

BIOLOGIC PARAMETERS OF POSTTRAUMATIC STRESS DISORDER

BIOLOGISCHEN PARAMETER BEI DEM POSTTRAUMATISCHEN STRESSSYNDROM

**Pavo Filaković, Jelena Barić, Dragutin Kadoić, Željka Crnčević-Orlić,
Ljiljana Grgurić-Radanović, Ivan Karner, Ivan Mihaljević & Nikola Mandić**

Summary: *The study included 32 hospitalized Croatian soldiers with posttraumatic stress disorder. A control group consisted of 32 hospitalized, age-, sex- and education-matched patients with psychoneurosis, who were not included in war actions. In the study group of patients with posttraumatic stress disorder, a coexistent somatic disease was present in nine patients, i.e. diabetes mellitus in three, hypertension in two, and ulcer disease in four patients. Serum cholesterol and triglyceride levels exceeded the upper normal limit in seven and nine patients, respectively. Transcranial Doppler sonography revealed cerebral hypoperfusion in five patients, and pointed to vasculospasm in 11 patients. In 23 patients, the coefficient of mental deterioration exceeded 10%. A significantly greater rate of somatic disturbances, significantly higher mean blood pressure, and significantly higher mean serum concentrations of cholesterol and triglycerides were recorded in the group of patients with posttraumatic stress disorder than in those with psychoneurosis. Attempts were made to identify the psychobiological mechanisms underlying organ abnormalities following psychotrauma, and found a significant correlation between the severity of symptoms of acute stress reaction and severity of symptoms of arousal in posttraumatic stress disorder.*

Key words: posttraumatic stress disorder (PTSD), biological parameters

Zusammenfassung: *Die vorliegende Studie umfasste 32 hospitalisierte kroatische Soldaten mit posttraumatischem Stresssyndrom. Die Kontrollgruppe umfasste 32 hospitalisierte Patienten mit Psychoneurosen ähnlichen Alters, Geschlechts und Ausbildung, die allerdings nicht an Kriegshandlungen teilgenommen hatten. Begleitende somatische Erkrankungen wurden bei neun Patienten der Versuchsgruppe diagnostiziert, u.z. Zuckerkrankheit bei drei, Bluthochdruck bei zwei und Magen-Darm-Geschwür bei vier. Der Cholesterin und Triglyzeridenspiegel lag oberhalb des Normbereichs jeweils bei sieben und neun Patienten. Transkranieller Doppler-Ultraschall zeigte verminderte Gehirndurchblutung bei fünf Patienten und vaskuläre Spasmen bei 11 Patienten. Bei 23 Patienten der Koeffizient der psychischen Verschlechterung über 10%. Ein signifikant höherer Prozentsatz an somatischen Störungen, signifikant höherer mittlerer Blutdruck und signifikant höhere Cholesterin- und Triglyzeridenspiegel wurden bei Patienten mit posttraumatischem Stresssyndrom im Vergleich mit der Kontrollgruppe festgestellt. Die Untersuchung psychobiologischer Mechanismen bei organischen Störungen als Folgen von psychischen Traumen deutete auf eine signifikante Korrelation zwischen dem Schweregrad der Symptome einer akuten Stressreaktion und dem Schweregrad der Symptome bei dem posttraumatischen Stresssyndrom.*

Schlüsselwörter: posttraumatisches Stresssyndrom, biologische Parameter

Sažetak: *Istraživanje je izvršeno u 32 bolnički liječena hrvatska vojnika s posttraumatskim stresnim poremećajem. Usporedna skupina sastojala se od 32 bolnički liječena pacijenta s psihoneurozom. Oni nisu sudjelovali u ratu, a bili su izjednačeni s eksperimentalnom skupinom prema dobi, spolu i obrazovanju. U skupini s posttraumatskim stresnim poremećajem čak 9 ispitanika imalo je tjelesnu bolest: 3 dijabetes, 2 povišen krvni tlak, 4 ulkusnu bolest. Serumska koncentracija kolesterola bila je u 7 ispitanika iznad gornje granice normale. Serumska koncentracija triglicerida bila je u 9 ispitanika iznad gornje granice normale. Transkranijalnom dopler sonografijom u 5 ispitanika nađena je hipoperfuzija mozga, a u 11 njih nalaz je upućivao na spazam krvnih žila. U 23 ispitanika koeficijent mentalne deterioracije iznosio je više od 10%. U skupini s posttraumatskim stresnim poremećajem nađen je značajno veći prosječni krvni tlak te značajno viša prosječna koncentracija kolesterola i triglicerida u serumu nego u skupini s psihoneurozom. Autori su pokušali ući u trag psihobiološkim mehanizmima koji dovode do organskih poremećaja poslije psihotraume i našli značajnu korelaciju između intenziteta simptoma akutne reakcije na stres i intenziteta simptoma pobuđenosti u posttraumatskom stresnom poremećaju.*

