



International Journal of Clinical and Health Psychology

www.elsevier.es/ijchp



ORIGINAL ARTICLE

Comorbidities with Posttraumatic Stress Disorder (PTSD) among combat veterans: 15 years postwar analysis



Dolores Britvić^a, Vesna Antičević^a, Mariano Kaliterna^{a,*}, Linda Lušić^a, Ardelko Beg^a, Igna Brajević-Gizdić^a, Mirjana Kudrić^b, Željana Stupalo^b, Vikica Krolo^b, Nela Pivac^c

^a University of Split Hospital and School of Medicine, Croatia

^b Private Family Practice, Croatia

^c Rudjer Boskovic Institute, Croatia

Received 7 August 2014; accepted 18 November 2014

Available online 25 December 2014

KEYWORDS

PTSD;
Combat;
Veterans;
Survey descriptive
study

Abstract The aim of this study was to investigate the differences in the prevalence of somatic diseases among combat veterans and their contemporaries who were not exposed to the traumatic experience at the battlefield, and to determine whether socio-demographic factors, exposure to war-time trauma and/or injury might predict individual somatic diseases. The study included 1,558 subjects living in south Croatia: 501 male combat veterans with Posttraumatic Stress Disorder (PTSD) and the corresponding control group of 825 men who were not exposed to combat experience. Veterans with PTSD, regardless of the length of time spent in war, suffered more often from cardiovascular, dermatological, musculoskeletal, pulmonary and metabolic diseases than corresponding control subjects who were not exposed to combat experience. The predictors of cardiovascular, musculoskeletal and malignant diseases in veterans were age, length of time spent in combat, having been wounded. A longer period in the combat zone was associated with arrhythmias in veterans with PTSD complicated with other psychiatric comorbidities. PTSD as a result of exposure to war trauma increases the possibility of developing somatic diseases.

© 2014 Asociación Española de Psicología Conductual. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

* Corresponding author at: University Hospital Split, Šoltanska 1, 21000 Split, Croatia.
E-mail address: mariano.kaliterna@gmail.com (M. Kaliterna).

PALABRAS CLAVE

TEPT;
 Combate;
 Veteranos;
 Estudio descriptivo
 mediante encuestas

Comorbilidades con el Trastorno de Estrés Postraumático (TEPT) entre veteranos de guerra: un análisis a los 15 años después de la guerra

Resumen El propósito de este estudio ha sido comparar la frecuencia de trastornos somáticos en veteranos de guerra y personas no expuestas a la experiencia traumática del campo de batalla, así como determinar si la exposición a factores socio-demográficos en tiempo de guerra pueden predisponer a traumas, alteraciones o trastornos somáticos. El estudio incluye 1,558 sujetos del sur de Croacia: 501 varones veteranos de guerra con síndrome de estrés postraumático (TEPT) y un grupo de control de 825 varones no expuestos a la experiencia de combate. Los veteranos con TEPT, independientemente del tiempo pasado en la guerra, desarrollan más a menudo alteraciones gastrointestinales, cardiovasculares, dermatológicas, locomotoras, pulmonares y metabólicas que los sujetos del grupo control. Los indicadores de alteraciones cardiológicas, locomotoras, entre otros, en veteranos han sido la edad, el tiempo pasado en combate y el daño allí sufrido. Un largo período en la zona de combate ha sido asociado con arritmias y otras complicaciones de tipo psiquiátrico. El TEPT, como resultado de la exposición a experiencias traumáticas del campo de batalla, incrementa la posibilidad de desarrollo de trastornos somáticos.

