

Low Respiratory Sinus Arrhythmia and Prolonged Psychophysiological Arousal in Posttraumatic Stress Disorder: Heart Rate Dynamics and Individual Differences in Arousal Regulation

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Background: There is extensive evidence that the parasympathetic branch of the autonomic nervous system can modulate psychophysiological arousal. To date, no studies have investigated associations between cardiac vagal tone and the time course of arousal during exposure to trauma-related stimuli in posttraumatic stress disorder (PTSD).

Methods: Thirty-one subjects, 29 with PTSD and 2 with partial PTSD, had electrocardiograms recorded during baseline and 2-minute traumatic and neutral script-driven imagery periods. Heart rate, respiratory sinus arrhythmia (RSA), and heart rate half-recovery to the trauma script were quantified, and subjects were divided into low and high baseline RSA groups.

Results: Across all participants, heart rate significantly increased from the neutral to the trauma script and RSA significantly decreased from baseline to trauma script ($p < .05$). As predicted, low RSA subjects had more prolonged heart rate increases to the trauma script than high RSA subjects ($p < .001$), and heart rate half-recovery was negatively correlated to baseline RSA ($r = -.50$, $p = .005$).

Conclusions: This study is the first to find decreased RSA in response to a traumatic reminder and an association between low baseline RSA and sustained conditioned arousal in PTSD. Low vagal tone may account for deficient arousal and emotion regulation capacities often observed in PTSD.

Key Words: PTSD, psychophysiology, arousal, vegetative system, emotion regulation

Psychophysiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event is a defining feature of posttraumatic stress disorder (PTSD) (American Psychiatric Association 1994). Two decades of research document heightened arousal reactions to trauma-related stimuli in subjects with posttraumatic stress disorder secondary to combat, motor vehicle accidents, child abuse, and other traumas (Orr and Roth 2000). From the outset (Blanchard et al 1982), a major focus of PTSD psychophysiology research has been diagnostic discrimination. This line of research is the most established among biological investigations of PTSD, and studies using psychophysiological data and discriminant functions to classify case status based on DSM-IV criteria have yielded respectable sensitivities and specificities ranging from 60% to 88% and 77% to 100%, respectively (Orr and Roth 2000).

A general consensus has also emerged on the relationship between PTSD psychophysiological research and treatment. The key problems are abnormal amygdala-mediated fear conditioning, overconsolidation of subcortical traumatic memories, and failure of extinction by mechanisms of cortical inhibition; effective exposure-based treatments modify a "fear structure" (Foa and Kozak 1986) with those biological correlates, and effective medications modulate subcortical activation and/or increase the capacity of cortical structures to do so (Pitman et al 2000).

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Received August 2, 2002; revised February 28, 2003; revised June 6, 2003; accepted June 13, 2003.

0006-3223/04/\$30.00
doi:10.1016/S0006-3223(03)00677-2

However, despite a broad consensus on fear conditioning and elevated psychophysiological arousal in PTSD, understanding of the underlying mechanisms is limited, particularly for individuals with histories of severe, chronic trauma and generalized impairments in the regulation of arousal and emotion (Ford 1999; van der Kolk 1996). The mechanisms and processes by which the amygdala and other subcortical structures affect the heart, for example, have not been well studied in humans with PTSD. Higher resting heart rate (HR) and greater heart rate reactivity to traumatic reminders in individuals with current PTSD, compared to trauma-exposed individuals without PTSD and individuals with other anxiety disorders, have been explained as effects of heightened noradrenergic arousal and associated overactivation of the sympathetic branch of the autonomic nervous system (ANS) (Pitman et al 2000).

Noradrenergic and sympathetic ANS-focused explanations draw on the classical stress model of Cannon (1925) and Selye and Fortier (1950) and certainly have validity. Over the past 2 decades, however, psychophysiological research has greatly advanced our understanding of the parasympathetic branch of the ANS, in addition to the sympathetic, and how both relate to stress responsivity and vulnerability (Pagani et al 1991). Recent work has supplanted the classic, but incorrect, view that the sympathetic and parasympathetic branches of the ANS are two strictly antagonistic systems which operate along a single dimension of autonomic control. Berntson et al (1991) synthesized this knowledge with a model of "autonomic space" constituted by two independent axes, the sympathetic and the parasympathetic, and three different modes of autonomic control: reciprocal (i.e., one branch's activity increases as the other decreases); coactivated (i.e., both increase together); and uncoupled (i.e., the activity of one increases or decreases with no concomitant change in the activity of the other).

