Vagal Modulation of Responses to Mental Challenge in Posttraumatic Stress Disorder

Tali Sahar, Arieh Y. Shalev, and Stephen W. Porges

Background: *Studies of the autonomic nervous system in posttraumatic stress syndrome (PTSD) have focused on the sympathetic modulation of arousal and have neglected the parasympathetic contribution. This study addresses the parasympathetic control of heart rate in individuals who have survived traumatic events.*

Methods: *Twenty-nine survivors, 14 with current PTSD and 15 without, participated in the study. The groups were comparable with regard to age, type of trauma, time since the latest traumatic event, and lifetime exposure to traumatic events. Electrocardiograms were recorded during rest and an arithmetic task. Heart period, respiratory sinus arrhythmia (RSA), and the amplitude of the Traube–Hering-Mayer wave were quantified.*

Results: *The groups did not differ on resting measures. During the arithmetic task, the past trauma group showed a significant increase in RSA (*$p < .007$*), whereas the PTSD group did not. In the past trauma group only, RSA and heart period were highly correlated (*$r = .75$*), thereby suggesting that the response to challenge was under vagal control.*

Conclusions: *Trauma survivors who develop PTSD differ from those who do not in the extent to which their heart rate response to challenge is controlled by vagal activity. Responses to challenge in PTSD may be mediated by nonvagal, possibly sympathetic mechanisms.* Biol Psychiatry 2001;49:637–643 © *2001 Society of Biological Psychiatry*

Key Words: Posttraumatic stress disorder, heart rate variability, respiratory sinus arrhythmia, challenge tests, human subjects

Introduction

Psychophysiologic research of posttraumatic stress disorder (PTSD) is expanding rapidly (for a review, see Orr 1997). Due to the prominence of hyperarousal symptoms in PTSD, research has focused primarily on the sympathetic branch of the autonomic nervous system. Previous studies have consistently shown an elevated phasic activation of the sympathetic nervous system in PTSD in response to trauma-related cues (Murburg et al 1995), to chemical challenges such as yohimbine (Southwick et al 1997), and to anxious expectation (e.g., McFall et al 1992). Elevated heart rate levels upon admission to an emergency room, following trauma, have been reported in individuals who later developed PTSD (Shalev et al 1998). However, baseline sympathetic activity is not believed to be higher in PTSD (McFall and Murburg 1994; Murburg et al 1995).

Overlooked in the psychophysiologic investigation of PTSD is the parasympathetic nervous system. The parasympathetic nervous system, and especially the vagal regulation of heart rate, is involved in stress reactions and the long-term consequences of stress (e.g., Porges 1992). The vagus nerve, the 10th cranial nerve, serves as a conduit from the brain stem to several visceral organs. The myelinated cardioinhibitory vagal fibers, which originate in the nucleus ambiguus and terminate on the cardiac sinoatrial node, contribute to the regulation of the heart rate response to and the recovery from stress. These vagal fibers functionally slow heart rate and actively inhibit the sympathetic influences to the heart (Vanhoutte and Levy 1979). The parasympathetic control of the heart is often synergistic and reciprocal with the energetic function of the sympathetic nervous system. For example, to support the metabolic demands associated with body movement, withdrawal of the "vagal brake" potentiates the expression of the sympathetic influences on the heart.

The vagal control of heart rate via the myelinated vagal fibers varies with respiration (Richter and Spyer 1990). Thus, the vagal influence to the heart may be evaluated by quantifying the amplitude of rhythmic fluctuations in heart rate that are associated with breathing frequencies (respiratory sinus arrhythmia [RSA]).

Methods for measuring vagal activity by quantifying RSA in humans have been validated and refined during the past decade (Berntson et al 1991, 1993, 1994a; Porges and Bohrer 1990; Porges and Byrne 1992). Time series analyses provide widely accepted methods to compute RSA

From The Center for Traumatic Stress, Department of Psychiatry, Hadassah University Hospital, Jerusalem, Israel (TS, AYS) and the Department of Human Development, University of Maryland, College Park, Maryland (SWP).
Address reprint requests to Arieh Y. Shalev, M.D., Hadassah University Hospital, Department of Psychiatry, P.O. Box 12000, Jerusalem 91120, Israel.
Received September 30, 1999; revised June 23, 2000; accepted July 28, 2000.

0006-3223/01/$20.00
PII S0006-3223(00)01045-3

(e.g., Berntson et al 1997; Porges and Bohrer 1990). In this study, RSA was defined as the heart rate variability in the frequency band between 0.12 and 0.40 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 (Porges 1995, 1997). The respiratory rhythm, although influenced by peripheral feedback, reflects a central respiratory rhythm emerging from the interneuronal communication between the nucleus ambiguus and the nucleus of the solitary tract (Richter and Spyer 1990).