© 2014 Asociación Española de Psicología Conductual. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Numerous studies with divergent results have examined the connection between physical and mental health, and the impact of stress and traumatic events on the hypothalamic-pituitary-adrenal (HPA) axis, with the consequent metabolic disorders and impairments of cortisol secretion and lipid status (Ginzburg & Solomon, 2011), or physical health in combat veterans with PTSD (O'Toole & Catts, 2008; Vasterling et al., 2008). These contradictory results support the complexity of this relationship, in addition to the important influences of genetic vulnerability, the HPA axis changes, smoking and substance abuse (Qureshi, Pyne, Magruder, Schultz, & Kunik, 2009; Zen, Whooley, Zhao, & Cohen, 2012). Some studies reported a higher incidence of arthritis, pulmonary disease (O'Toole & Catts, 2008), dermatological disorders (eczema), back and other musculoskeletal disorders, genitourinary disorders in the general population with PTSD (Glaesmer, Brähler, Gündel, & Riedel-Heller, 2011) and veterans (O'Toole & Catts, 2008), while others showed a significant association between PTSD and diabetes (Boyko et al., 2010), psoriasis, thyroid disease (Boscarino, 2004), cardiovascular diseases (Coughlin, 2011; Edmundson & Cohen, 2013) and ulcers (Fink, 2011). The fact that over 50% of veterans with PTSD also have another psychiatric diagnosis (Ginzburg, Ein-Dor, & Solomon, 2010) raises the question of the impact of psychiatric comorbidity on the occurrence of physical illnesses. We are not aware of any previous studies investigating the differences in the prevalence of somatic disorders among veterans with PTSD, with or without comorbid diagnoses. Given the large numbers of veterans with PTSD in Croatia in the aftermath of the 1991-1995 war, who undoubtedly represent a significant public health problem, there is a need to study their physical health.

The aim of this study was to investigate the differences in the prevalence of somatic diseases among combat veterans and their contemporaries who were not exposed to the traumatic experience in the battlefield, and to determine whether socio-demographic factors (education, marital

status, employment status), the effects of combat exposure to wartime trauma, and/or injury might be used as predictors of development of somatic diseases. The hypothesis was that veterans will have higher prevalence of somatic disorders compared to the general population matched for age and sex, and that those injuries and traumatic experiences will significantly influence the occurrence of somatic illnesses in veterans. Another aim was to elucidate a prevalence of somatic diseases among veterans with PTSD and psychiatric comorbidities, compared to subjects without comorbid diagnoses.

Method

Participants and instruments

This case control study included 1,558 subjects living in central Dalmatia in the region of Split-Dalmatia County. The test group consists of male combat veterans, 36 to 65 years of age, diagnosed with PTSD resulting from the combat experience after the Homeland war in Croatia, who were in outpatient treatment. The group was formed from a sample of all combat veterans who were diagnosed and/or treated at the Regional Center for Psychotrauma, Split Clinical Hospital Center, from May 2010 to May 2011. A total of 1,023 veterans were examined, of whom 759 were diagnosed with PTSD and 501 agreed to participate in the study. The remaining 258 were excluded from the study due to various reasons; 108 of them did not accepted to participate in the study, with the other 150 questionnaires were not properly filled, (49 of them Mississippi scale was not properly filled, and in 101 the data were insufficient). The diagnosis of PTSD was established according to the diagnostic criteria for PTSD based on the ICD-10 criteria (World Health Organization, 1992), but also with a Structured Clinical Interview (SCID) for DSM-IV (First, Spitzer, Gibbon, & Williams, 2000). All

participants were assessed systematically. Particular symptoms were evaluated using the self-report questionnaire of the Mississippi Scale for Combat Related Posttraumatic Stress Disorder (M-PTSD) (Keane, Cadell, & Taylor, 1988). PTSD assessed based on combat/military traumas only. This questionnaire is a 35-item self-report measure that assesses combat-related PTSD in veteran populations. This measure has demonstrated good test-retest reliability ($r = .97$, 1-week interval), internal consistency ($\alpha = .94$) and diagnostic accuracy (90% diagnostic efficiency) in a sample of Vietnam combat veterans (Kulka et al., 1991). Selected symptoms were collected and diagnoses established by three psychiatrists and two psychologists with an extensive experience in war related psychopathologies who were working with veterans with PTSD. Comorbid diagnoses were established using the ICD-10 and SCID according to DSM-IV.

