relative to a healthy control group (Rottenberg et al., 2007; Salomon et al., 2009). Similarly, self-reported depressive symptomatology has also been linked to blunted reactivity in non-clinical samples (Schwerdtfeger and Rosenkaimer, 2011), coronary artery disease patients (York et al., 2007), and large-scale community cohorts (Carroll et al., 2007; de Rooij et al., 2010). The traditional reactivity hypothesis links exaggerated reactivity to CVD risk; however, recent theorizing regarding allostatic load suggests that blunted reactivity and impaired recovery are also markers of poor health (McEwen, 1998). Specifically, McEwen argued that allostatic load may be indicated by inadequate mobilization of a stress–response system. Some degree of cardiovascular response to stress is functional in that it mobilizes energy toward coping efforts to manage the stressor. Thus, blunted reactivity, or inadequate responding, can be seen as maladaptive in some contexts. Further, blunted reactivity may be associated with unique and deleterious health consequences. As Carroll and colleagues have noted, reactivity is often positively associated with an up-regulation of immunity associated with host defense; thus by consequence, blunted reactivity may be associated with down-regulated immunity and compromised ability to fight infectious disease (Carroll et al., 2009).

While considerable evidence suggests that relatively robust reactivity is associated prospectively with increased risk for CVD (Chida and Steptoe, 2010), it has recently been argued that the relationship between reactivity and pathological states may be curvilinear (Lovatto, 2011). In other words, reactivity above or below the average range may indicate poor health. This argument is based on emerging evidence that comparatively low levels of reactivity in both the cardiovascular and HPA systems are related to a number of unhealthy states including obesity (Carroll et al., 2008), addiction (al’Absi et al., 2003; Panknin et al., 2002), disordered eating behavior (Ginty et al., 2012), exercise dependence (Heaney et al., 2011), fibromyalgia (Reyes del Paso et al., 2010) and fatigue among Veterans with Gulf War Illness (Peckerman et al., 2000), as well as states that confer risk for poor health such as racial/ethnic discrimination (Salomon and Jagusztyn, 2008) and low cognitive ability (Ginty et al.,...
Further, curvilinear relationships between physiological and psychological phenomenon is not without precedent. The classic Yerkes–Dodson law suggests that, when a task is difficult, performance exhibits a curvilinear relationship with arousal (Yerkes and Dodson, 1908). More recently, this relationship has been applied to the action of the locus corelesus–norepinephrine (LC–NE) system in the brain and its effects on memory and attention (Aston-Jones and Cohen, 2005). These models suggest the idea that flexibility and balance of physiological symptoms are also hallmarks of health. Rigidity of response in over or under responding reflects inflexibility and an inability to adapt. Thus, the idea that blunted reactivity may be related to pathology is reasonable.

Given that blunted reactivity may be seen as pathological, one key question is whether blunted reactivity in depression is a stable biomarker of risk for depression or is a marker of the depressed state. If blunted reactivity is a stable biomarker, then we would expect that those at risk for depression to exhibit it even when they are not depressed; i.e., prior to becoming depressed or after remitting from depression. Alternatively, if it is a phenomenon that marks the depressed state, we would expect those at risk to exhibit normative levels of reactivity. Prior data on this issue are scarce and inconclusive. In the same large-scale community cohort discussed above, blunted reactivity was positively associated with future depressive symptomatology, controlling for current symptomatology (Phillips et al., 2011). Elevations on depressive symptom measures may or may not indicate the presence of diagnosable depression. Fortunately, blunted cardiovascular reactivity has also been shown to predict a future depression, when depression is defined with structured clinical interviews (Rottenberg et al., 2005). These findings suggest that blunted reactivity may indicate a future risk for depression and not necessarily current depression.

Relatedly, it is unclear what constitutes the psychobiological basis of blunted reactivity in depression. Is blunted reactivity an indicator of physiological deficits in the integrity of the cardiovascular system or is it mediated by psychological processes? Lovallo (2011) has argued that what the pathological states associated with blunted reactivity may share, are dysregulated emotion and motivation systems. Depression, addiction, obesity, and disordered eating, among others, signal difficulties with mood regulation, behavior regulation, and, perhaps, impulsivity (Lovallo, 2011). In the context of acute laboratory task reactivity, emotional and motivational dysregulation may refer to a broad inability to regulate, i.e., abnormal differences in reactivity. Unfortunately, while task appraisals relate plain differences in reactivity. Unfortunately, while task appraisals relate performance, such as the persuasiveness of the speech, are arguably related to more psychological aspects of motivation and task engagement. In the present study, we sought to remedy this limitation. If blunted reactivity is related to decreased behavioral effort as a consequence of depressed mood, then those with depression should speak less and give less fluent speeches. If blunted reactivity is related to less motivational investment in the task, those with depression should give less persuasive speeches. Further, if negative mood leads to decreased effort in general, those with remitted depression, and thus, improved mood, should not exhibit blunted reactivity.