The model of autonomic space makes clear that the properties and states of the sympathetic branch alone are not the defining ANS characteristics of stress responses or stress vulnerability. As Cacioppo et al (1994) and others have demonstrated,

BIOL PSYCHIATRY 2004;55:284-290
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people who are “high HR reactors” may show either primarily sympathetic cardiac activation, primarily vagal cardiac withdrawal, or simultaneous vagal withdrawal and sympathetic activation. And consistent with the fact that parasympathetic input slows HR, low vagal tone has been implicated in the psychophysiological arousal and other symptoms associated with chronic stress activation, including in anxiety disorders (Yeragani et al 1993; Kawachi et al 1995; Friedman and Thayer 1998) and cardiovascular disease (Brosschot and Thayer 1998; Sloan et al 1999).

Until now, however, one could only speculate about such processes in PTSD, since the study of cardiac vagal control in PTSD is in its infancy. A key method in this work is assessing the amplitude of respiratory sinus arrhythmia (RSA), the rhythmic increase and decrease in HR associated with inspiration and expiration. This measure of heart rate variability (HRV) is also referred to as high frequency (HF) HRV, a reference to the relatively high frequency range above .12 Hz at which the parasympathetic but not the sympathetic branch of the ANS can respond to respiration and influence heart rate, and there are well-validated methods for assessing RSA (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). Respiratory sinus arrhythmia is used to assess tonic vagal control of the heart, though it should be noted that, in the absence of experimental or statistical control of respiratory parameters that can alter RSA via phasic vagal mechanisms, the term vagal tone is less precise but still generally accepted (Berntson et al 1997). Researchers have conducted many studies on HRV and RSA in other anxiety disorders than PTSD. Based on that work, some theorists have explained findings of lower HRV and RSA in generalized anxiety disorder and panic disorder using the construct of deficient self-regulation (e.g., Friedman and Thayer 1998; Thayer and Lane 2000). Similarly, in the child development and developmental psychopathology literature, more than a decade of empirical work has consistently associated higher resting vagal tone with greater capacities to regulate stress responsivity, emotional arousal, and attention (e.g., Bornstein and Suess 2000; Porges et al 1996; Stifter and Fox 1990).

The few studies of HRV in PTSD conducted thus far have had small sample sizes and have not employed script-driven imagery, the most standardized and widely used method in PTSD psychophysiology research. Studies by Cohen et al (1997, 1999, 2000), with samples of 9 to 14 PTSD subjects and long symptom provocation periods (15 to 20 minutes), have found evidence of both higher baseline HR and lower HF HRV relative to controls at baseline, consistent with low parasympathetic tone in PTSD. Yet, PTSD subjects' HR responses while recounting the traumatic event over 15- to 20-minute intervals were not greater than those of controls or, in the most recent study, subjects with panic disorder (Cohen et al 2000); however, it is possible that this laboratory's method of recording responses over the course of such long verbal trauma narratives is not well suited for eliciting, measuring, or comparing HR responses to trauma-related stressors. In a study of 14 subjects with history of trauma and PTSD and 15 subjects with trauma exposure but not PTSD, Sahar et al (2001) found no differences on resting measures of HRV, including RSA; however, only the non-PTSD group showed a significant increase in RSA during a 3.5-minute arithmetic challenge task, and RSA and heart period in response to challenge were highly correlated only for non-PTSD subjects as well. The latter finding led the authors to suggest that controls had greater vagal

control in response to challenge, while PTSD subjects' responses to challenge may be mediated primarily by sympathetic mechanisms. While these initial studies are important contributions to an emerging literature on HRV and RSA in PTSD, the small sample sizes and methodologies make it difficult to connect the findings to prior work on abnormal psychophysiological arousal and reactivity in PTSD.

