Depression is associated with protracted despondent mood, blunted emotional reactivity, and dysregulated parasympathetic nervous system (PNS) activity. PNS activity is commonly indexed via cardiac output, using indicators of its level (resting respiratory sinus arrhythmia [RSA]) or fluctuations (RSA reactivity). RSA reactivity can reflect increased or decreased PNS cardiac output (RSA augmentation and RSA withdrawal, respectively). Because a single index of a dynamic physiological system may be inadequate to characterize interindividual differences, we investigated whether the interaction of RSA reactivity and resting RSA is a better predictor of depression. Adult probands with childhood-onset depressive disorder histories (n = 113) and controls with no history of major mental disorders (n = 93) completed a psychophysiology protocol involving assessment of RSA at multiple rest periods and while watching a sad film. When examined independently, resting RSA and RSA reactivity were unrelated to depression, but their interaction predicted latent depression levels and proband status. In the context of high resting RSA, RSA withdrawal from the sad film predicted the lowest levels of depressive symptoms (irrespective of depression histories) and the greatest likelihood of having had no history of major mental disorder (irrespective of current distress). Our findings highlight the utility of combining indices of physiological responses in studying depression; combinations of RSA indices should be given future consideration as reflecting depression endophenotypes.

**Keywords:** depression, RSA, SEM, risk

Depressive disorders are characterized by impaired self-regulation of affect, cognition, attention, and energy. Unquestionably, however, protracted despondent mood and difficulties in regulating sad mood are the hallmarks of these conditions (American Psychiatric Association, 1994). Depression has also been associated with blunted reactivity to sad emotional stimuli (e.g., film clips; Rottenberg, 2005).

A growing body of literature has implicated the autonomic nervous system, particularly its parasympathetic branch (e.g., Beauchaine, 2001; Thayer & Lane, 2000), both in the experience of dysphoria (cf. Kreibig, 2010) and in mood regulation (Beauchaine, 2001). With respect to self-regulation, cardiac vagal control has been one commonly used index of parasympathetic nervous system functioning. Vagal efferent outflow to the heart has an inhibitory effect on heart rate and can be indexed by the magnitude of heart rate variability at the respiratory frequency (respiratory sinus arrhythmia [RSA]). This inhibitory effect on heart rate has been likened to the function of a “brake” (see Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996). One aspect of this dynamic system is resting RSA, which signals energy conservation (Porges, 2007) and has been shown to reflect trait self-regulatory capacity (cf. Beauchaine, 2001). For example, high resting RSA is associated with behavioral flexibility (Beauchaine, 2001; Porges, 2007), and low resting RSA is associated with anhedonia (Movius & Allen, 2005) and depression (Rottenberg, 2007). Environmental challenge typically elicits RSA reactivity: The normative RSA response to acute environmental stress and to sadness is to decrease cardiac vagal control (vagal withdrawal), (Kreibig, 2010) which promotes attention modulation and cognitive efficiency (Thayer & Lane, 2000). However, in some people, environmental challenge can also elicit increased cardiac vagal control (vagal augmentation), a pattern that predicts a prolonged course of depression (Rottenberg, Salomon, Gross, & Gotlib, 2005).

Most studies of RSA and depression have examined resting RSA and RSA reactivity separately (Rottenberg, 2007). However, Lacey’s (1959) classic work suggests that focusing on a single index of a physiological system may obscure the extent of interindividual differences. That is, people who are similar on one physiological index of a given system (e.g., resting RSA) may differ markedly on another related index (e.g., RSA reactivity). Indeed, depression findings, which have typically relied on single RSA indices, have often been inconsistent (cf. Rottenberg, 2007), suggesting the potential value of an approach that combines RSA indices.
Recent investigations of emotions focusing on moderation effects of RSA reactivity on resting RSA have explored this approach fruitfully. At high resting RSA levels, RSA withdrawal predicted lower internalizing symptoms in children 2 years later (Hinnant & El-Sheikh, 2009), and helped maintain positive affect in adults while recalling stressful events (Cribbet, Williams, Gunn, & Rau, 2011). In addition to representing physiological markers of depression, combined effects of RSA indices may also help to identify endophenotypes, which is an accepted way to reduce the clinical heterogeneity of depressive disorders (e.g., Stewart, Bismark, Towers, Coan, & Allen, 2010).

