CARDIAC VAGAL CONTROL AS A PROSPECTIVE PREDICTOR OF ANXIETY IN WOMEN DIAGNOSED WITH BREAST CANCER

Anya Kogan (Povzner), John J.B. Allen, Róisín O'Donnell, Amanda E. Brody, & Karen L. Weihs   The University of Arizona

Abstract

▪ Cardiac vagal control, as measured by respiratory sinus arrhythmia (RSA), indexes individual differences in ability to regulate emotions and respond to environmental demands.

▪ Across the literature, low cardiac vagal control has been associated with state and trait anxiety as well as anxiety spectrum disorders.

▪ The present study examined the association between resting RSA and anxiety in a sample of 40 women diagnosed with stage 0, I, II, or III breast cancer. At an oncology clinic visit, two 5-minute resting electrocardiographic segments were recorded; RSA values averaged across segments were used in the analysis.

▪ Participants completed the Taylor Manifest Anxiety Scale (TMAS) at the initial visit and then again every three months. Data for up to a year after the initial visit were used in the analyses.

▪ After accounting for the baseline level of anxiety at the initial visit, RSA was a significant predictor of change in anxiety in a 1-year period, such that lower RSA at baseline may place individuals at risk for increased anxiety and higher RSA at baseline may buffer against higher anxiety.

▪ These results are consistent with the hypothesis that resting RSA taps the ability to modulate anxiety in women coping with significant stressors of breast cancer diagnosis and treatment.

Introduction

▪ Within the framework of Polyvagal theory (Porges, 1995), cardiac vagal control, as measured by respiratory sinus arrhythmia (RSA), has been linked to regulation of emotion, attention, and communication.

▪ Data suggest that reduction in RSA is associated with anxiety-related phenomena. Several lines of research converge to indicate that low RSA is associated with clinical forms of anxiety as well as state and trait anxiety (Cohen & Benjamin, 2006; Friedman, 2007).

▪ Despite improvements in cancer treatments, being diagnosed with cancer remains a life-threatening event and cancer patients often experience emotional turmoil and symptoms of depression and anxiety immediately after the diagnosis (McGarvey et al., 1998). Data suggest that the first year post-diagnosis may be especially stressful for women with breast cancer as they are faced with multiple stressors of breast cancer treatment and transitioning to survivorship or reentry phase (Stanton et al., 2005).

▪ The present study investigated whether ability to regulate emotions, as indexed by RSA, is associated with ability to modulate anxiety as assessed by a trait measure of anxiety, the Taylor Manifest Anxiety Scale (TMAS), in women during 1-year period following breast cancer diagnosis.

▪ We predicted that after accounting for baseline level of anxiety, higher baseline cardiac vagal control, as indexed by RSA, will predict better emotional adjustment at a 1-year follow-up and will influence the trajectory of change in anxiety over the ensuing year after the initial assessment.

Method

Subjects

▪ A total of 106 female participants with stage 0, I, II, or III breast cancer participated in the study. All participants were tested in conjunction with oncology clinic visits.

▪ Participants who were currently taking anxiolytic medications, undergoing cardio-toxic chemotherapy regimens or taking medications that affect cardiac functioning were excluded from analyses. Additionally, only participants who filled out TMAS on at least 3 occasions were included in the analyses (min number of observations per subject = 3, max number of observations per subject = 5), leaving a final sample of 40 participants (Mean age = 53.5, SD = 9.4; Mean time since diagnosis = 4.5 months, SD = 4 months; min = 0.5 months, max = 15.9 months).

Procedure

▪ To record the ECG signal, J & J Amplifier System (Poulsbo, WA) was used. Gel free Ag – AgCl electrodes were attached to the left and right wrist and the ground electrode was attached to the lower right forearm. A sample rate of 512 Hz was used to record the ECG signal. No instructions on how to breathe were given to the participants.

▪ Two 5-minute resting ECG segments were obtained at the initial visit (T1). RSA values were averaged across two recording segments to produce an average baseline RSA value.

▪ Participants filled out a trait measure of anxiety, Taylor Manifest Anxiety Scale (TMAS), at the initial visit (T1) and then approximately every three months. Observations for up to a year after the initial visit (T2) were included in the analyses (mean time from T1 to T2 = 12 months, SD = 1.7 months).

ECG Data Reduction

▪ The raw digitized ECG signals from each 5-minute resting session were analyzed off-line. Interbeat interval (IBI) series from the raw ECG recording was extracted by using QRSTool Software (Allen, Chambers, & Towers, 2007). The extracted interbeat series was hand-corrected for artifacts such as missed, erroneous, or ectopic beats.

▪ An estimate of respiratory sinus arrhythmia was calculated with CMetX Cardiac Metric Software (Allen et al., 2007) by deriving heart rate variability in the HF band (0.12–0.4 Hz), which is assumed to be related to respiration. CMetX converts the IBI series to a time-series sampled at 10 Hz with linear interpolation and then applies a 241-point optimal finite impulse response digital filter designed using FWTGEN V3.8 (Cook & Miller, 1992) with half-amplitude frequencies of a .12–.40 Hz. The natural log of the variance of the filtered waveform was used as the estimate of RSA.

Results

▪ Consistent with literature on RSA, there was a significant negative correlation between RSA and age in the subset of subjects free of medications (r = -.329, p = .02). Therefore, age was entered in the regression model as a predictor of RSA and nonstandardized residuals were calculated. Values of RSA residualized on age were used in all of the following analyses.

▪ TMAS at T1 was a significant predictor of TMAS a year later (TMAS at T2) ($F_{1, 38}$ = 30.71, p < .000; R^2 = .353). Residualized regression slopes were obtained after partialling out influence of the intercepts. Cook's distance was greater than 0.1 for one subject who was excluded from further analyses on this basis.