Another measure of heart rate variability may be derived from quantifying the amplitude of an oscillation known as the Traube-Hering-Mayer (THM) wave (e.g., Hatch et al 1986) or 0.1 Hz wave (for overview, see Byrne and Porges 1992). The THM wave is characterized by a slower heart rate rhythm, usually observed between the frequencies of 0.06 and 0.1 Hz. The neurophysiologic mechanisms mediating the THM wave, although less understood, are assumed to be related to the regulation of blood pressure, since similar oscillations are observed in blood pressure. Since research has demonstrated that the two components of heart rate variability may respond differentially (e.g., Byrne and Porges 1992; Hatch et al 1986) and the cardiac contribution to blood pressure involves sympathetic influences, several researchers have assumed that the amplitude of the THM wave reflects sympathetic as well as vagal mechanisms (e.g., Akelrod et al 1981). However, since blocking the vagal influence on the heart with atropine removes both RSA and THM wave (e.g., Goddard et al 1995), the amplitude of the THM wave may reflect the joint effect of both vagal pathways originating from both vagal source nuclei in the medulla, the nucleus ambiguus, and the dorsal motor nucleus (Porges 1995).

Vagal influences to the heart serve to dampen the sympathetic reactions to stress and to promote calm behavioral states and self-regulation (Porges 1995). Consistent with this protective function of vagal tone, low-amplitude RSA has been associated with vulnerability to the effect of stress. Low-amplitude RSA has been associated with medically and psychologically stressed populations such as premature neonates (Fox and Porges 1985; Porges 1992), infants (Izrad et al 1991; Porges et al 1994), school-age children (Suess et al 1994), and neurosurgical patients (Donchin et al 1992). An increase in tonic levels of RSA has been observed in patients with major depressive disorder following successful treatment (Balogh et al 1993). Moreover, general anxiety disorder patients who exhibited less reduction in RSA following imipramine also exhibited greater symptom reduction (McLeod et al 1992).

In addition to the research on tonic levels of RSA, RSA is responsive to psychologic and behavioral demands. A marked reduction in RSA amplitude has been observed during procedures that produce panic symptoms (George et al 1989) as well as during tasks requiring sustained attention or increased motor activity (e.g., Hatfield et al 1998). Neurophysiologically, the amygdala may play a role in translating the psychologic experiences associated with fear and trauma into the vagal responses. The amygdala, a limbic structure that has been postulated to play a role in fear conditioning and in PTSD (e.g., Davis et al 1997), projects to the nuclei of the vagus in the brain stem (Schwaber et al 1980), and may effect the vagal response to fear.

Despite its hypothetical relevance to PTSD, there are only two published reports of parasympathetic activity in PTSD (Cohen et al 1997, 1998). Cohen and colleagues reported significantly lower resting RSA in PTSD, and absence of autonomic response to the recounting of the triggering stressful event. Our study was conducted to ask several questions relating vagal regulation of the heart in PTSD. First, the study evaluated whether base levels and reactivity of the amplitude of RSA were different in PTSD than they were in participants who had experienced trauma without developing PTSD. Second, the study evaluated the *vagal* contribution to the heart rate responses observed during the mental arithmetic challenge. It was hypothesized that the vulnerability to stress, characteristic of PTSD, would be paralleled by both low-amplitude RSA and a reliance on neural mechanisms, other than vagal, to mediate heart rate responses to stress.

Methods and Materials

Subjects

Included in this study were outpatients of the ambulatory psychiatric service of Hadassah University Hospital in Jerusalem with current PTSD (PTSD group, $n = 14$) and volunteers with past traumatic experiences but no current or past PTSD, recruited from the hospital staff (past trauma group, $n = 15$). To reduce gender- and age-related variability in parasympathetic activity (Ziegler et al 1992), only male subjects between the ages of 18 and 65 years were included in this study. All subjects had undergone a significant traumatic event, meeting DSM-IV "A" criterion for PTSD (see details below).

Subjects were not included in the study if they had current or lifetime psychotic disorder, an organic mental condition, head injury, or major thoracic or neck surgery, or if they regularly engaged in physical training exceeding 10 hours a week. Subjects with current or past alcohol and/or drug abuse were not included. Subjects were excluded from the study if they reported alcohol consumption within 24 hours of the evaluation session, or expected to have a stressful event on the testing day. Eligible subjects received detailed explanation about the study and signed an informed consent.

