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Cardiac vagal control as a prospective predictor of anxiety in women diagnosed with breast cancer☆

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ABSTRACT

Low cardiac vagal control (CVC) has been associated with state and trait anxiety and anxiety spectrum disorders. Studies indicate that diagnosis and treatments for breast cancer may be associated with anxiety. The current study examined whether CVC prospectively predicted a trajectory of change in anxiety following breast cancer diagnosis. Forty-three women diagnosed with non-metastatic breast cancer completed the Taylor Manifest Anxiety Scale and the Perceived Stress Scale, and a 5-min resting electrocardiographic (ECG) segment was recorded. Self-report measures were completed approximately every 3 months for a year. Respiratory sinus arrhythmia (RSA) significantly predicted the trajectory of change in anxiety over the follow-up period: participants with higher baseline RSA evidenced decreasing anxiety, whereas those with lower baseline RSA had increasing anxiety. These results are consistent with the hypothesis that CVC facilitates the modulation of anxiety in women coping with significant stressors of breast cancer diagnosis and treatment.

Cardiac vagal control (CVC), as measured by respiratory sinus arrhythmia (RSA), has been proposed as one of the indices of emotion regulation (Porges, 1995, 1997, 2007). In the literature, CVC has been found to predict outcomes in a variety of psychiatric (e.g., Beauchaine, 2001; Chambers and Allen, 2002; Licht et al., 2008) and medical conditions (e.g., Lindmark et al., 2003; Licht et al., 2010; Masi et al., 2007; Vanninen et al., 1993). Data suggest that higher resting RSA is associated with positive emotionality (Oveis et al., 2009), social engagement (Horsten et al., 1999), and coping with life stressors (Fabes and Eisenberg, 1997).

RSA, a measure of heart rate variability related to respiration, has been conceptualized as an index of physiological and psychological flexibility (Friedman and Thayer, 1998). RSA has been proposed to reflect integration and efficiency of central-peripheral neural feedback mechanisms implicated in flexibility and ability to adjust to environmental demands (Friedman, 2007). Given that anxiety is often marked by quick activation of threat responses and poor inhibition, this theoretical framework suggests reduced RSA in anxiety. Consistent with this view, studies indicate that low RSA is associated with clinical forms of anxiety, as well as state and trait anxiety (Cohen and Benjamin, 2006; Friedman, 2007). In a study of adolescents (Greaves-Lord et al., 2010), lower baseline RSA was predictive of anxiety in girls 2 years later. There are reports of a negative association between RSA and trait anxiety in healthy individuals (Fuller, 1992; Watkins et al., 1998). Among college students, reduced RSA during sleep was associated with self-reported state anxiety (Sakakibara et al., 2008). There is evidence indicating that reduced RSA is also associated with both trait (Delgado et al., 2009) and state worry (Hofmann et al., 2005). Additionally, lower RSA has been detected in individuals diagnosed with posttraumatic stress disorder (Blechert et al., 2007; Jovanovic et al., 2009; Woodward et al., 2009) and other anxiety disorders (Johnsen et al., 2003; Licht et al., 2009) as compared to healthy controls.

Despite numerous examinations of CVC and anxiety-related phenomena, CVC has been understudied in cancer patients. Despite improvements in cancer treatments, breast cancer remains a life-threatening condition and cancer patients often experience emotional turmoil and symptoms of depression and anxiety immediately after the diagnosis (Derogatis et al., 1983; Ganz et al., 1998; Nosarti et al., 2002; Palesh et al., 2006; Spiegel and Giese-Davis, 2003; Zabora et al., 2001). Even though studies of women with metastatic breast cancer identified the association between reduced RSA and depression (Giese-Davis et al., 2006) as well as sleep disruptions (Palesh et al., 2008), to date, there are no prospective studies examining whether CVC, as indexed by RSA, is associated with differences in coping with non-metastatic breast

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cancer. Given the existing evidence that RSA may prospectively predict anxiety (Greaves-Lord et al., 2010), prospective studies of RSA in breast cancer patients may have clinical utility as they could help identify those patients at risk for experiencing difficulties in coping with breast cancer diagnosis and treatments. Therefore, in the present study RSA was assessed as a prospective predictor of the trajectory of change in anxiety in non-metastatic breast cancer patients over a 1-year follow-up period. Given the reviewed literature, examination of depression in breast cancer patients would be of equal importance; however, the scope of the present investigation was limited by the unavailability of data on depression.