The average age of the participants was 47.5 ± 6.6 years. Most of them ($n = 384$) had a secondary school education (10–12 years of school). The majority ($n = 384$) were married, 78 were single, 37 were divorced and two were widowed. The largest number ($n = 358$) were retired, while 63 of them were unemployed and 80 veterans were employed. Most of the participants ($n = 202$) had spent more than three years on the battlefield, 104 between 2 and 3 years and 130 between 1 and 2 years. Of the total number, 47 had been wounded.

Control group. The total patient populations of three family medical practices in three different cities were examined, which included persons from urban, rural and island milieus, which were not exposed to war activities. There were a total of 5,000 subjects, of whom 2,389 were men and 825 met the criteria for participation in the study. The inclusion criteria were male gender between 36 and 65 years of age. The exclusion criteria were the existence of psychological problems or psychiatric treatment (all codes from F-01 to F-09, according to the ICD-10) and combat duty in the Homeland war. From all patient population, 913 were younger than 35 or older than 65 years, 561 subjects were involved in acts of war. From the subjects examined, 204 showed psychological problems, of which 114 as a result of participation in the war. Assessment of physical diseases was conducted by systematic examination of the medical records, medical examination by three experienced family physicians who received equivalent training, but unfortunately without rater-interrater reliability. Assessment of psychiatric disorders in the control group was conducted by a family physician, who found no criterion for the diagnosis of disorders of the F 00-F 99 ICD-10. In addition, inspection in the whole life medical records for each of the control respondents did not reveal presence of any psychiatric disorders. Average age of the control group was 46.9 ± 7.9 years. Out of 825 included control subjects, most of the participants ($n = 607$) had a secondary school education (10–12 years of school). The majority ($n = 643$) were married, 157 were single and 25 were divorced or widowed. The largest number were employed ($n = 591$), 148 were retired with pensions and 86 were unemployed.

Procedure and data analysis

Data were collected by three psychiatrists, two psychologists and four family physicians using a questionnaire

especially designed for this purpose. The questionnaire collected data on socio-demographic status (marital status, education, employment status, presence/absence at war and for the group of veterans the length combat duty and wounds). The data on physical illness were divided into gastrointestinal, cardiovascular, dermatological, neurological, metabolic, pulmonary, musculoskeletal systems, tumors, and other disease groups. Information on diseases was obtained from interviews with the subjects, medical examination and inspection of their medical records.

The resulting data described the sociodemographic data, data on the diseases in both groups (veterans and the general population) and differences in diseases, the length of combat duty during the war and wounds incurred, which represented predictors of individual physical illnesses. In the second analysis, the frequencies of physical illnesses in veterans with and without psychiatric comorbidity were compared.

Univariate logistic regression was performed in order to determine the odds ratio for a specific diagnosis in cases and controls. For this purpose, all the variables of a specific diagnose (including Diseases of the Gastrointestinal Tract, Cardiological Diseases, Dermatological Diseases, Diseases of the Locomotor Apparatus, Neurological Diseases, Metabolic Diseases, Pulmonary Diseases, Malignant Diseases and Other) were recoded into variables with two levels (YES= is diagnosed with the specific disease; NO= is not diagnosed with the specific disease). All the binary logistic regression analysis were performed with the inclusion of recoded variables in the model. The adjusted odds ratios were calculated after the inclusion of the following possible confounding factors in the multiple binary logistic regression model: age, education, marital status and employment status. Along with the adjusted odds ratios for a specific disease, Chi squares and a p value of a specific model including the possible confounding factors were reported. The variables were evaluated descriptively (presented as means and standard deviation), and analyzed using binary logistic regression. For a subsequent comparison between the groups, the Student's t -test and χ^2 test were used. The software program SPSS 12.0 for Windows (Chicago, IL: SPSS Inc., 2003) was used for data analysis, with the significance level set at .05.

The study was approved by the Ethics Committee of the University of Split Hospital Center. All the subjects were familiarized with the study and gave their written informed consent.