For our primary task we used a psychological stressor; preparing and giving a speech. This task is an active coping task and requires motivated performance that can be directly evaluated by others. Our secondary task was a forehead cold pressor. Individual differences in response to forehead cold pressor are well documented (Ruz, Uchino and Smith, 2006). The cold pressor is a passive task, requiring endurance, and reactivity to forehead cold is driven primarily by stimulating the “dive reflex,” characterized by a reduction in heart rate in response to cold temperature to the forehead region (e.g., Heath and Downey, 1990: Reyners et al., 2000). We included the cold pressor task because a pattern of blunted reactivity in a passive, physiologically-driven task might suggest a physiological basis for blunted reactivity in depression.

The present study sought to extend previous findings by comparing reactivity among a group with fully remitted depression (RMD) to those currently depressed (MDD) and healthy controls. We hypothesized that, as in our prior data, individuals with MDD would exhibit blunted reactivity to a speech stressor relative to healthy controls. In regard to the RMD group, our hypothesis was open. If blunted reactivity was a marker of risk for depression, we expected that the RMD group would also exhibit blunted reactivity relative to healthy controls similar to the MDD group. If blunted reactivity was indicative of the depressed state, we expected that the blunted effects would be restricted to the MDD group, and the RMD group would not differ from the healthy control group. We also sought to examine whether effort would explain reactivity differences by examining several aspects of performance during the speech task.

2. Method

2.1. Participants

2.1.1. Recruitment and clinical assessment

Participants were recruited from fliers and online forum postings in and around the Tampa Bay community. Individuals responding to research ads via email and phone were initially screened over the phone to determine eligibility. Screening items were based on diagnostic questions from the Structured Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR) Axis I Disorders, Research Version, Patient Edition with Psychotic Screen (SCID-I/P W/PSY SCREEN; First et al., 2002). A total of 820 potential participants were initially screened by telephone. Of those individuals, 271 were scheduled to complete the diagnostic interviews. Clinical psychology doctoral students completed the interviews and final diagnoses for study inclusion were based on responses to the SCID administration. Of those who completed the initial telephone screening, 31 individuals failed to attend their appointment and were unable to be rescheduled or decided they were no longer interested in participating. A total of 240 participants were consented and completed the SCID. Participants were excluded from further study if they reported diagnosed cardiovascular disease, use of medications with known strong effects on cardiovascular measures (e.g., antipsychotics, beta blockers, etc.), history of a major head injury, hearing impairment, diagnosis of bipolar disorder, substance abuse occurring within 6 months prior to entry into the study, or any history of primary psychotic symptoms. Participants were not excluded for regular antidepressant use; however antidepressant use was relatively uncommon in the sample. Less than 20% (n = 13) of the MDD/RMD participants (MDD n = 9, RMD n = 4) and none of the healthy controls reported taking antidepressants in the last month. Of those participants who completed a SCID, 97 were excluded for failing to meet inclusion or exclusion criteria, leaving 143 eligible participants
who were invited to participate in the psychophysiology assessment. Twenty-three individuals failed to complete the psychophysiological assessment at time 1, primarily due to scheduling difficulties. Participants who completed time 1 psychophysiology assessment fell into one of three categories, those who met criteria for MDD with a current episode (n = 50), those who met criteria for a history of MDD, but without a current episode (RMD, n = 25), and those who had no history of any Axis I disorder as assessed by the SCID (Healthy Controls, n = 45). We used strict criteria for remission requiring that individuals with RMD exhibited no more than one sub-threshold symptom and no sub-threshold depressed mood or anhedonia for at least 4 weeks. Current anxiety disorder was also assessed by the SCID. Comorbid anxiety disorders were common in the MDD (n = 37) and the RMD (n = 7) groups, and included panic (n = 4), social phobia (n = 11), obsessive-compulsive disorder (n = 2), post-traumatic stress disorder (n = 3), generalized anxiety disorder (n = 23) and not otherwise specified (n = 11). The demographic and clinical characteristics of the eligible sample are provided in Table 1.

2.1.2. Clinical symptom severity measures

At the time of the SCID interview, participants were also administered the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960), a well-validated clinician-rated measure designed to assess the presence and severity of depression symptomatology. Each item is scored on a 0–2 or 0–4 scale during a structured interview with the patient and the sum of these ratings is used as a score of global severity of depressive symptoms. The Beck Depression Inventory (BDI-II; Beck et al., 1996) and the Beck Anxiety Inventory (BAI; Beck et al., 1988) were also administered to measure depression and anxiety symptom severity. The BDI-II and the BAI are both 21-item well-validated self-report measures of depression and anxiety symptom severity.

