ORIGINAL ARTICLE

A Prospective Study of Heart Rate Response Following Trauma and the Subsequent Development of Posttraumatic Stress Disorder

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Background: Physiological arousal during traumatic events may trigger the neurobiological processes that lead to posttraumatic stress disorder (PTSD). This study prospectively examined the relationship between heart rate and blood pressure recorded immediately following a traumatic event and the subsequent development of PTSD.

Methods: Eighty-six trauma survivors who presentd at the emergency department of a general hospital were followed up for 4 months. Heart rate and blood pressure were recorded on arrival at the emergency department. Heart rate, anxiety, depression, and PTSD symptoms were assessed 1 week, 1 month, and 4 months later. The clinician-administered PTSD scale defined PTSD status at 4 months.

Results: Twenty subjects (23%) met PTSD diagnostic criteria at the 4-month assessment (PTSD group), and 66 (77%) did not (non-PTSD group). Subjects who developed PTSD had higher heart rates at the emergency department (95.5±13.9 vs 83.3±10.9 beats per minute, t=4.4, P<.001) and 1 week later (77.8±11.9 vs 72.0±9.5 beats per minute, t=2.25, P<.03), but not after 1 and 4 months. The groups did not differ in initial blood pressure measurement. Repeated-measures analysis of variance (ANOVA) for heart rate showed a significant group effect (P<.02), time effect (P<.001), and group × time interaction (P<.001). The time effect and group × time interaction remained significant when adjusted for sex, age, trauma severity, immediate response, and dissociation during the traumatic event.

Conclusion: Elevated heart rate shortly after trauma is associated with the later development of PTSD.

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POSTTRAUMATIC STRESS disorder (PTSD) is a pervasive anxiety disorder that occurs in 15% to 25% of trauma survivors. Symptoms of PTSD have been observed in up to 94% of trauma survivors 1 week following trauma.[1] Yet the intensity of such symptoms decreases in most survivors, leaving only a few with chronic PTSD.[2] The mechanism that links exposure to a traumatic event with the development of PTSD remains largely unidentified.

According to classical conditioning theory, the traumatic event serves as an unconditioned stimulus that evokes an immediate and "hardwired" response from the organism (unconditioned response).[3,4] Stimuli associated with the traumatic event then become conditioned stimuli, capable of subsequently eliciting conditioned responses in the form of PTSD symptoms (eg, reactivity "upon exposure to cues that symbolize or resemble an aspect of the traumatic event").[5] Additionally, the avoidance of stimuli associated with the traumatic event may be rewarded by a reduction in distress, and thereby be reinforced and fail to extinguish with time.[6,7]

The intensity of the traumatic event (unconditioned stimulus) has been shown to correlate with the subsequent development of PTSD.[8-11] However, it is the reaction to the traumatic event at the time of its occurrence (unconditioned response) that may hold the key to the pathogenesis of PTSD.[12,13] The psychological component of the immediate reaction has been the object of a few studies,[14,15] and is generally believed to contribute to the development of PTSD above and beyond the intensity of the exposure. The physiological component of the response to trauma, however, has received relatively little attention.

Physiological activation during stressful events may play a central role in the pathogenesis of PTSD. Peripheral administration of epinephrine immediately after aversive training enhances the consolidation of amygdala-mediated learning in animal models.[16,17] Low cortisol levels following rape have been found to be associated with a higher risk for developing PTSD,[18] and low corticosterone levels may

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SUBJECTS AND METHODS

SUBJECTS

The results presented here are part of a large-scale prospective study of the effect of trauma (see Shalev et al[21] for discussion of the parent project). Patients arriving at the emergency department of Hadassah University Hospital, Jerusalem, Israel, were recruited into the study during a period of 2 years. Patients were examined by a research psychiatrist and considered for the study if they were between 16 and 65 years of age and had experienced a traumatic event meeting the criterion A of the *DSM-III-R*.[22] Subject candidates received information about the study, were invited to participate, and gave written informed consent. They were subsequently interviewed 1 week, 1 month, and 4 months after the traumatic event. The follow-up interviews included self-reported psychometrics, structured clinical interviews, and assessments of resting heart rate. Blood pressure was measured in the emergency department but not during follow-up.

To reduce the heart rate and blood pressure variability that might result from severe physical injuries, treatment provided on the way to the hospital (eg, fluid substitution, medication), and different methods of vital sign monitoring in the emergency department (severely injured patients are monitored on-line), only patients with mild injuries who did not need surgical intervention and who were released to their homes within 12 hours of emergency department arrival were included. Other exclusion criteria were head injury, current or lifetime abuse of alcohol or illicit drugs (relatively rare in Israel), past or present psychosis, a life-threatening medical illness, and burn injury.