1. Methods

1.1. Study design

The present study added a specific aim to a larger prospective, longitudinal investigation of the association of close personal relationships with biobehavioral outcomes in patients newly diagnosed with breast cancer. This aim was based on the literature reviewed above, to test the hypothesis that higher baseline RSA would predict a more beneficial trajectory of change in anxiety whereas lower baseline RSA would predict an increase in anxiety over the ensuing year.

The participants were recruited from the Multidisciplinary Breast Oncology Clinic at the Arizona Cancer Center, and informed consent was obtained in accordance with procedures approved by the Human Subjects Protection Committee of the University of Arizona prior to any data collection. Electrocardiogram (ECG) and self-report questionnaires were collected at baseline, and self-report questionnaire data were obtained every 3 months with in-person interviews for 1 year after study enrollment. The inconvenience of the visits was minimized by scheduling the research assessments in conjunction with visits to the surgery clinic, medical oncology and radiation oncology clinics.

1.2. Participants and sample characteristics

Fifty participants (Age = 53 ± 8.8 years; Mean time since diagnosis = 4.9 ± 4.2 months, range of 0.5–17 months) who were not undergoing cardio-toxic chemotherapy regimens (1.9%; $n = 2$) or taking medications with anticholinergic properties or medications that produce a general effect on cardiac function (50.9%; $n = 54$) were included in this substudy. Participants who were taking medications that affected cardiovascular responses (i.e., anticholinergics, beta blockers, calcium channel blockers, angiotensin receptor blockers, angiotensin converting enzyme inhibitors, opioid agonists) were excluded due to potential alterations in RSA as the result of taking these medications. The parent study from which these 50 participants were drawn comprised 106 female participants (Age = 55.3 ± 9.3 years; Mean time since diagnosis = 4.3 ± 4.0 months; range of 0.3–17.7 months) with stage 0 ($n = 19$; 17.9%), I ($n = 43$; 40.6%), IIA ($n = 22$; 20.8%), IIB ($n = 12$; 11.3%), IIIA ($n = 4$; 3.8%), and IIIB ($n = 1$; 0.9%) breast cancer. Breast cancer severity was quantified with the Nottingham Prognostic Index (NPI; Galea et al., 1992). NPI is calculated based on tumor size, tumor histological grade, and lymph node stage, with higher NPI scores indicating greater disease severity.

From among these 50 participants, a final sample of 43 was used in the analyses. One participant who died during the data collection period was excluded from the analyses. At the beginning of the substudy, one participant (2%) was diagnosed with recurrent disease and thus was excluded from the analyses. Since the analysis focused on the assessment of change in anxiety over time, five participants (10%) who contributed fewer than three self-report observations were additionally excluded. If participants were diagnosed with recurrent breast cancer ($n = 1$; 2%) during data collection, data collected after recurrence were removed, since the diagnosis of recurrence was likely to affect the outcome measure of anxiety. This final sample of 43 participants did not differ from the full set of participants in the parent study by age, $t(146) = -1.2$, *ns*, time since diagnosis to the ECG assessment, $t(141) = 0.1$, *ns*, NPI, $t(142) = -0.5$, *ns*, anxiety, $t(142) = 1.1$, *ns*, or perceived stress $t(144) = 0.5$, *ns*, at baseline. The substudy participants included in analyses and participants in the parent study appeared comparable on other demographic and treatment variables displayed in Table 1.

1.3. Physiological data recording and reduction

At the participants' visit to the oncology clinic for this substudy, 5 min of resting ECG data were recorded. The participants were given instructions to sit quietly without talking or moving during the ECG recording. No instructions were given to the participants on how to breathe. The research nurse was present in the same room with the participants during the ECG recording. Among the 43 participants included in analyses, 20 had companions accompany them to the clinic visit. If present, a companion was in the same room with the participant and research nurse during the ECG recording.[1] If a companion was not present, only the participant and the research nurse were present in the room during the ECG recording. The presence of another person in the room during the ECG recording (a nurse or a companion) could have influenced the assessment of RSA, so the extent to which findings of the present study would generalize to solo recording conditions is unknown.