2.1.3. Diagnostic reliability

Diagnostic reliability was monitored on an ongoing basis. We conducted a formal reliability analysis of 15 cases that included both eligible and ineligible participants. Diagnostic agreement was assessed by having a second rater code SCID responses by listening to the audiotape records. The second rater was blind to the diagnostic decision of the original rater. For the classification of current MDD, and healthy control subjects the decision of the two raters agreed in all 15 cases, k = 1.00. For the classification of RMD, the raters agreed in 14 of 15 cases (k = .81). We also assessed inter-rater reliability on key clinician-rated scales for the same 15 cases. We found excellent inter-rater reliability for the Global Assessment of Functioning (GAF; α = .96) Scale and Hamilton Rating Scale for Depression (HAM-D; α = .98)

2.2. Procedure for cardiovascular assessment

Cardiovascular assessments were conducted within 3 weeks of the clinical assessment sessions. If more time had passed due to scheduling difficulties, some participants were again administered the mood modules of the SCID to ensure diagnostic status had not changed. One person was deemed no longer eligible because of a change in diagnostic status.

After obtaining informed consent, participants completed a packet of questionnaires. Each participant then was assessed for height and weight with a fixed steel tape and a beam scale. Waist circumference was measured in cm at the level of the umbilicus. Next, the experimenter attached the measurement sensors. Participants were seated comfortably in a small recording room. The experimenter noted the presence of a video camera and informed the participants that they would be monitored throughout the protocol. Participants then viewed a neutral travelogue film for a 10-min acclimation and baseline assessment. The two cardiovascular reactivity tasks were then administered in counterbalanced order. The speech task required participants to prepare a speech on a specific topic (i.e., defending themselves against a traffic ticket), and to deliver the speech. The preparation and delivery phases of the speech task were each 3 min. To increase evaluation apprehension during the speech task, a research-assistant was present in the room and silently observed and took notes and participants were made aware of the camera recording their speech. The second task consisted of a forehead cold pressor. A cold ice pack was placed on participants' foreheads for 2 min. Each task was separated by a 5-minute recovery where participants rested and a 5-minute buffer period where participants watched more of the travelogue film. After the second task, sensors were removed, and participants were paid, debriefed, and thanked.

2.3. Data recording, reduction, and processing

A digital camera was used to record behavior throughout the experiment. ECG and impedance cardiography was recorded continuously. Impedance and ECG data were collected continuously during baseline, task, and recovery phases. We collected systolic (SBP) and diastolic (DBP) blood pressure according to published guidelines (Shapiro et al., 1996) using an Accutorr Plus blood pressure monitor (Datascope Corp., Mahwah, NJ). Participants' electrocardiograms (ECG) were obtained according to published guidelines (Jennings et al., 1981). Cleartrace LT disposable Ag/AgCl electrodes (Conmed Andover Medical, Haverhill, MA) were placed in a modified Lead II configuration on the chest, and ECG was amplified using a Biopac MP150 system with an ECG100 amplifier (Biopac Instruments Inc., Goleta, CA). We collected impedance cardiography according to the guidelines outlined by Sherwood et al. (1990) using four mylar-band electrodes fully encircling the neck and torso with the Biopac NIC0100C monitor and Z0 & dz/dt signals were digitized, acquired, and stored using a PC and Biopac AcqKnowledge software.

BP recordings were taken at two-minute intervals during study phases. During the 10-minute resting baseline, BP was recorded at the fifth, seventh and ninth minutes because ECG and impedance cardiography signals were obtained during the last 5 min of baseline only. During the three-minute speech preparation and speech delivery phases, BP recordings were obtained at the first and third minute of each phase. For the three-minute cold pressor task, BP was measured during the first and third minutes. During both recovery phases, BP recordings were obtained during the first, third and fifth minutes.

Table 1

Demographic, physical, and clinical characteristics of the eligible recruited sample.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>MDD</th>
<th>RMD</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 50</td>
<td>n = 25</td>
<td>n = 45</td>
<td></td>
</tr>
<tr>
<td>Age (years), M (SD)</td>
<td>31.93 (11.77)</td>
<td>30.03 (10.26)</td>
<td>29.41 (12.07)</td>
<td></td>
</tr>
<tr>
<td>Age, range</td>
<td>19–56</td>
<td>19–57</td>
<td>18–59</td>
<td></td>
</tr>
<tr>
<td>Caucasian ethnicity, N (%)</td>
<td>32 (59.30%)</td>
<td>19 (52.80%)</td>
<td>34 (66.70%)</td>
<td></td>
</tr>
<tr>
<td>Female gender, N (%)</td>
<td>45 (83.30%)</td>
<td>20 (55.60%)</td>
<td>37 (72.50%)</td>
<td></td>
</tr>
<tr>
<td>BMI, M (SD)</td>
<td>28.59 (8.89)</td>
<td>27.13 (8.05)</td>
<td>24.18 (5.74)</td>
<td></td>
</tr>
<tr>
<td>Waist circumference, M (SD)</td>
<td>91.14 (15.57)</td>
<td>91.94 (17.86)</td>
<td>83.60 (12.69)</td>
<td></td>
</tr>
<tr>
<td>Income, M (SD)*</td>
<td>4.95 (2.87)</td>
<td>5.91 (3.04)</td>
<td>6.10 (3.43)</td>
<td></td>
</tr>
<tr>
<td>BDI, M (SD)</td>
<td>31.11 (9.49)</td>
<td>6.75 (5.30)</td>
<td>2.58 (4.16)</td>
<td></td>
</tr>
<tr>
<td>BDI, range</td>
<td>15–49</td>
<td>0–19</td>
<td>0–25</td>
<td></td>
</tr>
<tr>
<td>BAI, M (SD)</td>
<td>19.22 (8.86)</td>
<td>6.97 (7.87)</td>
<td>1.79 (2.99)</td>
<td></td>
</tr>
<tr>
<td>BAI, range</td>
<td>3–39</td>
<td>0–41</td>
<td>0–15</td>
<td></td>
</tr>
<tr>
<td>Comorbid anxiety disorder</td>
<td>74.0%</td>
<td>28.0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Antidepressant use past month</td>
<td>16.7%</td>
<td>19.4%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