Ključne riječi: posttraumatski stresni poremećaj (PTSP), biološki parametri

* * * * *

INTRODUCTION

Posttraumatic stress disorder (PTSD) is an extended or delayed psychopathologic reaction to a potent environmental stressor. According to this definition, PTSD is a purely psychopathologic disorder. Nevertheless, both researchers and clinicians have observed various neurohormonal, endocrinometabolic, psychosomatic, or somatic impairments in patients with PTSD (1-8). The more so, the individuals resistant to the occurrence of psychic symptoms appear to be at a higher risk of the development of severe somatic disturbances after stress (9,10). The pathophysiology of PTSD is known to include dysfunction of a number of brain structures (e.g., amygdala, locus caeruleus, hippocampus, etc.) and neurochemical systems (noradrenergic, dopaminergic, opiate, CRF, etc.). In stress, these brain structures and neurochemical systems activate a series of adaptive physiologic and behavioral responses needed for survival. If the stress exceeds their tolerability threshold, these responses become uncoordinated, converting into the extended psychologic and neurobiologic dysfunction (11,12). It remains obscure, though, what is the inter-relationship between the PTSD symptoms and accompanying biological impairment.

The aim of the study was to determine the type and prevalence of pathophysiological changes in PTSD patients, as well as their relationship with psychic symptoms, and to try to define the psychobiological mechanisms leading to physical dysfunction after psychic trauma.

PATIENTS AND METHODS

The study was conducted in 1996, in a group of 32 Croatian Army soldiers with PTSD, mean age 34.1 ± 7.1 years, who had been actively included in war actions in 1991 and 1992. A control group consisted of 32 hospitalized patients with psychoneurosis, who had not been included in war actions. The control group patients matched the study group patients by age (33.0 ± 7.5 years), sex (males), and level of education. All study subjects were included in the study consecutively, according to their admission for hospital treatment. On admission, physical examination was performed. On the next morning, blood pressure was measured in supine position and blood samples were obtained for laboratory analysis. Further diagnostic examinations depended on these findings. Both groups of patients underwent testing with various psychologic techniques, i.e. interview. Wechsler Adult Intelligence Scale, Bender-Gestalt test, attention test by T. Đurić, Ž. Bele-Potočnik and B. Hruševar, and Minnesota Multiphasic Personality Inventory. The PTSD patients were additionally evaluated by a number of scales for PTSD evaluation, i.e. Scale of Combat Exposure, Scale of Acute Reaction, PTSD Questionnaire according to DSM-III R, and Los Angeles Symptom Checklist (adult version-LASC 01).

Arterial blood pressure of $>150/90$ mmHg brain hypoperfusion on transcranial Doppler sonography (vascular spasm was considered a borderline finding), mental deterioration coefficient of $>10\%$, serum cholesterol level of >8 mmol/l, serum triglyceride level of >3 mmol/l, and serum glucose level of >6.4 mmol/l were considered pathologic findings.

RESULTS

In the patients with PTSD, the mean scores on evaluation scales ranged from 53.3% to 87.5% of the maximal scores possible, indicating difficult combat experience and severe form of PTSD (Table 1).

Table 1. Mean scores on various evaluation scales in PTSD patients (N = 32)

EVALUATION SCALE	DIAGNOSTIC CATEGORY	SCORE RANGE	MEAN SCORE
Scale of combat exposure		1-6	4.6 ± 1.0
Scale of acute	psychologic	0-3	1.6 ± 0.7
	affective	0-3	2.0 ± 0.7
LASC-01	category A	0-4	3.5 ± 0.6
	category B	0-4	2.9 ± 0.5
	category C	0-4	3.1 ± 0.5
DSM-III R	category A	0-7	5.2 ± 0.8
	category B	0-7	4.9 ± 0.8
	category C	0-7	5.4 ± 0.8

In the study group (PTSD), the severity of acute affective-cognitive stress reaction significantly exceeded their physiologic reaction ($N = 32$, 2.0 ± 0.7 : 1.6 ± 0.7 , $t = 2.35$, $P < 0.05$). However, this group included nine patients with a coexistent somatic disease (arterial hypertension in two, diabetes mellitus in three, and ulcer disease in four patients). In the control group of psychoneurosis patients, a coexistent somatic disease (ulcer disease) was present in only two patients. The difference was statistically significant ($\chi^2 = 3.95$, $P < 0.05$, $df = 1$). A large number of pathophysiologic abnormalities were recorded in PTSD patients (Table 2).