The present study examined whether combining indices of resting RSA and RSA reactivity can clarify the contribution of this physiological system to depression. Our clinical sample consisted of rigorously diagnosed young adult probands, whose first depressive episode had onset by age 14. Narrowing the age of depression onset reduces one important source of heterogeneity in depression phenotypes. Additionally, focusing on very early onset cases indexes a familial, recurrent, and serious form of depressive illness (Kauffman, Martin, King, & Charney, 2001). Resting RSA was assessed during multiple rest periods and RSA activity was assessed while viewing a sad film clip. We focused on sadness because it is a cardinal symptom of depression (American Psychiatric Association, 1994), is theorized to be relevant to the self-regulatory difficulties of depressed people (Kovacs, Rotenberg, & George, 2009), and is known to affect RSA (Kreibig, 2010). We hypothesized that at high resting RSA levels, robust RSA withdrawal in response to sad material will predict low levels of depressive symptoms and lowest likelihood of being a depressed proband. Conversely, we expected that at low resting RSA levels, RSA augmentation in response to the sad material will predict high levels of depressive symptoms and highest odds of being a depressed proband. Given the increased measurement precision that is associated with latent variables (see Bollen, 1989), these hypothesized relationships were tested in two sets of structural equation models (SEMs) in which a resting RSA factor was estimated from three protocol rest periods. The first set of models utilized self-report and interview measures as indices of latent depression, which was regressed on the first- and second-order effects of resting RSA factor and RSA reactivity (latent depression model). To account for anxiety and depression severity that are known to affect RSA levels, the second set of models employed self-report and interview measures of anxiety and depression symptoms to estimate a general distress factor (see Bleil, Gianaro, Jennings, Flory, & Manack, 2008). General distress was then added as a covariate in predicting proband group membership from the first- and second-order effects of resting RSA factor and RSA reactivity (group membership model).

### Method

The initial sample included 212 subjects in a longitudinal project (PP) on risk factors for juvenile-onset depression (JOD). Six subjects were deleted due to missing physiological (n = 2) and extreme ∆RSA (n = 4) values. The final sample contained 206 subjects (74% women): 78% were Caucasian, 18% were African American, and 4% had “other” ethnicity. Probands (n = 113) and the 93 normal controls were comparable in sex and racial distributions but differed in age (Mcontrols = 29.04, SD = 5.41; MJOD = 25.97, SD = 3.82); t(205) = 4.76, p < .001.

For probands, mean age at onset of first depression was 10.10 years (SD = 2.83 years), they had three prior depressive episodes (SD = 2.06) on average. At the time of RSA assessment, 41 probands (37%) were in a depressive episode and 31 (28%) were in an episode of an anxiety disorder. Thirty-seven probands were prescribed antidepressants in addition to mood stabilizers (n = 9), atypical antipsychotics (n = 7), and benzodiazepines (n = 9). The controls had no major psychiatric disorders and were free of psychotropic medication.

### Subject Recruitment and Diagnosis

Probands were recruited from among adults who had participated in research studies of depression and anxiety when they were children, or through clinical sites or advertisements in the community. Controls were recruited via the Cole Directory, a cross-reference listing of residential telephone numbers and addresses that is commonly used for business and marketing purposes, as well as through community advertisements and by approaching adults who previously served as controls in pediatric studies. Criteria for study entry included either a verifiable diagnosis of a depressive disorder by the age of 14 years or a history free of major psychiatric disorders.