*Income was assessed on a 6-point scale with higher numbers representing higher income – a score of 5–6 represents an income range of $25,000 and $34,999.

Note. BDI = Beck Depression Inventory, 2nd Edition, BAI = Beck Anxiety Inventory, BMI = Body Mass Index. Means not sharing the same subscript differ at p < .05.
HR and the impedance-derived measures of stroke volume (SV), pre-ejection period (PEP), and cardiac output (CO) were obtained using MindWare IMP 2.56 software (MindWare Technologies, Ltd., Gahanna, OH). The ECG and dZ/dt signals were ensemble-averaged over 60-s epochs. The data were screened for artifact by visual inspection. Total peripheral resistance (TPR) was estimated using the formula TPR = (MAP/CO) * 80 in dyne-s/cm² with mean arterial pressure (MAP) calculated as (SBP + (2 * DBP)) / 3. Baseline, task, and recovery values for each measure were computed by averaging the available values for each phase. Reactivity scores were calculated as the arithmetic difference between task and baseline averages. Recovery scores were calculated as the arithmetic difference between recovery and baseline values, such that smaller values indicate greater recovery.

2.4. Behavioral measures

Speech behavior was coded for 97 participants; 15 participants (13%) had missing videos due to technical difficulties, such as the research assistant forgetting to record the video or partial recordings of speeches. The recording was transcribed by two research assistants. The text was used to compute objective indicators of task engagement such as the number of words spoken, number of prompts from the experimenter for the participant to continue the speech for the allotted time, and number of words indicating dysfluency (i.e., "um"). The transcriptions were also analyzed with the Linguistic Inquiry and Word Count (LIWC2007) program to identify words signaling positive and negative emotionality used during the speech. Video recording of the participants delivering the speech was used to code persuasiveness of the speech. Persuasiveness of the speech was determined using a global measure based upon the entirety of the 3-minute speech. In making decisions about the degree of persuasiveness, the coder was instructed to attend to the level of detail presented, logical flow of the story, whether the participant spoke with conviction, and whether the speaker made a compelling and believable argument. The speeches were coded on a 0 to 10 scale, where 10 is the most persuasive. Persuasiveness was double coded for 20% (n = 20) of the cases and reliability was computed (α = .75).

2.5. Data analysis

First, a series of analyses of covariance (ANCOVAs) was conducted to examine group differences in baseline SBP, DBP, and HR levels including BMI and sex as covariates. To examine group differences in speech responses, a series of repeated measures ANCOVAs was conducted with group (MDD, RMD, healthy control) as the between-subjects factor, and phase (baseline, speech preparation, speech delivery, recovery) as the within-subjects factor with SBP, DBP, HR, SV, CO, PEP, and TPR as the dependent measures and BMI and sex included as covariates. Parallel repeated measures ANCOVAs were conducted for the cold pressor task with three phases (baseline, cold, cold recovery).

Additional analyses were conducted to examine group differences in reactivity and recovery separately. We conducted a series of ANCOVAs with group (MDD, RMD, healthy control) as the between-subjects factor and reactivity change scores as the dependent measures, again with BMI and gender entered as covariates. To examine group differences in recovery, we conducted a series of ANCOVAs with group as the between-subjects factor and recovery change scores as the dependent measures, with BMI, sex, and reactivity score entered as covariates. For ANCOVAs that revealed significant differences among the groups, a Tukey’s LSD post-hoc analysis was conducted to determine which groups differed significantly.

To examine group differences in speech behavior, we conducted a series of ANOVAs with group as the between-subjects factor, and speech behavior (persuasiveness, number of words produced, number of words indicating dysfluency, and number of prompts needed to continue the speech) as the dependent measures. For ANOVAs that revealed significant differences among the groups, a Tukey’s LSD post-hoc analysis was conducted to determine which groups differed significantly.

3. Results

3.1. Demographic, physical, and clinical variables

Demographic, physical, and clinical characteristics of the sample are presented in Table 1. There were no significant differences among the three groups on any of the demographic variables. The healthy control group had significantly lower BMI and smaller waist circumferences relative to the current and remitted depressed groups, but the depressed and remitted depressed groups did not differ on these variables. As expected, current and remitted depressed participants reported more depressive and anxiety symptoms than healthy controls, and currently depressed participants reported more depressive and anxiety symptoms relative to the remitted group.