Results

Differences in the sociodemographic factors

There was no significant difference in age of the veterans and control group ($t = 1.36$ $p = .174$). However, significant difference was detected in marital status ($\chi^2 (2) = 16.77$; $p = .0005$) and employment status ($\chi^2 (2) = 426.13$; $p = .0005$). In the control group, there was a marginally higher number of unmarried men and a lower number of divorced men and widowers. Regarding employment status, the veterans were more frequently retired and subjects in the control group were more frequently employed (Table 1).

Table 1 Differences in the sociodemographic factors between veterans with PTSD and the control group.

	PTSD <i>n</i> =501	%	Control <i>n</i> =825	%	χ^2	<i>p</i>
<i>Education</i>						
Uneducated	5	1	5	0.6	2.556	.465
Elementary school	58	11.6	111	13.5		
Secondary school	384	76.6	607	73.6		
Associate/bachelor's degree	54	10.8	102	12.4		
<i>Marital Status</i>						
Married	384	76.6	643	77.9	16.771	<.0005
Unmarried	78	15.6	157	19		
Divorced/widowed	39	7.8	25	3		
<i>Employment Status</i>						
Employed	80	16	591	71.6	426.131	<.0005
Unemployed	63	12.6	86	10.4		
Pensioners	358	71.5	148	17.9		

Differences in physical morbidities between the veterans with PTSD and control group

The difference in the overall prevalence of physical illnesses between these two groups was significant (χ^2 (1)=8.67; $p=.003$) in the morbidity from gastrointestinal, cardiac, dermatological, musculoskeletal, respiratory and metabolic diseases (Table 2). With the exception of gastrointestinal illnesses, all other somatic diseases were more prevalent among the combat veterans suffering from PTSD compared to control group. In the group of subjects with gastrointestinal illnesses, ulcer disease was more common in the general population, while gastritis and ulcerative colitis were more prevalent among the combat veterans (Table 2). Although total cardiovascular diseases were significantly more common among the combat veterans, arterial hypertension was more common in the control group, while myocardial infarction, arrhythmia and other illnesses were more common in the group of combat veterans. Out of dermatological diseases, psoriasis was more common in the control population, but allergies, alopecia and other diseases were more frequent in the group of veterans (χ^2 (4)=51.14; $p=.001$). All diseases of the musculoskeletal system were more frequent in combat veterans (χ^2 (4)=104.69; $p<.001$), which include spinal disorders, arthritis and rheumatoid arthritis, compared to control subjects. All neurological diseases were more common in the group of combat veterans (χ^2 (4)=66.36; $p=.001$), with the most common consisting of headache, epilepsy and cerebrovascular insult(s). Metabolic diseases were more common in combat veterans (χ^2 (2)=24.432; $p<.001$), such as diabetes mellitus and thyroid disease, than in control subjects. There were no differences in the frequencies of malignant and other diseases between these two groups (Table 2). All stated differences are statistically significant also when the influence on length of time spent in combat is controlled, and it means that differences in more often physical illnesses in veterans are mainly results of PTSD rather than duration of trauma exposure (Table 3).

The results of the binary logistic regression confirmed that the patients with PTSD were statistically significantly

more likely to be diagnosed with cardiological, dermatological, neurological, metabolic diseases and diseases of the locomotor apparatus (Table 4). When adjusted for possible confounding factors among the cases and controls, including age, education, marital status and employment status, the adjusted odds ratios were still statistically significant in all variables that proved significant in the univariate regression model. After the adjustment, PTSD patients were almost 4 times more likely to be diagnosed with neurological diseases (odds ratio 3.856; 2.381-6.246; $p<.001$), and two times more likely to be diagnosed with diseases of the locomotor apparatus (odds ratio 2.141; 1.602-2.862; $p<.001$) and dermatological diseases (odds ratio 2.021; 1.185-3.445; $p=.010$). Odds ratio for metabolic (odds ratio 1.779; 1.089-2.907; $p=.021$) and cardiological diseases (odds ratio 1.423; 1.016-1.993; $p=.040$) were somewhat smaller, but still statistically significant after the adjustment.