Recruitment and diagnostic procedures have been described in detail previously (Miller et al., 2002). Briefly, all diagnoses were based on information from subjects and second informants (parents); were derived by experienced, masters-level clinicians via semistructured psychiatric interviews (e.g., Structured Clinical Interview of DSM–IV Disorders [SCID-I]; First, Spitzer, Gibbon, & Williams, 1995); met Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM–IV; American Psychiatric Association, 1994) criteria, with an interrater reliability of κ = .92 for major depressive disorder and κ = .63 for dysthymic disorder; utilized medical and related records to verify age at depression onset; and were finalized via best-estimate consensus procedures by pairs of psychiatrists.

### Rating Scales

Severity of depression symptoms was assessed by the self-rated Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961); clinician-rated severity of depressive symptoms was derived via our own Follow-Up Depression Scale (FDS), consisting of 24 items (each rated on a 0- to 4-point scale) and completed based on a structured interview. In this study, the FDSs had excellent internal consistency (α = .94) and interrater reliability (intraclass correlation coefficient = 0.97). Subjects also completed the self-rated Beck Anxiety Inventory (BAI; Beck, Epstein, Brown & Steer, 1988); clinician-rated severity of anxiety symptoms was derived via our own Follow-Up Anxiety Scale (FAS), consisting of 11 items (each rated on a 0- to 4-point scale), and completed in a structured interview. The FAS had excellent internal consistency (α = .87) and interrater reliability (intraclass correlation coefficient = 0.87) in this study.

Subjects also rated the subjective intensity of five discrete emotions (happy, sad, angry, fearful, and disgust) on a 0- to 8-point Likert-type scale after specific affective stimuli (see Pro-
These intensity ratings were used as a manipulation check.

**Procedures**

The data reported in this article were collected as part of a larger electrophysiological protocol targeting emotional reactivity and regulation. After arrival at the laboratory, each subject received the structured clinical evaluation and completed the self-rated scale, along with a questionnaire regarding recent caffeine consumption, smoking, and current medications. Then, he or she was connected to equipment that continuously monitored multiple physiological parameters during a protocol that involved rest periods and experimental tasks, including emotion inductions via short film clips (i.e., joy, fear, sadness, anger, and disgust). The present report focuses on subjects’ resting RSA during an initial rest period and two later intertask intervals, and RSA while watching a sad film clip. The 172-s sad clip from “The Champ” was selected based on Gross and Levenson (1995).

**Physiological Data Acquisition and Reduction**

Subjects were seated upright in a comfortable chair facing a computer monitor. Resting ECG data were collected during a 384-s pretask period, during which participants sat quietly. Then, they watched a series of film clips, in a fixed order, that were intended to elicit discrete emotions (sequence order: neutral, happy, sad, fear, anger, and disgust film clips). The film clips were followed by a 120-s intertask interval, during which participants sat quietly, one further task (not reported here), and then another 120-s rest interval. For a manipulation check, affect ratings after the sad film were compared with those of the preceding neutral and happy film clips.

Standard guidelines were followed in ECG data acquisition and reduction using software and equipment from the James Long Company (Caroga Lake, NY; Bernston et al., 1997). Ag/AgCl ECG electrodes were placed axially on the left and right rib cage, approximately at heart level. The bioamplifier was set for bandpass filtering with frequencies of 0.01 and 1.000 Hz. The ECG signal was amplified with a gain of 500, and data were digitized with a sampling rate of 512 Hz and resampled off-line at 1,000 Hz to increase precision of R-wave detection (Bernston et al., 1997). Mean heart rate for the initial and the two intertask resting periods ranged from 70.27 to 71.75. Heart rate variability (HRV) is the power band of HRV that occurs in the typical range of respiration.

**Analytic Approach**

Descriptive analyses were conducted in SPSS 19 software (SPSS, Inc., 2011); latent variable and logistic regression models were fit in Mplus version 7.0 software (Muthén & Muthén, 2008–2012). Robust full information maximum likelihood (MLR) was used to estimate parameters adjusted for randomly missing values of dependent variables, which comprised on average 0% to 11% of the sample. Listwise deletion of exogenous predictors yielded sample sizes that varied from 180 to 206. Following Hu and Bentler (1999), CFI values of .95 or greater and RMSEAs of .06 or lower indicate excellent model fit.

