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Depression is associated with increased vagal withdrawal during unpleasant emotional imagery after cardiac surgery

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ABSTRACT

Background: The aim of this study was to examine the influence of depression on heart rate and heart rate variability (HRV) during emotional imagery in patients after cardiac surgery.

Methods: Based on the scores of the Center for Epidemiological Studies of Depression (CES-D) scale, 28 patients after cardiac surgery were assigned either to the group with depression (CES-D scores ≥ 16; $N = 14$) or the one without depression (CES-D scores < 16; $N = 14$). Each patient completed a rest period and an emotional imagery including pleasant, neutral and unpleasant scripts. Inter-beat intervals (IBIs) and HRV were measured during the entire protocol.

Results: Compared to nondepressed patients, those with depression had greater reductions in high frequency expressed in normalized units (HF n.u.) during the imaging of the unpleasant script ($p = .003$, Cohen's d = 1.34). Moreover, HF n.u. were lower during the imaging of the unpleasant script than the pleasant one in depressed patients only ($p = .020$, Cohen's d = 0.55). CES-D scores were also inversely correlated with residualized changes in IBIs ($r = -.38$, $p = .045$) and HF n.u. ($r = -.49$, $p = .008$) from rest to the imaging of the unpleasant script.

Conclusions: The relationship between depression and increased vagal withdrawal during unpleasant emotional imagery extends to patients after cardiac surgery. The present study suggests that increased vagal withdrawal to negative emotions in patients after cardiac surgery may mediate the conferral of cardiac risk by depression.

1. Introduction

Depression is an important and independent risk factor for the onset, the adverse course and outcomes in patients with coronary artery disease (CAD) (Carney et al., 2005; Wulsin and Singal, 2003). Specifically, there is evidence that depression is associated with a 60% greater likelihood of having CAD (Wulsin and Singal, 2003). Patients with depression are also more likely to have a major cardiac event within a year of the diagnosis of CAD (Carney et al., 1988) and/or to die in the years following the diagnosis (Barefoot et al., 1996). Moreover, it has been consistently reported that depression is a risk factor for cardiac morbidity and/or mortality in patients who had undergone cardiac surgery (Blumenthal et al., 2003; Lespérance et al., 2000).

The autonomic nervous system (ANS) has been identified as a pivotal site of dysregulation, with reduced parasympathetic and/or increased sympathetic nervous system activity leading to arrhythmias and sudden cardiac death (Musselman et al., 1998; Podrid et al., 1990; Schwartz and Vanoli, 1981). Given that depression itself is associated with reduced parasympathetic and/or increased sympathetic activity (Kemp et al., 2010), the presence of depression may potentiate the impaired parasympathetic control and increased sympathetic activity observed in patients with CAD. In turn, these depression-related ANS abnormalities, especially a reduced cardiac vagal tone, may further predispose depressed patients with CAD to ventricular tachycardia, ventricular fibrillation, myocardial ischemia, and sudden cardiac death (Carney et al., 2002, 2005).

In line with these findings, there is abundant and converging evidence that, compared to nondepressed individuals, depressed patients with CAD or after myocardial infarction have reduced heart rate variability (HRV), which is associated with excessive sympathetic modulation and/or inadequate cardiac vagal control (Carney et al., 2001, 2002, 2005). Intriguingly, it has been recently shown that a depression-reduced HRV association extends also to patients who underwent cardiac surgery (Patron et al., 2012, 2014). In particular, Patron et al. (2012, 2014) observed that, compared to patients without depression, those with depression have reduced HRV, especially an impaired cardiac vagal tone, at discharge from the hospital, thus suggesting an association between postoperative depression and

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cardiac vagal dysfunctions after cardiac surgery. Based on this finding, reduced HRV has been suggested as one possible pathophysiological marker of depression-related ANS dysregulation that has been implicated as a risk factor for cardiac morbidity and/or mortality in post-surgical patients (Blumenthal et al., 2003; Lespérance et al., 2000).

In addition to the depression–ANS dysregulation relationship at rest, some studies have shown depression-related abnormalities in vagal activity during psychophysiological stressors such as the speech task or the cold pressor task, indicating reduced ability to regulate cardiac activity to meet task demands (Appelhans and Luecken, 2006; Hughes and Stoney, 2000; Sheffield et al., 1998). Specifically, it has been reported that, compared to individuals without depression, CAD or healthy individuals with depression are characterized by greater decreases in vagal activity, as reflected by reduced high frequency (HF) power of HRV, during a speech task — a stressor that generally elicits reduction in HF power (Berntson et al., 1994; Hughes and Stoney, 2000; Sheffield et al., 1998). Consistent with these studies, a recent meta-analysis reported that depression is associated with increased heart rate reactivity, especially in those patients with cardiovascular diseases (Kibler and Ma, 2004). In particular, Kibler and Ma (2004) suggested that the depression-related autonomic imbalance may predispose depressed patients with cardiovascular diseases to exaggerated physiological stress reactions and therefore increase cardiac risk.