Table 2. Some pathophysiologic abnormalities in PTSD patients ($N = 32$)

PARAMETER	NORMAL (N)	BORDERLINE (N)	PATHOLOGIC (N)
Arterial blood pressure	24	6	2
Transcranial Doppler sonography	16	11	5
Coefficient of mental retardation	3	5	24
Serum cholesterol level	16	9	7
Serum triglyceride level	19	4	9
Serum glucose level	28	1	3

Comparison of some of these findings with those obtained in the control group of patients with psychoneurosis revealed a significantly higher prevalence in the PTSD group (Table 3). The mean mental deterioration was 17% in PTSD patients, and within the normal limits in all control group patients with psychoneurosis.

Table 3. Comparison of the groups of patients with PTSD ($N = 32$) and psychoneurosis ($N = 32$) according to systolic and diastolic blood pressure, and serum levels of cholesterol, triglycerides and glucose (mean \pm SD)

PARAMETER	PTSD	PSYCHONEUROSIS	t	P <
Blood pressure				
systolic (mmHg)	131.4 \pm 12.8	122.8 \pm 11.7	2.80	0.01
diastolic (mmHg)	89.2 \pm 11.1	79.5 \pm 8.7	3.90	0.01
Serum cholesterol	5.8 \pm 1.6	4.6 \pm 1.1	3.43	0.01
Serum triglycerides	2.9 \pm 3.2	1.4 \pm 0.6	2.63	0.05
Serum glucose	5.2 \pm 1.4	5.0 \pm 0.8	0.71	NS

There was no significant correlation between any of the observed biological abnormalities and either type or severity of PTSD symptoms. No correlation was found between the type of acute stress reaction and late symptoms of the disorder either. A significant correlation was observed between the severity of immediate physiologic and effective-cognitive stress reaction, and level of pooled symptom severity score of D category on the Los Angeles Scale (physiologic reaction/symptom D category: $X_1 = 1.6 \pm 0.7$, $X_2 = 3.1 \pm 0.5$, $r = 0,440$, $t = 2.684$, $P < 0.02$; affective-cognitive reaction/symptom D category: $X_1 = 2.0 \pm 0.7$, $X_2 = 3.1 \pm 0.5$, $r = 0,390$, $t = 2,320$, $P < 0.05$).

All possible permutations of the relationship between the severity of individual acute stress reaction symptoms and severity of individual D category symptoms on the Los Angeles Scale were tested and those yielding positive correlation were singled out (Table 4).

Table 4. Correlation of the severity of acute and late stress reaction D category symptoms on the Los Angeles Scale of symptoms (LASC-01) in the group of PTSD patients (N = 32)

STRESS REACTION mean score	LASC-01 SYMPTOM mean score	r	t	P <
Tremor 2.1±1.1	Agitation (D4) 3.4±1.4	0.36	2.11	0.05
Tremor 2.1±1.1	Panic attacks (D38) 2.4±1.4	0.43	2,61	0.02
Perspiration 2.3±1.0	Agitation (D4) 3.4±1.4	0.40	2.39	0.05
Perspiration 2.3±1.0	Extreme neurosis (D34) 2.4±1.2	0.35	2.05	0.05
Anxiety 2.2±1.0	Extreme neurosis (D34) 2.4±1.2	0.35	2.05	0.05
Fear from being killed 2.0±1.3	Concentration difficulties (D34) 3.0±1.1	0.43	2.61	0.02

DISCUSSION

The real nature of PTSD as an extended or delayed stress reaction of the entire body is masked by a concept according to which PTSD is a purely psychopathologic diagnostic category. This is supported by the results of numerous biological studies of extended stress reaction of the body (2-4,8,13,14). Neuroadrenergic dysfunction has a special role in the pathophysiology of chronic PTSD. It is considered responsible for recurrent intrusive recollections of the traumatic event, hypersensitivity for signs reminding of the trauma, as well as for continuous presence of the symptoms of psychic and physical arousal (15-18).