**Measurement models.** Two measurement models (the latent depression model and the group membership model) were estimated to determine the fit of latent depression, general distress, and resting RSA factors. The BDI and FDS were used to estimate the latent depression factor for the latent depression model. To account for high correlations between depression and anxiety symptoms (r = .74 to .87) that are known to reduce RSA activity, the BDI, FDS, BAI, and FAS were used as indicators for a common general distress factor in the group membership model, akin to one estimated by Bleil and colleagues (2008). In both models, a latent resting RSA factor was estimated from the 384-s pretask rest epoch and the 120-s postfilm and end of protocol rest intervals (RSA1, RSA2, and RSA3). RSA reactivity (ΔRSA) was defined as the difference between RSA1 and RSA3 during the sad film. Latent factors and ΔRSA were centered at a zero value in all models, and no restrictions were made on latent covariance terms. Residual correlations between RSA1 and ΔRSA were tested, given that ΔRSA is mediated by RSA values. Negative ΔRSA values indicate vagal augmentation and positive values indicate vagal withdrawal.

Latent depression and group membership measurement models demonstrated excellent fit (latent depression, χ²[27] = 26.35, p = .50, CFI = 1.00, RMSEA = .00; group membership, χ²[32] = 46.71, p = .05, CFI = .97, RMSEA = .05). Removing residual covariance between RSA1 and ΔRSA resulted in significantly reduced fit of both models, and was therefore retained (residual rs = .41 to .43, Wald χ²[1] = 13.56–13.63, ps < .001). Latent resting RSA was unrelated to RSA reactivity in both models (rs = −.03, ps = .62). Latent depression correlated with demographic characteristics, anxiety symptom measures, current depression diagnosis, and proband status, but was unrelated to RSA or ΔRSA. Likewise, proband group membership correlated with general distress and age but was unrelated to RSA (results available upon request).

A series of structural models evaluated our primary hypotheses, which concerned main and interactive effects of RSA on the latent depression factor and subject group membership. Latent variable interactions were modeled using latent moderated structural equations (LMS; Klein & Moosbrugger, 2000). The incremental value of each RSA interaction term was evaluated through a Wald chi-square test. Post hoc probes followed approaches outlined by Preacher, Curran, and Bauer (2006).
Results

Consistent with the intended manipulation, repeated measures ANOVAs showed that the sad film clip evoked strong reported feelings of sadness, unlike the neutral or happy films, irrespective of proband status (sadness ratings: $M_{\text{sad-film}} = 4.95, SD = 2.14$; $M_{\text{neutral-film}} = .29, SD = .94$; $M_{\text{happy-film}} = .53, SD = 1.37, F(2, 197) = 432.35, p < .001$; proband status: $F(2, 203) = 2.45, p = .09$). The sad clip also elicited vagal withdrawal, as expected, across both genders ($M_{\Delta\text{RSA}} = .28, SD = .50, t[200] = 8.00, p < .001$), and was more pronounced in men than in women ($F(1, 199) = 3.90, p = .05$; Men: $M_{\Delta\text{RSA}} = .39, SD = .55, t[52] = 5.25, p < .001$; Women: $M_{\Delta\text{RSA}} = .24, SD = .47, t[147] = 6.16, p < .001$). When the bivariate associations reported in Table 1 were examined in a multivariate setting, the significant associations remained, with the following exceptions: (a) sex was no longer related to RSA$_3$, or $\Delta$RSA, and (b) current anxiety disorder was no longer related to depressive symptom measures.

Racial background was unrelated to depression measures, and, along with caffeine consumption and smoking, it also was unrelated to resting RSA indicators and $\Delta$RSA (not shown in Table 1). As warranted in a specific analysis, significant effects shown in Table 1 were statistically controlled.