A total of 239 subjects agreed to participate in the parent study and 191 (79.9%) completed all 3 follow-up interviews. Of these, 105 failed to meet the more stringent exclusion criteria of the current study, leaving a total of 86 participants (45% of all completers). Subjects who were excluded from this study did not differ from those included in type of traumatic events (83% motor vehicle crashes; χ^2 test, 0.02; P=.9) and in prior and event-related variables (ie, age [29.3±10.4 years among excluded patients], number of past traumatic events [4.2±1.8 among excluded patients], event severity [5.0±1.6], Peritraumatic Dissociation Responses Questionnaire[14] (PDEQ) score [18.7±7.6] and immediate response scores [73.2±27.7]; multivariate analysis of variance [MANOVA] $F_{5,186}$=1.56; P=.2). The subgroups did not differ in the prevalence of 4-month PTSD (17% in the parent sample; χ^2 test, 2.54; P=.12), in 1-week and 1-month scores on the Impact of Events Scale[23] (IES) (36.4±15.5 and 24.8±15.4, Fs<1), in 1-month scores on the Mississippi Scale for Combat-Related PTSD–Civilian Version[24] (MISS) (70.6±20.7; F<1) and in 1-month scores on the Clinician-Administered PTSD Scale (CAPS) (23.9±26.2, F<1). Finally, the subgroups did not differ in heart rate measures at 1 week (75.1±10.3 among those excluded, t=0.41), 1 month (72.6±9.4, t=0.67) and 4 months (73.0±11.2, t=0.44).

PSYCHOMETRICS

Self-report instruments included the IES, State-Trait Anxiety Inventory,[25] (STAI), MISS, PDEQ, an immediate-response questionnaire, and a trauma history questionnaire.

The IES, STAI, and MISS have been used in numerous studies of PTSD and other disorders and will not be described here (see Shalev[21] for detailed discussion of psychometric properties and predictive power) in this study's sample. The PDEQ is an 8-item questionnaire about experiences related to the construct of dissociation, validated by Marmar et al[14] with 238 male Vietnam war veterans and by Shalev et al[15,21] in civilian trauma survivors.

prolong the adrenergic response to stress[19] and enhance the effect of catecholamines on memory consolidation in animals.[20]

Studying bodily responses to traumatic stress is therefore of particular interest. It is also important to know whether measurable dimensions of such responses can improve the prediction of PTSD over and above predictions made from psychometrics. Our study prospectively evaluates the relationship between 2 measures of physiological activation recorded immediately following the trauma, heart rate and blood pressure, and the subsequent development of PTSD.

RESULTS

DIAGNOSTIC CLASSIFICATION AND DEMOGRAPHIC DATA

Eighty-six trauma survivors (34 women and 52 men) were included in this study. Thirty-three (38%) met diagnostic criteria for PTSD at 1 month, and 20 (23%) had PTSD at the 4-month assessment (PTSD group). Sixty-six (77%) did not have PTSD at 4 months (non-PTSD group). Traumatic events in the PTSD group included motor vehicle crashes (n=17, 85%), terrorist attacks (n=2, 10%) and a mechanical accident occurring at home (n=1, 5%). Traumatic events in the non-PTSD group included motor vehicle crashes (n=53, 80%), work-related accidents (n=5, 7.5%) terrorist attacks (n=4, 6%), mechanical accidents occurring at home (n=3, 4.5%), and witnessing violence (n=1, 1.5%). The difference between the groups in type of traumatic events (motor vehicle crashes vs all others) was not statistically significant (χ^2 test, 0.22; P=.64).

Eight PTSD subjects (40%) and 16 non-PTSD subjects (24%) had at least 1 *DSM-III-R* Axis I disorder prior to the traumatic event (χ^2 test, 1.89; P=.16). Lifetime diagnoses in the PTSD group (more than one per subject allowed) included simple phobia (n=6), social phobia (n=3), major depression (n=3), panic disorder (n=1), bipolar disorder (n=1), and agoraphobia without panic attacks (n=1). Lifetime diagnoses in the non-PTSD group included major depression (n=6), social phobia (n=5), somatoform disorders (n=4), simple phobia (n=1), and panic disorder (n=1).

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The immediate-response questionnaire included 14 items that assessed the intensity of physical (eg, pain), emotional (eg, fear, anger), and negative cognitive (eg, expectation of doom) experiences during the event. Each item was rated from 1 to 10 (1=none, 10=highest possible intensity), yielding response intensity scores ranging from 10 to 140.

