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

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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.

Keywords

RSA reactivity; Major Depressive Disorder; depression trajectory; sadness specificity

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

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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 & 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, Sellaro, 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 & 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, Plonskaia, & Porges, 2001). Vagal suppression has been considered an emotion regulation index, which may reflect a person's ability to respond flexibly to environmental demands (Bornstein & 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 a variety of environmental demands, such as coping with negative emotion (Beauchaine, 2001; Friedman & 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, Fitzpatrick, Hendricks, & Paige, 1993; Carney et al.,

2000; Chambers & Allen, 2002; de Geuvara et al., 2004), others found no relationship between resting RSA and course (Rottenberg, Clift, Bolden, & Salomon, 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; Rottenberg, Wilhelm, Gross, & Gotlib, 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, 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 – *t*s < 1.91, *p*s > .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, 2005) 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 modelled 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). Retrospective symptom assessments have been noted to have good interrater reliability. For example, Warshaw, Dyck, Allsworth, Stout, Keller (2001) found substantial interrater reliability of symptom report at 25–28 weeks post baseline (ICC = .69) and found comparative reliability of bi-monthly symptoms report with 6 month symptom report among MDD participants (ICC = .76). Our main outcome was each week's total number of MDD symptoms. Because some participants returned later than six months due to scheduling difficulties, the analyses presented here focused only on the first 30 weeks post intake, which were common across participants.

2.3. Psychophysiological assessment

At Time 1, psychophysiological assessments were conducted within 3 weeks of the initial clinical assessment. If more time had passed due to scheduling difficulties, participants were re-administered the SCID mood modules to confirm eligibility. After obtaining informed consent, participants completed questionnaires and were assessed for height, weight, and waist circumference. Next, the experimenter attached cardiovascular sensors, and 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 continuously monitored.

Participants then viewed a neutral travelogue film for a 10-minute acclimation and assessment of resting RSA, followed by a 4-minute paced breathing baseline where participants were instructed to pace their breathing to a rising and falling tone. Following this, participants viewed three emotion films (sad, fear, happy) and then completed the speech stressor task.

Participants watched the 3 emotion films in a randomized order, separated by a 60 second buffer task in which participants completed simple math problems on a computer as a distractor. Film selection was based on criteria recommended by Rottenberg et al. (2007). The fear film was 140s and depicted heavy turbulence in the cabin of a commercial airline. The sad film was 170s in length and depicted a boy who was distraught at the death of his father. The amusing film lasted 120s and depicted antic, slapstick-type comedy (Rottenberg et al, 2007). The speech task was completed after the films were viewed.

The speech stressor required participants to listen to instructions, prepare, and deliver a speech on a specific topic (i.e., defending themselves against a traffic ticket). The preparation and delivery phases of the speech task were each 3 minutes. To increase evaluation apprehension during the speech task, participants were made aware of the camera recording their speech, and an experimental observer was present and silently pretending to take notes on the participant's behavior. The speech stressor was followed by a 5-minute recovery period, during which participants rested.

2.4. Data recording, reduction, and processing

Electrocardiogram (ECG) and respiration signals were continuously recorded on a PC with AcqKnowledge 3.7.2 software, sampled at 1000Hz. Cleartrace LT disposable Ag/AgCl electrodes (Conmed Andover Medical, Haverhill, MA) were placed in a modified Lead-II configuration on the chest. ECG signals were amplified using Biopac MP150 with an ECG100 amplifier (Biopac Instruments Inc., Goleta, CA). Respiration rate and amplitude were measured with two RSP100C amplifiers, each with a TSD100C respiratory transducer (one transducer was placed around the abdomen at the level of the umbilicus; the other was placed around the chest, crossing under the armpits and atop the breastbone).

