EXAMINING THE RELATION BETWEEN RESPIRATORY SINUS ARRHYTHMIA AND DEPRESSIVE SYMPTOMS IN EMERGING ADULTS: A LONGITUDINAL STUDY

by

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STATEMENT OF THESIS APPROVAL

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ABSTRACT

College students are at elevated risk for depression due to the unique stressors of this developmental stage. Among potential biomarkers, there has been a strong interest in respiratory sinus arrhythmia (RSA), a measure of parasympathetic influences on cardiac activity. Research suggests resting RSA may mark individual differences in self-regulation abilities and higher levels of resting RSA indicate increased physiological flexibility and self-regulation capacity. However, the precise relation between RSA and depression is inconsistent in the adult literature. We investigated the association between resting RSA and depressive symptoms across approximately 1 year in an emerging adult sample (n = 185). We hypothesized that lower resting RSA at year one (Y1) would predict higher depressive symptoms at Y2. Results indicate Y1 resting RSA is indeed associated with Y2 depressive symptoms in emerging adults, even after controlling for several confounding variables. Findings provide support for RSA as a promising biomarker for understanding and predicting psychopathology, specifically depressive symptoms.

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INTRODUCTION

College students are at elevated risk for depression due to the unique stressors of this developmental stage (e.g., increased autonomy, academic pressures, and changes to social support networks; Hirsch, Webb, & Jeglic, 2011; Rawson, Bloomer, & Kendall, 1994). Indeed, even though college is perceived to be a time of intellectual and interpersonal growth, many students report heightened distress during this time (Eisenberg, Gollust, Golberstein, & Hefner, 2007). When surveyed, many university students describe problems with grades, finances, relationships, and feelings of loneliness, hopelessness, and helplessness (Furr, Westefeld, McConnell, & Jenkins, 2001). According to the American College Health Association, approximately 10% of college students meet criteria for major depressive disorder (MDD; National College Health Assessment, 2010). Some young adults also show worsening depression during this stage (Fisher & Hood, 1987), which may indicate a more protracted form of the disorder, heightened risk for suicide, or a more severe clinical course. Thus, identifying predictors of depressive symptoms could lead to earlier identification or targeted prevention of MDD for adults attending college.

RSA as a Biological Marker of Depression

Over the past several decades, scientists have sought to identify biomarkers of depression and depressive symptoms (Cowen & Wood, 1991; Gentzler, Rottenberg, Kovacs, George, & Morey, 2012; Rottenberg, Clift, Bolden, & Salomon, 2007; Schmidt,

Shelton, & Duman, 2011). Among potential biomarkers, there has been a strong interest in respiratory sinus arrhythmia (RSA, known alternatively as cardiac vagal control, vagal tone, or high-frequency heart-rate variability; Rottenberg, 2007), a measure of parasympathetic influence on cardiac activity. RSA is the beat-to-beat variability in heart rate that corresponds with the breathing cycle in which inhalation suppresses vagal activity and increases heart rate, and exhalation resumes vagal activity and decreases heart rate. When an individual is at rest, higher resting RSA indicates conservation of resources and is therefore considered adaptive. Research findings also suggest resting RSA may mark individual differences in self-regulation abilities (Beauchaine, 2001; Porges, 1995, 2007). Specifically, higher levels of resting RSA appear to indicate increased physiological flexibility, self-regulation capacity, and ability to adapt when faced with environmental stressors (Porges, 1995, 2007).

The interest in RSA as a potential marker of depression follows from a growing literature examining the relation between RSA and several other physical and mental health outcomes. For example, high RSA is associated with social competence (Eisenberg et al., 1995) resilience among individuals faced with stressors (Fabes & Eisenberg, 1997), and the ability to respond flexibly to environmental demands (Porges, 2007). Alternatively, low levels of resting RSA are associated with several disorders and problems in children and adults, including poor impulse control (Beauchaine, 2001), anxiety (Thayer, Friedman, & Borkovec, 1996), as well as negative health conditions, such as cardiovascular disease (Hinkle, Carver, & Plakun, 1972) and sudden cardiac death following myocardial infarction (Peltola et al., 2008).