The trauma history questionnaire[26] assessed the nature and number of previously experienced traumatic events (eg, natural and man-made disasters, war, motor vehicle crashes, rape, physical assault, and others). The number of distinct traumatic events endured by each subject constituted the questionnaire's score.

In addition to the above, 12 mental health professionals, blinded as to subjects' PTSD status, listened to audiotaped scripts describing each of the traumatic events (for detailed procedure see[21,26-28]) and independently rated the severity of the traumatic event on a 1 to 10 scale (1=not severe at all, 10=extreme severity). The average score of the 12 observers is reported.

STRUCTURED CLINICAL INSTRUMENTS

These included Hebrew versions of the Hamilton Depression and Hamilton Anxiety scales,[29] CAPS,[30] and the Structured Clinical Interview for *DSM-III*[31] (SCID). All instruments had been previously validated and used in studies of PTSD,[15,28,32,33] and all were administered by clinicians (D.B., S.F., T.P., and A.S.) with extensive experience in PTSD diagnosis and treatment. The PTSD status at 4 months was determined according to *DSM-III-R* criteria as measured by the CAPS. Current and lifetime diagnoses of other mental disorders were identified via the SCID.

HEART RATE AND BLOOD PRESSURE

Heart rate and blood pressure were obtained from all patients on presentation to the emergency department. A registered nurse, using a vital signs monitor (Critikon Dynamap, Tampa, Fla), measured and then immediately transcribed these measures into the patient's medical record. During subsequent assessments, resting heart rate was recorded as part of a larger study of responses to auditory startle in the psychophysiological laboratory of the Center for Traumatic Stress, Hadassah University Hospital, according to a previously described procedure.[33,34] A Coulbourn Modular Instrument System (Coulbourn Inc, Allentown, Pa), interfaced with a personal computer through a Coulbourn Lablinc Computer Interface was used to record heart rate via standard limb electrocardiogram leads connected to a high-gain bioamplifier and inputting to a Coulbourn Tachometer. The analog signal was sampled and digitized by a Coulbourn Lablinc Analog-to-Digital Converter at a rate of 2 Hz. The laboratory sessions took place in an 3.2×2.4-m humidity- and temperature-controlled room, connected via wires to an adjoining portion of the laboratory in which the experimental apparatus was located. The subject was seated in a comfortable armchair. After the subject was familiarized with the laboratory, the electrodes were attached, and he or she was asked to sit quietly for 5 minutes. Heart rates were sampled continuously during this period and averaged to yield a measure of resting heart rate.

STATISTICAL ANALYSIS

Statistical analyses follow the general linear model for group comparisons (ANOVAs and MANOVAs), group × time comparisons (repeated-measures ANOVA), control of confounds (analysis of covariance [ANCOVA]), and analyses of multiple correlations (multiple regression). Logistic regression was used to assess the prediction of PTSD. An α level of .05 conferred statistical significance. All values are given as mean±SD unless otherwise indicated.

PSYCHOMETRICS

Table 1 provides demographic and psychometric information for the 2 groups. The groups did not differ in the average number of past traumatic events, but did differ in objective ratings of current event severity, self-reported severity of the immediate response, and PDEQ (MANOVA $F_{3,81}=3.56$, $P<.02$). Group differences at 1 and 4 months are consistent with the group selection procedure and reflect the presence vs absence of PTSD. More importantly, these differences significantly increased with time (**Table 2**).

HEART RATE AND BLOOD PRESSURE

Differences Between PTSD Subjects and Non-PTSD Subjects

Repeated-measures ANOVA for heart rate revealed a significant main effect of diagnostic group ($F_{1,84}=5.73$, $P<.02$), a significant main effect of time ($F_{3,252}=62.2$, $P<.001$), and a significant group × time interaction ($F_{3,252}=8.71$, $P<.001$). **Figure 1** illustrates changes in mean heart rate over time.

The PTSD group had higher heart rates in the emergency department (96.4±13.9 vs 83.3±10.9 beats per minute; $t[84]=4.40$; $P<.001$) and higher 1-week heart rates (77.8±12.9 vs 72.0±9.46 beats per minute; $t[84]=2.26$; $P<.03$) than the non-PTSD group. **Figure 2** illustrates the distribution of individual heart rate measurements in the emergency department and 1 week later, showing an overlap between the groups and the lack of remote outliers in the PTSD group. The groups did not differ in 1-month heart rate measurements (74.06±12.8 vs 74.02±10.52 beats per minute; $t[84]=0.02$) or in 4-month heart rate measurements (72.7±13.3 vs 72.2±9.78 beats per minute; $t[84]=0.21$). The groups did not differ in emergency department systolic (139.8±24.9 vs 128.2±17.8 mm Hg; $t[84]=0.53$) or diastolic (79.8±12.4 vs 78.5±9.04 mm Hg, $t=0.52$) blood pressure.