ECG was recorded using a J & J Amplifier System (Poulsbo, WA). Gel free Ag–AgCl electrodes were attached to the left and right wrist, and the ground electrode was attached to the lower right forearm. The ECG signal was sampled at 512 Hz. Respiration was recorded from each participant using a respiration sensor (J & J Engineering; Poulsbo, WA).

The off-line analysis of the raw digitized ECG signal was performed by extracting interbeat interval (IBI) series from the raw ECG recording by using QRSTool Software (Allen et al., 2007). Since even a single artifact can distort an index of RSA (Berntson and Stowell, 1998), each extracted interbeat series was hand-corrected for artifacts such as missed, erroneous, or ectopic beats.

According to the guidelines for the quantification of the heart rate variability (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Berntson et al., 1997), the high frequency band (HF) of the heart rate spectrum is assumed to represent vagal influences. Heart rate variability in the HF band (.12–.4 Hz), which is assumed to be related to respiration, was derived with CMetX Cardiac Metric Software (Allen et al., 2007) and used to calculate an estimate of respiratory sinus arrhythmia. The CMetX program converted IBI series to a time-series sampled at 10 Hz with linear interpolation. A 241-point optimal finite impulse response digital filter designed using FWTGEN V3.8 (Cook and Miller, 1992) with half-amplitude frequencies of a .12–.40 Hz was applied to the 10 Hz time-series representation of the IBI series. The natural log of the variance of the filtered waveform was used as the estimate of RSA. All participants were verified to be breathing within the respiratory frequency range (.12–.40 Hz), assessed by examining the dominant frequency in the power spectrum of the respiration waveform. This validation check was performed in order to confirm that participants were breathing neither too slowly nor too quickly to ensure the RSA metric adequately captured their respiratory related variations in heart rate.

2. Self-report measures

Participants completed questionnaires at the initial visit and then again approximately every 3 months. Data collected every 3 months for up to a year after the initial visit (up to 5 assessments) were used in the analyses. Some subjects missed one or more assessments due to illness related constraints or other factors. The participants filled out a short version of the Taylor Manifest Anxiety Scale (TMAS; Bendig, 1956), which has been shown to have a comparable reliability to the longer version of the scale (Taylor, 1953). The short TMAS consists of 20 true or false items that assess typically experienced signs of anxiety (e.g., I believe I'm no more nervous than most others; I sometimes feel that I am about to go to pieces), with higher scores indicating greater level of anxiety. The internal consistency reliability of the 20-item TMAS scale is .76 (Bendig, 1956).

A 10-item version of the Perceived Stress Scale (PSS; Cohen et al., 1983) was administered to all participants. The scale comprises items measuring the degree to which situations in one's life are perceived as stressful (e.g., How often have you felt you could not cope with all the things you had to do? How often have you felt nervous and "stressed?"). The total score on this scale is the total of all item responses (0 = Never, 4 = Very often). The internal consistency reliability of 10-item PSS is .89 (Roberti et al., 2006).

3. Statistical analyses

RSA was examined as a predictor of change in anxiety as measured by TMAS over the year following the initial ECG assessment. One RSA assessment obtained at baseline and up to five self-report assessments of stress and anxiety obtained approximately every 3 months were used in analyses. Demographic and treatment variables (race, ethnicity, education, marital status, disease

[1] There were no statistically significant differences in RSA between those participants who had companions present in the room during the ECG recording and those who did not.

Table 1
Demographics and treatment variables for the sample included in analyses and the entire sample from the parent study.