### Predicting Depression Symptom Severity

A structural model was fit to test the first-order effects of resting RSA and $\Delta$RSA on depression, while controlling for effects of age, sex, anxiety symptoms, psychotropic medication use, current depressive disorder diagnosis, and proband group membership (Figure 1, Panel A). This first-order effects model fit the data well and was used as the base for subsequent analyses, $\chi^2(40) = 64.31, p = .01$, CFI = .98, RMSEA = .06. Although the covariates accounted for a large portion of variance in the depression factor ($R^2 = .86$), there were no significant relationships between depression and resting RSA or $\Delta$RSA ($\tilde{p}_{\text{RSA}} = -.06, p = .09$; $\tilde{p}_{\Delta\text{RSA}} = .03, p = .40$).

The next model included a latent resting RSA $\times$ $\Delta$RSA interaction term. As we hypothesized, including the second-order effects of resting RSA and RSA reactivity significantly improved the fit of the first-order effects model, Wald $\chi^2(1) = 5.82, p < .05$, $\Delta$AIC = 55.43, $\Delta$adj. BIC = 56.03. Specifically, the resting RSA $\times$ RSA interaction term significantly predicted variance in the depression factor ($\beta = -.09, t(179) = 2.48, p < .05$). Post hoc probes revealed that high resting RSA was associated with reduced depression symptom in the context of RSA withdrawal (uncentered $\Delta$RSA > .18; see Figure 2). Contrary to expectation, vagal augmentation was associated with elevated depressive symptoms across the range of resting RSA levels.

### Predicting Proband Status

The structural model testing first-order effects of RSA and $\Delta$RSA on proband status fit the data well, $\chi^2(39) = 60.89, p = .01$, CFI = .96, RMSEA = .05 (Figure 1, Panel B). Again, neither resting RSA nor $\Delta$RSA emerged as significant predictors ($\tilde{p}_{\text{RSA}} = -.04, p = .68$; $\tilde{p}_{\Delta\text{RSA}} = .15, p = .07$).

Consistent with our hypothesis, adding the second-order latent resting RSA $\times$ $\Delta$RSA interaction term significantly improved the model fit, Wald $\chi^2(1) = 4.54, p < .05; \beta = -.15, p < .05$. Post hoc probes of the interaction term revealed that, controlling for general distress (i.e., depressive and anxiety symptoms), high resting RSA reduced the likelihood of proband status in the context of high RSA withdrawal (uncentered $\Delta$RSA $\approx .89$). For example, in the context of high RSA withdrawal, high resting RSA (1 SD above the mean) increased the probability of control group membership by 91%, compared with low resting RSA levels (1 SD below the mean; OR = 9.60, 95% CI [1.01, 91.06]). Contrary to expectation, at low resting RSA, vagal augmentation did not significantly increase the risk of proband membership.

Discussion

This study investigated the value of combining RSA indices for predicting depressive symptoms and depressive disorder histories. Consistent with our hypotheses, combined effects of resting RSA and an index of RSA reactivity emerged as strong predictors of depression (whereas single indices made no contribution). In the context of robust RSA withdrawal in response to a sad emotional challenge, resting RSA predicted reduced depressive symptoms (irrespective of depression histories) and an increased likelihood of control group membership (irrespective of current distress). These findings held even after statistically controlling for several possible confounds, including anxiety symptoms, psychotropic medication use, and current depressive disorder diagnosis.

A protective effect of high resting RSA combined with RSA withdrawal in response to a dysphoric challenge is consistent with other reports: This physiological pattern has been found to protect against internalizing symptoms (Hinnant & El-Sheikh, 2009) and to help maintain positive affect during stressors (Cribbet et al., 2011). Laboratory-induced vagal withdrawal in response to negative valenced stimuli is associated with emotional responsiveness (Weinberg & Tronick, 1996), and is also the normative reaction among healthy adults to themes of loss (Kreibig, 2010). Given individual associations between high resting RSA and good executive functioning (Hansen, Johnsen, & Thayer, 2003; Thayer & Lane, 2000), and between RSA withdrawal and attention modulation, the combination of RSA withdrawal in the presence of high resting RSA may facilitate appropriate attentional and emotional responsiveness to changing environmental demands.

