

NEUROBIOLOGICAL AND CLINICAL CONSEQUENCES OF POST-TRAUMATIC STRESS DISORDER

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SUMMARY - Thirty-two male patients, mean age 34.1 ± 7.1 , Croatian soldiers from 1991-1992 war, suffering from post-traumatic stress disorder (PTSD) diagnosed on the basis of psychiatric examination and use of graduation scales DSM III and LASC-01, were included in the study. In order to identify possible organic disorders, the patients were submitted to neuropsychological testing, laboratory testing, hemodynamic testing of cerebral hemodynamics by the method of transcranial Doppler ultrasonography (TCD), and analysis of risk factors for cerebrovascular disease related to an unhealthy lifestyle. Neuropsychological examination showed mental deterioration which surpassed the allowable level in 21, impaired memory in 19, significant mnemonic control disorders in 30 and confabulation in 15 patients, while other tests pointed to an organic basis of the mental abnormalities observed (attention, visuomotor co-ordination). Laboratory analysis pointed to the following disturbances: elevated blood glucose in 3, cholesterol in 7 and triglycerides in 10 patients; decreased HDL in 10 and increased LDL in 6 patients; increased white blood cell count in 16 and increased erythrocyte sedimentation rate in 5 patients. TCD analysis revealed functional impairments of cerebral circulation in 16 patients, i.e. vasospasm in 11 and hypoperfusion in 5 patients. A significant presence of unhealthy lifestyle indicators was recorded, i.e. smoking in 30, alcoholism in 15, and physical inactivity and overweight in 10 patients each. Study results confirmed the correlation of mental and physical mechanisms in the occurrence of PTSD as well as the presence of organic indicators of the nervous system lesions, and psychosomatic and organic damage to other body systems. This small, uncontrolled pilot study suggested the need of a complex approach to patients with PTSD.

Key words: *Stress disorders, post-traumatic; Stress disorders, post-traumatic - physiopathology; Combat disorders*

Introduction

Reactions on severe stress and adaptability disorders are classified in the latest International Classification of Diseases under the code F 43, and post-traumatic stress disorder (PTSD) under the code F 43.1¹. According to literature data, chronic PTSD is followed by pathophysiological syndromes and biological alterations caused by adaptable reactions of brain structures, all of which can later bring

forth significant physical disorders^{2,3}. During the war in Croatia (1991 - 1992), a huge number of people were recorded as having PTSD, especially among soldiers, Croatian defenders. Thus, a study conducted in the Osijek surroundings revealed PTSD to be present in about 13% of soldiers who had taken part in most intensive war actions during 1991 - 1992⁴.

The aim of this multidisciplinary clinical study was to assess the presence of pathophysiological changes and somatic disorders in individuals with chronic PTSD. The specific goals of the neurological team included in the project were focused on the detection of disorders which would show the existing or future damage to the nervous system.

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Patients and Methods

A randomized sample of 32 patients, Croatian soldiers from the 1991 - 1992 war, with the diagnosis of PTSD according to the estimated DSM III grade (criteria A - traumatic experience; B - symptoms of repetition; C - symptoms of avoiding; and D - symptoms of excitement) and LASC-01 were included in the study⁵. All study subjects were male, mean age 34.1 ± 7.1 years. During hospitalization at the Department of Psychiatry in Osijek, study subjects underwent neuropsychological testing, laboratory testing, clinical examination, and testing of cerebral hemodynamics by transcranial Doppler ultrasonography (TCD).

Laboratory analysis of venous blood, performed at least 12 hours after the last meal, consisted of a series of hematologic and biochemical parameters, reported in the literature to be changeable during stress reaction. On neuropsychological examination, the following parameters were estimated: intelligence (general, verbal and non-verbal), signs of mental deterioration, memorizing, learning, remembering and recognition, attention, visuomotor co-ordination, and visuoconstructional abilities. The battery of neuropsychological instruments included: Wechsler-Bellevue intelligence scale (WB-II), Rey auditory verbal learning test (RAVLT), Bender-Gestalt test of visuomotor co-ordination and visuoceptive abilities, block design test (from Wechsler scale for assessment of visual-constructive abilities), and attention test (Djurić, Bele-Potočnik, Hruščevar, Ljubljana, 1985). TCD examination was performed with a 3-D TCD scanner (EME), with a probe of 2 MHz pulsating ultrasound. Blood flow velocities (BFV) in basal brain arteries of the Willis circle (middle, systolic and diastolic BFV), hemodynamic chart and sound phenomena were analyzed. The measured values were compared with normal values⁶. Data were collected on psychosomatic disorders and factors of unhealthy lifestyle from medical documentation and history. Results were analyzed by standard statistical methods, and are presented in figures and tables.