Sociodemographic indicators as predictors of the incidence of physical illnesses in veterans and the control group

In the group of veterans suffering from PTSD, the predictors of the incidence of physical illness were age ($B=-0.067$, $p=.005$), the length of time spent on the battlefield ($B=0.182$, $p=.063$), and whether they were wounded. Higher age was significant predictor of cardiovascular ($B=-0.071$, $p<.005$), musculoskeletal ($B=-0.047$, $p=.002$) metabolic ($B=-0.078$, $p=.001$) and malignant ($B=-0.231$, $p=.003$) diseases. Secondary or higher education was a predictor of gastrointestinal diseases ($B=0.701$, $p=.035$) (Table 4). A predictor of cardiovascular ($B=0.221$, $p=.026$), musculoskeletal ($B=0.254$, $p=.004$), neurological ($B=0.264$, $p=.018$) and pulmonary ($B=-0.475$, $p=.013$) diseases was the length of time spent on musculoskeletal ($B=-0.582$, $p=.073$) and malignant ($B=-1.972$, $p=.038$) diseases.

In the control group, age was a predictor of the occurrence of total physical diseases ($B=-0.068$, $p<.005$) but also gastrointestinal ($B=-0.034$, $p=.012$), cardiovascular ($B=-0.113$, $p<.005$) and malignant ($B=-0.088$, $p=.019$) diseases,

Table 2 Differences in morbidity from physical diseases between veterans with PTSD and the control group.

	PTSD		CONTROL		χ^2	<i>p</i>
	<i>n</i> = 501	%	<i>n</i> = 825	%		
<i>Physical illnesses</i>						
Yes	345	69	502	61	8.675	.003
No	156	32	323	40		
<i>Diseases of the Gastrointestinal Tract</i>						
No	396	79	672	82	168.413	<.001
Ulcer	27	6	153	19		
Gastritis	58	12	0	0		
Ulcerative Colitis	3	1	0	0		
Other	17	4	0	0		
<i>Cardiological Diseases</i>						
No	362	73	657	80	80.241	<.001
Arterial hypertension	92	19	168	21		
Myocardial Infarction	11	3	0	0		
Arrhythmia	27	6	0	0		
Other	9	2	0	0		
<i>Dermatological Diseases</i>						
No	451	90	782	95	56.14	<.001
Psoriasis	20	4	43	6		
Alopecia	4	1	0	0		
Allergies	12	3	0	0		
Other	14	3	0	0		
<i>Diseases of the Locomotor Apparatus</i>						
No	266	53	584	71	104.698	<.001
Diseases of the Spine	184	37	241	30		
Diseases of the Joints	40	8	0	0		
Rheumatoid Arthritis	7	2	0	0		
Other	4	1	0	0		
<i>Neurological Diseases</i>						
No	410	82	785	96	66.365	<.001
Headaches	81	17	40	5		
Epilepsy	3	1	0	0		
Cerebrovascular Insult	2	1	0	0		
Other	5	1	0	0		
<i>Metabolic Diseases</i>						
No	444	89	775	94	24.432	<.001
Diabetes Mellitus	45	9	50	6		
Diseases of the Thyroid	12	3	0	0		
<i>Pulmonary Diseases</i>						
No	474	93	782	95	20.969	<.001
Bronchitis	16	4	43	6		
Asthma	2	1	0	0		
Other	9	2	0	0		
<i>Malignant Diseases</i>						
Yes	8	2	21	3	1.311	.333
No	493	99	804	98		
<i>Other</i>						
Yes	79	16	104	13	2.62	.119
No	422	85	721	88		

Table 3 Predictors of morbidity from physical diseases in the combat veterans with PTSD.