3.2. Resting baseline levels

As displayed in Table 2, the groups did not significantly differ on resting levels of any of the cardiovascular measures (all ps > .05).

3.3. Speech task responses

For the repeated measures ANCOVAs on speech task responses, significant group by phase interactions occurred for HR, F(4, 217.6) = 6.36, p < .001, η²p = .108, PEP, F(4, 230.7) = 5.53, p < .001, η²p = .098, and CO, F(4, 224.9) = 3.14, p < .005, η²p = .058. The interaction for TPR approached significance, F(5, 237.4) = 2.19, p < .06, η²p = .044. No other group by phase interactions were significant (all ps > .18). Significant main effects of phase were found for SBP, F(2, 239, 253.01) = 20.45, p < .001, η²p = .162, DBP, F(2, 215.78) = 20.47, p < .001, η²p = .162, HR, F(2, 217.76) = 28.43, p < .001, η²p = .215, PEP, F(2, 226, 230.69) = 17.06, p < .001, η²p = .143, SV, F(2, 229, 233.33) = 10.51, p < .001, η²p = .093, and TPR, F(2, 250, 237.36) = 3.08, p < .05, η²p = .031, but not CO, F(2, 212, 216.06) = 2.08, p > .12, η²p = .020. A significant main effect of group emerged for SBP, F(2, 106) = 5.21, p < .01, η²p = .089. Post-hoc tests indicated that the MDD group had lower overall SBP levels (M = 117.23, SE = 1.50) than the control group (M = 123.27, SE = 1.51) and the RMD group (M = 123.94, SE = 2.08), whereas the latter two did not significantly differ. Table 2 presents the mean cardiovascular levels for each speech phase by group.

As described earlier, to distinguish between reactivity and recovery, ancillary analyses were conducted on change scores. For the speech preparation period, significant effects on reactivity for group were found for SBP, F(2, 108) = 3.74, p < .05; η²p = .065, HR, F(2, 103) = 5.61, p < .05, η²p = .098; and PEP, F(2, 103) = 4.32, p < .05, η²p = .077, with the MDD group exhibiting significantly less HR, PEP, and SBP reactivity than the healthy controls. The MDD group significantly differed from the RMD group for preparation HR and PEP. Reactivity in the RMD group did not significantly differ from that of healthy controls on any of the measures. No significant group differences were found for DBP, SV, CO, or TPR reactivity during the speech preparation period (all ps > .05).

For the speech delivery period, significant group differences in reactivity were found for HR, F(2, 102) = 8.14, p = .001, η²p = .138, PEP, F(2, 102) = 9.33, p < .001, η²p = .155, CO, F(2, 102) = 4.68, p < .05, η²p = .084, and TPR, F(2, 97) = 3.15, p < .05, η²p = .061. Post-hoc tests indicated that the MDD group again exhibited significantly less reactivity than the healthy controls for delivery HR, CO, PEP and TPR. The MDD group significantly differed from the RMD group for delivery HR, CO and PEP. Reactivity in the RMD group did
not significantly differ from that of healthy controls on any of the measures. No significant group differences were found for SBP, DBP, SV, or CO reactivity during the speech delivery period.

For the speech recovery period, significant group differences were found for SBP, $F(2, 107) = 3.45$, $p < .05$, $\eta^2_p = .060$. The MDD group exhibited less recovery than the RMD group and healthy controls. No significant group differences were found for the other cardiovascular measures (all $p$s > .11). Fig. 1 presents the means for speech reactivity and recovery change by group and phase.

### 3.4. Cold pressor responses

For the cold pressor task, no significant group by phase interactions were found (all $p$s > .29). Significant main effects of phase were found for DBP, $F(1.85, 201.80) = 3.62$, $p < .05$, $\eta^2_p = .032$, HR, $F(1.83, 191.68) = 4.69$, $p < .05$, $\eta^2_p = .043$, and CO, $F(1.35, 141.86) = 3.61$, $p < .05$, $\eta^2_p = .033$. No significant main effects of group were found, although the effect for SBP approached significance, $F(2, 109) = 2.91$, $p < .06$, $\eta^2_p = .051$. Similarly, no significant group differences