Controlling for Prior Variables, Event Severity, and Immediate Responses

Repeated-measures ANCOVA for heart rate (emergency department, 1 week, 1 month, and 4 months), using PTSD as grouping factor and controlling for sex, age, past Axis

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Table 1. Means and SDs of Demographic and Psychometric Variables in PTSD Subjects and Non-PTSD Subjects*

	PTSD Subjects (n = 20)	Non-PTSD Subjects (n = 66)	*t* (*df* = 84)	*P*
Demographic variables				
Age, y	27.4 (10.6)	27.3 (10.5)	0.04	.96
Sex, M/F	13/7	53/13	0.22*	.6
No. of past traumatic experiences†	4.1 (2.1)	3.92 (3.0)	0.24	.8
Event-related variables				
Event severity	6.2 (2.09)	4.9 (1.25)	3.28	.002
Immediate response	80.7 (32.9)	66.1 (27.2)	2.00	.05
Peritraumatic dissociation (PDEQ)‡	22.6 (10.4)	19.7 (7.0)	1.46	.14

*χ^2 Test.
†Number of past traumatic experiences as assessed by the Trauma History Questionnaire.
‡PDEQ indicates Peritraumatic Dissociation Responses Questionnaire.[14]

Table 2. Means, SDs, and Repeated-Measures Analyses of Variance (ANOVA) of Psychometric Measures*

				ANOVA					
				Group		Time		Group × Time	
Measure	1 wk	1 mo	4 mo	$F_{1,84}$	*P*	$F_{2,168}$	*P*	$F_{2,168}$	*P*
IES Intrusion									
PTSD subjects	26.4 (8.1)	24.0 (10.3)	24.5 (9.2)	31.06	<.001	10.84	<.001	4.08	.02
Non-PTSD subjects	17.5 (10.5)	13.9 (10.7)	9.37 (8.7)						
IES Avoidance									
PTSD subjects	13.5 (6.3)	12.6 (5.4)	14.2 (4.5)	2.96	.09	0.10	.9	2.29	.11
Non-PTSD subjects	11.2 (6.4)	11.8 (7.7)	9.7 (7.6)						
STAI-State									
PTSD subjects	60.1 (9.6)	53.8 (16.5)	54.5 (17.8)	24.8	<.001	17.33	<.001	2.89	.06
Non-PTSD subjects	49.6 (11.6)	43.1 (12.9)	37.5 (11.0)						
STAI-Trait									
PTSD subjects	45.6 (9.1)	50.2 (12.9)	47.3 (11.9)	29.03	<.001	2.00	.14	6.39	.003
Non-PTSD subjects	40.11 (9.9)	40.2 (9.2)	37.0 (9.1)						
HAM-A									
PTSD subjects	14.5 (10.0)	23.4 (12.3)	15.0 (8.4)	91.71	<.001	17.05	<.001	8.02	.001
Non-PTSD subjects	7.9 (7.3)	7.8 (10.1)	3.4 (5.1)						
HAM-D									
PTSD subjects	15.45 (11.8)	28.1 (11.6)	18.3 (11.1)	51.18	<.001	32.33	<.001	9.86	<.001
Non-PTSD subjects	8.60 (8.7)	10.6 (11.5)	5.0 (8.2)						
MISS†									
PTSD subjects	. . .	107.3 (22.1)	113.1 (18.6)	57.5	<.001	0.03	.9	6.84	.02
Non-PTSD subjects	. . .	78.7 (21.5)	72.1 (18.6)						
CAPS total score†									
PTSD subjects	. . .	64.9 (27.8)	58.5 (18.1)	99.4	<.001	14.5	.001	1.9	.17
Non-PTSD subjects	. . .	24.5 (23.7)	10.8 (12.7)						

*IES indicates Impact of Events Scale; PTSD, posttraumatic stress disorder; STAI, State-Trait Anxiety Scale; HAM-A, Hamilton Anxiety Scale; HAM-D, Hamilton Depression Scale; MISS, Mississippi Rating Scale for Combat-Related PTSD–Civilian Version; CAPS, Clinician-Administered PTSD Scale; and ellipses, not applicable.
†$F_{1,84}$ for time and group × time interaction.