In our study, the pathophysiologic abnormalities were significantly more common in the group of PTSD patients than in those with psychoneurosis. The type of the pathophysiologic abnormalities recorded also pointed to a significant effect of noradrenergic dysfunction in their genesis (15,16,19).

In the group of PTSD patients, there was no significant correlation of any of the observed biological abnormalities with the type or severity of PTSD symptoms. There was no correlation of the type of acute stress reaction with the type or severity of PTSD symptoms either, but there was a significant correlation between the severity of acute physiologic and affective-cognitive stress reaction, and severity of D category symptoms on the Los Angeles Scale (insomnia, agitation, irritability, anxiety, concentration difficulties, strong neurosis, palpitations, and panic episodes). Interestingly enough, no correlation was found between the severity of acute stress reaction and severity of B and C category symptoms on the Los Angeles Scale. These two symptom categories (intrusive recollections and nightmares, emotional anesthesia, avoiding reminders, loss of interest, etc.) actually include the traumatic event re-experiencing and psychological defense against the trauma-induced arousal. Therefore, their severity depends on the person's psychological reflexiveness and his/her capacity for psychological reexperiencing rather than on the severity of acute stress reaction. Peritraumatic dissociation is discussed by van der Kolk and van der Hart (20), relying on Janet's concept of traumatic dissociation, whereas Shalev et al. (21) consider it to be of a predictive value for subsequent development of PTSD. Other authors also found a significant correlation between a tendency to dissociative reaction and occurrence of PTSD symptoms following a traumatic event (22-24). This correlation, though, refers only to some of the B and C category symptoms on the Los Angeles Scale. Thus, only the symptoms of arousal in PTSD (D category on LA Scale) would be a direct consequence of acute stress reaction, while other symptoms would rather be determined by the personality structure, i.e. type of the activated mechanisms of defense. As the diagnosis of PTSD cannot be made in the absence of the latter, it appears quite justified to pose the following question: what happens with those who have been exposed to stress but their psychological reflexiveness is significantly obliterated due to the personality structure, upbringing or training, and they do not meet all the criteria for the psychiatric diagnosis of PTSD? In his editorial that has appeared in the American Journal of Psychiatry in 1995 Nemiah (9) comments on his observation that psychologically stable individuals with normal development during their childhood and stable family situation, and who are additionally well trained and motivated for military service, may seem to be protected from the occurrence of PTSD upon exposure to stress, but virtually are at an increased risk of developing severe frequently lethal physical diseases. He points to the need of developing a psychosomatic model of arousal treatment in such persons, i.e. he suggests that in these persons, the stress-induced arousal is directly converted into physical dysfunction. Other authors also emphasize the psychosomatic model of the development of biological derangements and disorders in PTSD patients (10,25), thus the diagnostic and prognostic role of biological parameters of PTSD remains an open issue.

CONCLUSION

Somatic disturbances and various pathophysiologic disorders are significantly more common in patients with PTSD than in those with psychoneurosis. In PTSD, there is a positive correlation between the severity of the symptoms of psychic and vegetative arousal, and severity of acute stress reaction.