We believe that the most common observation in the field, of increased HR responses to script-driven imagery and other relatively brief trauma-related reminders in PTSD, could be explained, at least in part, by a regulatory deficit associated with low cardiac vagal tone. Thus, we sought to begin answering two questions with the current study: Regardless of the extent of sympathetic arousal in response to a reminder, could low vagal tone account for slower HR deceleration once peak rates have been reached? If so, could lower vagal tone (at least partly) account for greater average HRs over the relatively short intervals typically studied? Since our primary aim was to assess modulation of trauma-related arousal over time, we modified the script-driven imagery paradigm typically utilized by Pitman et al (1987) and Orr and Kaloupek (1997). We used a single script with a duration of 2 minutes and assessed both mean HR change from baseline and HR as a time series over the entire script period. Given extensive evidence that vagal influences on the heart serve to dampen the effects of sympathetic reactions to stress and promote self-regulation and calm psychobiological states, we had two hypotheses. First, we hypothesized that vagal tone assessed via RSA would be significantly lowered during presentation of an individualized trauma script due to a stress-related suppression of vagal control. Second, we predicted that PTSD subjects with lower baseline RSA would show more sustained physiologic arousal to reminders of their traumatic memories than PTSD subjects with higher baseline RSA.

Methods and Materials

Participants

Thirty-one PTSD patients (10 male patients, 21 female patients) with an average age of 38.9 ± 9.2 years were recruited from an outpatient clinic with specialization in the treatment of psychological trauma. The subject pool was part of a treatment outcome study, and data were gathered at pretreatment assessments. Subject selection was designed to recruit patients likely to respond to less than 3 months of treatment with cessation of PTSD. That is, exclusion criteria were comorbid personality disorders or complex posttraumatic stress disorder resulting from multiple traumatizations in childhood. All assessment interviews were administered by the first author, who is experienced in assessment with structured interviews. Diagnosis of PTSD was confirmed by administering the German translation of the Structured Clinical Interview for DSM-III-R (SCID) module for PTSD (Wittchen et al 1997). Comorbid diagnoses were drawn using checklists for ICD-10 diagnoses (Hiller et al 1995). Trauma histories were assessed by clinical interview, and the following exposures were reported: accident, 17 or 54.8%; severe illness, 8 or 25.8%; physical assault, 16 or 51.6%; and sexual assault, 10 or 32.3%. Four of the women but none of men reported trauma (sexual abuse) in childhood. All subjects (including the four subjects reporting sexual abuse) were seeking therapy for symptoms caused by a single trauma in adulthood. Trauma scripts were prepared for the following situations: accident ($n = 17$), sexual assault as an adult ($n = 8$), and other forms of interpersonal violence ($n = 6$). Twenty-nine subjects fulfilled all DSM-IV

Table 1. Low Versus High RSA Group Comparisons: Psychometric Measures

Variables	Low RSA (n = 15)		High RSA (n = 16)		ANOVA		
	Mean	SD	Mean	SD	F	df	p
Age (years)	40.4	9.6	37.5	9.0	.72	30	ns
SUD	6.6	2.1	7.1	1.7	1.83	30	ns
DES	12.7	11.6	10.2	6.7	.53	29	ns
CES-D	19.2	9.1	24.5	8.6	2.57	28	ns
STAI-X2	47.8	9.9	65.0	12.2	3.82	27	.062
SCL-90 GSI	.83	.49	1.08	.53	1.63	25	ns
IES Total	45.0	11.7	50.3	12.7	1.37	28	ns
IES-Avoidance	19.1	9.3	25.0	8.0	3.17	28	.078
IES-Intrusion	25.9	4.9	25.3	8.7	.05	29	ns
PDS Total	1.64	.47	1.82	.52	.59	29	ns
PDS-Intrusion	1.83	.52	1.92	.88	1.73	29	ns
PDS-Avoidance	1.48	.62	1.84	.85	.12	29	ns
PDS-Arousal	1.72	.74	1.68	.85	.02	29	ns

SUD, subjective units of discomfort; DES, Dissociative Experience Scale; CES-D, Center of Epidemiologic Studies Depression Scale; STAI-X2, State and Trait Anxiety Inventory, State Only; SCL-90 GSI, Symptom Check List 90-R Global Severity Index; IES, Impact of Event Scale; PDS, Posttraumatic Diagnostic Scale; RSA, respiratory sinus arrhythmia; ANOVA, analysis of variance.

diagnostic criteria for PTSD, and two subjects fulfilled criteria for partial PTSD (three of four required criteria); the partial PTSD subjects were included because, despite having two rather than three avoidant/numbing symptoms (criterion C), they experienced significant distress and impairment requiring treatment.