However, the precise relation between RSA and depression is less clear. In

several studies, low resting RSA is associated with higher depression or more depressive symptoms, as would be expected. In one such study, Gentzler and colleagues (2012) followed children between the ages of 5-14 at high risk for MDD, defined as having a parent with a childhood-onset mood disorder. The high-risk group did not show the same developmental increase in resting RSA as the low risk group. This suggests that young people at risk for depression demonstrate an atypical trajectory of resting RSA over time. Another study examined RSA as a marker of emotion dysregulation in a sample of 8-12 year old children and found that lower resting RSA was associated with depression (Pang & Beauchaine, 2012). Moreover, in a large sample of adults diagnosed with MDD the authors found the expected association between depression and decreased RSA. However, the authors were not able to rule out a possible effect of medications (Licht et al., 2008).

In spite of theoretical and empirical evidence that depression should be associated with lower resting RSA, adult findings are not consistent. Lehofer and colleagues (1997) investigated parasympathetic influences on heart rate in individuals diagnosed with MDD compared with age and sex matched controls and found no resting RSA differences. RSA has also been examined as a predictor of MDD severity and recovery (Rottenberg, Wilhelm, Gross, & Gotlib, 2002) in a sample of 55 adults, all of whom were diagnosed with MDD. The researchers found that resting RSA was not related to depression severity, but was positively associated with sadness and negatively associated with suicidality (i.e., lower RSA correlated with higher suicidality). Paradoxically, higher levels of resting RSA at year one (Y1) predicted a more malignant course of depression by year two (Y2). Given these inconsistent findings, Rottenberg (2007) conducted a

meta-analysis to determine the relation between depression and RSA across 13 studies. This meta-analysis revealed a small to moderate effect in both healthy participants (d = 0.33) and participants with compromised cardiovascular functioning (d = 0.28), with lower RSA corresponding to higher depression.

In sum, lower RSA is a promising marker for depression but the findings are inconsistent. Possible reasons for this include the presence of comorbid disorders such as anxiety, medication effects, and physical health (Molgaard, Hermansen, & Bjerregaard, 1994; Rottenberg, et al., 2007). Specifically, anxiety, poor physical health (e.g., obesity), and certain medications are also associated with low resting RSA (Watkins, Grossman, Krishnan, & Blumenthal, 1999), leading researchers to question whether the association between resting RSA and depressive symptoms may be driven by these other factors (Molgaard, et al., 1994). Disregarding these variables could produce inconsistent estimates of the association between RSA and depression.

In addition, most of the previous studies are cross-sectional, which precludes tests of the temporal association between resting RSA and depressive symptoms. Ideally, biomarkers such as RSA could serve as a predictor of later depression, which could improve early intervention and prevention efforts. Finally, most studies have examined the association between RSA and depressive symptoms in smaller clinical samples. Examining only one extreme of the distribution neglects the continuum of depressive symptoms and could produce unexpected associations between these variables (Beauchaine, 2009). Thus, the role of RSA as a predictor of depressive symptoms in a normative adult sample is not well understood, suggesting a strong need for longitudinal research (Berntson, Cacioppo, & Grossman, 2007).

The Current Study

In the current study, we examine the association between resting RSA and depressive symptoms in a large sample of college students over a 12-month time period. In contrast to prior research, we have assessed several covariates that may have clouded the relation between these variables previously, including anxiety, body mass index (BMI), and use of psychiatric medication. We also measured resting RSA and depressive symptoms at two time points approximately 12 months apart. This allowed us to examine the longitudinal association between resting RSA and depressive symptoms during a developmental stage in which psychopathology often increases. We hypothesized that lower resting RSA would be associated with higher depressive symptoms scores at both time points (Y1 and Y2). Further, we hypothesized that lower levels of Y1 RSA would predict higher Y2 depressive symptoms. Importantly, because both RSA and depression show high stability over time (Beauchaine, Neuhas, Brenner, & Gatzke-Kopp, 2008; Sloan, Shapiro, Bagiella, Gorman, & Bigger, 1995), we tested a model where Y1 RSA predicted Y2 depressive symptoms while accounting for the stability in RSA and depressive symptoms across the two time points.

METHODS

Participants

At year one, 371 college students were recruited through a psychology department participant pool. Of those, 336 provided consent for future contact and were therefore considered eligible for the longitudinal component of the study. These individuals were contacted approximately 12 months after their Y1 visit and invited to participate in the study follow-up. Due to the presence of nontraditional students at the university, we made no age restrictions for the study. However, as expected, the majority of the participants were young adults (mean age = 25; mode = 23). Given the wide age range (18-64), age was also included as a covariate in statistical models.