	Age	Education				Marriatal status			Employment status		
		Uneducated	Elementary school	Secondary school	Associate /bacc. degree	Married	Unmarried	Divorced /widowed	Employed	Unemployed	Pensioners
Physical illnesses	B	-0.067	1.449	0.355	0.048		0.411	0.4		0.002	0.186
	<i>p</i>	<.001 .384	.153	.419	.891	.609	.321	.391	.838	.995	.558
Diseases of the Gastrointestinal Tract	B	-0.02	20.442	1.048	0.701		-0.043	-0.229		0.429	-0.11
	<i>p</i>	.266 .116	.999	.027	.035	.817	.922	.647	.393	.21	.748
Cardiological Diseases	B	-0.071	-0.829	-0.148	-0.037		-0.167	-0.188		-0.097	-0.22
	<i>p</i>	<.001 .873	.449	.735	.917	.922	.7	.702	.777	.736	.497
Dermatological Diseases	B	-0.028	-18.417	-0.649	-0.394		-0.385	-0.867		-0.199	0.682
	<i>p</i>	.228 .806	.999	.324	.485	.362	.614	.285	.368	.608	.228
Diseases of the Locomotor Apparatus	B	-0.047	1.313	0.013	-0.015		-0.163	-0.138		-0.298	0.287
	<i>p</i>	.002 .724	.267	.973	.961	.904	.655	.743	.261	.258	.334
Neurological Diseases	B	-0.027	19.559	0.334	-0.169		-0.675	0.115		-0.127	2.185
	<i>p</i>	.142 .666	.999	.53	.667	.082	.226	.862	.79	.689	.639
Metabolic Diseases	B	-0.078	18.955	-0.383	-0.279		0.22	0.09		0.501	-0.009
	<i>p</i>	.001 .932	.999	.523	.567	.888	.682	.885	.523	.264	.984
Pulmonary Diseases	B	-0.041	18.235	0.589	-0.167		0.24	-0.024		0.876	-0.767
	<i>p</i>	.178 .807	.999	.54	.804	.856	.729	.976	.1	.257	.114
Malignant Diseases	B	-0.231	16.826	0.316	0.194		0.098	-0.605		-0.605	-0.681
	<i>p</i>	.003 .996	.999	.815	.842	.847	.942	.712	.713	.525	0.497
Others	B	-0.023	-0.413	-0.785	-0.355		0.904	0.599		0.388	0.23
	<i>p</i>	.25 .509	.735	.145	.432	.074	.027	.215	.56	.324	0.562

Table 4 Odds ratio for specific diseases in PTSD patients compared to controls in univariate and multiple logistic regression models.

	Univariate		Adjusted		Logistic regression model*	
	OR	95% CI	OR	95% CI	χ^2 (df)	p
Diseases of the Gastrointestinal Tract	1.165	0.882-1.537	0.950	0.674-1.337	484.78 (9)	<.001
Cardiological Diseases	1.502	1.159-1.945	1.423	1.016-1.993	488.92 (9)	<.001
Dermatological Diseases	2.016	1.320-3.080	2.021	1.185-3.445	491.45 (9)	<.001
Diseases of the Locomotor Apparatus	2.141	1.699-2.697	2.141	1.602-2.862	511.48 (9)	<.001
Neurological Diseases	4.356	2.948-6.437	3.856	2.381-6.246	517.29 (9)	<.001
Metabolic Diseases	1.990	1.337-2.960	1.779	1.089-2.907	490.05 (9)	<.001
Pulmonary Diseases	1.036	0.632-1.699	0.969	0.534-1.760	484.70 (9)	<.001
Malignant Diseases	0.621	0.273-1.413	0.478	0.187-1.223	487.15 (9)	<.001
Other	1.298	0.946-1.781	1.006	0.680-1.489	484.69 (9)	<.001

Note. *Including the specific diagnosis and confounding variables age, education, marital status and employment status. CI = 95% confidence intervals; OR = odds ratio for negative change; Univariate = univariate binary logistic regression; Adjusted = adjusted or multivariate binary logistic regression controlling for age, education, marital status and employment status.

as well as the prediction limit for musculoskeletal diseases ($B = -0.022$, $p = .057$). Higher education was a predictor of musculoskeletal diseases and cancer, while being single was a predictor of gastrointestinal diseases. Being employed was a predictor of general physical diseases, particularly regarding dermatological (psoriasis) and neurological (headache) diseases (Table 5).