	Included sample ($N = 43$)			Parent study sample ($N = 106$)		
	M	*SD*	Range	*M*	*SD*	Range
Age (years)	53.2	9.2	27–72	55.2	9.3	27–76
Time from diagnosis to ECG assessment (months)	4.2	3.9	0.5–15.9	4.7	4.4	0.5–19
	N	%		*N*	%	
Race						
African American	0	0.0		0	0.0	
Asian	0	0.0		1	0.9	
Caucasian	36	83.7		88	83.1	
Hispanic	7	16.3		16	15.1	
Other	0	0.0		1	0.9	
Marital status						
Married	26	60.5		64	60.4	
Divorced	8	18.6		23	21.7	
Separated	0	0.0		1	0.9	
Widowed	2	4.7		3	2.8	
Living together	3	6.9		8	7.6	
Single	4	9.3		7	6.6	
Education						
College degree or higher	23	53.5		48	45.3	
Missing	1	2.3		1	0.9	
Stage of disease						
0	11	25.6		19	17.9	
I	15	34.9		43	40.6	
IIA	11	25.6		22	20.8	
IIB	4	9.3		12	11.3	
IIIA	1	2.3		4	3.8	
IIIB	0	0.0		1	0.9	
Missing	1	2.3		5	4.7	
Type of surgery						
Mastectomy	18	41.9		44	41.5	
Lumpectomy	24	55.8		55	51.9	
Biopsy only	1	2.3		1	0.9	
Missing	0	0.0		6	5.7	
Adjuvant treatment						
Chemotherapy only	7	16.3		20	18.9	
Antihormonal therapy only	3	7.0		6	5.7	
Radiation only	6	14.0		12	11.3	
Chemotherapy and antihormonal therapy	0	0.0		2	1.9	
Chemotherapy and radiation therapy	4	9.3		7	6.6	
Chemotherapy, radiation, and antihormonal therapy	0	0.0		2	1.9	
Radiation and antihormonal therapy	4	9.3		10	9.4	

severity, current disease status, type of treatment, time from diagnosis to initial assessment, use of antidepressant medications, use of antianxiety medications[2]), and perceived stress were examined in separate models as predictors of TMAS. Those variables that were significant predictors of TMAS (either as main effects or in their interaction with time: education, time from diagnosis to initial assessment, perceived stress) were then included in an expanded model with RSA and the interaction with RSA. All of the analyses were conducted using multilevel modeling in the PROC MIXED routine of SAS 9.2 software (Singer, 1998). PROC MIXED allows modeling of the growth parameters for each individual as random effects and individual-level covariates as fixed effects. The effect of growth parameters and individual-level covariates alone as well as the effect of their interaction on the dependent variable can be examined using this approach. Additionally, multilevel modeling allows variability with regard to spacing and number of measurement occasions, which is advantageous for longitudinal studies, in which participants may not be available at the desirable times of measurement or drop out of the study. In this study, participants with at least three assessment time points were included in order to appropriately address the question of the trajectory of change in anxiety over time. A maximum likelihood estimation procedure and an unstructured error structure were specified in the models.

4. Results

4.1. RSA and age

A preliminary analysis revealed the expected significant negative correlation between RSA and age ($r = -.48$, $p < .01$), consistent with that reported in the RSA literature (Masi et al., 2007; DeMeersman and Stein, 2007). Because of this association, RSA values were age-adjusted to account for age-related variance in RSA, and age-adjusted values were used in all subsequent analyses. Age at recruitment was entered in a regression model as a predictor of RSA, and non-standardized residuals were calculated and saved for all subsequent analyses.[3] Importantly, age at recruitment was not significantly correlated with TMAS ($r = -.20$, *ns*), so that age was not confounded with either the predictor or criterion variables (cf. Miller and Chapman, 2001).

[2] Based on the lack of information and rare occurrence of smoking in the study sample, smoking status was not included as a variable in the analyses.

[3] Results of analyses using raw RSA values (RSA unadjusted for age) replicate the age-adjusted findings presented in this manuscript.