All components of this study were approved by the institutional review board. Participants were included if they were 18 years of age or older and attending the University of Utah. Exclusion criteria included a history of seizures or other neurological conditions that could be exacerbated by 3D stimuli (used for another aspect of the study protocol; reported elsewhere). Participants were not excluded for use of beta-blockers or psychiatric medication; however, medication use was noted and later controlled for in the model. Upon meeting eligibility criteria, participants were assessed at two time points approximately 12 months apart. Participants were initially recruited through the university participant pool, then invited to participate in the Y2 follow-up visit using methods that participants selected in their Y1 consent form, including (1) mailing flyers;

(2) phone calls; and (3) e-mails. Interested participants were asked to contact study personnel by phone or e-mail to schedule an appointment. Participants were compensated with 3 hours of research credit at Y1, and given two options for compensation at Y2: (1) 2 hours of participant pool credit and $30, or (2) $40 and no participant pool credit.

Procedure

Year 1 Visit

Participants were seated in a quiet, comfortable room. Once consent was obtained, participants were asked to complete the Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996), a demographics form (e.g., age, height, weight, ethnicity, etc.), and several self-report questionnaires related to depression, emotion regulation, and psychopathology (described below). Next, a brief video was shown to inform participants of the electrode placement and describe the physiology equipment used in the study. A research assistant who was matched to the participant's sex then placed electrodes before obtaining resting RSA for the last minute of a 5 min resting period. At the end of the study visit, the electrodes were removed and participants were debriefed and compensated. Participants completed an IRB-approved re-contact form to either decline or provide consent for future contact.

Year 2 Visit

After consent was obtained, participants were asked to complete the Beck Depression Inventory (BDI-II) used to identify and measure depressive symptoms. Participants were then shown the video used at Y1 describing electrode placement and an identical protocol was used to obtain resting RSA. Participants were assessed in the same

room for both Y1 and Y2 and all equipment, hardware, and software were identical. Participants also completed questionnaires related to demographics, and completed other self-report measures initially given at Y1. Participants were then debriefed, compensated, and completed a re-contact form.

Measures

Participants were asked to complete a battery of self-report questionnaires regarding symptoms of depression and anxiety, and a demographics form. Resting RSA was collected during the same study session.

Self-Report Measures

The Demographics Form is a brief multiple choice and free response self-report form in which we collected data on participant age, biological sex, height and weight (later used to calculate BMI), and medication use over the prior 2 weeks. A measuring tape and scale were provided to facilitate accurate reporting of height and weight. Participants were asked to list all medications taken in the past 2 weeks leading up to the visit date. Consistent with other psychophysiological studies, the following medications were presumed to affect physiological responding: beta-blockers, antihistamines, tricyclic antidepressants, stimulants, and seizure medication (Cacioppo, Tassinary & Berntson, 2007). Tests of our primary hypotheses were conducted with and without these participants to determine whether effects were due to medication use.

The Beck Depression Inventory-II (Beck, Steer & Brown, 1996) is a 21-item questionnaire used to measure the severity of depression by assessing cognitive, affective, behavioral, and physiological symptoms. The BDI-II is a widely used

instrument that has been shown to have good test-retest reliability ($r = 0.93$, $p < .001$), moderate to high convergent validity with the Short Form General Health Survey ($r = -.19$ to $-.65$), and high internal consistency ($r = .54$ to $.74$). The instrument is not used to diagnose depression, but rather to identify depressive symptoms that are consistent with diagnostic criteria. Responses on the BDI-II are rated from 0 (low intensity) to 3 (high intensity). Scores range from 0-63 with higher scores indicating higher depressive symptoms. Total scores of 0-13 are considered in the minimal range, 14-19 is mild, 20-28 is moderate, and 29-63 scores of are considered severe.

The State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970) is an instrument used to help diagnose anxiety and a general propensity to being anxious. The STAI has two subscales (state anxiety and trait anxiety) with 20 items each. The STAI defines trait anxiety as the stable aspects or qualities of anxiety rather than a temporary condition. Items are on a 4-point scale from *Almost Never* to *Almost Always*, where higher scores on the STAI indicate greater anxiety. Internal consistency coefficients range from .86 to .95, and test-retest reliability coefficients range from .65 to .75. Although the STAI examines state and trait anxiety, we selected trait anxiety for our analyses because traits are presumably better predictors of later depression than anxious states.