Results

Use of graduation scales DSM III and LASC-01 revealed a very high percentage (>70%) of characteristic symptoms, including the symptoms of repetition, avoiding and excitement as well as a high presence of disorders in general (Fig. 1). Neuropsychological examination showed an intellectual level within the average values (IQ = 104

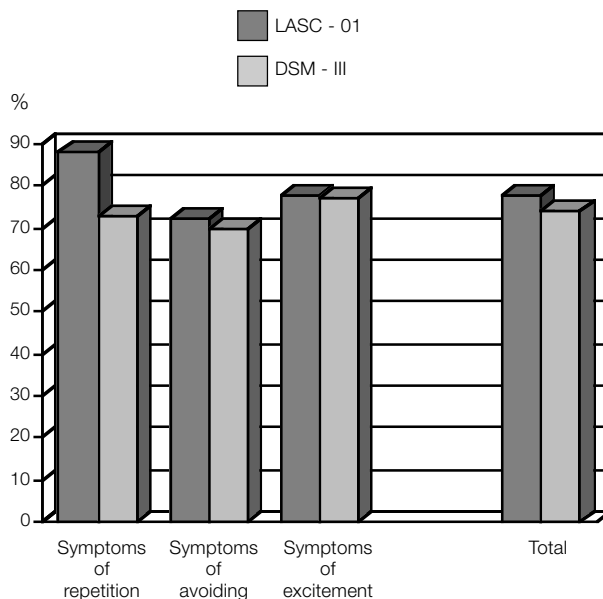


Fig. 1. Severity of symptoms in PTSD patients according to LASC-01 and DSM III scales.

± 13.4 , verbal IQ = 102.5 ± 12.6 , non-verbal IQ = 97.4 ± 14.3). In 21 subjects, mental deterioration was increased, yielding a mean value of 17.1% vs 10% of tolerated rate. On attention testing, the achievement rate was at 41st centile and corresponded to the lower average rate. Distractibility and faster losing attention were recorded in many subjects. The mean number of errors on visuomotor co-ordination testing was 6.4, which corresponded to marginal values and referred to incipient deficits. The visuoconstructional abilities were within the average limits. The abilities of memory and learning were within the average limits; the number of memorized words on the test of verbal auditive memorizing and learning was 45.8, which was worse than the expected values of 50-52 (Fig. 2). Verbal learning test showed lower immediate recalls, slower learning ability, and decrement in retention following exposure to an intervening word list. The ability of recognition showed no major fall (12.9 words in relation to 15 presented). Disorders of mnemonic control were found in 30, and confabulations in 15 subjects (Fig. 3).

TCD analysis of cerebral hemodynamics showed normal BFV in 16 (50%), mild acceleration of BFV in all blood vessels of the circle of Willis (vasospasm) in 11 (34.4%), and deceleration of BFV (hypoperfusion) in 5 (15.6%) subjects (Fig. 4). The most common TCD alterations of cerebral hemodynamics (vasospasm) found in the study subjects are presented in Fig. 5.