I disorders (as a dummy 0,1 variable), event severity, response severity, and peritraumatic dissociation, yielded a nearly significant group effect ($F_{1,77}$=2.94, *P*=.09), a significant main effect of time ($F_{3,249}$=61.06, *P*<.001), and a significant group × time interaction ($F_{3,249}$=8.63, *P*<.001). The adjusted mean heart rate in the emergency department was 95.1 beats per minute for PTSD subjects and 84.7 beats per minute for non-PTSD subjects ($F_{1,78}$=10.92, *P*<.002). The adjusted mean heart rate at 1 week was 77.3 beats per minute for PTSD subjects and 72.6 beats per minute for non-PTSD subjects ($F_{1,78}$=2.78, *P*=.09).

Correlations Between Emergency Department Heart Rate and Other Measures

Prior Variables. Heart rate levels in the emergency department were higher in male (88.6±13.6 beats per minute) than in female subjects (82.9±11.03 beats per minute). Two-way ANOVA failed to show a sex × PTSD interaction ($F_{1,82}$=0.11), while showing a significant main effect of PTSD ($F_{1,82}$=16.75, *P*<.001) and a trend toward a main effect of sex ($F_{1,82}$=3.39, *P*<.07). The correlations with age and with peritraumatic dissociation were not significant.

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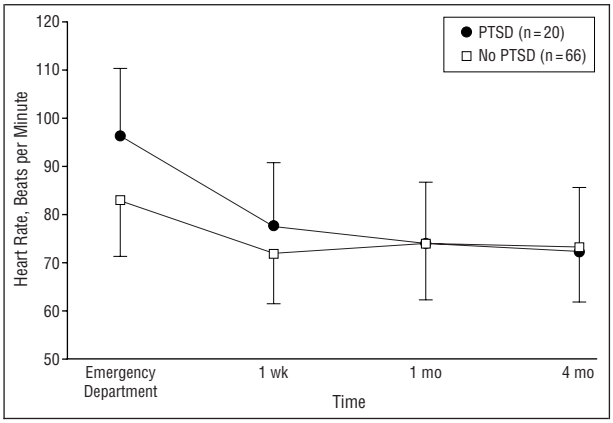

Figure 1. *Means and SDs of heart rates in subjects with and without posttraumatic stress disorder (PTSD).*

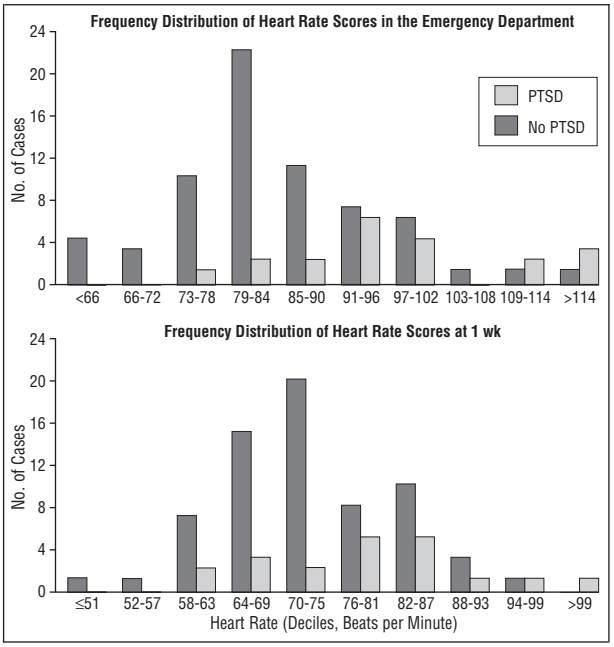

Figure 2. *Frequency distribution of heart rate scores in the emergency department and 1 week later. PTSD indicates posttraumatic stress disorder.*

Trauma-Related Variables. Heart rate levels in the emergency department showed a small but significant correlation with systolic blood pressure (r=0.24, P<.03), diastolic blood pressure (r=0.32, P<.01), event severity (r=0.36, P<.001), and immediate response (r=0.26, P<.02).

Continuous Outcome Variables. Heart rate scores in the emergency department produced significant correlation with 4-month IES Intrusion subscale scores (r=0.43, P<.001) IES Avoidance subscale scores (r=0.28, P=.02), STAI-State scores (r=0.31, P<.01), MISS scores (r=0.24, P=.03), and total CAPS score (r=0.31, P<.005). Systolic and diastolic blood pressure did not correlate significantly with any of the 4-month variables.