All subjects were interviewed using the Clinician Adminis-

tered PTSD Scale (CAPS; Blake et al 1990). Subjects with PTSD ($n = 14$) met all four CAPS diagnostic criteria for PTSD (i.e., a traumatic event, re-experiencing symptoms, avoidance symptoms, symptoms of hyperarousal) and had a mean total CAPS score of 63.5. Among past trauma control subjects ($n = 15$), only one met CAPS/PTSD criterion B (intrusive thoughts and feelings), and the mean CAPS score was 9.32. Six PTSD subjects and 10 past trauma control subjects had experienced combat events, four PTSD subjects and five past trauma control subjects had had severe car accidents, and four subjects with PTSD had been victims of terrorist attacks.

No attempt was made to alter any subject's medication regimen for the purpose of this study. Seven subjects from the PTSD group were taking medications: six were taking benzodiazapines, one was on a selective serotonin reuptake inhibitor (SSRI), and two were taking both benzodiazepines and SSRIs. To examine the effect of including medicated patients in this study, we used the Mann-Whitney *U* test to compare the medicated PTSD subjects with those who were not medicated. Posttraumatic stress disorder subjects on medication did not differ from those without medication in any of the psychologic or physiologic measures.

Psychometrics

Each subject completed the following psychometric questionnaires: the revised Impact of Event Scale (Horowitz et al 1979), a 21-item questionnaire that includes avoidance, intrusion, and arousal; the Beck Depression Inventory (Beck et al 1961); the State and Trait Anxiety Inventory (Spielberger 1983); and the Trauma History Questionnaire (Green et al 2000). All instruments, including their Hebrew versions, had been used extensively in studies of PTSD and other mental conditions (Shalev et al 1997, 1998).

Quantification of Heart Period Data

The electrocardiogram signals were recorded via standard limb electrocardiogram leads connected to a high-gain bioamplifier (Coulbourn, Allentown, PA) and stored on an FM tape recorder (C-4, Vetter, Rebersburg, PA). The data were quantified offline by replaying the tape into a Vagal Tone Monitor (Delta-Biometrics, Bethesda, MD). The Vagal Tone Monitor detects the peak of the R wave to the nearest millisecond and times the interval between sequential R-wave detections (i.e., R–R intervals or heart periods [HPs]) to the nearest millisecond. Files of sequential HPs were stored on an IBM-compatible computer. MXedit software (Delta-Biometrics) was used to graphically display the HP data, to edit outliers, and to quantify the HP and the amplitudes of RSA and the THM wave.

Heart period was selected as the metric for the cardiac rate analyses for statistical and neurophysiologic reasons (e.g., Berntson et al 1995). However, since heart period is less intuitive than heart rate to discuss, although our analyses are based on HP data, we use *heart rate* in the Abstract, Introduction, and Discussion.

The MXedit software incorporates the following procedural steps to quantify RSA: 1) the HPs (i.e., the time between successive heart beats) are converted to time-based data by resampling the sequential HPs at successive 500-msec intervals, 2) the time-based data are detrended with a 21-point cubic moving polynomial filter to remove the variance associated with the complex changing baseline and oscillations slower than RSA, 3) the detrended data are processed by a digital bandpass filter with 25 coefficients to extract the variance in the frequency band 0.12–0.40 Hz (i.e., the frequency of spontaneous breathing for adults), and 4) the bandpassed variance is transformed to its natural logarithm and used to quantify RSA. MXedit employs a similar procedure to calculate THM wave variance. However, a 51-point moving polynomial filter and a bandpass filter passing frequencies between 0.06 and 0.10 Hz are used. These methods are consistent with the procedures developed and tested previously (Porges 1985).

Table 1. Means (and SDs) of Demographic and Psychometric Measures

	PTSD ($n = 14$)	Past trauma ($n = 15$)	*Z*, adjusted	*p*
Age (years)	41.5 (15.2)	41.6 (9.22)	−0.17	.86
Time since trauma (months)	133.6 (125)	154.7 (110)	−0.46	.64
Number of lifetime traumatic events	9.10 (4.3)	7.3 (1.9)	−1.49	.14
IES				
Intrusion	27.09 (8.4)[a]	4.21 (6.6)[a]	−4.00	.0001
Avoidance	15.46 (6.1)[a]	2.53 (3.3)[a]	−3.93	.0001
Arousal	20.54 (6.3)[a]	2.46 (3.5)[a]	−4.17	.0001
STAI Trait	53.58 (13.7)	36.25 (8.25)	−3.01	.003
STAI State	59.27 (12.6)	35.41 (8.67)	−3.67	.001
BDI	25.38 (13.1)	4.57 (5.5)	−3.22	.002

[a] $p < .05$ (Mann-Whitney *U* test).