One question raised by our findings is how might the combination of high resting RSA and RSA withdrawal reduce the risk for depression? One potential pathway may be through their effects on mood regulation. For example, high resting RSA is associated with adaptive emotion regulatory responses (Volokhov & Demaree,
Table 1
Descriptive Statistics and Correlations Among Study Variables

<table>
<thead>
<tr>
<th>Measures</th>
<th>$M$ (SD)</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td>27.35 (4.84)</td>
<td>.20**</td>
<td>- .32**</td>
<td>- .12</td>
<td>- .27**</td>
<td>- .25**</td>
<td>- .26**</td>
<td>- .02</td>
<td>- .16*</td>
<td>- .21**</td>
<td>- .18**</td>
<td>- .13</td>
<td>- .21**</td>
<td>- .09</td>
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<tr>
<td>2. Sex (0 = Male)</td>
<td>—</td>
<td>.01</td>
<td>.05</td>
<td>- .10</td>
<td>- .11</td>
<td>- .16*</td>
<td>- .14*</td>
<td>.13</td>
<td>.14*</td>
<td>.02</td>
<td>.10</td>
<td>.14*</td>
<td>.09</td>
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<td>3. Proband (0 = No)</td>
<td>—</td>
<td>.43**</td>
<td>.05</td>
<td>.09</td>
<td>.05</td>
<td>.12</td>
<td>.54**</td>
<td>.58**</td>
<td>.46**</td>
<td>.48**</td>
<td>.58**</td>
<td>.39**</td>
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<td>4. Meds (0 = No)</td>
<td>—</td>
<td>- .13</td>
<td>- .06</td>
<td>- .09</td>
<td>- .03</td>
<td>.45**</td>
<td>.42**</td>
<td>.48**</td>
<td>.42**</td>
<td>.37**</td>
<td>.46**</td>
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<tr>
<td>5. RSA1</td>
<td>6.76 (1.16)</td>
<td>.89**</td>
<td>.86**</td>
<td>.12</td>
<td>.09</td>
<td>.04</td>
<td>.07</td>
<td>.16*</td>
<td>.09</td>
<td>- .05</td>
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<td>6. RSA2</td>
<td>6.76 (1.22)</td>
<td>.87**</td>
<td>.02</td>
<td>.09</td>
<td>.05</td>
<td>.13</td>
<td>.18**</td>
<td>.11</td>
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<td>7. RSA3</td>
<td>6.57 (1.17)</td>
<td>—</td>
<td>.05</td>
<td>.05</td>
<td>.08</td>
<td>.14</td>
<td>.14</td>
<td>.11</td>
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<td>8. $\Delta$RSA</td>
<td>.28 (.50)</td>
<td>.02</td>
<td>.09</td>
<td>.06</td>
<td>- .04</td>
<td>.07</td>
<td>.03</td>
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<tr>
<td>9. BDI</td>
<td>7.57 (9.10)</td>
<td>.87**</td>
<td>.60**</td>
<td>.77**</td>
<td>.76**</td>
<td>.39**</td>
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<td>10. FDS</td>
<td>9.98 (11.43)</td>
<td>.66**</td>
<td>.74*</td>
<td>.85**</td>
<td>.43**</td>
<td></td>
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<td>11. DepDx (0 = No)</td>
<td>—</td>
<td>.48*</td>
<td>.56**</td>
<td>.54**</td>
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<td>12. BAI</td>
<td>6.61 (8.10)</td>
<td>.72**</td>
<td>.40**</td>
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<tr>
<td>13. FAS</td>
<td>5.31 (5.31)</td>
<td>.45**</td>
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<td>14. AnxDx (0 = No)</td>
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<td>—</td>
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</table>

Skewness $M$ (SE) | .68 (.17) | — | — | — | — | — | — | — | — |
Kurtosis $M$ (SE) | -.15 (.34) | — | — | — | — | .82 (.34) | .22 (.34) | .02 (.36) | .51 (.34) | 2.46 (.34) | 1.10 (.35) | — | 3.92 (.34) | .08 (.35) | — |

Note. $N$ between 167 and 206. AnxDx = current anxiety disorder; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; DepDx = current depressive disorder; FAS = Follow-Up Anxiety Scale; FDS = Follow-Up Depression Scale; meds = psychotropic medication; RSA1, RSA2, and RSA3 = prefilm, postfilm, and end of protocol resting RSA; $\Delta$RSA = change in prefilm to during film.