Predicting PTSD From Prior Variables, Immediate Responses, and Heart Rate

Stepwise hierarchical logistic regression, estimating the effects of sex, age, trauma history, event severity, immediate response, dissociation, and initial (emergency department) heart rate (in that order) on 4-month PTSD status showed a significant effect of event severity (χ^2 test, 0.01; P<.04) and a significant additional effect (increase in χ^2 test, 9.97; P=.002) of initial heart rate (total χ^2 test, 20.37; P=.005), with no other variable contributing significantly to 4-month PTSD.

COMMENT

The results of this study showed that on arrival to an emergency department following a traumatic event, and regardless of whether PTSD developed, survivors of traumatic events showed elevated heart rates, which later normalized. Survivors who subsequently developed PTSD showed higher emergency department and 1-week heart rates than those who did not. The heart rate difference between diagnostic groups was not accounted for by rated intensity of the trauma nor by self-reported responses. This finding suggests that heart rate expresses a dimension of the response to traumatic events that is not entirely captured by psychometrics. Initial blood pressure measurements did not differentiate the groups, nor did they correlate with any of the outcome measures.

There are several limitations to this study, mostly resulting from its "naturalistic" design. First, while all subjects had come to the emergency department directly from the site of their trauma, the exact timing of their arrival relative to the time of their traumatic incident was unavailable. However, traumatic events are not limited to the impact phase but often include the evacuation phase as well. Second, heart rate levels in the emergency department were obtained by single measurement, while those obtained at 1 week represent an average of 5 minutes of continuous recording. However, the persistence of higher heart rate levels at 1 week in PTSD supports the validity of the study's main finding. Data on blood pressure, in contrast, rely on a single measurement.

Within the above-mentioned conditioning model, the finding of elevated heart rate in the emergency department in the PTSD group may be interpreted as reflecting higher intensity of the unconditioned response. Theoretically, excessive adrenergic activation may contribute to the development of PTSD through enhanced memory consolidation of the traumatic event (unconditioned stimulus).[4,19] The lack of blood pressure elevation in this study, despite heart rate increase, suggests a mainly adrenergic as opposed to noradrenergic activation.

Our study does not exclude a possible effect of a prior trait (eg, hyperresponsiveness) on both heart rate response and the development of PTSD. Posttraumatic stress disorder has been associated with increased physiological responses to trauma-related cues[3,27,28,35-37] and to other stimuli, including loud tones[33,34]; nontraumatic stressors, such as waiting to receive medical treatment[38]; and chemical stimulation, such as yohimbine

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administration.[39] Hypothetically, increased physiological responsiveness may precede the traumatic event, be expressed during the event, and become part of PTSD after the trauma. The source of such hyperresponsiveness may be genetic. A twin study of Vietnam veterans has shown that about 30% of the liability to developing PTSD symptoms of hyperarousal and avoidance are accounted for by heredity.[40] Alternatively, the elevated heart rate responses in PTSD patients may reflect the priming effect of earlier traumatization or a combination of inherited vulnerability and lifetime exposure. A family history of mental disorders has been associated with increased likelihood of both exposure to traumatic events and of developing PTSD on such exposure.[41]

Interestingly, the heart rate responses of the 2 groups overlapped (Figure 2) and were not extreme. This finding does not support theories postulating that PTSD typically results from "extreme" or "catastrophic" responses to stress.[42] Indeed, these results are in line with previous research showing that moderate sympathetic activation has a greater effect on learning and memory than more extreme activation.[17]

Despite increasing differences in symptom intensity, the 2 study groups had similar resting heart rates 1 and 4 months after trauma. This may reflect a slow return to baseline following the trauma and/or habituation to the laboratory setting. Studies of resting heart rate in PTSD[37] are often confounded by an expectation of a stressful task, such as psychophysiological testing. Conversely, when PTSD subjects were maintained in supine position for 30 minutes without an expectation of a challenge, their heart rate, blood pressure, and plasma norepinephrine levels were not found to differ from those of controls.[43] Accordingly, Prins et al[35] concluded that baseline heart rate may not be higher in PTSD. It is possible that in the emergency department and during the first visit to the laboratory, PTSD subjects reacted as toward a challenge, and therefore showed higher heart rate levels. By their second and third visits to the laboratory, however, they may have became accustomed to the setting and learned that they were not in a threatening environment, so that no differences were seen.

Previous studies have suggested that an alteration in noradrenergic brain functions may exist in chronic PTSD.[36,37,39] This study does not address central noradrenergic mechanisms, nor those through which peripheral hormones affect central catecholamines and memory consolidation. The effect of peripheral epinephrine on memory may be mediated through the brainstem nucleus of the solitary tract, projecting into the locus ceruleus,[44] or through epinephrine-related increase in circulating glucose levels.[17] Future prospective studies should explore such endocrine and metabolic variables shortly after trauma. They should also address the interaction between circulating catecholamines and cortisol during acute stress[43] and its relationship with subsequent PTSD.