Procedure and Instruments

Psychometrics. Each participant completed the following psychometric questionnaires (translated versions in German language): Impact of Event Scale (IES) (Horowitz 1979); State and Trait Anxiety Inventory (STAI) (Spielberger et al 1970) state anxiety only; Posttraumatic Diagnostic Scale (Foa 1995); Dissociative Experiences Scale (Bernstein and Putnam 1986); Symptom Check List 90-R (Derogatis et al 1973); and Center of Epidemiology Study Depression Scale (Radloff 1977). Descriptive results of the questionnaires are presented in Table 1.

Script-Driven Imagery. The procedure initially described by Pitman et al (1987) was modified using script-reading periods of 2 minutes duration instead of the typical 30 seconds, since we were interested in regulatory and arousal modulation capacities and not diagnostic discrimination. In addition, pilot work indicated that some patients needed more than 30 seconds to “get into” their traumatic memory.

All trauma scripts were prepared by the first author (MS) and described, in the present tense and first person, sequentially unfolding details of the most disturbing traumatic event. Scripts were then read to the patient to check for any inconsistencies with their memories. A script was accepted as valid when a subject reported a subjective unit of distress (SUD) level at least of 7 on a 0 to 10 scale. A 2-minute recording of the script was made on audiotape. Psychophysiological assessment was conducted in a second session, approximately 1 week after script preparation, which took place in the therapy office to assure a sense of safety and maximum familiarity with the situation. Subjects were seated in a comfortable chair and asked to sit still during the recording procedure. After electrocardiogram (ECG) electrode placement and a 5-minute adaptation period, a sequence of five scripts was played back via a tape recorder, in a fixed order: 1) 2-minute scripted relaxation exercise followed by a 1-minute break; 2) 2-minute neutral script of imagining washing dishes followed by 1-minute break; 3) 2-minute trauma script followed by a 5-minute break; 4) repeat of relaxation script/

exercise and 1-minute break; and 5) repeat of neutral script. Levels of subjective discomfort (SUD) were immediately assessed at the end of the trauma script. The design of the study was approved by the ethics committee of Hannover Medical School, Germany. All subjects gave their informed consent.

Psychophysiological Assessment

Electrocardiogram signals were obtained via three commercial disposable Ag-AgCl electrodes placed on the chest and recorded in a miniaturized amplifier (Par-Port/F, Par-Elektronik, Berlin, Germany). Sampling rate of ECG data for acquisition of interbeat intervals (IBIs) was 1000 Hz. Data were transferred to a PC and a time series of interbeat intervals was generated. The time series of heart period data were visually displayed to edit outliers. Except for singular premature heart beats in four cases, which were edited with a standard averaging procedure, all ECG data were free from artifacts and no further corrections were required.

Power spectral densities of the RR-interval variability were computed by Fast Fourier Transform using commercial software (Nevrokard, Medistar Inc., <http://www.nevrokard.medistar.si>). According to published recommendations (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996), spectral power was partitioned into low frequency (LF) (.04–.15 Hz) and HF (.15–.4 Hz) frequency bands. Low frequency and HF power were transformed with natural logarithms to reduce the skewness of their distributions. In addition, the ratio of LF to HF power, a measure which has been used to estimate sympathovagal balance (Pagani et al 1991), was computed. Respiratory sinus arrhythmia was defined as the heart rate variability in the frequency band between .15 and .40 Hz. This frequency band selectively reflects the activity of the vagal efferent fibers originating in the nucleus ambiguus and is characterized by a respiratory rhythm (Berntson et al 1997).

Data Reduction and Statistical Analyses

Mean values of HR were calculated for the first 60 seconds of each script. Heart rate data were also averaged as segments of consecutive 5-second intervals. Half recovery time was calculated, beginning from the start of the script, as the total of