PTSD, posttraumatic stress disorder; IES, Impact of Events Scale (revised); STAI, Spielberger State and Trait Anxiety Scale; BDI, Beck Depression Inventory.

Procedure

The laboratory session took place in a 3.2 × 2.4-m, humidity- and temperature-controlled room. The physiologic monitoring equipment was in an adjoining room. The subject was seated in a comfortable armchair. After familiarization with the laboratory, the electrodes were attached and the subject was allowed another 5 min before the recording started. The subject was asked to sit still during the whole procedure. Electrocardiograms were recorded during a 7-min resting period (i.e., baseline) and during a 3.5-min mental arithmetic task. During the mental arithmetic task the subject was instructed to sequentially add and subtract a series of integers and to retain the final result. Although Hatch et al (1986) used a 60-sec period to employ a similar protocol of sequential subtraction, we conservatively selected a minimum of 3 min of heart rate data to obtain a more reliable measure of RSA.

Results

Table 1 presents results of Mann-Whitney *U* tests, comparing group means of psychometric questionnaire and demographic data. Examination of the results indicates

Table 2. Means (and SDs) of Physiologic Measures

	PTSD (n = 14)	Pasttrauma (n = 15)	Z, adjusted	p
HP rest	840.4 (173)	843.7 (161)	−0.087	.93
HP math	836.5 (175)	837.0 (157)	−0.26	.79
ΔHP	−3.949 (32.7)	−6.743 (36.1)	−0.05	.97
RSA rest	4.867 (1.26)	4.953 (1.53)	−0.48	.63
RSA math	4.846 (1.16)	5.367 (1.60)	−0.96	.34
ΔRSA	−0.021 (0.34)	0.414 (0.61)	−2.34	.02[a]
THM rest	3.831 (1.20)	3.691 (1.29)	−0.17	.86
THM math	3.539 (1.19)	3.903 (1.46)	−0.68	.50
ΔTHM	−0.293 (0.47)	0.211 (0.60)	−2.27	.03[a]

PTSD, posttraumatic stress disorder; HP, heart period; RSA, respiratory sinus arrhythmia; THM, Traube-Hering-Mayer wave; ΔRSA, the difference between RSA during the arithmetic task and RSA at rest; ΔTHM, the difference between THM during the arithmetic task and THM at rest.

[a] $p < .05$ (Mann-Whitney U test).

that the groups were comparable with regard to age, lifetime history of trauma (total number of traumatic events), and time elapsed since the most traumatic life event. As expected, the groups differed in all psychometric scores, PTSD subjects showing significantly more symptoms than control subjects.

Physiologic Measures

Table 2 presents the group means of HP, RSA, and THM wave, at rest and during the arithmetic task. Table 2 also presents the average change in each of the physiologic parameters between the level recorded during the task and the resting level (ΔHP, ΔRSA, and ΔTHM wave). Mann-Whitney U tests revealed no differences between the groups in any of these physiologic response parameters. The past trauma group, however, had an increase in RSA during the arithmetic task, whereas RSA slightly decreased in the PTSD ($Z_{adj} = -2.337$, $p < .02$). The past trauma group also had an increase in the THM wave during the arithmetic task, whereas the THM wave decreased in the PTSD group ($Z_{adj} = -2.27$, $p < .03$).

Wilcoxon matched-pairs tests were used to compare, within each group, the baseline levels of HP, RSA, and the THM wave with those recorded during the arithmetic task. There were no within-group differences in resting HP and HP during the arithmetic task. The past trauma group showed a significant increase in RSA during the task ($T = 13$, $p < .007$).

To evaluate whether vagal influences mediated the HP changes and to assess the relative contribution of each of these change scores to changes in HP, stepwise regression analyses were performed using ΔRSA and ΔTHM wave, in this order, to predict ΔHP (Table 3). For the past trauma group, the results indicate a significant contribution of ΔRSA ($R^2 = .572$, $p < .0011$) to ΔHP, whereas ΔRSA has no such effect in the PTSD group ($R^2 = .0143$, $p < .689$).