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REFERENCES

1. Rothbaum BO, Foa EB. Subtypes of posttraumatic stress disorder and duration of symptoms. In: Davidson JRT, Foa EB, eds. *Posttraumatic Stress Disorder:* DSM-IV *and Beyond*. Washington, DC: American Psychiatric Press; 1993: 23-35.
2. Kesslar RC, Sonega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*. 1995;52: 1048-1060.
3. Kolb LC, Multipassi LR. The conditioned emotional response: a subclass of the chronic and delayed posttraumatic stress disorder. *Psychiatr Ann*. 1982;12: 979-987.
4. Pitman RK. Posttraumatic stress disorder, hormones, and memory. *Biol Psychiatry*. 1989;26:221-223.
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, DC: American Psychiatric Association; 1994.
6. Mowrer OH. *Learning Theory and Behavior*. New York, NY: John Wiley & Sons; 1960.
7. Keane TM, Zimmering RT, Caddell JM. A behavioral formulation of posttraumatic stress disorder in Vietnam veterans. *Behav Ther*. 1985;8:9-12.
8. Foy DW, Rueger DB, Sipprelle RC, Carroll EM. Etiology of posttraumatic stress disorder in Vietnam veterans: analysis of premilitary, military, and combat exposure influences. *J Consult Clin Psychol*. 1984;52:79-87.
9. Breslau N, Davis GC. Posttraumatic stress disorder: the stressor criterion. *J Nerv Ment Dis*. 1987;175:255-264.
10. Goldberg J, True WR, Eisen SA, Henderson WG. A twin study of the effects of the Vietnam war on posttraumatic stress disorder. *JAMA*. 1990;263: 1227-1232.
11. March JS. What constitutes a stressor? the criterion A issue in posttraumatic stress disorder. In: Davidson JRT, Foa EB, eds. *Posttraumatic Stress Disorder:* DSM-IV *and Beyond*. Washington, DC: American Psychiatric Press; 1993: 37-54.
12. Feinstein A, Dolan R. Predictors of post-traumatic stress disorder following physical trauma: an examination of the stressor criterion. *Psychol Med*. 1991;21: 85-91.
13. Perry S, Difede J, Musngi G, Frances AJ, Jacobsberg L. Predictors of posttraumatic stress disorder after burn injury. *Am J Psychiatry*. 1992;149: 931-935.
14. Marmar CR, Weiss DS, Schlenger WE, Fairbank JA, Jordan BK, Kulka RA, Hough RL. Peritraumatic dissociation and posttraumatic stress in male Vietnam theater veterans. *Am J Psychiatry*. 1994;151:902-907.
15. Shalev AY, Peri T, Canetti L, Schreiber S. Predictors of PTSD in injured trauma survivors: a prospective study. *Am J Psychiatry*. 1996;153:219-225.
16. McGaugh JL, Liang KC, Bennet C, Sternberg DB. Adrenergic influence on memory storage: interaction of peripheral and central systems. In: Lynch G, McGaugh JL, Weinberger NM, eds. *Neurobiology of Learning and Memory*. New York, NY: Guilford Press; 1984:313-332.
17. Gold PE, McCarthy RC. Stress regulation of memory processes: role of peripheral catecholamines and glucose. In: Friedman MJ, Charney DS, Deutch AY, eds. *Neurobiological and Clinical Consequences of Stress*. Philadelphia, Pa: Lippincott-Raven Publishers; 1995:151-162.
18. Resnick HS, Yehuda R, Pitman RK, Foy DW. Effect of previous trauma on acute plasma cortisol level following rape. *Am J Psychiatry*. 1995;152: 1675-1677.
19. Munck A, Guyre PM, Holbrook NJ. Physiological functions of glucocorticoids in stress and their relation to pharmacological actions. *Endocr Rev*. 1984;93: 9779-9783.
20. Bohus B. Humoral modulation of learning and memory processes: physiological significance of brain and peripheral mechanisms. In: Delacour J, ed. *The Memory System of the Brain*. Singapore: World Scientific; 1984:337-364.
21. Shalev AY, Freedman S, Peri T, Brandes D, Sahar T. Predicting PTSD in civilian trauma survivors: prospective evaluation of self report and clinician administered instruments. *Br J Psychiatry*. 1997;170:558-564.
22. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*. Washington, DC: American Psychiatric Association; 1987.
23. Horowitz M, Wilner N, Alvarez W. Impact of Events Scale: a measure of subjective stress. *Psychosom Med*. 1979;41:209-218.