Table 2. Low Versus High RSA Group Comparisons: Physiological Measures

Variables	Low RSA (n = 15)		High RSA (n = 16)		ANOVA		
	Mean	SD	Mean	SD	F	df	p
LF Neutral 1 (ms ²)	6.45	1.5	7.69	.92	7.7	30	.010
LF Trauma Script (ms ²)	5.89	1.0	7.20	1.3	9.5	30	.004
HF Neutral 1 (ms ²)	5.52	.95	7.74	.61	60.7	30	<.001
HF Trauma Script (ms ²)	5.29	1.15	6.94	1.58	11.0	30	.002
LF/HF Neutral 1	1.17	.15	.99	.10	14.0	30	<.001
LF/HF Trauma Script	1.13	.15	1.06	.18	1.28	30	ns
HR Relaxation 1 (bpm)	77.7	9.7	72.0	10.2	2.6	30	ns
HR Neutral 1 (bpm)	80.4	9.6	74.9	11.1	2.1	30	ns
HR Trauma Script (bpm)	88.9	16.1	86.9	14.5	.31	30	ns
HR Relaxation 2 (bpm)	78.3	9.8	71.8	7.7	4.3	30	.048
HR Neutral 2 (bpm)	78.5	10.4	72.2	7.6	3.6	30	.060
Half Recovery Time (s)	46.3	31.9	24.4	21.7	5.09	30	.032

RSA, respiratory sinus arrhythmia; LF, low frequency heart rate variability; HF, high frequency heart rate variability; LF/HF, ratio of LF/HF; HR, heart rate; bpm, beats per minute; s, seconds; ANOVA, analysis of variance.

all 5-second intervals with HRs above a threshold equaling half of the difference between the maximum and baseline heart rates. To characterize subjects' baseline RSA, we used both a dichotomous variable based on a median split and a continuous variable. Because RSA was significantly negatively correlated with age ($r = -.53$, $p < .01$), consistent with the well-known relationship between these two variables (Agelink et al 2001; Sinnreich et al 1998), age-corrected RSA values were computed and used for group comparisons.

To test our first hypothesis, RSA during the first neutral script, used as the baseline, and RSA during the trauma script were calculated from the time series of IBIs over the 120 seconds of the corresponding scripts, and t tests were used to compare these. For descriptive purposes and to check for potential confounds in our planned analyses, correlations among key variables were computed with Pearson correlation statistics.

To test our second hypothesis concerning predicted differential pattern of heart rate over time among subjects with low versus high RSA, we used two approaches: a repeated measures analysis of variance (ANOVA) using the General Linear Model (GLM) to test for differential patterns of HR change over time in the high and low basal RSA groups and a correlation analysis to assess the relationship between basal RSA and HR half-recovery time. We predicted that PTSD subjects in the low RSA group would display more sustained arousal than those in the high RSA group, as indicated by a significant group-by-time interaction effect of RSA on HR in the repeated measures ANOVA. We also predicted that there would be a significant positive correlation between basal RSA and half-recovery time. Significance levels were set at .05 for all statistical analyses, which were performed using the SPSS 10 statistical package (SPSS Inc., Chicago, Illinois).

Results

Across all participants ($n = 31$), the presentation of the individualized trauma script led to significant psychophysiological arousal. Mean values for heart rate during the listening conditions were as follows: relaxation 1: 74.7, SD = 10.2; neutral 1: 77.6, SD = 10.5; trauma script: 87.5, SD = 14.2; relaxation 2: 74.9, SD = 9.3; neutral 2: 75.3, SD = 9.5. Heart rate increased significantly from the first neutral script to the trauma script, with a mean acceleration of 9.9, SD = 9.6 beats per minute ($t_{30} = -5.7$, $p < .001$). As predicted by our first hypothesis, our HF HRV measure of RSA decreased significantly from baseline to trauma

script (mean = 6.66 ln[ms]², SD = 1.4, versus 6.14 ln[ms]², SD = 1.4; $t_{30} = 2.2$, $p = .034$). Low frequency HRV also decreased significantly during the trauma script (mean = 7.1 ln[ms]², SD = 1.4 versus 6.6 ln[ms]², SD = 1.4; $t_{30} = 2.0$, $p = .05$) such that LF/HF ratio did not change. Mean SUD level during the trauma script was 6.7, SD = 1.9.

In terms of gender differences, these were only present for the SCL-Global Severity Index, with men having significantly higher scores (women: .80, SD = .41, men: 1.35 SD = .65; ANOVA: $F(25) = 8.04$, $p = .009$), and for heart rates during script-driven imagery, with women having higher rates than men for all scripts, although a statistically significant difference was only found for the first neutral script (men: 71.4, SD = 7.5 vs. women: 81.5, SD = 9.8; ANOVA: $F(25) = 8.42$, $p = .007$).