Table 3. Relative Contribution of ΔRSA and ΔTHM to Change in Heart Period

	Step	Multiple R	Multiple R^2	R^2 change	F, to enter	p level	Variables included
PTSD							
ΔRSA	0	.1196	.0143			.69	1
ΔTHM	1	.5110	.2611	.2468	3.67	.09	2
Past trauma group							
ΔRSA	0	.7565	.5723			.002[a]	1
ΔTHM	1	.7768	.6034	.0310	0.94	.35	2

Stepwise regression was preformed; ΔHP was taken as the dependent variable, using the difference between respiratory sinus arrhythmia during the arithmetic task and RSA at rest (ΔRSA) and the difference between Traube-Hering-Mayer wave (THM) during the arithmetic task and THM at rest (ΔTHM) in this order.

Discussion

The two main findings of this study are 1) the PTSD and past trauma groups had similar levels of resting parasympathetic activity and 2) the magnitude of the heart rate response to mental challenge correlated with our index of vagal activity (i.e., RSA) in the past trauma group, but not in PTSD.

Resting Activity

The similarity between the groups in the resting physiologic measures is consistent with previous reports of similarities in resting heart rate between PTSD and healthy control subjects (e.g., McFall et al 1990, 1992; for discussion, see McFall and Murburg 1994; Prins et al 1995). However, the Cohen et al (1997, 1998) report of lower resting heart rate and parasympathetic tone in PTSD differs from our results. These differences may be due to the unique characteristics of the control subjects and not a correlate of PTSD. Cohen et al reported a very low average heart rate (61.9 bpm) in control subjects. Such resting heart rate does not reflect levels associated with a random sample, but is characteristic of healthy adults who are extremely fit. For example, Hatfield et al (1998) reported a similar heart rate (61.2 bpm) in athletically fit college students, who possessed a minimum of 3 years of training and competing in cross-country events. Thus, it is possible that the low heart rate in Cohen and colleagues' control group represented participants with an atypically high vagal tone. Accordingly, the difference between control subjects and PTSD in the Cohen et al study might have resulted from the atypically high parasympathetic tone among control subjects, rather than from low parasympathetic tone in the participants diagnosed with PTSD.

Another difference between the studies is the frequency band selected to quantify RSA. Cohen et al used a variable defined as high frequency heart rate variability. This variable is similar but not identical to our measure of RSA. In the Cohen et al study high frequency heart rate

variability was quantified within a frequency range of 0.15 Hz and 0.50 Hz. In our study RSA was quantified within a frequency range of 0.12 Hz and 0.40 Hz. The 0.12–0.40 Hz band was selected because it captures the representative frequencies associated with spontaneous breathing. In contrast, the selection of the 0.15–0.50 Hz tends to miss the slower breathing frequencies (i.e., breaths slower than nine per minute) frequently observable in fit adults at rest, while tracking breathing activity faster than that observed in the adult at rest (i.e., 30 breaths per minute). The low observed heart rate in the Cohen et al control group suggests that the participants were fit, and thus possibly breathing at a slow rate. Thus, it is likely that the 0.15-Hz low frequency cutoff missed a substantial component of the heart rate variability associated with RSA.

Similarly, the low frequency heart rate variability measure in the Cohen et al study (0.04–0.15 Hz) is not identical to our measure of the THM wave (0.06–0.10 Hz). The band selected for the low frequency heart rate variability component by Cohen et al is likely to be confounded by including the effect of slow breathing (at the higher frequencies within this band).

Our finding that there were no differences between PTSD subjects and control subjects in the physiologic parameters monitored during rest is consistent with previous reports suggesting that PTSD is primarily associated with increased phasic response to challenge, and mainly with responses to trauma-related cues or to sudden loud tones (e.g., Blanchard et al 1991; McFall et al 1990, 1992; Murburg et al 1995).

Challenge Test

The second finding of this study concerns the arithmetic task. In the past trauma control subjects, change in RSA was highly correlated with changes in heart rate. From a physiologic perspective, this would suggest that vagal mechanisms contribute to the regulation of the heart rate changes. Statistically, the vagal regulation (i.e., changes in RSA) accounted for more than 50% of the change in heart rate. In contrast, heart rate and RSA responses during the arithmetic task were not related in the PTSD group.

These findings suggest that the neural mechanisms that modulate heart rate responses to mental challenge differ between the PTSD and the past trauma groups. In the past trauma group, the relation between heart rate and RSA is consistent with the reports of a tight coupling between RSA and heart rate reported in healthy subjects during exercise (Hatfield et al 1998), posture shift (Umhau et al, unpublished data), and rest (Reed et al 1999). In contrast, heart rate and RSA responses did not covary in individuals with PTSD. These findings are consistent with reports that the decoupling of heart rate and RSA may reflect a physiologic state associated with difficulties in behavioral self-regulation. For example, in spouse abusers heart rate and RSA were decoupled relative to age-matched control subjects (Umhau et al, unpublished data) and heart rate and RSA were decoupled as an acute consequence of alcohol consumption (Reed et al 1999).