2.5. Computation of RSA

RSA was calculated using MindWare HRV 2.51 (MindWare Technologies, Ltd., Gahanna, OH). R-wave markers in the ECG signal were evaluated for artifacts by the MAD/MED artifact detection algorithm (Bernston, 2007) and visual inspection, and suspected artifacts were manually corrected. Our approach accords with current guidelines for frequency domain methods to determine heart rate variability and is well suited for short-term (~5 min) recordings (Task Force, 1996). To compute minute-by-minute estimates of heart rate and RSA during baselines and tasks, a 60s time series of interbeat intervals was created from an interpolation algorithm that has a 250ms sample time, which were then: (a) linearly-detrended, (b) mean-centered, and (c) tapered using a Hanning window. Spectral-power values were determined (in ms^2/Hz) with fast Fourier transformations, and the power values in the 0.15–0.50 Hz spectral bandwidth were integrated (ms^2). These spectral-power values were natural-log transformed prior to statistical analyses because of distributional violations, and the natural-logged (ln) spectral-power value in the high frequency (HF) 0.15–0.50 Hz bandwidth was used as the measure of RSA for each task epoch. RSA reactivity was computed by subtracting baseline RSA from each mean task RSA.

2.6. Statistical analyses

Given the nested nature of the data used in the presented analyses, we implemented multi-level models (MLM) to examine changes in depressive symptoms over the 30 week period, as well as to evaluate predictors over time (Hox, 2010; Raudenbush and Byrk, 2002; also see Shek and Ma (2011) for a discussion of longitudinal analyses using linear mixed models). Specifically, the MLM models were employed to test the specificity of RSA reactivity to predict overall symptom improvement, as well as symptom changes over time. Separate models were run for each of the RSA reactivity scores to the employed tasks. Longitudinal changes in our main outcome, total weekly depressive symptoms, were modeled by linear, quadratic, and cubic terms to evaluate non-linearity of effects. Several covariates were tested as control variables: baseline MDD symptoms, baseline resting RSA, baseline anxiety symptom severity, and psychotropic medication since these factors have been shown to affect RSA reactivity in previous studies (e.g., Licht et al., 2008). Negative log likelihood (−2LL) and Akaike's Information Criterion (AIC) were used to evaluate model goodness of fit. Analyses were implemented using SPSS statistical software package Version 22 (IBM, 2013).

3. Results

3.1. Level 1 model and baseline effects

First, to examine individual variability in total depressive symptoms over the course of 30 weeks, we established a level 1 model of individual variability to compare with our level 2 task reactivity models. The most parsimonious level 1 model that accounted for the greatest amount of variance in the course of total depressive symptoms over time was retained for hypothesis testing.

The intercept-only model of overall MDD symptoms indicated that 40.7% of the variance in depression symptoms was between individuals, suggesting sufficient individual variability to examine inter-individual effects. A random-effects model including linear, quadratic, and cubic time variables showed a significant increase in fit from the intercept only model (−2LL = 853.63, AIC = 4879.46) and demonstrated significant change in total depressive symptoms related to linear time ($b = -.391$, $p < .05$), which was retained as a random effect in all subsequent models. The standardized coefficients indicated that, on the whole, MDD participants tended to initially decrease in depressive symptoms ($b = -.391$, $p < .05$) and later plateau in their improvement over subsequent weeks given non-significant quadratic and cubic time main effects (quadratic: $b = .003$, $p > .05$; cubic: $b = .0002$, $p > .05$).

Next, to complete our baseline level 1 model, we tested a series of control variables. Specifically, baseline RSA (controlling for baseline respiration rate and respiration amplitude), baseline MDD symptoms, baseline BAI score, and psychotropic medication were evaluated as potential control variables by including them as fixed effect covariate predictors in the random-effects model. Baseline RSA was the only significant control variable ($b = -.81$, $p = .036$); there were no other significant main effects for any of the potential control variables (all other ps > .05). Thus, baseline RSA was the only covariate retained in further models. Our final level 1 model was the mixed time effects model that included the random intercept and linear time, fixed quadratic and cubic time variables and baseline RSA (Table 2). This was compared to level 2 models to test our hypotheses in subsequent analyses.

3.2. Was the sad film reactivity a specific predictor of depression course?

We tested models for each task separately controlling for baseline RSA, respiratory rate and amplitude reactivity during each film type, delivery of speech instructions, speech preparation, and speech delivery (see descriptive statistics of psychophysiological data presented in Table 1). Consistent with our prediction that greater RSA reactivity to the sad film would predict overall symptomatic improvement over a 30 week course, we found a fixed main effect of RSA reactivity to a sad film ($b = 5.18$, $p = .002$) indicating that diminished RSA withdrawal during the sad film predicted an overall worse course of MDD symptoms over time (see Figure 1). Consistent with specificity, there were no main effects for RSA reactivity to the fear or happy films, or to the delivery of speech instructions, speech preparation, or actual speech delivery (all ps > .05).