No significant differences were found between the low versus high basal RSA groups for the demographic variables of gender, age, education level, or marital status. Comparisons of those groups on psychometric scales are presented in Table 1. There were nonsignificant trends toward higher levels of state anxiety (STAI) and avoidance (IES) in the high RSA group. Comparison of the high and low RSA groups on psychophysiological measures suggests that the low RSA group is characterized by a higher basal heart rate, as indicated by significant differences in HRs during the second relaxation and neutral scripts and nonsignificant trends for this difference during the first relaxation and neutral scripts (Table 2).

Both RSA groups were characterized by increasing HRs from the first relaxation period through the first neutral script and the 1-minute break preceding the trauma script. General Linear Model repeated measures ANOVA on HR responses to the trauma script revealed a significant main effect of time on heart rate ($F = 4.1$, $p < .001$). In addition, and as predicted, there was a significant group by time interaction ($F = 3.1$, $p < .001$), with the low RSA group exhibiting a more prolonged HR response to the traumatic reminder than the high RSA group. Figure 1 clarifies these relationships by depicting mean HRs for both high and low RSA groups, from the 60 seconds before the trauma script through its 120-second duration. Both groups have comparable rates of HR acceleration, beginning with an apparent 10-second anticipatory period before the trauma script; however, during exposure to the trauma script, mean HR values of the high RSA group reach their peak HR earlier and show a relatively faster deceleration to baseline levels than in the low RSA group, which

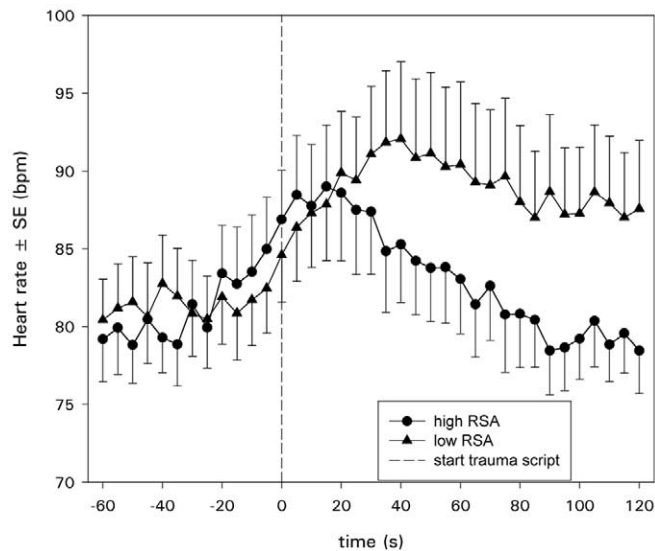


Figure 1. Group comparison of heart rate immediately before and during trauma script. RSA, respiratory sinus arrhythmia.

exhibits higher peak values, delayed deceleration, and heightened HR levels even at the end of the 120-second script period.

Also, as predicted, half-recovery time during exposure to the trauma script was significantly negatively correlated with basal RSA ($r = -.50, p = .005$). Consistent with this finding, half-recovery time was negatively correlated with RSA during trauma script ($r = -.61, p < .001$). These significant negative correlations were even stronger in partial correlations that controlled for trauma script SUD ratings ($r = -.57, p = .001$ and $r = -.65, p < .001$, respectively). Finally, the low RSA group had a significantly longer half-recovery time than the high RSA group (Table 2).

Discussion

To our knowledge, this PTSD study is the first to show decreased RSA in response to a traumatic reminder and an association between baseline RSA and sustained conditioned arousal. These findings, yielded by the well-established script-driven imagery methodology, suggest that significant insights may result from assessing both state and trait heart rate variability and parasympathetic function in this disorder. They also suggest that investigation of the parasympathetic branch of the ANS can illuminate psychophysiological processes and individual differences associated with dysregulated arousal in PTSD.

As predicted, RSA decreased significantly from baseline to the trauma script. These RSA suppressions, corresponding to decreases of parasympathetic outflow to the heart, were accompanied by significant increases in heart rate and considerable levels of subjective distress. Given the rapid adaptation capacity of the vagal system, we were more likely to find RSA suppression with a 2-minute exposure time than were previous studies of PTSD subjects that used longer trauma-related and arithmetic stressors (Cohen et al 1998; Sahar et al 2001).