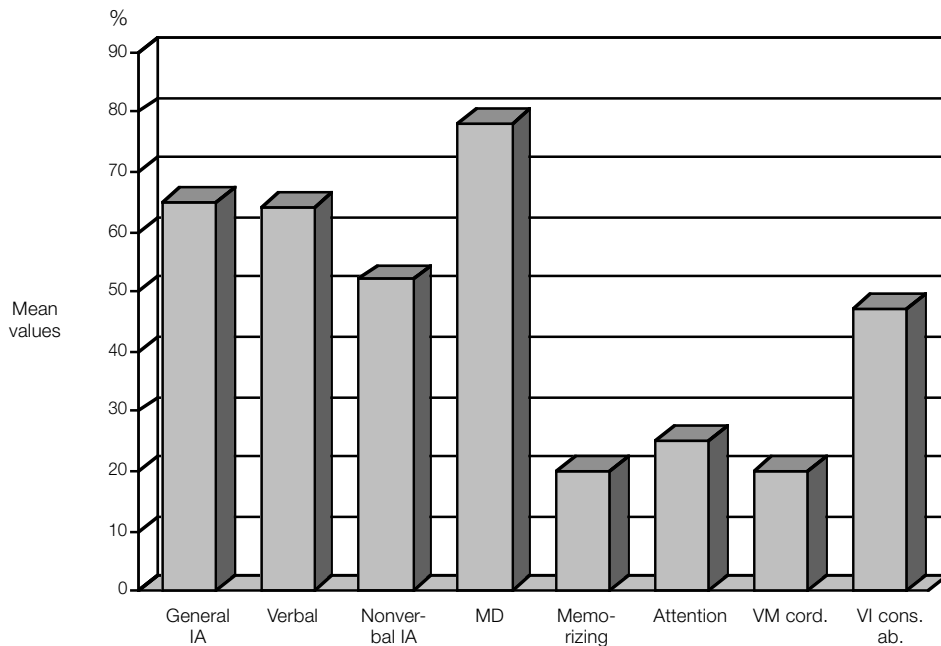
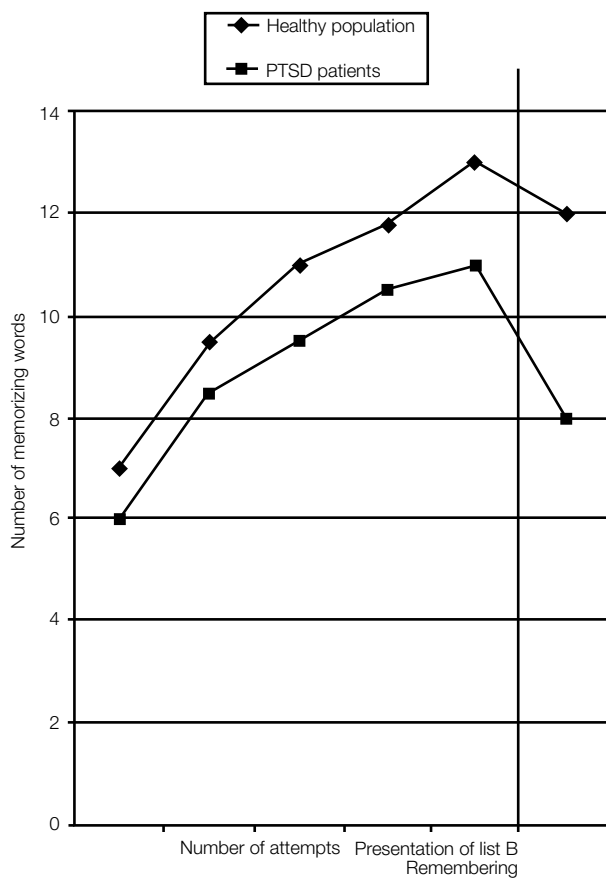


Fig. 2. Cognitive abilities in PTSD patients: intelligence (general, verbal, non-verbal), mental deterioration, memorizing, attention, visuomotor co-ordination, visuoconstructional abilities.



The following psychosomatic diseases were detected: duodenal ulcer in 2, gastritis in 2, diabetes mellitus in 3, and arterial hypertension in two patients.

Laboratory tests yielded the following findings: elevated blood glucose in 3, cholesterol in 7 and triglycerides in 10 patients; decreased HDL lipoprotein in 10, and increased LDL lipoprotein in 6 patients; increased white blood cell (WBC) count in 16, and increased erythrocyte sedimentation rate (ESR) in 5 patients (Table 1).

Table 1. Laboratory abnormalities in PTSD patients

Laboratory abnormality	n	%
Blood glucose increase	3	9.4
Increased cholesterol	7	21.9
Increased triglycerides	10	31.2
Decreased HDL	10	31.2
Increased LDL	6	18.7
Increased WBC	16	50.0
Increased ESR	5	15.6

Fig. 3. Results of verbal-auditive memorizing and learning testing in comparison with healthy population.