REFERENCES

1. Andreasen NC: *Posttraumatic stress disorder: psychology, biology, and the manichaeon warfare between false dichotomies (editorial)*. Am J Psychiatry 1995;152:963-5.
2. Resnick HS, Yehuda R, Pitman RK & Foy DW: *Effect of previous trauma on acute plasma cortisol level following rape*. Am J Psychiatry 1995;152:1675-7.
3. Reist C, Kauffmann CD, Chicz-Demet A, Chen CC & Demet EM: *REM latency, dexamethasone suppression test, and thyroid releasing hormone stimulation test of posttraumatic stress disorder*. Prog Neuropsychopharmacol Biol Psychiatry 1995;19:433-43.
4. Lemieux AM & Coe CL: *Abuse-related posttraumatic stress disorder: evidence for chronic neuroendocrine activation in women*. Psychosom Med 1995;57:105-15.
5. Yehuda R, Kahana B, Binder-Brynes K, Southwick SM, Mason JW & Giller EL: *Low urinary cortisol excretion in Holocaust survivors with posttraumatic stress disorder*. Am J Psychiatry 1995;152:982-6.
6. Yehuda R, Boisoneau D, Lowy MT & Giller EL Jr: *Dose-response changes in plasma cortisol and lymphocyte glucocorticoid receptors following dexamethasone administration in combat veterans with and without posttraumatic stress disorder*. Arch Gen Psychiatry 1995;52:583-93.
7. Holsboer F, Grasser A, Friess E & Wiedemann K: *Steroid effects on central neurons and implications for psychiatric and neurological disorders*. Ann NY Acad Sci 1994;746:345-61.
8. Van der Kolk BA & Fisler RE: *The biologic basis of posttraumatic stress (review)*. Prim Care 1993;20:417-32.
9. Nemiah JC: *A few intrusive thoughts on posttraumatic stress disorder (editorial)*. Am J Psychiatry 1995;152:501-3.
10. Nemiah JC: *Alexithymia and psychosomatic illness*. In: Flach F. ed. Stress and its management. New York: Norton, 1989.
11. Goldstein S & Halbreich U: *Hormones and stress*. In: Nemeroff CB, Loosen PT. eds. Handbook of clinical psychoneuroendocrinology. Chichester-New York-Brisbane-Toronto-Singapore: John Wiley and Sons, 1987:460-9.
12. Charney DS, Deutch AY, Krystal JH, Southwick SM & Davis M: *Psychobiologic mechanisms of posttraumatic stress disorder*. Arch Gen Psychiatry 1993;50:294-305.
13. Krystal JH, Kosten TR, Perry BD, Southwick SM., Mason JW & Giller EL Jr: *Neurobiological aspects of PTSD: review of clinical and preclinical studies*. Behav Ther 1989;20:177-98.
14. Bauer M, Priebe S, Kurten I, Graf KJ & Baumgartner A: *Psychological and endocrine abnormalities in refugees from East Germany: Part I. Prolonged stress psychopathology and hypothalamic-pituitary-thyroid axis activity*. Psychiatry Res 1994;51:61-73.
15. Pitman RK, Orr SP, Fogue DF, Dejong JB & Claiborn JM: *Psychophysiologic assessment of post-traumatic stress disorder in Vietnam combat veterans*. Arch Gen Psychiatry 1987;44:970-5.
16. Southwick SM, Krystal JH, Morgan CA & et al: *Abnormal noradrenergic function in posttraumatic stress disorder*. Arch Gen Psychiatry 1993;50:266-74.
17. Murburg MM, McFall ME, Lewis N & Veith RC: *Plasma norepinephrine kinetics in patients with posttraumatic stress disorder*. Biol Psychiatry 1995;38:819-25.
18. Mellman TA, Kumar A, Kulick-Bell R, Kumar M & Nolan B: *Nocturnal/daytime urine noradrenergic measures and sleep in combat-related PTSD*. Biol Psychiatry 1995;38:174-9.
19. Hayward C, Taylor CB, Roth WT, King R & Agras WS: *Plasma lipid levels in patients with panic disorders or agoraphobia*. Am J Psychiatry 1989;146:917-9.
20. Van der Kolk BA & van der Hart O: *Pierre Janet and the breakdown of adaptation in psychological trauma*. Am. J Psychiatry 1989;146:1530-40.
21. Shalev AY, Peri T, Canetti L & Schreiber S: *Predictors of PTSD in injured trauma survivors: a prospective study*. Am J Psychiatry 1996;153:219-25.
22. Carlson EB & Rosser-Hogan R: *Trauma experiences, posttraumatic stress, dissociation, and depression in Cambodian refugees*. Am J Psychiatry 1991;148:1548-51.
23. Bremner JD, Southwick S, Brett E, Fontana A, Rosenbeck R & Charney DS: *Dissociation and posttraumatic stress disorder in Vietnam combat veterans*. Am J Psychiatry 1992;149:328-32.

24. Koopman C, Classen C & Spiegel D: *Predictors of posttraumatic stress symptoms among survivors of the Oakland/Berkeley, Calif. firestorm*. Am J Psychiatry 1994;151:888-94.
25. Yehuda R, Resnick H, Kahana B & Giller EL: *Longlasting hormonal alterations to extreme stress in humans: normative or maladaptive?* Psychosom Med 1993;55:287-97.

Correspondence:

*Pavo Filaković, M.D., Ph.D., Department of Psychiatry, Osijek University Hospital,
Huttlerova 4, HR-31000 Osijek, Croatia*