### Table 2

<table>
<thead>
<tr>
<th>Phase</th>
<th>Baseline</th>
<th>Prep</th>
<th>Speech</th>
<th>Speech recovery</th>
<th>Cold</th>
<th>Cold recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg) MDD</td>
<td>111.28</td>
<td>117.66</td>
<td>129.20</td>
<td>114.98</td>
<td>114.44</td>
<td>112.71</td>
</tr>
<tr>
<td></td>
<td>116.33</td>
<td>126.67</td>
<td>136.11</td>
<td>123.96</td>
<td>121.72</td>
<td>118.93</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>112.94</td>
<td>123.92</td>
<td>133.00</td>
<td>118.71</td>
<td>115.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.18)</td>
<td>(2.54)</td>
<td>(1.73)</td>
<td>(1.84)</td>
</tr>
<tr>
<td>DBP (mm Hg) MDD</td>
<td>69.22</td>
<td>74.68</td>
<td>82.41</td>
<td>70.93</td>
<td>71.20</td>
<td>70.11</td>
</tr>
<tr>
<td></td>
<td>69.13</td>
<td>77.59</td>
<td>85.02</td>
<td>73.81</td>
<td>73.35</td>
<td>72.65</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>68.43</td>
<td>75.65</td>
<td>84.00</td>
<td>70.96</td>
<td>72.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.36)</td>
<td>(1.37)</td>
<td>(1.25)</td>
<td>(1.16)</td>
</tr>
<tr>
<td>HR (bpm) MDD</td>
<td>73.90</td>
<td>78.66</td>
<td>83.98</td>
<td>74.98</td>
<td>69.77</td>
<td>73.33</td>
</tr>
<tr>
<td></td>
<td>71.94</td>
<td>82.18</td>
<td>90.85</td>
<td>74.27</td>
<td>69.77</td>
<td>72.66</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>68.42</td>
<td>72.25</td>
<td>86.77</td>
<td>69.00</td>
<td>65.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(1.36)</td>
<td>(1.86)</td>
<td>(1.43)</td>
<td>(1.48)</td>
</tr>
<tr>
<td>PEP (ms) MDD</td>
<td>109.54</td>
<td>105.28</td>
<td>101.27</td>
<td>105.77</td>
<td>108.29</td>
<td>108.06</td>
</tr>
<tr>
<td></td>
<td>112.61</td>
<td>102.89</td>
<td>94.55</td>
<td>104.94</td>
<td>109.76</td>
<td>110.49</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>108.77</td>
<td>99.90</td>
<td>90.52</td>
<td>101.24</td>
<td>107.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2.25)</td>
<td>(2.41)</td>
<td>(3.09)</td>
<td>(2.46)</td>
</tr>
<tr>
<td>SV (ml) MDD</td>
<td>112.91</td>
<td>111.87</td>
<td>110.65</td>
<td>116.62</td>
<td>120.80</td>
<td>114.20</td>
</tr>
<tr>
<td></td>
<td>128.95</td>
<td>123.20</td>
<td>124.71</td>
<td>136.16</td>
<td>131.24</td>
<td>127.76</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>120.07</td>
<td>117.76</td>
<td>116.62</td>
<td>125.50</td>
<td>122.88</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5.80)</td>
<td>(5.67)</td>
<td>(5.70)</td>
<td>(6.78)</td>
</tr>
<tr>
<td>CO (l/min) MDD</td>
<td>8.15</td>
<td>8.59</td>
<td>9.11</td>
<td>8.52</td>
<td>8.18</td>
<td>8.15</td>
</tr>
<tr>
<td></td>
<td>9.11</td>
<td>9.96</td>
<td>11.18</td>
<td>10.91</td>
<td>9.08</td>
<td>9.24</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>8.49</td>
<td>8.95</td>
<td>10.01</td>
<td>8.90</td>
<td>8.27</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.42)</td>
<td>(0.45)</td>
<td>(0.53)</td>
<td>(0.43)</td>
</tr>
<tr>
<td>TPR (dyne-s/cm$^5$)MDD</td>
<td>942.72</td>
<td>988.26</td>
<td>998.09</td>
<td>937.00</td>
<td>999.33</td>
<td>952.08</td>
</tr>
<tr>
<td></td>
<td>850.81</td>
<td>887.91</td>
<td>783.93</td>
<td>811.87</td>
<td>874.67</td>
<td>855.62</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>888.96</td>
<td>949.82</td>
<td>924.20</td>
<td>906.38</td>
<td>940.43</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(71.30)</td>
<td>(86.90)</td>
<td>(83.06)</td>
<td>(78.41)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(81.97)</td>
<td>(92.73)</td>
<td>(41.12)</td>
<td>(58.75)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(62.37)</td>
<td>(78.11)</td>
<td>(72.68)</td>
<td>(82.78)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(86.68)</td>
<td>(75.49)</td>
</tr>
</tbody>
</table>

**Note.** Numbers in parentheses are standard errors.

a. Significant speech task phase main effect.
b. Significant speech task group main effect.
c. Significant cold pressor phase main effect.
d. Significant speech task group by phase interaction.

Fig. 1. Mean reactivity and recovery change scores by group and phase. Note. *$p < .05$; **$p < .01$. Means for speech preparation, speech delivery, and speech recovery are adjusted for gender and BMI. HR = heart rate, SBP = systolic blood pressure, CO = cardiac output, and PEP = pre-ejection period.
in reactivity or recovery were found for any of the cardiovascular measures (all ps > .14). Table 2 presents the means for cold task levels by group.