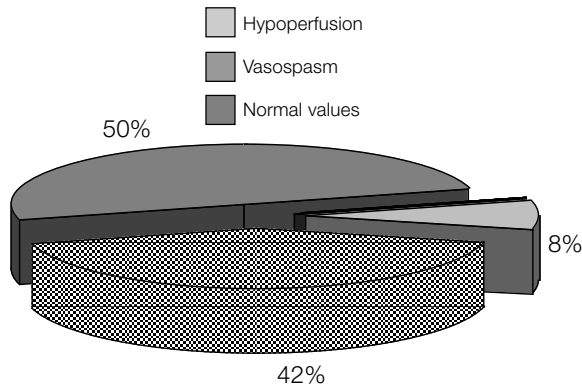


Fig. 4. Results of TCD examination according to type of TCD abnormalities.

Among unhealthy lifestyle indicators, smoking was recorded in as many as 30 (93.7%), alcoholism in 15 (46.9%), and physical inactivity and overweight in 10 (31.2%) study subjects each (Table 2).

Table 2. Unhealthy lifestyle indicators in PTSD patients

Indicator	n	%
Smoking	30	93.7
Alcoholism	15	46.9
Physical inactivity	10	31.2
Overweight	10	31.2

Discussion

Study results showed a high proportion of neuropsychological alterations. The intensity and quality of neuropsychological alterations found in this study as well as the very quality of test profiles constituted the suspected organic basis of impairment, especially those of brain structures, which take part in the function of memorizing. Traumatic events which cause PTSD do not only produce psychological effects but also induce an enormously elevated activity

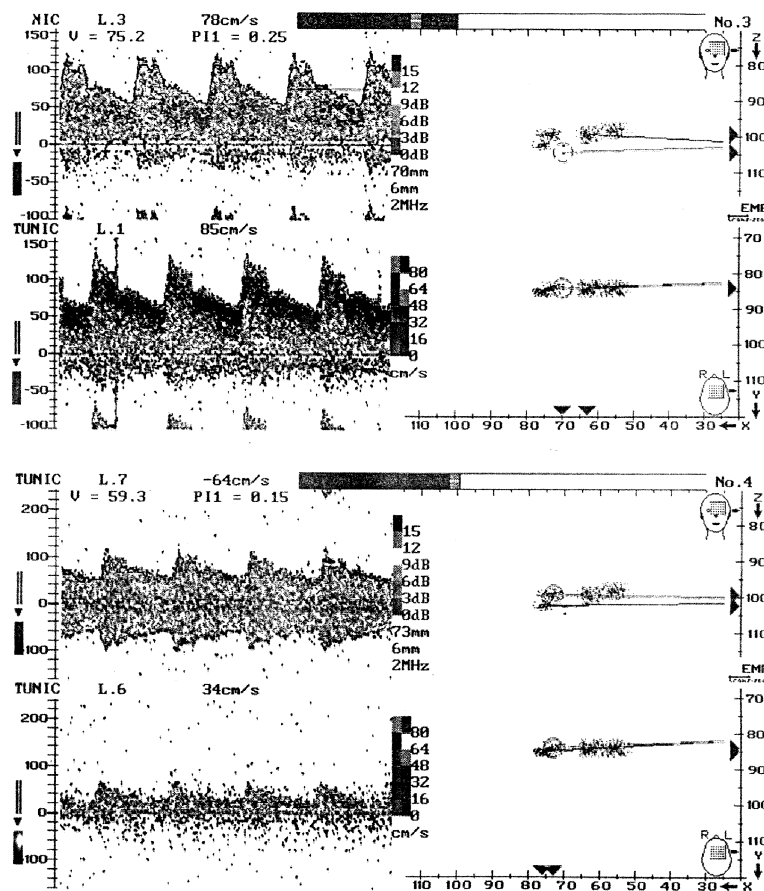


Fig. 5. Most common TCD alterations of cerebral hemodynamics (vasospasm) recorded in study patients.

of the autonomic nervous system with all consequential pathophysiological alterations. Biological alterations in the noradrenergic and serotonergic function, hypothalamo-hypophyseal-adrenaline axis, and endogenous opiate system gradually lead to organic disorders^{7,8}.

Due to the autonomic innervation of cerebral blood vessels, the effect of catecholamine and predominance of the sympathetic system can lead to acceleration of the blood circulation, usually in all blood vessels of the circle of Willis, as the result of vasospasm. Similar TCD changes have been described in smokers, and are explained by direct nicotine effects upon receptors in the central nervous system (CNS) and increased release of catecholamine, followed by elevated blood pressure and heart rate⁹. TCD changes as evaluated according to the type of mild vasospasm, found in PTSD patients, could probably be explained by these mechanisms.