Psychiatric comorbidity in combat veterans with PTSD

All veterans examined were PTSD diagnosed. Psychiatric comorbidity was present in 62% of the subjects, most commonly Enduring Personality Change After Catastrophic Experience (EPCACE) (F62.0), detected in over half of the subjects, followed by depressive disorder in 38%, and less frequently, anxiety depressive disorder and addictions.

Differences in the sociodemographic indices and physical illnesses in combat veterans, with and without psychiatric comorbidity

Sociodemographic data were similar between the two groups. However, veterans with psychiatric comorbidities spent a significantly longer period of time on the battlefield than veterans without comorbidities ($\chi^2 (3) = 12.44$; $p = .006$). Significantly more frequent cardiovascular diseases (hypertension and myocardial infarction) occurred in veterans without comorbidities ($\chi^2 (4) = 14.49$; $p = .006$), while arrhythmias were somewhat more frequent in veterans with comorbidities (Table 6). There were no significant differences in the incidence of other diseases between veterans with or without psychiatric comorbidities.

As presented in Table 7, PTSD patients with psychiatric comorbidity were statistically significantly less likely to be diagnosed with cardiological (odds ratio 0.537; 0.361-0.800; $p = .002$) and dermatological (odds ratio 0.487; 0.270-0.877; $p = .016$) diseases, in comparison with PTSD patients without psychiatric comorbidity, even after the adjustment for confounding sociodemographic variables (Table 7).

Discussion

The results of this case-control study indicate that combat veterans suffer more often from physical comorbidities, i.e., cardiovascular, dermatological, musculoskeletal, pulmonary and metabolic diseases, than the corresponding control group who was not exposed to combat traumatic experiences in the battlefield. These differences remain even after controlling the possible impact of sociodemographic characteristics. PTSD patients were almost 4 times more likely to be diagnosed with neurological diseases, two times more likely to be diagnosed with diseases of the locomotor apparatus and dermatological diseases, odds ratio for metabolic and cardiological diseases were somewhat smaller, but still statistically significant after the adjustment.

The predictors of illnesses were age, length of time spent on the battlefield for veterans with cardiovascular, musculoskeletal, neurological and pulmonary diseases, and having been wounded for the occurrence of cardiovascular, mus-

Table 5 Predictors of morbidity from physical diseases in the control group.

		Age		Education			Marriatal status			Employment status		
		Uneducated	Elementary school	Secondary school	Associate /bacc. degree	Married	Unmarried	Divorced /widowed	Employed	Unemployed	Pensioners	
Physical illnesses	B	-0.068		-0.783	-0.212	-0.298		-0.184	-0.349		0.745	0.956
	<i>p</i>	<.001	.584	.508	.48	.191	.638	.683	.466	.007	.004	.004
Diseases of the Gastrointestinal Tract	B	-0.034		-0.615	-0.276	-0.788		1.052	1.069		0.245	0.026
	<i>p</i>	.012	.053	.604	.515	.021	.054	.016	.03	.529	.333	.943
Cardiological Diseases	B	-0.113		0.15	-0.039	-0.41		-0.22	0.027		0.305	0.304
	<i>p</i>	<.001	.352	.906	.92	.174	.683	.668	.963	.435	.204	.422
Dermatological Diseases	B	0.031		-0.47	2.017	0.551		1.614	1.138		0.916	1.401
	<i>p</i>	.199	.083	.709	.017	.189	.042	.019	.135	.071	.037	.056
Diseases of the Locomotor Apparatus	B	-0.022		-0.298	-0.565	-1.151		0.261	0.679		0.413	0.622
	<i>p</i>	.057	<.001	.799	.132	<.001	.161	.555	.163	.105	.064	.062
Neurological Diseases	B	-0.021		-1.06	-0.349	-0.023		-0.364	-1.015		1.139	0.387
	<i>p</i>	.404	.749	.415	.586	.967	.276	.731	.355	.021	.008	.492
Metabolic Diseases	B	-0.038		18.882	0.064	0.375		0.486	1.152		0.385	1.212
	<i>p</i>	.086	.761	.999	.905	.372	.345	.461	.165	.268	.307	.124
Pulmonary Diseases	B	0.003		-0.894	1.504	0.106		1.014	0.512		0.552	2.15
	<i>p</i>	.908	.216	.473	.079	.82	.235	.203	.556	.117	.202	.049
Malignant Diseases	B	-0.088		-1.058	0.508	1.058		-17.865	-17.618		0.839	17.784
	<i>p</i>	.019	.143	.435	.495	.07	.957	.998	.998	.315	.129	.997
Others	B	-0.029		-1.309	0.052	-0.087		-0.562	-0.929		0.379	0.34
	<i>p</i>	.074	.573	.187	.904	.794	.312	.457	.24	.422	.19	.427