Psychophysiological Assessment

Psychophysiological assessments were conducted in a sound attenuated room that was monitored with audio-video recording equipment. Electrodes were placed on the participant's torso using a standard spot configuration (Qu, Zhang, Webster, & Tompkins, 1986). The ECG signal was sampled at 1 kHz. RSA was measured for the last

2 min of a 5 min resting period using a MindWare BioNex 3711-08 chassis and MindWare Biolab 3.0.9 acquisition software (MindWare Technologies, Ltd., Gahanna, OH, USA). Physiological data were scored in 30-second epochs and averaged to create a single resting RSA score for each time point. R-wave markers were evaluated for artifacts through visual inspection, and were corrected manually. In order to examine the parasympathetic influences on heart rate variability, spectral analysis was performed with MindWare software and all variables were log transformed by the software to reduce skew, as is standard for RSA.

RESULTS

Retention

At Y1, a total of 363 participants took part in the study. Resting RSA data from 15 participants were unusable due to experimenter mistake or equipment failure. Two hundred and twenty nine participants (63% of eligible participants) participated in a component of the Y2 follow-up approximately 12 months later. Of these 229 participants, 44 either declined to return to the laboratory for the physiological component of the study or RSA scores were unusable due to equipment failure. All 229 participants at Y2 consented to completing online questionnaires related to demographics, mood, emotion and psychopathology. Thus, data at Y2 are available for 229 participants for self-report measures and 185 participants for RSA.

Demographic Characteristics

At Y1, participants were 63% female, 86% Caucasian, and between the ages of 17-63 (M = 23.71, SD = 6.42). At year two, participants were 61% female, 90% Caucasian, and between the ages of 19-64 (M = 24.15, SD = 5.77). Table 1 summarizes additional participant information at year one and year two including height, weight, body mass index (BMI), medication use, resting RSA levels and BDI scores. In order to test whether there were significant differences between the participants at year one and those who returned for year two, a series of t-tests were performed. Results indicate no differences in age, height, weight, and BMI (all ts < 1.6, all ps > .05). However,

significant differences between Y1 and Y2 emerged for resting RSA levels, $t(391) = -5.48$, $p < .001$, and BDI scores, $t(405) = 4.39$, $p < .001$. That is, resting RSA scores at Y1 were significantly lower than resting RSA scores at Y2, and BDI scores at Y1 were significantly higher than BDI scores at Y2. This suggests that participants with the lowest RSA and highest depression scores were also the least likely to return for follow-up.

Preliminary Analyses

Data were analyzed using SPSS, version 20.0 (SPSS Inc, Armonk, New York). Characteristics across participants at Y1 and those who returned at Y2 were compared using one sample *t*-tests and chi square statistics. Prior to conducting analyses, we performed correlations in order to examine the cross sectional associations between resting RSA and depressive symptoms at each time point, and to assess stability between Y1 and Y2 variables (see Table 2). Correlations indicated that Y1 resting RSA was negatively associated with Y1 depressive symptoms ($r = -.11$, $p < .05$), as predicted. However, Y2 resting RSA was not associated with Y2 depressive symptoms. Across the two time points, Y1 and Y2 resting RSA were highly correlated ($r = 0.50$, $p < .001$), as were Y1 and Y2 BDI ($r = 0.60$, $p < .001$).

We also performed correlations to examine associations between Y1 resting RSA and potential confounding variables including age, body mass index, and comorbid anxiety. Y1 age was negatively associated with Y1 RSA ($r = -.31$, $p < .001$) and therefore added to the model to control for effects. In addition, BMI was included as one estimate of physical health. Y1 BMI was negatively associated with Y1 resting RSA ($r = -.11$, $p < .05$) and was also included in the model to control for effects. Symptoms of trait anxiety were assessed using Y1 STAI responses. Correlations indicated a strong association

between trait anxiety and depressive symptoms at Y1 (r = .78, p < .001) and Y2 (r = .53, p < .001), and with Y1 resting RSA (r = -.11, p < .05).