Our finding of an increment in RSA during arithmetical challenge is in contrast with previous studies of healthy individuals, in which sustained attention was linked with a reduction in RSA (e.g., Allen and Crowell 1989; Berntson et al 1994a, 1994b). This discrepancy may be explained by an element of perceived stress that can be found in the above-cited studies, in addition to the focused attention. For instance, stress can be perceived when there is an increase in the difficulty of the task (Allen and Crowell 1989), when correct answers are rewarded, or when the subjects receive feedback on their mistakes during the task (Berntson et al 1994a, 1994b). In support of the stress or metabolic cost model, Bazhenova and Porges (1997) reported increases in RSA when infants were experiencing positive affect and engagement with objects and people, whereas RSA decreased during movement and increases in negative affect.

Conclusion

Before generalizing from this study's results one should be aware of its inherent limitations. This study addressed a small sample of trauma survivors with various traumatic experiences. Some PTSD patients have been on medication, and the reported lack of statistically significant difference between those on medication and those without may be due to lack of statistical power. Finally, the challenge task administered was neutral—that is, not related to the traumatic event. The results of our study suggest, however, a potential difference in parasympathetic control of heart rate response to mental challenge between trauma survivors with PTSD and those without. The observed difference consists of lack of vagal modulation of heart rate response to challenge in PTSD, and presence of such modulation among control subjects. As suggested above, such "decoupling" between heart rate and RSA may be associated with difficulties in behavioral self-regulation in PTSD. Another explanation is that in PTSD a sympathetic activation (i.e., stress-related "alarm" mechanism) is preferentially involved in responding to challenges. This may be due to an impaired appraisal of challenge as being potentially harmful—a dysfunction that may be mediated by the amygdala and could be typical in PTSD (e.g., Davis 1997).

Alternatively, the difference in vagal modulation of heart rate may be due to a compromised corticobulbar regulation of brain-stem structures. Porges (1997) described an integrated social engagement system with both

somatomotor and visceromotor components that relies on the cortical regulation via corticobulbar pathways of the medullary nuclei of several cranial nerves. The somatomotor component (i.e., the striated muscles of the face and head) regulates behavioral engagement with the environment (i.e., looking, listening, facial signaling, head tilting, vocalizing, ingesting). The visceromotor component (i.e., the vagal regulation of the heart, bronchi, and thymus) regulates the physiologic state to promote engagement or withdrawal with the environment. According to Porges, corticobulbar pathways, directly from frontal areas to the brain stem, provide an efficient neural mechanism that at times can override or circumvent the limbic system in the regulation of emotion and affective state (Porges 1997). The defective vagal regulation of heart rate observed in PTSD may index a compromised integrated social engagement system. Thus, several of the behavioral features observed in PTSD (i.e., poor social behavior, lack of positive emotional expressivity) may be dependent on difficulties in the neural regulation of the muscles of the face and head, whereas several of the features related to autonomic state regulation may be due to difficulties in the vagal regulation of the heart and bronchi.

To better understand the neural mechanisms mediating the unique physiologic response profile of PTSD, it will be necessary to assess additional features of the social engagement system (e.g., facial expressivity, facial electromyogram, intonation) and indices of the sympathetic nervous system. Future research needs to determine how sympathetic activity might compensate for the inability of the vagal system to efficiently and reliably regulate heart rate. In addition, since the mental arithmetic challenge created only minor physiologic reactions, future research should include trauma-related tasks.

This study was supported by a Public Health Service research grant (MH-50379) to AYS.

References

Akelrod SD, Gordon D, Ubel FA, Shannon DC, Barger DC, Cohen RJ (1981): Power spectrum analysis of heart rate fluctuations: A quantitative probe of beat-to-beat cardiovascular control. *Science* 213:220–222.

Allen MT, Crowell MD (1989): Patterns of autonomic response during laboratory stressors. *Psychophysiology* 26:603–614.

Balogh S, Fitzpatrik DF, Hendriks SE, Paige SR (1993): Increases in heart variability with successful treatment in patients with major depressive disorder. *Psychopharmacol Bull* 29:201–206.

Bazhenova OV, Porges SW (1997): Vagal reactivity and affective adjustment in infants: Convergent response system. *Ann N Y Acad Sci* 807:469–471.

Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961): An inventory for measuring depression. *Arch Gen Psychiatry* 4:561–571.

Berntson GG, Bigger JT, Cacioppo JT, Eckberg DL, Grossman P, Kaufmann PG, et al (1997): Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology* 34:623–648.