3.3. RSA reactivity as a predictor of the trajectory of symptomatic improvement

While RSA reactivity to the sad film was specifically predictive of *overall* symptomatic improvement, it was not a specific predictor of the symptom *trajectory* over the course of 30 weeks. Specifically, interaction effects evidenced several findings: greater RSA reactivity to the sad film ($b = -.65$, $p = .001$) and speech preparation ($b = -.36$, $p = .027$) both predicted quicker initial decreases in MDD symptoms over time by showing significant interactions with the linear time effect. Although the positive coefficients of the higher order quadratic growth of these two variables indicated that RSA reactivity predicted a subsequent deceleration in symptom improvement, the final negative coefficients of the higher order cubic growth revealed that such deceleration gradually slowed down supporting the idea that RSA reactivity was also implicated in maintenance of gained symptomatic improvements over time (see Table 2). Furthermore, the quadratic growth by fear film reactivity interaction and cubic growth by speech instructions reactivity interaction revealed similar patterning for symptom trajectory (see Table 2). Interestingly, speech RSA reactivity was the only variable that predicted acceleration of initial symptom improvements by showing a negative interaction with the quadratic time effect ($b = -.003$, $p = .005$). Therefore, the data did not support our second hypothesis that RSA reactivity to a sad stimuli would specifically be related to a faster trajectory of symptomatic improvement (McLeod et al, 1992). Rather, greater RSA reactivity to negative stimuli, including the sad film, predicted a faster initial improvement of depression symptoms and/or maintenance of improvements.

4. Discussion

Preliminary evidence supports the idea that robust reactivity to a sad context may predict which depressed persons are most likely to recover (Fraguas, 2007; Rottenberg, 2005). We conducted a more comprehensive test of this hypothesis with a battery of four laboratory reactivity tasks and a retrospective assessment of weekly depressive symptoms over a 30 week follow-up period. Furthermore, because we had weekly symptom counts, the current study had temporal resolution to evaluate the trajectory of symptomatic improvement, an outcome of particular importance given clear evidence that early improvement predicts a more benign depression course over the longer term (Stoolmiller, Kim, & Capaldi, 2005).

We found that robust RSA withdrawal during a sad film uniquely predicted overall improvement in depressive symptoms over 30 weeks. Our prediction of specificity was supported on two accounts. First, RSA reactivity to the happy or fear films showed no predictive value for overall depression course over 30 weeks. Likewise, RSA withdrawal before and during speech, which has differentiated depressed persons cross-sectionally in this same sample (Bylsma et al, 2014), did not predict overall depression course. These results reinforce previous observations that RSA to a sad film and not fear or happy films predicts improvement in depression (Fraguas, 2007; Rottenberg, 2005). Recent work on emotion regulatory skills lends further credibility to the idea that emotion regulation in a sad context is linked to RSA withdrawal and relevant to depression course. In a recent study, engaging in cognitive distraction versus rumination led to more robust RSA withdrawal among depressed individuals (LeMoult et al, 2015). A greater ability to tolerate negative

emotion and to actively modify undesired emotions predicted subsequent depression improvement (Radkovsky et al, 2014).

By contrast, all our negative stimuli (i.e., fear film, speech instructions, preparation, and delivery) were associated with symptomatic improvement and/or maintenance of improvement over time. Thus, our study can provide only qualified support to the hypothesis that sad contexts provide etiological specificity for depression course, as we found that a range of negative stimuli influenced the speed of improvement among those who were initially depressed. Elsewhere, diminished RSA reactivity across a range of stressors has been interpreted under the framework of reduced autonomic flexibility (Friedman & Thayer, 2008), and a broad-based blunting of cardiovascular response, has been associated with poorer adaptation, including future depression (Phillips, Hunt, Der, & Carroll, 2011) among other adverse psychological and physical health outcomes (de Rooij, 2013; Phillips, Ginty, & Hughes, 2013).

