International Journal of Psychophysiology 99 (2016) 108–113

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Respiratory sinus arrhythmia reactivity to a sad film predicts depression symptom improvement and symptomatic trajectory

Vanessa Panaite [a], Alexandra Cowden Hindash [a], Lauren M. Bylsma [b], Brent J. Small [c], Kristen Salomon [a], Jonathan Rottenberg [a,*]

[a] Department of Psychology, University of South Florida, Tampa, FL, USA
[b] Psychiatry Department, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA
[c] School of Aging Studies, University of South Florida, Tampa, FL, USA

ARTICLE INFO

Article history:
Received 18 August 2015
Received in revised form 7 November 2015
Accepted 6 December 2015
Available online 8 December 2015

Keywords:
RSA reactivity
Major depressive disorder
Depression trajectory
Sadness specificity

ABSTRACT

Respiratory sinus arrhythmia (RSA) reactivity, an index of cardiac vagal tone, has been linked to self-regulation and the severity and course of depression (Rottenberg, 2007). Although initial data supports the proposition that RSA withdrawal during a sad film is a specific predictor of depression course (Fraguas, 2007; Rottenberg, 2005), the robustness and specificity of this finding are unclear. To provide a stronger test, RSA reactivity to three emotion films (happy, sad, fear) and to a more robust stressor, a speech task, were examined in currently depressed individuals (n = 37), who were assessed for their degree of symptomatic improvement over 30 weeks. Robust RSA reactivity to the sad film uniquely predicted overall symptom improvement over 30 weeks. RSA reactivity to both sad and stressful stimuli predicted the speed and maintenance of symptomatic improvement. The current analyses provide the most robust support to date that RSA withdrawal to sad stimuli (but not stressful) has specificity in predicting the overall symptomatic improvement. In contrast, RSA reactivity to negative stimuli (both sad and stressful) predicted the trajectory of depression course. Patients' engagement with sad stimuli may be an important sign to attend to in therapeutic settings.

1. Introduction

Major depressive disorder (MDD) is a devastating mood disorder that will affect about 20% of the population over the life course (Kessler et al., 2005). Despite increasing efforts to better understand and treat the condition, depression is projected to become the leading cause of disability by 2030 (WHO, 2011). The high burden of depression is in part due to the tendency of depressive episodes to recur, which has spawned inquiries into what predicts its course. In the current study we consider a biological index of cardiac vagal control, respiratory sinus arrhythmia (RSA), which may help predict the course of depression.

Prediction of depression course has proven challenging. Much work has focused on clinical factors that may explain heterogeneity in depression outcome over long periods of time (Kerr et al., 1972; Angst et al., 1973; Keller et al., 1982; Keller and Boland, 1998). It has been shown that depressed people vary on demographic, clinical, and biological factors: age of onset, presence of prior episodes (Judd et al., 1998), severity indicators (e.g., suicidal ideation and intent; Lewinsohn et al., 1994), and biological indicators, such as cardiac vagal control (see a review of conflicting results by Rottenberg, 2007), that all potentially contribute to variability in length of time to recovery, remission, and maintenance of recovery (see Boland and Keller, 2009 for a review; Angst et al., 2000). For instance, first symptoms (Iacoviello et al., 2010), early recovery from depression (generally in response to treatment; Szegedi et al., 2009), and cardiac vagal tone (Chambers and Allen, 2002; Carney et al., 2000) have predicted fewer symptoms or subsequent remission. Despite this knowledge, there remains considerable room to improve our ability to predict depression course. To address this issue, we examine the predictive role of cardiac vagal control index, RSA, in the symptomatic course of depression over 30 weeks (McLeod et al., 1992).