Resting Year One RSA as a Predictor of Year Two Depressive Symptoms

A regression analysis was performed to test the hypothesis that lower resting RSA at Y1 predicts higher depressive symptoms (BDI-II score) at Y2. To account for the stability in depressive symptoms, BDI-II scores at Y1 were included in the model in order to control for baseline depressive symptoms. BDI-II scores at Y2 were regressed onto resting RSA at Y1 (see Figure 1). As hypothesized, a significant negative association emerged between Y2 BDI-II and resting RSA at Y1 (B = -0.92, *Beta* = -.16, p = 0.02), indicating that individuals with lower resting RSA at Y1 showed higher depressive symptoms at Y2 while accounting for the stability in both scores over time (see Figure 2). The model accounted for 46% of the variance in Y2 depressive symptoms, F (3, 172) = 48.08, p <.001, R^2 = 0.46.

To assess potential effects of age, BMI and trait anxiety (all measured at Y1), these variables were included in the model as predictors of Y2 depressive symptoms. Results indicated none of these variables were significant predictors of Y2 depressive symptoms (all ps > .05). In order to examine the effects of medication on the association between resting RSA and depressive symptoms, we first ran the model with all participants regardless of medication use. Because medication use was measured dichotomously (yes or no) and dosages were not assessed, we chose to re-run this model excluding participants who reported medications use with known effects on psychophysiology (e.g., beta-blockers, tricyclic antidepressants, antihistamines,

stimulants and benzodiazepines). This analysis indicated that the association between Y1 resting RSA and Y2 depressive symptoms was maintained even after excluding participants who reported medication use (B = -1.02, *Beta* = -.19, p = .01).

Table 1
Demographics for Participants at Year One and Year Two

	Year 1		*Year 2*	
	M(SD)	**Range**	***M(SD)***	**Range**
Age	23.7(6.4)	17-63	24.2(5.8)	19-64
Sex (% female)	63%	--	60.5%	--
Race (% Caucasian)	85.8%	--	90.3%	--
Height (in)	67.6(4.1)	58-81	67.7(4.0)	58-78
Weight (lbs)	155.1(47.5)	95-370	156.1(35.9)	97-400
BMI	23.9(4.6)	17.2-53.2	23.9(4.7)	17.4-61.0
Resting RSA	6.2(1.4)	0.9-13.1	6.5(1.2)*	2.9-9.5
BDI Score	8.7(7.5)	0-42	7.1(7.8)*	0-41

* Denotes mean differences from Y1, $p < .05$

Table 2
Correlations between Variables Across Both Time Points

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.
1. RSA1	-	.50***	-.11*	-.15*	-.31**	-.10	.00	-.11*	.10*	-.04	-.10	-.08	-.07	-.11
2. RSA2	.50**	-	-.04	-.04	-.25**	.05	-.01	.08	.15*	-.01	.04	-.04	.08	-.08
3. BDI1	-.11*	-.04	-	.60***	.02	.08	-.02	.10	.10	-.02	.07	-.03	.11	.12
4. BDI2	-.15*	-.04	.60***	-	-.08	.05	-.11	.13*	.02	.12	.12	-.08	.19*	.22**
5. Age1	-.31***	-.25**	.02	-.08	-	.25***	.08	.26***	.05	.08	.30***	.14	.27***	.02
6. WT1	-.10	.05	.08	.05	.25***	-	.59***	.86***	.07	.02	.94***	.49***	.80***	-.04
7. HT1	-.00	-.01	-.02	-.11	.08	.59***	-	.09	-.06	-.03	.54***	.84***	.12	-.12
8. BMI1	-.11*	.08	.10	.13*	.26***	.86***	.09	-	.12*	.06	.80***	.09	.89***	.03
9. Rx1	.10*	.15*	.10	.02	.05	.07	-.06	.12*	-	-.05	.07	.01	.08	-.06
10.Age2	-.04	-.01	-.02	.12	.08	.02	-.03	.06	-.05	-	-.00	-.08	.05	-.02
11.WT2	-.10	.04	.07	.12	.30***	.94***	.54***	.80***	.07	-.00	-	.52***	.86***	-.06
12. HT2	-.08	-.04	-.03	-.08	.14	.49***	.84***	.09	.01	-.08	.52***	-	.01	-.15*
13.BMI2	-.07	.08	.11	.19*	.27***	.80***	.12	.89***	.08	.05	.86***	.01	-	.02
14.Rx2	-.11	-.08	.12	.22**	.02	-.04	-.12	.03	-.06	-.02	-.06	-.15*	.02	-