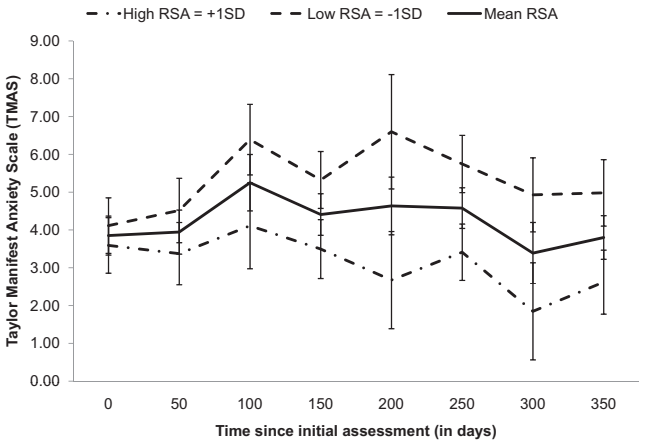

Fig. 1. Effect of the interaction between RSA adjusted for age and Time since initial assessment on TMAS over a 1-year period. Although RSA is a continuous variable, for illustrative purposes, its effect on TMAS is plotted at ±1 SD from the mean. Error bars represent standard errors. RSA: respiratory sinus arrhythmia; SD: standard deviation; TMAS: Taylor Manifest Anxiety Scale.

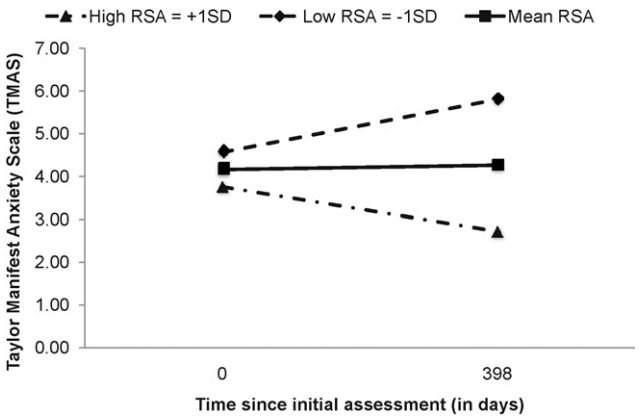

Fig. 2. Simple slopes depicting the two-way interaction between RSA and Time from initial assessment (in days). The simple slopes become significant 180.2 days after the initial assessment, and the effect continues to increase thereafter. RSA: respiratory sinus arrhythmia; TMAS: Taylor Manifest Anxiety Scale.

4.2. Baseline RSA and trajectory of change of anxiety

Consistent with characteristics of a trait measure, the intraclass correlation of 0.71 indicated that 71% of the variance in anxiety measure (TMAS) was attributable to between-person as opposed to within-person variations in anxiety. Nevertheless, anxiety increased in twenty-two participants (51%) over time, thus RSA was examined as a possible predictor of change. To examine the effect of RSA on change in anxiety, in the growth model with TMAS as the dependent variable, Time from initial assessment to each questionnaire assessment (in days) was entered as a within-participant independent variable, RSA (uncentered, since adjustment for age produced a meaningful 0 on this measure) was entered as a between-participant independent variable, and TMAS was entered as a dependent variable. The model revealed no significant main effect of Time since initial assessment, $F(1, 150) = 0.1$; $\beta = -.0002$, $t = 0.2$, *ns*, and no main effect of RSA, $F(1, 150) = 0.6$; $\beta = -.34$, $t = -0.8$, *ns*; however, the predicted significant interaction between Time since initial assessment and RSA emerged, $F(1, 150) = 6.2$, $\beta = -.002$, $t = -2.5$, $p < .05$, indicating that although there was no observed overall change in anxiety over time, in those participants who did evidence change in anxiety, the trajectory of this change was predicted by RSA. More specifically, participants with lower baseline RSA evidenced an increase in anxiety over the follow-up period, whereas participants with higher baseline RSA evidenced a decrease (see Fig. 1 for the illustration of the interaction between RSA and Time since initial assessment).