By contrast, however, a growing body of research has shown that depression may be associated with attenuated rather than increased cardiovascular reactivity in healthy individuals (e.g., Carroll et al., 2007; Schwerdtfeger and Rosenkaimer, 2011), as well as in patients with major depression disorder (e.g., Salomon et al., 2009), and in patients with CAD (York et al., 2007). In line with these findings, it should be noted that the effect sizes of the relationship between depression and exaggerated cardiovascular reactivity reported by Kibler and Ma (2004) were only small to moderate. The latter may be due to the fact that the vast majority of studies examining whether and how cardiac vagal activity could be modulated by depression used non-emotional tasks (e.g., mental arithmetic, cold pressor or Stroop task) (Kibler and Ma, 2004). Conversely, the number of studies that investigated the influence of depression on cardiac vagal activity during *emotional* stressors is much more limited. This is surprising given that it is well-established that depression is characterized by a bias toward negative affect or emotion, namely the *mood-congruent bias* (Eizenman et al., 2003; Erickson et al., 2005; Mogg and Bradley, 1998; Murphy et al., 1999), which, in turn, has been found to potentiate emotional and psychophysiological reactivity to negative stimuli or context (Golin et al., 1977; Lewinsohn et al., 1973).

In order to examine the influence of depression on cardiac vagal activity during an emotional task in patients who have undergone cardiac surgery, a useful tool is the emotional imagery paradigm. Specifically, the emotional imagery task can effectively be used as an emotional stressor in order to induce and/or manipulate emotional states (e.g., happiness, fear), and related physiological responses (e.g., Lang, 1979; Lang et al., 1990). That is, the emotional imagery task can influence both the intensity of the affective experience and the physiology associated with the affective experience during mental imagery (Lang, 1979). For example, at the subjective level, the imagery of stress-evoking vs. neutral scripts has been shown to be effective in increasing symptoms associated with anxiety (e.g., Williams and Cumming, 2012; Williams et al., 2010). At the physiological level, emotional imagery has been found to elicit somatic and autonomic responses that are isomorphic with those typically reported in the referenced behavioral context (Cuthbert et al., 1991; Lang et al., 1990). Among autonomic responses, there is considerable evidence that imagery elicits significant cardiac acceleration in response to emotionally arousing than neutral scripts (e.g., Gollnisch and Averill, 1993; Lang et al., 1990; vanOyen Witvliet and Vrana, 1995; Vrana et al., 1988; Williams et al., 2010), reflecting the activation of the approach- and withdrawal-related behaviors (Bradley, 2000).

In light of these considerations, the present study was designed to examine whether postoperative depression would be associated with increased vagal withdrawal in patients after cardiac surgery during an emotional imagery task, including pleasant, neutral and unpleasant conditions. Given that depression is characterized by increased psychophysiological reactivity to negative stimuli, post-surgical patients with depression were expected to exhibit greater heart rate increase and vagal withdrawal, as reflected by lower HF power of HRV, during the imaging of the unpleasant vs. the neutral and the pleasant scripts compared to patients without depression.

2. Materials and methods

2.1. Participants

After receiving the local ethics committee's approval, 28 patients who had undergone first-time cardiac surgery were enrolled in this study after their written informed consent was obtained. Based on the presence of clinically significant depression [i.e., scoring greater than 16 on the Center for Epidemiologic Studies of Depression (CES-D) scale] (Radloff, 1977; Italian version by Fava, 1982), the patients were classified into one of two groups: with depression ($N = 14$) or without depression ($N = 14$). CES-D is a 20-item, self-reporting questionnaire designed to measure the presence of common symptoms of depression over the previous week. CES-D score ranges from 0 to 60, with the higher scores indicating greater depressive symptoms. Each patient was administered the validated Italian version of the CES-D questionnaire, which has shown good psychometric properties (Fava, 1982). All patients had undergone cardiac surgery at a regional specialized hospital and were admitted for rehabilitation in a highly specialized hospital between July 2012 and December 2012. Patients underwent heart valve surgery ($N = 12$), coronary artery bypass graft (CABG) surgery ($N = 12$), and combined surgery (heart valve plus CABG surgery) ($N = 4$). Each patient had the same protocol of cardioplegia and a mild hypothermic cardiopulmonary bypass. Ages greater than 75, incapability to read or understand Italian language, visual or auditory impairments, use of psychotropic drugs, other life-threatening medical illness, and prior cerebrovascular and/or neurological diseases were the exclusion criteria.

2.2. Imagery task

Three narratives, selected from the Affective Norms of English Text (ANET) (Bradley and Lang, 2007) based on standardized ratings of valence and arousal, were translated and adapted for the Italian population while maintaining the meaning and the intention of the original items, and categorized as pleasant (narrative 8500: Valence, $M = 8.5$, $SD = 1.5$; Arousal, $M = 8.2$, $SD = 1.7$), neutral (narrative 2610: Valence, $M = 5.4$, $SD = 1.3$; Arousal, $M = 3.1$, $SD = 1.7$) or unpleasant (narrative 6020: Valence, $M = 1.9$, $SD = 1.2$; Arousal, $M = 8.2$, $SD = 1.5$). The scripts from the English original and Italian translation and adaptation are presented in Appendix A. All patients were instructed to listen to the script read by the same experimenter and upon offset vividly imagine themselves in the event described. The experimenter read the scripts slowly (for a total duration of 30 s each), in order for the patients to fully understand each script. Each imagery trial consisted of 2 min of active imagery. After each imagery trial, in order to ascertain that the participants imagined the specific scene, the experimenter asked them to describe the details of the scene they imagined and the emotions experienced during the imagery. Then, valence and arousal of the affective state associated with the scene imagined were rated using the Self-Assessment Manikin (SAM) scale (Bradley and Lang, 1994). On both the valence and the arousal dimensions, the SAM scores range from 1 (valence: very unpleasant; arousal: very calm) to 9 (valence: very pleasant; arousal: very aroused). After each description and self-reported assessment of valence and arousal of the affective