Note. 1 & 2 correspond with year data was collected. RSA- Resting respiratory sinus arrhythmia, BDI – Beck Depression Inventory year one, WT- weight, HT- height, BMI- Body mass index, Rx- Medications currently taking.
*p <.05. **p <.01 ***p <.001

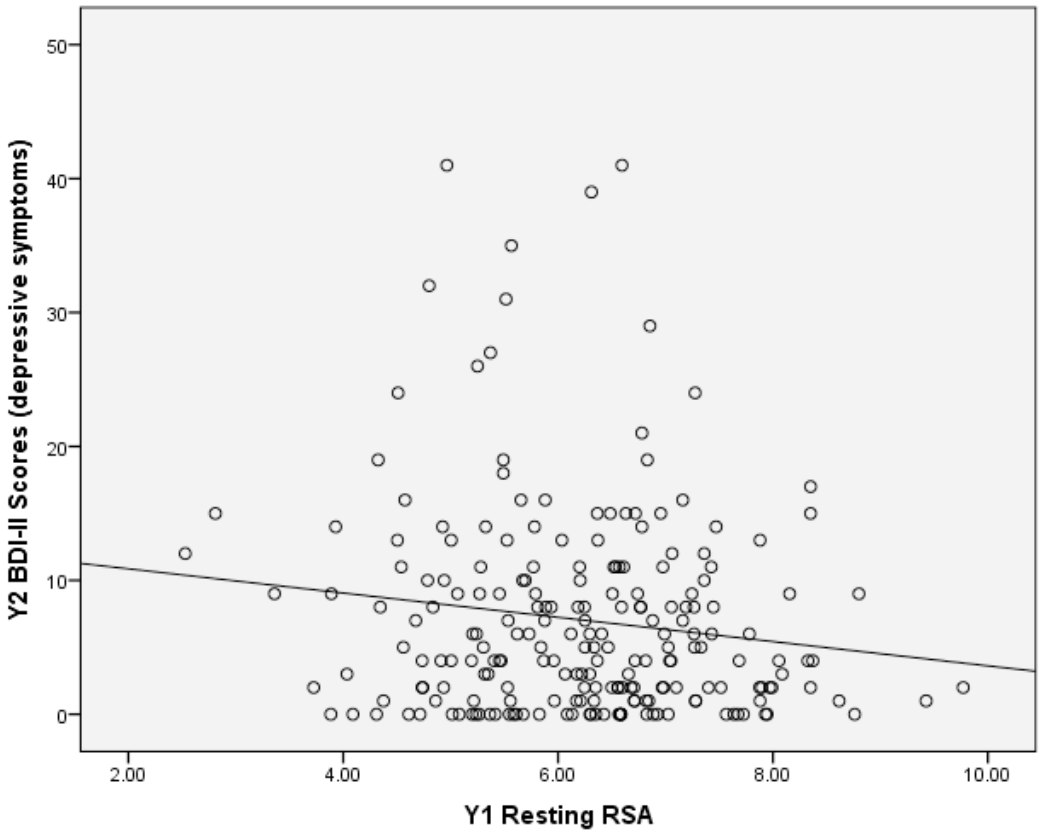
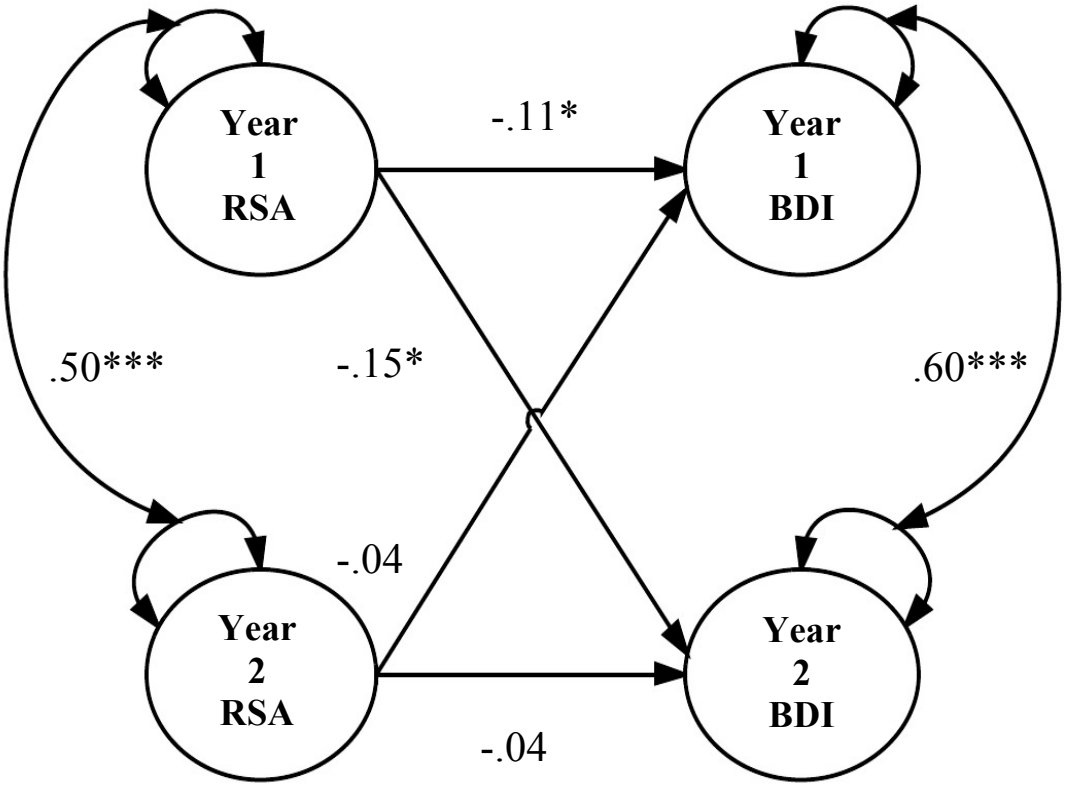