In the follow-up analyses using the covariates mentioned above, in all instances the RSA by Time interaction remained significant in all models, but the effect of other covariates remained significant only for time from diagnosis to initial assessment and for perceived stress measured by PSS (as main effects). Thus in the final model, these two variables were included to assess whether the effect of RSA on the trajectory of anxiety remained after accounting for variance in anxiety due to these variables. In this final model, Time since initial assessment and PSS were entered as within-participant independent variables, RSA and Time from diagnosis to initial assessment were entered as between-participant independent variables, and TMAS was entered as a dependent variable. As previously reported, there was no main effect of Time since initial assessment in this model, $F(1, 149) = 0.4$, $\beta = .0007$, $t = 0.7$, *ns*, and no main effect of RSA, $F(1, 149) = 1.6$, $\beta = -.51$, $t = -1.3$, *ns*; however, the interaction between Time since initial assessment and RSA remained significant, $F(1, 149) = 5.4$, $\beta = -.002$, $t = -2.3$, $p < .05$. The effects of time from diagnosis to initial assessment, $F(1, 149) = 5.4$, $\beta = .009$, $t = 2.3$, $p < .05$, and PSS, $F(1, 149) = 9.6$, $\beta = .26$, $t = 3.1$, $p < .01$, also remained significant. This model suggests that although there was no systematic group-level pattern of change in anxiety over the 1-year follow-up period, the individual differences in the trajectory of change in anxiety were predicted prospectively by RSA, and that perceived stress and time from diagnosis to the initial assessment were predictors of overall anxiety level (but not change in anxiety). The direction of the effects indicate that participants first assessed closer to initial diagnosis and those with lower perceived stress had lower anxiety scores, and that those with lower RSA experienced an increase in anxiety, whereas participants with higher RSA experienced a decrease in anxiety (see Table 2 for a summary of this model's parameters).

A computational tool for the decomposition of simple slopes in multilevel models (Preacher et al., 2006) was used to examine the nature of the interaction effect between baseline RSA and Time from initial assessment. The significance of the simple slopes was tested at the very beginning of the study (Time from initial assessment = 0 days), at the mean time from initial assessment (Time from initial assessment = 175.3 days), and at the maximum available time point (Time from initial assessment = 398 days). The decomposition of the simple slopes indicated that significant differences between participants based on their RSA levels were not evident at the beginning of the study ($t = -0.8$, *ns*). The differences were approaching significance at the mean time from the initial assessment ($t = -2.0$, $p = .054$), and the examination of the region of significance of the time-variant predictor, Time since initial assessment, revealed that the interaction between RSA and time from the initial assessment became significant 180.2 days after the initial assessment. The differences between participants based on their RSA continued to increase up until the maximum assessment point ($t = -2.9$, $p < .05$) (see Fig. 2 for the depiction of simple slopes).

5. Discussion

5.1. Cardiac vagal control as a predictor of anxiety

Consistent with the study hypothesis, the results of this study indicated that RSA at baseline was significantly and prospectively associated with the trajectory of change in anxiety over the follow-up period, such that those participants with higher baseline RSA evidenced a decrease in anxiety, whereas participants with lower baseline RSA were more likely to have increasing anxiety during the follow-up period. This suggests that RSA may index the ability

Table 2
Parameters of the model with multiple predictors of trajectory of change in TMAS.

Parameter	Variable level	DF	*B*	*SE β*	*T*	*p*
Intercept		40	2.98***	0.68	4.4***	<.0001
Time since initial assessment	1	149	0.0007	0.001	0.7	*ns*
PSS	1	149	0.26**	0.08	3.1**	<.01
RSA	2	149	−0.51	0.41	−1.3	*ns*
Time from diagnosis to initial assessment	2	149	0.009*	0.004	2.3*	<.05
RSA × Time since initial assessment	n/a	149	−0.002*	0.0009	−2.3*	<.05

Note. The estimate of the fit of this model (AIC) = 912.1; RSA: respiratory sinus arrhythmia; PSS: Perceived Stress Scale; DF: degrees of freedom; SE: standard error.
* $p < .05$.
** $p < .01$.
*** $p < .0001$

to modulate anxiety in this sample of breast cancer patients. The present findings are consistent with the premise of Polyvagal theory (Porges, 1995, 1997, 2007) that RSA indexes emotion regulation and the ability to adapt to stressors.