This study had several limitations. One limitation was the relatively small study sample, which limited the scope of post hoc analyses. We were, for instance, unable to examine the potential differential effects of comorbid anxiety. The small sample size limited investigation of possible mediators or moderators of depression trajectory and pace of improvement, such as gender. Next, although a detailed timeline was used to orient the subject and pinpoint major life experiences over the course of follow up, all follow-up data was recorded retrospectively and we did not record these life stress data for analysis. Investigating the mediating and moderating roles of variables such as gender and subsequent life events on the relationship between RSA and depressive symptoms over time would certainly be insightful and further elucidate current findings. Finally, depressive symptom data were recorded retrospectively and we did not assess the reliability of these reports. Mitigating this limitation somewhat, prior findings show high comparative reliability of bi-monthly symptoms report with 6 month symptom report among MDD participants (ICC = . 76; Warshaw et al., 2001).

Despite limitations, the study has significant strengths. Our study was the first to investigate the relationship of RSA reactivity to both emotional films and a speech task to MDD symptomatic improvement independent of other predictors such as baseline RSA, medication at baseline or anxiety level. The careful reconstruction of a 30-week follow up period also allowed us to assess depression symptom trajectories over time. Results consistently pointed to robust RSA withdrawal to a sad context as most clearly linked to a more benign depression course overall and a broader pattern RSA reactivity to negative contexts as predicting initial symptomatic improvement. Overall, these data speak to the viability of using biological variables in both sad and stressful contexts to predict the course of depression. Patients' engagement with sad stimuli may be an important sign to attend to in therapeutic settings.

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Highlights

- We examined RSA reactivity to emotion films (happy, sad, fear) and a speech task.
- We examined changes in MDD symptom level week-to-week during 30 weeks.
- Robust RSA reactivity to the sad film predicted overall decreases in MDD symptoms.
- The predictive effect of RSA was specific to the sad film.
- All negative stimuli had predictive value for symptomatic trajectory of depression.

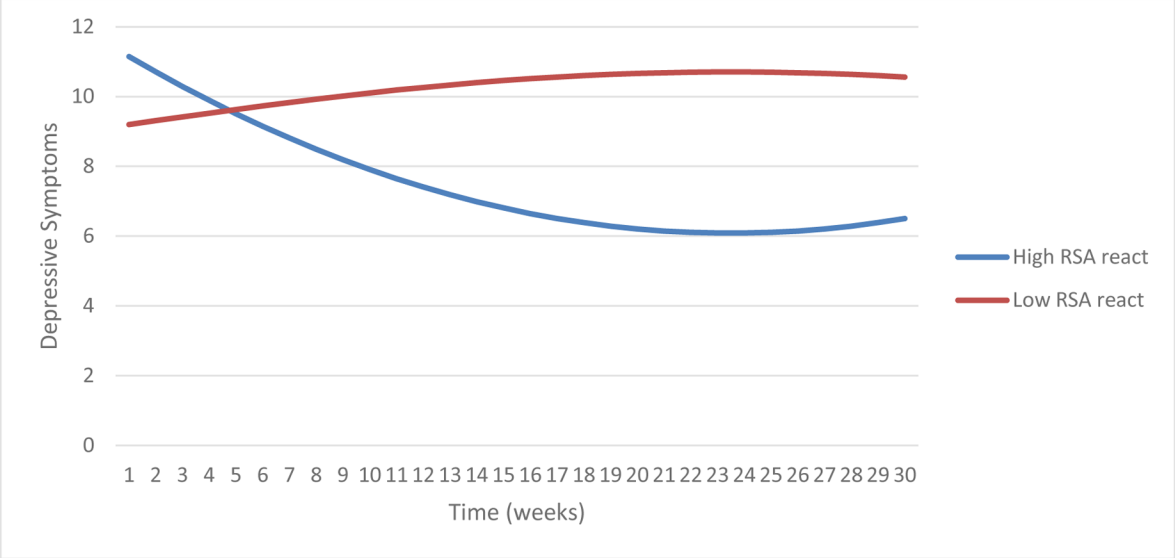

Figure 1.

Depressive symptom trajectory for those exhibiting high RSA reactivity and low RSA reactivity to the sad film (groups created through median split of RSA reactivity to the sad film for illustrative purposes).

Table 1

Descriptive statistics for RSA, RSA reactivity, and respiratory rate at baseline and in response to each task.