Our main and predicted finding is that, compared to PTSD subjects with high RSA, those with low basal RSA exhibited prolonged HR elevation over a 2-minute individualized trauma script. Both the repeated measures ANOVA and half-recovery analyses confirmed this result. In addition, basal RSA and RSA during the trauma script were negatively correlated with half-recovery time, consistent with the positive chronotropic effect of

withdrawn vagal input to the heart. These findings shed light on the role that vagally mediated regulation of cardiac function can play in arousal responses to trauma-related stimuli in subjects with PTSD.

Our findings on RSA and HR responses to a trauma-related stimulus also suggest that the excessive stress-related autonomic lability and tachycardia observed in PTSD patients, typically explained solely in terms of exaggerated sympathetic arousal, may in some cases be associated with a reciprocal mode of autonomic control characterized by deficient parasympathetic control in the presence of increased sympathetic arousal. Indeed, from the perspective of emotion regulation, this particular reciprocal mode of autonomic “control” constitutes a mode of dysregulation and dyscontrol. Similarly, our finding of higher baseline HR in the low RSA or vagal tone group, though we did not predict it, is consistent with lower tonic vagal activity at the heart’s sinoatrial node, thus less of an inhibitory influence to counter excitatory sympathetic input (Berntson et al 1994). Thus, while this study did not compare PTSD with control subjects on these variables, this between-groups effect suggests that the potential contribution of low vagal tone to elevated basal HR in PTSD (Buckley and Kaloupek 2001) warrants further study.

Because these findings are the first linking low RSA and sustained HR responses to reminders in PTSD, it is helpful to place these findings in the context of research on parasympathetic function in normal subjects, people with other anxiety disorders, and animals. Pharmacological blockade studies have revealed a dominance of parasympathetic over sympathetic influences in regulation of heart rate: in healthy humans with normal baseline heart rates, approximately two thirds of heart rate acceleration in response to arousing stimuli is controlled via vagal influences (Saul et al 1991; Berntson et al 1994). Empirical work with animals shows that the parasympathetic control of heart rate is even higher during severe stressors, such that the fear-conditioned freezing states in the classic work of LeDoux (2000) can be coactivated states in which increased parasympathetic activity dampens sympathetic effects on heart rate (Iwata and LeDoux 1988; Nijssen et al 1998). Thus, many studies have shown that poor control of HR and vulnerability to tachycardia is an important consequence of chronic increased sympathetic activity paired with decreased vagal tone (Bernston et al 1998). As Porges (1995) has argued, RSA may serve as an index of stress reactivity and stress vulnerability. High vagal tone enhances cardiac control in terms of beat-to-beat adjustments to environmental demands. Low vagal tone, in contrast, is associated with a more rigid and inflexible system, one vulnerable to dysregulated excessive and sustained responses to real and imagined stressors (Berntson et al 1998).

Finally, we believe it is important to place our findings within theoretical and empirical approaches to anxiety disorders, including PTSD, that emphasize deficient inhibition capacities as central to problems of self-regulation. For example, a model of neurovisceral integration recently proposed by Thayer and Lane (2000), which incorporates autonomic, attentional, and affective systems into a functional and structural network, views inhibitory processes as negative feedback circuits that allow for the interruption of ongoing behavior and redeployment of resources to currently relevant tasks. They propose that when these negative feedback mechanisms are compromised, positive feedback loops may develop as a result of disinhibition. From this perspective, the baseline sympathetic arousal of anxiety disorders, including PTSD, may be a condition of disinhibition, resulting from compromised baseline parasympathetic inhibition. In terms

of PTSD specifically, impaired inhibitory control may be a key psychobiological dimension of the disorder. Transient suppressions of vagal cardiac control and its reinstatement for self-regulation and self-soothing necessarily involve both subcortical and cortical structures. Thus, cardiac arousal regulation is a critical biological function, one that straddles the interface where evolved involuntary responses and automatic behaviors can interact with learned, inhibitory, and executive cognitive and attentional capacities. By studying arousal regulation in terms of heart rate dynamics and assessing baseline and state-dependent parasympathetic function, psychophysiology researchers can contribute to the integration of emotion (not merely fear) and self-regulation into biological models of PTSD, in line with a continuing trend in neuroscience and cognitive neuroscience (Panksepp 1998; Damasio et al 2000; Gray et al 2002; Pochon et al 2002).