The increased strain of the vegetative and endocrine system, and later of the cardiocirculatory and immune system is followed by various alterations of laboratory parameters. Glucose intolerance, increased blood lipids, changes of blood coagulability, increased ESR and WBC, and other abnormalities have been described in the literature and practically confirmed in this study. The psychosomatic alterations (duodenal ulcer, gastritis, diabetes mellitus and essential arterial hypertension) confirm the connection of affective, behavioral and physiological mechanisms, and the complexity of the biopsychosocial human nature⁵.

A significant role of unhealthy lifestyle shows that PTSD patients can additionally contribute to the increased development of organic diseases by their behavior. Chronic smoking habit, escape from reality by uncontrolled alcohol consumption, and physical inactivity with resulting adiposity lead to metabolic disorders and accelerate the development of multifactorial diseases, especially atherosclerosis and degenerative diseases^{3,5}. Because of the complexity of all these indicators and mechanisms, the approach to a PTSD patient should be multidisciplinary, including 'organic' specialists beside the psychiatrist in order to make a comprehensive assessment of the disorder.

Conclusion

In this small, uncontrolled study, various pathophysiological alterations were found in patients with PTSD: abnormalities of laboratory parameters, neuropsychological alterations, and changed results of functional diagnostic examinations. In PTSD patients, a rather high contribution of unhealthy lifestyle was recorded, including smoking, alcoholism, and physical inactivity and overweight, which can have unfavorable consequences and contribute to the development of vascular, degenerative and other somatic diseases. On the basis of the facts established in this pilot study, we consider that PTSD patients require a multidisciplinary approach which will include a follow-up of due quality and duration.

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Sažetak

NEUROBIOLOŠKE I KLINIČKE POSLJEDICE POSTTRAUMATSKOG STRESNOG POREMEĆAJA

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Studijom su bila obuhvaćena 32 bolesnika, hrvatski branitelji iz Domovinskog rata 1991./1992., s dijagnozom posttraumatskog stresnog poremećaja (PTSP) postavljenom psihijatrijskim pregledom i primjenom ocjenskih ljestvica DSM III. i LASC-01. Svu su ispitanici bili muškog spola, srednje dobi $34,1 \pm 7.1$ godina. Radi otkrivanja mogućih organskih poremećaja ispitanici su podvrgnuti neuropsihologijskim i laboratorijskim pretragama, hemodinamskom ispitivanju moždanog krvotoka metodom transkranijске doplerske sonografije (TCD) te analizi čimbenika rizika za cerebrovaskularnu bolest, koji se odnose na nezdrav način života. Neuropsihologijskim ispitivanjem nađena je mentalna deterioracija koja je prelazila dozvoljenu razinu u čak 21 bolesnika, oštećenje pamćenja u 19, značajne smetnje mnestičke kontrole u 30 te sklonost konfabuliranju u 15 bolesnika. Ostale su pretrage ukazivale na organsku podlogu zabilježenih mentalnih abnormalnosti (pozornost, vizuomotorna koordinacija). Laboratorijske pretrage ukazale su na sljedeće poremećaje: povišenu glukozu u krvi u 3, povišen kolesterol u 7, povišene trigliceride u 10, snižen HDL u 10, povišen LDL u 6, povišene leukocite u 16 i povišenu sedimentaciju eritrocita u 5 bolesnika. Analiza TCD pokazala je funkcionalne promjene moždane cirkulacije u 16 bolesnika (vazospazam u 11, a hipoperfuziju u 5 bolesnika). Zabilježen je značajan udjel pokazatelja nezdravog načina života: pušenje u 30, prekomjerne uporabe alkohola u 15, smanjene tjelesne aktivnosti u 10 te prekomjerne tjelesne težine u 10 bolesnika. Ispitivanje je potvrdilo povezanost psihičkih i tjelesnih mehanizama u nastanku sindroma PTSP-a, ali i prisutnost organskih pokazatelja oštećenja živčanog sustava te psihosomatskih i organskih oštećenja drugih tjelesnih sustava. Ova mala, nekontrolirana pokusna studija ukazala je na potrebu stalnog praćenja navedenih parametara, kao i multidisciplinarnog pristupa bolesniku s PTSP-om.

Ključne riječi: Stresni poremećaji, posttraumatski; Stresni poremećaji, posttraumatski – fiziopatologija; Ratni poremećaji