3.5. Speech behavior

A series of ANOVAs revealed that there were no significant differences among the three groups for any of the indices of behavioral engagement, including number of words produced, number of words indicating dysfluency, and number of prompts needed to continue the speech, and words signaling positive and negative emotionality (all ps > .12). However, group differences were observed for speech persuasiveness, \( F(2, 94) = 4.50, p < .05 \). A post-hoc analysis revealed that the effect was driven by the fact that the MDD participants produced less persuasive speeches than healthy controls (\( p < .05 \)). To ensure that differences in coders’ ratings were not influenced by the sex or BMI of the participant, we repeated analyses on persuasiveness controlling for these two factors. The results were nearly identical to those reported above. Means and standard deviations for speech behavior are provided in Table 3.

3.6. Covariate analyses

Because the groups significantly differed on ratings of speech persuasiveness, we examined whether persuasiveness, as a proxy for behavioral mobilization, explained the differences in reactivity and recovery. When persuasiveness was entered as a covariate into all significant ANCOVAs, results were unchanged. Therefore, speech persuasiveness did not account for the differences in reactivity and recovery among MDD, RMD, and healthy controls.

We repeated all analyses including antidepressant medication use as a covariate to examine if medications explained differences in reactivity. Antidepressant use was dummy-coded (1 = used antidepressants regularly in past month, 0 = did not use antidepressants regularly in past month). Similarly, we repeated all analyses including dummy-coded comorbid anxiety disorder as a covariate (1 = present, 2 = absent). The results were virtually identical to those reported above and neither medication use nor comorbid anxiety disorder was a significant covariate.

4. Discussion

Depression has been repeatedly associated with blunted cardiovascular reactivity, but the psychobiological basis of this effect is unclear. The present study was designed to determine if the blunted reactivity associated with MDD fluctuates with the depressed state or if it is a stable biomarker of risk for depression. The present findings suggest the former. In this sample, those diagnosed with MDD exhibited a pattern of attenuated reactivity relative to healthy controls, replicating prior findings in MDD (Salomon et al., 2009), but those who had previously suffered a major depressive episode, but were currently no longer depressed exhibited a similar pattern of reactivity to the healthy controls. If blunted reactivity was a biomarker of risk for depression, we would expect that the remitted-depressed group would look similar to the depressed group in terms of reactivity. While these findings suggest that the blunted reactivity seen during a major depressive episode remits along with depression, returning to normative levels of cardiovascular reactivity, the cross-sectional nature of the current study prevents strong conclusions on this score. To better test this idea, a longitudinal design would be optimal.

Relatedly, we sought to isolate the psychobiological basis of blunted reactivity in depression. If blunted reactivity reflects a fundamental compromise in the capacity for physiological response, then we would expect that the MDD group would show also blunted reactivity to a cold pressor relative to healthy controls. This was not the case. Our findings are in agreement with others finding depression-related blunted reactivity to active coping, beta-adrenergic stressors (Carroll et al., 2007; Phillips et al., 2011; York et al., 2007) but not passive coping, alpha-adrenergic stressors (Salomon et al., 2009). However, Schwerdtfeger and Rosenkaimer (2011) suggest that task self-relevance, not hemodynamic profile, may be critical for finding blunted reactivity associated with depression. They used three tasks: a beta-adrenergic speech task (giving a speech) and two alpha-adrenergic tasks (watching the video of their speech and a cold pressor). They found an association between depressive symptomatology and blunted reactivity during both speech stressors — one active/beta-adrenergic and one passive/alpha-adrenergic. Thus, their findings suggest that the self-relevance of the task is of greater importance than the specific adrenergic response that the task elicits (Schwerdtfeger and Rosenkaimer, 2011). Neither our present nor prior studies include an alpha-adrenergic self-relevant task so we cannot make this comparison, but we agree with Schwerdtfeger & Rosenkaimer, and feel that our data supports their views regarding task self-relevance and blunted reactivity in depression. Finally, one further consideration with the present findings is that the cold pressor task did not elicit the same degree of reactivity as the speech task. Thus the lack of group differences in cold pressor reactivity may be due to an overall lower level of reactivity.

Differences were only observed on a self-relevant speech task that required active coping. We reasoned that if blunted reactivity during the speech task reflects motivational deficits, that we would be able to see signs that depressed participants were withholding effort during the task. We examined effort by coding participants’ speeches for indices of emotional content, behavioral mobilization and motivational investment. No differences in the number of positive or negative emotional words used during the speech emerged between groups. Although evidence suggests that depressed individuals use more negative and fewer positive words in their speech (Pennebaker et al., 2003; Rude et al., 2004), our study suggests that these differences do not occur in the context of a laboratory reactivity speech task. The groups also did not differ on indices of behavioral mobilization. Those with MDD spoke as many words, spoke them with similar fluency, and required a similar number of prompts to continue as participants in the other groups. The only difference was that the speeches given by the MDD group were rated as less persuasive than the speeches given by the other two groups. While persuasiveness does imply effort, it suggests a lack of motivational investment in performing well, not necessarily a lack of behavioral effort to engage in the task. However, the differences in persuasiveness did not explain the differences in cardiovascular reactivity.