Task	RSA M(SD)	RSA React M(SD)	RR M(SD)	RR React M(SD)
Baseline	5.86(1.38)	--	14.11(3.44)	--
Sad Film	5.67(1.40)	−.176(.537)	14.67(3.86)	.331(4.90)
Happy Film	5.64(1.34)	−.214(.803)	14.92(3.85)	.642(3.85)
Fear Film	5.69(1.30)	−.136(.563)	14.85(5.29)	.403(5.19)
Instructions	5.70(1.29)	−.147(.721)	15.64(4.35)	1.281(5.22)
Prep	5.82(1.15)	−.027(.672)	14.29(4.34)	−.098(4.29)
Speech	5.46(1.23)	−.404(1.094)	14.16(3.97)	−.153(3.30)

Note: RSA = Respiratory Sinus Arrhythmia; React = Reactivity; RR = respiratory rate; RA = respiratory amplitude; M = mean; SD = standard deviation.

Table 2

Final models* showing Intercept, Time, and RSA reactivity as predictors of MDD symptoms over 30 weeks.

Random Effects only	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	12.37	0.78	<.001
a Time	−0.39	0.16	.022
a Time_sq	.003	0.01	.824
a Time_cub	.0002	0.00	.440
Sad Film RSA Reactivity	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	13.38	0.91	<.001
a Time	−0.60	0.12	<.001
b $Time^2$	0.02	0.01	.010
b $Time^3$	−0.00	0.00	.234
b Sad Film RSA reactivity	5.18	1.61	.002
b Sad Film RSA reactivity* Time	−0.65	0.20	.001
b Sad Film RSA reactivity* $Time^2$	.04	0.01	.003
b Sad Film RSA reactivity* $Time^3$	−0.001	0.00	.003
Happy Film RSA Reactivity	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	12.74	0.91	<.001
a Time	−0.49	0.11	<.001
b $Time^2$	0.01	0.01	.075
b $Time^3$	−0.00	0.00	.716
b Happy Film RSA reactivity	1.09	0.60	.079
Fear Film RSA Reactivity	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	12.64	0.99	<.001
a Time	−0.50	0.12	<.001
b $Time^2$	0.01	0.01	.073
b $Time^3$	−0.00	0.00	.614
b Fear Film RSA reactivity	0.77	1.65	.642
b Fear Film RSA reactivity* Time	0.11	0.11	.326
b Fear Film RSA reactivity* $Time^2$	−0.004	0.002	.034
Speech Instructions RSA Reactivity	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	12.42	0.95	<.001
a Time	−0.51	0.11	<.001

Random Effects only	Coefficient	Standard Error	*p* Value
b Time^2	0.02	0.01	.037
b Time^3	−0.001	0.00	.474
b Instructions RSA reactivity	−0.48	1.27	.710
b Instructions RSA reactivity* Time	−0.16	0.15	.299
b Instructions RSA reactivity* Time^2	0.20	0.01	.055
b Instructions RSA reactivity* Time^3	−0.0004	0.00	.037
Speech Prep RSA Reactivity	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	1246	0.92	<.001
a Time	−0.49	0.11	<.001
b Time^2	0.01	0.01	.090
b Time^3	−0.00	0.00	.820
b Speech Prep RSA reactivity	−0.44	1.36	.744
b Speech Prep RSA reactivity* Time	−0.36	0.16	.027
b Speech Prep RSA reactivity* Time^2	0.04	0.01	.001
b Speech Prep RSA reactivity* Time^3	−0.001	0.00	<.001
Speech RSA Reactivity	**Coefficient**	**Standard Error**	***p* Value**
a Individual Intercept	12.28	0.99	<.001
a Time	−0.45	0.11	<.001
b Time^2	0.01	0.01	.104
b Time^3	−0.00	0.00	.706
b Speech RSA reactivity	−0.58	0.82	.479
b Speech Prep RSA reactivity* Time	0.11	0.06	.062
b Speech Prep RSA reactivity* Time^2	−0.003	0.001	.005

Note: RSA = Respiratory Sinus Arrhythmia;

*a*Random effect;

*b*Fixed effect;

*2*A quadratic effect

*Presented models are the result of step-wise backward exclusion of non-significant higher order effects; all presented analyses do not include control variables as they remained unchanged when controlling for baseline RSA, respiratory rate reactivity, and respiratory amplitude reactivity to the tasks.