Figure 1

The association between Y1 resting RSA and Y2 BDI-II scores



* $p < .05$ *** $p < .001$

Figure 2

Model demonstrating associations between resting RSA and BDI-II scores

DISCUSSION

Resting RSA level has often been interpreted as an index of physiological flexibility and self-regulatory capacity; however, prior research demonstrates mixed findings for the association between RSA and psychopathology. In this study, we investigated whether resting RSA predicted depressive symptoms across a 12-month period while accounting for the stability in RSA and depressive symptoms over time. Consistent with our primary hypothesis, we found that resting RSA was negatively associated with BDI at Y1. We also found that lower resting RSA at Y1 predicted higher depressive symptoms at Y2 after controlling for effects of age, BMI, symptoms of anxiety, and medication use. However, the cross-sectional association between RSA and BDI was not significant at Y2. We suspect this is due to the fact that participants with more moderate to severe depressive symptoms did not return for the follow-up visit. Unlike several other studies, we examined potential confounds of this association including age, BMI, use of specific psychiatric medications, and symptoms of anxiety. Previous research has recommended identifying and controlling for these variables when examining associations between RSA and depressive symptoms (Rottenberg, 2007). Including these variables in our model indicates that the association between Y1 resting RSA and Y2 depressive symptoms in this sample is not likely due to effects of age, BMI, symptoms of anxiety, or medication use. Symptoms of anxiety were also positively associated with depressive symptoms at both time points; however, trait anxiety was not a

significant predictor of later depressive symptoms with Y1 RSA in the model.

Many scholars hypothesize that RSA is a biomarker of emotion dysregulation and may mark risk for a range of clinical diagnoses (e.g., Austin, Riniolo, & Porges, 2007; Crowell et al., 2005; Pang & Beauchaine, 2012). In most studies, RSA is assessed cross-sectionally or in clinical samples. Fewer studies have examined RSA as a predictor of later depressive symptoms in a young, healthy, nontreatment seeking sample. Results from our study support the notion that RSA is a viable biomarker associated with future development of depressive symptoms in emerging adulthood. This holds promise for studies that seek to identify those at risk for depression and other forms of psychopathology.

Limitations and Future Directions

Although this study has several strengths, including the relatively large sample, examination of several covariates, and a longitudinal component, our findings should be interpreted in the context of several limitations. First, we acknowledge that BDI-II scores are only one measure of depressive symptoms and should not be viewed as a solitary tool to identify and diagnose depression. Thus, future research should look at BDI-II scores as only one measure in a multimethod approach for detecting and diagnosing depression. Second, RSA was measured at rest rather than during exposure to a stressor. Rottenberg (2005) provides evidence that differences may exist when examining the association between depressive symptoms and resting RSA when compared to RSA reactivity. Therefore, future research should examine a combination of RSA indices of physiological responses among depressed participants, as suggested by Yaroslavsky (2013). Third, this study looked at only one physiological index (i.e., resting RSA) as a predictor of

depressive symptoms, but perhaps accounting for multiple physiological indices would produce different findings.