Berntson GG, Cacioppo JT, Binkley PF, Quigley KS (1994a): Autonomic cardiac control. I. Estimation and validation from pharmacological blockades. *Psychophysiology* 31:572–585.

Berntson GG, Cacioppo JT, Binkley PF, Uchino BN, Quigley KS, Fieldstone A (1994b): Autonomic cardiac control. III. Psychological stress and cardiac response in autonomic space as revealed by pharmacological blockades. *Psychophysiology* 31:599–608.

Berntson GG, Cacioppo JT, Quigley KS (1991): Autonomic determinism: The modes of autonomic control, the doctorine of autonomic space, and the laws of autonomic constraint. *Psychol Rev* 98:459–487.

Berntson GG, Cacioppo JT, Quigley KS (1993): Respiratory sinus arrhythmia: Autonomic origins, physiological mechanisms, and psychological implications. *Psychophysiology* 30: 183–196.

Berntson GG, Cacioppo JT, Quigley KS (1995): The metrics of cardiac chronotropism: Biometric perspective. *Psychophysiology* 32:162–171.

Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Klauminzer G, Charney DS, et al (1990): A clinician rating scale for assessing current and lifetime PTSD: The CAPS-1. *Behav Therapist* 13:187–188.

Blanchard EB, Kolb LC, Prins A, Gates S, McCoy G (1991): Changes in plasma norepinephrine to combat related stimuli among Vietnam Veterans with PTSD. *J Nerv Ment Dis* 179:371–373.

Byrne EA, Porges SW (1992): Frequency-specific amplification of heart rate rhythms using oscillatory tilt. *Psychophysiology* 29:120–126.

Cohen H, Kotler M, Matar MA, Kaplan Z, Loewnthal U, Miodownik H, et al (1998): Analysis of heart rate variability in posttraumatic stress disorder patients. *Biol Psychiatry* 44:1054–1059.

Cohen H, Kotler M, Matar MA, Kaplan Z, Miodownik H, Cassuto Y (1997): Power spectral analysis of heart rate variability in posttraumatic stress disorder patients. *Biol Psychiatry* 41:627–629.

Davis M, Walker DL, Lee Y (1997): Role of the amygdala and the bed nucleus of the stria terminals in fear and anxiety: Possible relevance to PTSD. *Ann N Y Acad Sci* 821:305–331.

Donchin Y, Constantini S, Sold A, Byrne EA, Porges SW (1992): Cardiac vagal tone predicts outcome in neurosurgical patients. *Crit Care Med* 20:942–949.

Fox NA, Porges SW (1985): The relation between neonatal heart period patterns and developmental outcome. *Child Dev* 56: 28–37.

George DT, Nutt DJ, Walker WV, Porges SW, Adinoff B, Linnolia M (1989): Lactate and hyperventilation substantially attenuate vagal tone in normal volunteers: A possible mechanism of panic provocation? *Arch Gen Psychiatry* 46:153–156.

Goddard PH, Porges SW, Fleg J, Wright J (1995): The effects of

sympathetic and parasympathetic blockade on heart rate oscillations. *Psychophysiology* 32:S35.

Green BL, Krupnick JL, Rowland JH, Epstein SA, Stockton P, Spertus I, Stern N (2000): Trauma history as a predictor of psychologic symptoms in women with breast cancer. *J Clin Oncol* 18:1084–1093.

Hatch JP, Klatt K, Poregs SW, Schroeder-Jasheway L, Supik JD (1986): The relation between rhythmic cardiovascular variability and reactivity to orthostatic, cognitive and cold pressor stress. *Psychophysiology* 23:48–56.

Hatfield BD, Santa Maria DL, Porges SW, Potts JT, Spalding T, Byrne EA (1998): Respiratory sinus arrhythmia during exercise in aerobically trained and untrained men. *Med Sci Sports Exerc* 30:206–214.

Horowitz M, Wilner N, Alvarez W. (1979): Impact of Event Scale: A measure of subjective stress. *Psychosom Med* 41:3.

Izrad CE, Porges SW, Simons RF, Haynes OM, Hyde C, Parisi M, et al (1991): Infant cardiac activity: Developmental changes and relations with attachment. *Dev Psychol* 27:432–439.

McFall ME, Murburg MM (1994): Psychophysiological studies of combat related PTSD: An integrated view. In: Murburg MM, editor. *Catacholamine Function in Posttraumatic Stress Disorder—Emerging Concepts.* Washington, DC: American Psychiatric Press, 161–173.