If subsequent research replicates our main finding, treatment implications should be carefully considered. Deficient self-soothing and self-regulatory capacities are major problems for many people with PTSD. Indeed, these can be among the most far-reaching—and difficult to treat—effects of extreme and prolonged psychological trauma in both children and adults (van der Kolk 1996, 2001). Our finding that PTSD subjects with low RSA exhibited sustained HR elevation after exposure to trauma-related reminders suggests that low RSA can be a biological correlate of impaired self-regulation and a possible biological target for psychological and pharmacological treatments aimed at specifically addressing self-regulatory deficits. Also, as noted above, the potential physical costs in terms of cardiovascular risk and related treatment needs could be important areas for further research.

This study has several limitations. First, because respiratory rate and amplitude were not recorded, RSA analyses did not control for respiratory influences as recommended in recent guidelines (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). Second, we had no direct measure of sympathetic influence on heart rate or contractility (i.e., impedance cardiography) (Sherwood et al 1990); thus, we cannot know the contribution of the sympathetic branch of the ANS to our findings. Third, body mass and physical fitness, factors known to influence parasympathetic tone and RSA (Rossey and Thayer 1998) and thus potential confounds, were not measured or controlled for in analyses. Fourth, respiratory irregularity due to arousal might have influenced our RSA suppression data (Grossman and Kollai 1993; Yeragani et al 2002); however, even if systematic differences in these factors caused the RSA differences between the groups, it would still be an important individual difference associated with sustained arousal in response to trauma-related stimuli and would not necessarily invalidate our interpretations of the findings.

There are two other issues that could challenge our interpretation of the findings in terms of vagally mediated self-regulatory mechanisms. First, the finding of a statistical trend for higher anxiety levels on the STAI and IES avoidance scales in the high-RSA subgroup could raise the concern that their faster HR decelerations are due to an avoidance of emotional engagement with the script-driven imagery. Though we did not assess emotional engagement with the script, there are at least two reasons for not drawing this conclusion. Our finding of higher RSA associated with trait anxiety is inconsistent with most findings in the empirical literature, which indicates lowered RSA levels in subjects with various anxiety disorders, and in a partial

correlation of basal RSA and half-recovery controlling for STAI scores, the correlation between RSA and half-recovery was even higher. Thus, we regard the nonsignificant correlations of basal RSA and STAI and the IES avoidance subscale as spurious, though future research in this area should include measures of emotional engagement (Foa and Hearst-Ikeda 1996), as well as PTSD and dissociative symptomatic responses to script-driven imagery. Second, because when the trauma script started, the mean HR of the high RSA group had already increased to 86 bpm (time 0 in Figure 1) from an apparent baseline of approximately 72.5 bpm (i.e., mean value of relaxation 1, relaxation 2, and neutral 2 HRs), it could be argued that these subjects' HRs had already "maxed out" due to anticipatory anxiety (Grillon 2002) and that their decreasing HR during the trauma script was essentially regression to the mean. This interpretation cannot be ruled out, and the trend for greater progressive anticipatory HR increases before the trauma script in the high RSA group is noteworthy.

In summary, the relationship between low vagal tone and prolonged arousal found in our study supports the speculation that phasic hyperarousal in PTSD can be partly mediated by deficient inhibitory control of heart rate. This finding is consistent with several other lines of HRV research in normal subjects, anxiety disorders, and cardiac risk populations, and can be understood in terms of the model of autonomic space and the construct of self-regulation. Furthermore, it may be that low parasympathetic activity and not just elevated sympathetic activity as conventionally discussed in the PTSD psychophysiology literature is a key mechanism underlying higher basal heart rate in PTSD. Clearly, more research is needed on the parasympathetic branch of the ANS, the temporal dynamics of baseline and stress-induced cardiovascular parameters, and the regulation of psychophysiological arousal. Only by including such approaches can PTSD psychophysiology adequately address the self-regulatory deficiencies often associated with this disorder. Finally, future research should investigate the limbic and paralimbic structures and circuits that control vagal output to the heart and regulate the arousal dimension of emotion.

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