Fourth, while the objective of the current study was to examine associations in resting RSA and depression among college students, participants recruited for this study are in a life stage characterized by unique stressors. Thus, findings may not generalize to other developmental stages or to individuals not facing the particular stressors of a college student. Further, given the large number of participants in this sample who report minimal to mild depressive symptoms, the present data may not extend to individuals in the general population who report more moderate to severe depressive symptoms. Fifth, there was a high attrition rate in this sample due to participants graduating and/or moving out of state. However, analyses indicate participants with *higher* depressive symptoms were less likely to return for Y2. This introduced a conservative bias into our analyses. Despite this high attrition rate, results from this Y2 sample (i.e., lower reported depressive symptom severity compared to Y1 average) show that lower resting RSA was still associated with higher depressive symptoms over time.

Finally, although it is important to consider biological vulnerabilities in the development of psychopathology, it is only one level of analysis among many factors that could affect risk for depression. According to Beauchaine and colleagues (2008), biological vulnerabilities may moderate the association between environment and behavioral adjustment. That is, when individuals are exposed to environmental risks, higher RSA serves as a protective factor from psychopathology development. In this study, environmental factors that may have influenced the development of depressive symptoms over a 12-month period were not assessed. Examples of these potentially

important environmental factors include perceived social support from family members or peers, and frequency and severity of stressful events. Future research should continue assessing biology × environment interactions in examining the etiology and maintenance of depressive symptoms over time.

Additionally, since depression is characterized by a variety of presenting symptoms, future work should closely examine these individual symptoms of depression and how they are associated with resting RSA. Research by Rottenberg and colleagues (2002) indicates that particular depressive symptoms such as crying and sadness were associated with higher levels of RSA while suicidal ideation was associated with lower levels of RSA. Further, associations between resting RSA and depressive symptoms may change depending on one or more specific depressive symptoms rather than overall symptom severity. Perhaps further examination of symptom heterogeneity will provide answers as to why prior associations between RSA and depressive symptoms have produced mixed results.

Implications for Research and Treatment

This study expands upon previous research examining associations between resting RSA and depressive symptoms in smaller, cross-sectional samples. By including a larger sample of participants across a 12-month period, we are able to assess longitudinal associations within our variables of interest. Similar to previous findings that have documented resting RSA stability in samples of children and adults, RSA appears to be a fairly stable index of parasympathetic activity in emerging adults. In order to explore reasons for mixed findings regarding the association between RSA and depressive symptoms, researchers have begun to examine potential confounding variables. By

assessing multiple potential confounds, the relation between resting RSA and depressive symptoms in our study is likely not due to effects of age, BMI, medication use, or symptoms of anxiety. Results from this study suggest that resting RSA may be a viable prospective biomarker of depressive symptoms.

This has potential implications for preventing later depression. For example, two studies found that biofeedback increased RSA and reduced depressive symptoms in individuals with PTSD (Zucker, Samuelson, Muench, Greenberg, & Gevirtz, 2009) and in a group of post-cardiac surgery patients (Patron et al., 2012). Vagus nerve stimulation has also been proposed as a treatment for chronic, treatment-resistant depression. Berry and colleagues (2013) conducted a meta-analysis which provides some evidence that there is a significant and lasting difference in response and remission rates between treatment resistant, depressed individuals in the intervention group (i.e., vagal nerve stimulation therapy) compared to the treatment as usual group.

Further, psychological interventions targeted towards decreasing depressive symptoms may be a promising direction to pursue. For example, behavioral activation therapy (BA) is a well-established treatment for depression (Dimidjian et al., 2006; Jacobson et al., 1996); however, there is a lack of research that examines whether BA or other effective interventions may increase resting RSA. Examining increases in RSA from biological and psychological intervention approaches may shed more light on the association between RSA and depressive symptoms. In sum, understanding biomarkers (e.g., RSA) as a potentially viable predictor of psychopathology may assist with identification of developing disorders and could ultimately serve as a means of early intervention for individuals at risk for depression.

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