While we believe that persuasiveness captures a key aspect of motivational investment in the present study, we also think it is possible that more subtle motivational deficits in depression may explain blunted reactivity during active coping tasks like a speech stressor. For example, persuasive speeches may be a downstream result of reduced motivational investment during the speech preparation phase, which we did not assess. Future work could address this issue through a thought sampling technique which might determine the number of
blunted reactivity recently has been proposed as a marker of emotion and motivation dysregulation (Carroll et al., 2009; Lovallo, 2011). According to these authors, reactivity outside the normative range, either blunted or exaggerated, may have implications for poor health. Blunted reactivity has been linked to a number of disorders and psychological states associated with deficits in emotional and motivational regulation such as depressive symptomatology (Carroll et al., 2007), disordered eating (Ginty et al., 2012), obesity (Carroll et al., 2008), and risk for addiction (Lovallo, 2007; Panknin et al., 2002). Further, blunted reactivity has been associated with a number of conditions that are associated with poor health including fibromyalgia (Reyes del Paso et al., 2010), fatigue (Peckerman et al., 2000), racial/ethnic discrimination (Salomon and Jagusztyn, 2008) and low cognitive ability (Ginty et al., 2011). Our findings provide some tentative support for motivational dysregulation in depression. While seemingly putting forth as much behavioral effort during speech, depressed participants were unable to be as persuasive as the remitted and healthy control participants. Similar to obese individuals (Peckerman et al., 2000), racial/ethnic discrimination (Salomon and Jagusztyn, 2008) and low cognitive ability (Ginty et al., 2011), our findings suggest the contentment that blunted reactivity is an indicator of risk for poor psychological and physical health.

Our findings also demonstrated group differences in SBP recovery such that the MDD group evidenced impaired recovery relative to the RMD and control groups. Although differences during the recovery period were modest, this finding also replicates and extends our previous work. In addition, a lack of recovery has been identified as one pattern of allostatic load (McEwen, 1998). Impaired recovery is specifically significant because of its link to increased risk for cardiovascular disease (Chida and Steptoe, 2010; Hocking Schuler and O’Brien, 1997; Steptoe et al., 2006; Steptoe and Marmot, 2006), indicating one potential pathway placing those with depression at greater risk for disease. Impaired cardiovascular recovery has been linked to a number of processes likely to operate in depression, such as perseverative cognition (Nolen-Hoeksema, 2000; Spasojevic and Alloy, 2001), including anxiety, worry, and rumination (Brosschot et al., 2006; Glynn et al., 2002). Thus it is possible that depression leads to increased perseveration after the task, and thus, impaired recovery.

Most published research showing blunted cardiovascular reactivity examined only heart rate and blood pressure responses. The present study adds to this literature by demonstrating the autonomic and hemodynamic underpinnings of blunted reactivity. Namely, the PEP and CO responses seen in the MDD group suggest that the blunted HR and SBP responses are driven by sympathetic cardiac influences. Additionally, findings from our prior sample, as well as the current sample show that respiratory sinus arrhythmia reactivity is also blunted in MDD (Salomon et al., 2009; Bylsma et al., under review) suggesting that blunted HR reactivity is concurrently driven by a lack of withdrawal of parasympathetic control during stress.

The present study utilized a sample of currently and formerly depressed people that was reasonably representative and thus contained individuals who had other conditions and were taking medication. Additional covariate analyses including comorbid anxiety disorder and medication use suggested that these were not confounds but with our design, we cannot entirely rule out the possibility of confounding with comorbid anxiety and medication use. The generalizability of the present findings is also limited by the relatively small sample size. Requiring MDD as determined by clinical interviews is resource intensive and often result in smaller samples than those utilizing normative levels of self-reported depressive symptomatology. For this reason, it is reassuring that the present findings converge with evidence showing that symptoms of depression are associated with blurred reactivity in a large prospective cohort (Carroll et al., 2007; Phillips et al., 2011).

In sum, individuals with MDD exhibited less reactivity relative to never-depressed healthy controls and asymptomatic formerly depressed individuals. Future research should involve longitudinal methods to better address whether blunted reactivity tracks episodic depression within the same individuals. Also, a better understanding of the specific emotional and motivational deficits associated with blunted reactivity is warranted, given that blunted reactivity seems to be associated with not only depression, but a number of maladaptive psychological profiles.

Acknowledgments

The authors would like to acknowledge April Taylor-Clift, Bethany Morris and Kristina Przywaski for their assistance in conducting this study. This study was funded by NIH/NIMH R21MH077669-01A1.

References


Please cite this article as: Salomon, K., et al. Is blunted cardiovascular reactivity in depression mood-state dependent? A comparison of major depressive... International Journal of Psychophysiology (2013), http://dx.doi.org/10.1016/j.ijpsycho.2013.05.018

Relevant references for stress and cardiovascular reactivity are included here, leading to a deeper understanding of the topic.