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24. Keane TM, Caddell JM, Taylor KL. Mississippi Scale for Combat-Related Posttraumatic Stress Disorder: three studies in reliability and validity. *J Consult Clin Psychol*. 1988;56:85-90.
25. Speilberger CD. *Manual for State-Trait Anxiety Inventory*. Palo Alto, Calif: Consulting Psychologists Press; 1983.
26. Green BL. Psychometric review of Trauma History Questionnaires (Self Report). In: Stamm BH, ed. *Measurement of Stress, Trauma, and Adaptation*. Lutherville, Md: Sidran Press; 1996.
27. Pitman RK, Orr SP, Forgue DF, de Jong JB, Claiborn JM. Psychophysiological assessment of posttraumatic stress disorder imagery in Vietnam combat veterans. *Arch Gen Psychiatry*. 1987;44:970-975.
28. Shalev AY, Orr SP, Pitman RK. Psychophysiologic assessment of traumatic imagery in Israeli civilian patients with post-traumatic stress disorder. *Am J Psychiatry*. 1993;50:620-624.
29. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960; 23:56-62.
30. Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Klauminzer G, Charney DS, Keane TM. A clinician rating scale for assessing current and lifetime PTSD: the CAPS-1. *Behav Ther*. 1990;13:187-188.
31. Spitzer RL, Williams JBA, Gibbon M. *Structured Clinical Interview for* DSM-III-R: *Patient Version*. New York, NY: New York State Psychiatric Institute; 1987.
32. Solomon Z, Benbenishty R, Neria Y, Abramowitz M, Ginzburg K, Ohry A. Assessment of PTSD: validation of the revised PTSD Inventory. *Isr J Psychiatry Relat Sci*. 1993;30:110-115.
33. Shalev AY, Orr SP, Peri T, Schreiber S, Pitman RK. Physiologic responses to loud tones in Israeli posttraumatic stress disorder patients. *Arch Gen Psychiatry*. 1992; 49:870-875.
34. Orr SP, Lasko N, Shalev A, Pitman RK. Physiologic responses to loud tones in Vietnam veterans with PTSD. *J Abnorm Psychol*. 1995;104:75-82.
35. Prins A, Kaloupek DG, Keane TM. Psychophysiological evidence for autonomic arousal and startle in traumatized adult populations. In: Friedman MJ, Charney DS, Deutch AY, eds. *Neurobiological and Clinical Consequences of Stress*. Philadelphia, Pa: Lippincott-Raven Publishers; 1995:291-314.
36. Murburg MM, McFall ME, Veith RC. Basal sympathoadrenal function in patients with PTSD and depression. In: Murburg MM, ed. *Cathecholamine Function in Posttraumatic Stress Disorder: Emerging Concepts*. Washington, DC: American Psychiatric Press; 1994:175-188.
37. McFall ME, Murburg MM. Psychophysiological studies of combat-related PTSD: an integrated view. In: Murburg MM, ed. *Cathecholamine Function in Posttraumatic Stress Disorder: Emerging Concepts*. Washington, DC: American Psychiatric Press; 1994:161-173.
38. Geraradi RJ, Keane TM, Cahoon BJ, Klauminzer GW. An in vivo assessment of physiological arousal in posttraumatic stress disorder. *J Abnorm Psychol*. 1994; 103:825-827.
39. Southwick SM, Krystal JH, Morgan CA, Johnson D, Nagy LM, Nicolaou A, Heninger GR, Charney DS. Abnormal noradrenergic function in posttraumatic stress disorder. *Arch Gen Psychiatry*. 1993;50:266-274.
40. True WR, Rice J, Eisen SA, Heath AC, Goldberg J, Lyons MJ, Nowak J. A twin study of genetic and environmental contributions to liability for posttraumatic stress symptoms. *Arch Gen Psychiatry*. 1993;50:257-264.
41. Breslau N, Davis GC, Andreski P, Peterson E. Traumatic events and posttraumatic stress disorder in an urban population of young adults. *Arch Gen Psychiatry*. 1991;48:216-222.
42. Hobfoll SE. *The Ecology of Stress*. New York, NY: Hemisphere Publishing Corporation; 1988.
43. McFall ME, Veith RC, Murburg MM. Basal sympathoadrenal function in PTSD. *Biol Psychiatry*. 1992;31:1050-1056.
44. Williams CL, McGaugh JL. Reversible inactivation of the solitary tract impairs retention performance in an inhibitory avoidance task. *Behav Neural Biol*. 1992; 58:204-210.

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