RSA indexes cardiac vagal control, or variability in heart rate in response to cardiac control by the brain stem through the vagal nerve, which is gated by the respiratory cycle. Vagal control has been studied as a key support for self-regulation (Porges, 1995), which may be compromised in depression and other mental conditions (Beauchaine, 2015). The capacity to robustly suppress parasympathetic activation during physical and psychological challenges is useful as it prepares the body for appropriate responses to the environment (Bazhenova et al., 2001). Vagal suppression has been considered an emotion regulation index, which may reflect a person's ability to respond flexibly to environmental demands (Bornstein and Suess, 2000). Specifically, the flexible gating of vagal control allows an organism both to limit its energy use under rest conditions and to expend energy in adjusting to

* Corresponding author at: Department of Psychology, University of South Florida, PCD 4118G Tampa, FL, USA.
E-mail address: rottenberg@usf.edu (J. Rottenberg).

http://dx.doi.org/10.1016/j.ijpsycho.2015.12.002
0167-8760/

a variety of environmental demands, such as coping with negative emotion (Beauchaine, 2001; Friedman and Thayer, 1998; Thayer et al., 1996), and extreme threats (George et al., 1989). Given the important role of RSA during rest and motivated behavior, research on depression has examined whether the disorder is characterized by changes in resting RSA and/or RSA reactivity (i.e., change in RSA in response to challenge; see Rottenberg, 2007 for a review).

The role of resting RSA in depression course has been closely investigated. Cross-sectional evidence often finds that persons in a depressive state have lower resting RSA than controls (Chang et al., 2012; Rottenberg, 2007). However, effect sizes for group differences are modest, and found to be subject to confounds, such as antidepressant medication use (Licht et al., 2010). Evidence that high resting RSA predicts a more benign course of depression is mixed. Although several studies found that low resting RSA levels were associated with a worse depression course (Balogh et al., 1993; Carney et al., 2000; Chambers and Allen, 2002; de Guevara et al., 2004), others found no relationship between resting RSA and course (Rottenberg et al., 2007), and in at least one instance high resting RSA actually predicted a worse course of disorder (Rottenberg et al., 2002).

The inconclusive evidence for resting RSA has spurred a smaller body work on RSA reactivity to emotional or stressful situations as a risk factor for depression. The premise of this work is that high degree of RSA reactivity is considered to be adaptive (e.g. Porges et al., 1996; Cohen et al., 2000). Consistent with this idea, several studies have found reduced RSA reactivity in depressed persons (Bylsma et al., 2014; Rottenberg et al., 2007, 2002) and in internalizing disorders more broadly (Yaroslavsky et al., 2013). Although reduced RSA reactivity to depression is often found, not all findings are supportive (Straneva-Meuse et al., 2004).

Preliminary evidence suggests that diminished RSA reactivity predicts a worse depression course. We were the first to report in a prior study in an independent sample that diminished RSA reactivity to a sad film predicted failure to remit from MDD 6 months later (Rottenberg et al., 2005). Another group of investigators subsequently found that smaller RSA reactivity to a sad film at a pre-treatment assessment predicted a poorer symptomatic response to 8 weeks of treatment in clinically depressed patients (Fraguas et al., 2007). Interestingly, both findings were specific to a sad film and did not generalize to fear or happy films, raising the possibility that RSA reactivity to sad contexts has specific predictive significance for depression course (Fraguas et al., 2007; Rottenberg, 2005). Given that elevated sadness is a cardinal symptom of depression (APA, 2013), this finding has potential theoretical and clinical significance.

While film stimuli are well-controlled and can elicit discrete emotional responses, the degree of RSA reactivity during emotional films is modest. Conceivably, tasks that elicit larger changes in RSA could be superior for predicting depression course. One strong candidate is a speech task, which elicits robust changes in RSA among healthy subjects, and has been shown repeatedly to cross-sectionally differentiate depressed and non-depressed persons (Rottenberg et al., 2007; Bylsma et al., 2014).