Interestingly, although a trait measure of anxiety was used as the outcome measure in this study, the analysis indicated changing levels of anxiety over time on this measure as a function of RSA. Perhaps this illustrates the profound effect of stressors associated with breast cancer diagnosis and treatment on what is believed to be a relatively stable, trait-like level of anxiety. In the present study, perceived stress was also associated with the outcome measure of anxiety; however, even after accounting for the effect of the perceived stress, the effect of RSA on change in anxiety remained significant. Additionally, time from the diagnosis to the initial RSA assessment was associated with anxiety. Interestingly, in this sample of breast cancer patients, greater time from the diagnosis to the initial RSA assessment was associated with greater anxiety. The direction of this effect is surprising as it might be expected that the time around the breast cancer diagnosis would be associated with greater anxiety compared to the later stages of breast cancer treatment and recovery. However, greater time since diagnosis may be indicative of the ending phases of treatment and transitioning to survivorship phase, and although most women adjust well to the end of treatment, for some patients this milestone in cancer trajectory may be anxiety provoking due to reduced social and medical support, fears of recurrence, or an increased sense of vulnerability (Stanton et al., 2005a,b).

In the present study, women may have been experiencing stress and anxiety from treatments themselves as well as due to concerns of recurrence and transitioning to survivorship or re-entry phase. In this context, RSA may reflect the extent to which women in the present study adaptively coped with the stressors of breast cancer diagnosis, treatment, and recovery. Future studies will need to establish what other factors may influence the trajectory of change in anxiety in breast cancer patients as well as in other high risk populations under stress.

6. Study limitations

One of the limitations of this study is a relatively small sample size. More than half of the participants in the parent study used medications with anticholinergic properties or medications with a general effect on cardiac functioning (i.e., medications for hypertension); therefore, many of the participants were excluded from analyses since the effect of these medications could potentially obfuscate the RSA assessment. Another important limitation in the present study was heterogeneity in timing of assessments since diagnosis. The assessment of RSA was added to the protocol after the parent study began, and thus the first seventeen participants in the parent study received their first RSA assessment not during their first study visit, but at the next available study visit. This introduced heterogeneity to the stage of treatment at which RSA was assessed, and complicated the interpretation of the finding that anxiety was higher among those assessed later after their initial diagnosis. Given the co-morbidity between anxiety and depression, both in the general population (e.g., Kessler et al., 2003) and in those diagnosed with breast cancer (e.g., Vahdaninia et al., 2010), the findings of the present investigation would have been strengthened by the examination of depressive symptoms, but unfortunately, no measure of depression was included in the study. Another methodological limitation, all too common in studies of phenomena that cannot be experimentally manipulated, is that a true causal relationship between CVC and anxiety could not be established due to the non-experimental nature of the study. Nonetheless, the results of the present study support the predictive validity of vagal control and suggest that vagal control may hold an important clinical utility in helping to identify a high-risk sample of patients, who may benefit from emotionally supportive interventions. Additionally, the research nurse and sometimes a companion were present in the same room with participants at the time of the ECG recording; therefore, there is a possibility that the presence of the nurse or a companion might have had an influence on RSA of participants. Yet another limitation of the present study is the assumption that RSA provides an accurate measure of CVC. Given that this assertion cannot be confirmed with non-invasive methods, there is always a question of how precisely RSA reflects vagal control, although the assumption that RSA accurately reflects vagal control when assessed in quiet resting conditions is fairly well supported (Houtveen et al., 2002), and the fact that all participants in the present study were verified to be breathing within the identified respiratory band further supports this assumption. The assumption that RSA is indeed the index of vagal control is extensively made in human literature; therefore, the presented findings are comparable in that regard to the large extant literature on this topic.

7. Conclusion

The present study revealed promising findings in a relatively small but clinically relevant sample of women following the diagnosis of breast cancer. These findings suggest that future investigations might examine the extent to which higher vagal control would be similarly associated with a more favorable trajectory in other stressful medical conditions. Moreover, the findings suggest that the role of CVC in adjustment and coping with illness might provide important implications for clinical care; for example, patients low in vagal control at illness onset might constitute a vulnerable group in need of emotionally supportive interventions to improve coping with illness and treatment. Taken together, the results of the present study provide support for Polyvagal theory's perspective that those with higher vagal control will have better regulatory resources when confronted with emotional challenges (Porges, 1995, 1997, 2007). The findings suggest that CVC, as assessed by RSA, may be an index of emotional coping capacity

in women diagnosed with breast cancer. These results are especially important as they suggest potential mechanisms that impact emotional well-being during coping with disease.

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