* No significant differences between probands and controls.  ** Means/frequencies significantly higher for probands than controls ($ps < .0001$).

*p ≤ .05.  **p ≤ .01.
2010) and has been shown to facilitate effective mood regulation by reducing the intensity of negative arousal (Dywan, Mathewson, Choma, Rosenfeld, & Segalowitz, 2008; Fabes & Eisenberg, 1997). Likewise, RSA withdrawal negatively correlates with the use of maladaptive coping responses (e.g., Colder, 2001; Healy, Treadwell, & Reagan, 2011) and predicts faster recovery from depressive episodes (Rottenberg et al., 2005). Thus, future work on combined effects of resting RSA and RSA reactivity may speak not only to mood regulation but also to mechanisms of depression genesis, and pathways to its treatment.

Our results also showed that RSA augmentation was associated with depression across the range of resting RSA levels. This finding is interpretable if RSA augmentation is seen as an atypical response to sadness (Kreibig, 2010) and one that predicts a more enduring course of depression (Rottenberg, Salomon, Gross, & Gotlib, 2005). Taken in the context of our findings on RSA withdrawal and other studies showing negative associations between resting RSA and depression (Rottenberg, 2007), one possibility is that RSA augmentation inhibits salubrious effects of resting RSA. This possibility should be explored in future investigations.

That we obtained null findings for single RSA indices was not entirely surprising. The extant literature shows inconsistent association between RSA and a current diagnosis of depression (Rottenberg, 2007). It is important to point out that our study population was adults with prior histories of juvenile onset depression. Nonsignificant effects of single RSA indices on depression may in part reflect the features of our study population.

In light of the lack of main effects, the significant moderation effects of RSA reactivity on resting RSA underscores the value of our measurement approach to characterizing complex physiologic systems (Lacey, 1959). As noted by El-Sheikh and Erath (2011), a combination of PNS levels and fluctuations may be needed to understand its role in adaptive functioning. The clear pattern in our data suggests value in reanalyzing existing resting RSA and RSA reactivity data on depressed cases to test whether the interaction of the two indices yields superior predictive power over individual metrics.

Dynamic relations between RSA levels and fluctuations in depressed patients should be given consideration as depression endophenotypes. It has been reported that never-depressed offspring of depressed parents exhibit aberrant resting RSA (Field, Pickens, Fox, & Nawrocki, 1995) and fail to show normative RSA development (Gentzler, Rottenberg, Kovacs, George, & Morey, 2012). We also have preliminary findings indicating that the joint effects of resting RSA and RSA reactivity (comparable with those reported here) differentiate youth at high risk for depression from normal controls. In the context of familial depression transmission models (e.g., Goodman & Gotlib, 1999), atypical PNS functioning
that is captured by the RSA profiles may represent dysfunctional neuroregulatory mechanisms that increase the risk of depression.

To our knowledge, this study is the first to investigate the combined effects of resting RSA and RSA reactivity on depression symptoms and histories in adults with JOD, and it has several strengths. Using a sample of juvenile-onset probands controlled for age of depression onset, a key contributor to phenotypic heterogeneity in depression. Structural equation modeling attenuated measurement error and controlled for key variables known to confound RSA. Finally, a sadness film challenge as a means to probe RSA reactivity had both ecological and empirical validity. However, our findings should also be interpreted in the context of several limitations. Because we did not measure respiration, we cannot rule out the possibility that respiration influenced our findings. As our sample consisted of early onset depression cases, our findings have unknown generalizability to adult-onset depression. Finally, although we sought to investigate the contribution of the PNS to depression, we recognize that PNS activity is partly influenced by the sympathetic nervous system (Bernston et al., 1997). Future studies that address the limitations noted here could help to further clarify the role of RSA in depression.

References


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