With these considerations in mind, the current study investigated RSA reactivity to emotion eliciting films and a speech stressor as a predictor of both overall depression burden (i.e., average symptom level) and speed of improvement (i.e., slope of symptoms over time). We sought to provide a stronger test for the idea that greater RSA reactivity in a sad context is a specific predictor of a more benign depression course. Furthermore, we examined whether RSA reactivity is also related to a faster trajectory of symptomatic improvement (McLeod et al., 1992), itself a clinically-significant endpoint that is known to predicts a better subsequent MDD course (Stoolmiller, Kim, & Capaldi, 2005).

To test our *first hypothesis*, RSA reactivity was assessed during sad, happy, and fear-inducing films, and during listening instructions about, the preparation, and delivery of a speech. We hypothesized that high RSA reactivity to a sad film, but not happy or fear films, would predict overall symptom improvement over time. To strengthen tests of specificity, we included a speech task, which has been shown to be sensitive to depression status cross-sectionally (Bylsma et al., 2014). To test our *second hypothesis*, that high RSA reactivity to the sad film will predict faster initial change and maintenance of improvement over the course of 30 weeks independent of baseline RSA, we assessed weekly depressive symptoms over the course of six months, which resulted in thirty independent time points (30 weeks).

2. Methods

2.1. Participants

The present analyses focus on 37 MDD persons who returned for a six month follow-up. The current sample is a subset of a larger investigation that recruited 143 participants who met the screening and diagnostic criteria for MDD ($n = 49$), remitted MDD ($n = 24$), or healthy controls ($n = 45$) (see Bylsma et al., 2014 for full details). Attrition analyses indicated that MDD diagnosed individuals those who completed the six month follow up ($n = 37$) did not differ from those that did not return for the 6 month follow-up ($n = 12$) on any of the predictor variables (age, gender, baseline RSA, all RSA reactivity variables — $ts < 1.91$, $ps > .05$). Of the 37 MDD participants, 28 reported recurrent depressive episodes and 24 were diagnosed with a comorbid anxiety disorder. At the baseline clinical assessment, the MDD sample had a mean age of 30.41 ($SD = 11.96$), and was 83.8% female. Further, 25.1% of the sample had attained a bachelor's degree or higher, 41.9% had an annual income of less than $20,000, and 54.1% had never been married, 29.7% were currently married/partnered, and 29.9% had children.

2.2. Clinical diagnostic assessments

Detailed recruitment and screening procedures have been reported elsewhere (Bylsma et al., 2014). In brief, participants were recruited from the community and initially screened by phone to determine eligibility. Participants who were deemed potentially eligible were invited to the lab to complete a clinical assessment, including the Structured Clinical Interview for DSM-IV (SCID; First et al., 1995) to determine lifetime and current Axis-I diagnoses. Interviews were conducted by doctoral students in clinical psychology (interview procedures and reliability are reported in Bylsma et al., 2014). Participants were excluded at the phone pre-screen or SCID interview for the following reasons: diagnosed cardiovascular disease, diagnosed hypertension or hypotension, insulin-dependent diabetes, use of beta-blockers or antihistamines, history of a major head injury, hearing impairment, history of mania, substance abuse occurring within 6 months prior to study entry, or history of psychotic symptoms. Participants were not excluded for antidepressant use, and 11 individuals in the MDD group were on some form of psychiatric medication during the month prior to the baseline interview. Medication was tested as a potential control variable in a baseline model; this variable was dropped from analyses once deemed a null predictor (procedure described below).

Six months after their initial participation (Time 2), all participants were invited to return for a follow-up clinical assessment where they completed a modified version of the SCID. This modified interview retrospectively assessed each MDD symptom on a week-by-week basis over the follow-up period (30 weeks). Prior to this assessment, the interviewer worked with the participant to construct a timeline of life events to assist with recall, a procedure that was explicitly modeled after the well-established Longitudinal Interval Follow-up Evaluation (Keller et al., 1987). We (e.g., Rottenberg et al., 2005) and other groups have used similar procedures successfully to reconstruct depression course (e.g., Keller et al., 1992; Lewinsohn, Joiner, Rohde, 2001).