McFall ME, Murburg MM, Ko GN, Veith RC (1990): Autonomic responses to stress in Vietnam combat veterans with posttraumatic stress disorder. *Biol Psychiatry* 27:1165–1175.

McFall ME, Veith RC, Murburg MM (1992): Basal sympathoadrenal function in PTSD. *Biol Psychiatry* 31:1050–1056.

McLeod DR, Hoehn-Saric R, Porges SW, Zimmerli WD (1992): Effects of Alprazolam and imipramine on parasympathetic cardiac control in patients with generalized anxiety disorder. *Psychopharmacology* 107:535–540.

Murburg MM, McFall ME, Lewis N, Veith RC (1995): Plasma norepinephrine kinetics in patients with posttraumatic stress disorder. *Biol Psychiatry* 38:819–825.

Orr SP (1997): Psychophysiologic reactivity to trauma-related imagery in PTSD. Diagnostic and theoretical implications of recent findings. *Ann N Y Acad Sci* 821:114–124.

Porges SW, inventor (1985, April 16): Method and apparatus for evaluating rhythmic oscillations in aperiodic physiological response systems. U.S. patent 4,510,944.

Porges SW (1992): Vagal tone: A physiologic marker of stress vulnerability. *Pediatrics* 90:498–504.

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

Porges SW (1997): Emotion: An evolutionary by-product of the neural regulation of the autonomic nervous system. *Ann N Y Acad Sci* 807:62–77.

Porges SW, Bohrer RE (1990): The analysis of periodic processes in psychophysiological research. In: Cacioppo JT, Tassinary IG, editors. *Principles of Psychophysiology: Physical, Social and Inferential Elements.* New York: Cambridge University Press, 708–753.

Porges SW, Byrne EA (1992): Research methods for measurement of heart rate and respiration. *Biol Psychol* 34:93–130.

Porges SW, Doussard-Roosevelt J, Portales AL, Suess PE (1994): Cardiac vagal tone: Stability and relation to difficultness in infants and 3-years-old. *Dev Psychobiol* 27:289–300.

Prins A, Kaloupek DG, Keane TM (1995): Psychophysiological evidence for autonomic arousal and startle in traumatized adult populations. In: Freidman MJ, Charney DS, Deutch AY, editors. *Neurobiological Clinical Consequences of Stress.* Philadelphia: Lippincott-Raven, 291–314.

Reed SF, Porges SW, Newlin DB (1999): Effects of alcohol on vagal regulation of cardiovascular function: Contributions of the polyvagal theory to the psychophysiology of alcohol. *Exp Clin Psychopharmacol* 7:484–492.

Richter DW, Spyer KM (1990): Cardiorespiratory control. In: Loewy AD, Spyer KM, editors. *Central Regulation of Autonomic Function.* New York: Oxford University Press, 189–207.

Schwaber JS, Kapp BS, Higgins G (1980): The origin and extent of direct amygdala projections to the region of the dorsal motor nucleus of the vagus and the nucleus of the solitary tract. *Neurosci Lett* 20:15–20.

Shalev AY, Freedman S, Peri T, Brandes D, Sahar T (1997): Predicting PTSD in civilian trauma survivors: Prospective evaluation of self report and clinician administered instruments. *Br J Psychiatry* 170:558–564.

Shalev AY, Sahar T, Freedman S, Peri T, Glick N, Brandes D, et al (1998): Prospective study of heart rate response to trauma and subsequent PTSD. *Arch Gen Psychiatry* 55:553–559.

Southwick SM, Krystal JH, Bremner JD, Morgan CA III, Nicolaou AL, Nagy LM, et al (1997): Noradrenergic and serotonergic function in posttraumatic stress disorder. *Arch Gen Psychiatry* 54:749–758.

Spielberger CD (1983): *Manual for State Trait Anxiety Inventory.* Palo Alto, CA: Consulting Psychologists Press.

Suess PE, Porges SW, Plude DJ (1994): Cardiac vagal tone and sustained attention in school-age children. *Psychophysiology* 31:17–22.

Vanhoutte PM, Levy MN (1979): Cholinergic inhibition of adrenergic neurotransmission in the cardiovascular system. In: Brooks CM, Koizumi K, Sato A, editors. *Integrative Functions of the Autonomic Nervous System.* Tokyo: University of Tokyo Press, 159–176.

Ziegler D, Laux G, Dannehl K, Spuler M, Muhlen H, Mayer P, et al (1992): Assessment of cardiovascular autonomic function: Age-related normal ranges and reproducibility of spectral analysis, and standard tests of heart rate variation and blood pressure responses. *Diabet Med* 9:166–175.