Results (cont.)

▪ Initial level of RSA (RSA at T1) prospectively predicted anxiety scores on TMAS at a 1-year follow-up (TMAS at T2).

$$\text{TMAS at T2} = B_0 + B_1 \times \text{TMAS at T1} + B_2 \times \text{RSA at T1}$$

Table 1. Predicting TMAS at Time 2

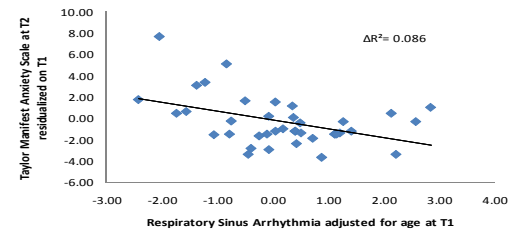| IV	B	SE	β	t	p
Model 1					
Constant	0.79	0.60		1.31	0.20
TMAS at T1	0.82	0.12	0.74	6.64	<.001
Model 2					
Constant	0.99	0.55		1.80	0.08
TMAS at T1	0.80	0.11	0.72	7.08	<.001
RSA at T1	-0.81	0.28	-0.29	-2.90	0.01

Figure 1. After accounting for initial level of anxiety (TMAS at T1), baseline RSA (RSA at T1) was a significant predictor of anxiety at a 1-year follow-up (TMAS at T2). In the resulting model ($F_{2, 36}$ = 30.642, p < .001), TMAS at T1 accounted for 54.4% of the variance (R^2 = .544) and inclusion of RSA in the model accounted for an additional 8.6% of the variance (ΔR^2 = .086).

▪ RSA predicted the slope of change in TMAS scores assessed at multiple time points over a 1-year period.

$$\text{TMAS regression slope} = B_0 + B_1 \times \text{RSA at T1}$$

Table 2. Predicting TMAS regression slope

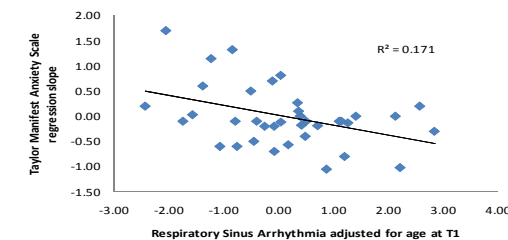| IV	B	SE	β	t	p
(Constant)	0.01	0.09		0.16	0.88
RSA at T1	-0.20	0.07	-0.41	-2.76	0.01

Figure 2. Slope of change in TMAS over the year following diagnosis was calculated by obtaining unstandardized Beta coefficients separately for each subject using regression model (IV = Time, DV = TMAS). In the resulting model ($F_{1, 37}$ = 7.615, p = .009), baseline RSA (RSA at T1) accounted for 17.1% of variance in TMAS slope (R^2 = .171).

Discussion

▪ Consistent with the literature on RSA and anxiety in individuals free from cancer diagnosis (Friedman, 2007), higher RSA was associated with a beneficial trajectory in anxiety over time. Those participants who had higher baseline RSA evidenced decrease in anxiety, whereas participants with lower baseline RSA appeared to be at a higher risk for stable or increasing anxiety during the first year after being diagnosed with breast cancer.

▪ Two methods were used to investigate predictive power of RSA. Assessment of anxiety after a 1-year period, adjusted for baseline anxiety, produced comparable results to the assessment of change in anxiety at multiple time points, suggesting that RSA may indeed be an index of anxiety modulation in this sample of breast cancer patients.

▪ RSA has been proposed to index emotion regulation and the ability to adapt to stressors (Porges, 1995), and the present findings are consistent with this idea. In this study, women were undergoing transitioning from active treatment phase and may have been experiencing stress and anxiety from treatments themselves as well as due to concerns of recurrence. In this context, RSA may reflect the extent to which these women 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-stress/high risk-populations.

References

Allen, J.J.B, Chambers, A.S., & Towers, D.N. (2007). The many metrics of cardiac chronotropy: A pragmatic primer and a brief comparison of metrics. *Biological Psychology, 74*, 243–262.

Cohen, H., & Benjamin, J. (2006). Power spectrum analysis and cardiovascular morbidity in anxiety disorders. *Autonomic Neuroscience, 128*, 1–8.

Cook III, E.W., & Miller, G.A. (1992). Digital filtering: Background and tutorial for psychophysiologists. *Psychophysiology, 29(3)*, 350–367.

Friedman, B.H. (2007). An autonomic flexibility – neurovisceral integration model of anxiety and cardiac vagal tone. *Biological Psychology, 74*, 185–199.

Ganz, P.A., Kwan, L., Stanton, A.L., Krupnick, J.L., Rowland, J.H., Meyerowitz, B.E., Bower, J.E., Belin,T.R. (2004). Quality of life at the end of primary treatment of breast cancer: first results from the moving beyond cancer randomized trial. *Journal of the National Cancer Institute, 96*, 376–387.

McGarvey, E.L., Canterbury, R.J., Koopman, C., Clavet, G. J.,Cohen, R., Largay, K. et al. (1998). Acute stress disorder following diagnosis of cancer. *International Journal of Rehabilitation and Health, 4*, 1–15.

Porges, S.W. (1995). Orienting in a defensive world: Mammalian modifications of our evolutionary heritage. A polyvagal theory. *Psychophysiology, 32*, 301–318.

Stanton, A.L., Ganz, P.A., Rowland, J.H., Meyerowitz, B.E., Krupnick,J.L., & Sears, S.R. (2005). Promoting adjustment after treatment for cancer. *Cancer, 104*, 2608–2613.

Handouts available: www.psychofizz.org.

THE UNIVERSITY OF ARIZONA
TUCSON ARIZONA