Table 6 Differences in morbidity from physical diseases in veterans suffering from PTSD with and without psychiatric comorbidity.

	PTSD without Psychiatric Comorbidity <i>n</i> = 191		PTSD with Psychiatric Comorbidity <i>n</i> = 310		χ^2	<i>p</i>
		%		%		
<i>Diseases of the Gastrointestinal Tract</i>						
No	149	37.6	247	62.4	5.04	.283
Ulcer	10	37	17	63		
Gastritis	23	39.7	35	60.3		
Ulcerative Colitis	3	100	0	0		
Other	6	35.3	11	64.7		
<i>Cardiological Diseases</i>						
No	123	34	239	66	14.491	.006
Arterial Hypertension	40	43.5	52	56.5		
Myocardial Infarction	6	54.5	5	45.5		
Arrhythmia	15	55.6	12	44.4		
Other	7	77.8	2	22.2		
<i>Dermatological Diseases</i>						
No	164	36.4	451	63.6	6.444	.168
Psoriasis	12	60	20	40		
Alopecia	2	50	4	50		
Allergies	6	50	12	50		
Other	7	50	14	50		
<i>Diseases of the Locomotor Apparatus</i>						
No	94	35.3	172	64.7	9.807	.44
Diseases of the Spine	78	42.4	106	57.6		
Diseases of the Joints	11	27.5	29	72.5		
Rheumatoid Arthritis	5	71.4	2	28.6		
Other	3	75	1	25		
<i>Neurological Diseases</i>						
No	154	37.6	256	62.4	2.901	.575
Headache	35	43.2	46	56.8		
Epilepsia	1	33.3	2	66.7		
Cerebrovascular Insult	0	0	2	100		
Other	1	20	4	80		
<i>Metabolic Diseases</i>						
No	169	38.1	275	61.9	0.844	.656
Diabetes mellitus	16	35.6	29	64.4		
Thyroid Diseases	6	50	6	50		
<i>Pulmonary Diseases</i>						
No	179	37.8	295	62.2	0.513	.916
Bronchitis	7	43.8	9	56.3		
Asthma	1	50	1	50		
Other	4	44.4	5	55.6		
<i>Malignant Diseases</i>						
Yes	5	62.5	3	37.5	2.048	.152
No	186	37.7	307	62.3		
<i>Other</i>						
Yes	30	38	49	62	0.001	.976
No	161	38.2	261	61.8		

culoskeletal and malignant diseases. Veterans with PTSD complicated with other psychiatric comorbidities most often spent a long period on the battlefield, but suffered less often from all cardiovascular diseases, except arrhythmias.

These results indicate a far greater tendency among combat veterans to suffer from the majority of somatic diseases (Beckham et al., 2003; O'Toole & Catts, 2008; Qureshi et al., 2009). It seems that PTSD more often

Table 7 Odds ratio for specific diseases in PTSD patients with psychiatric comorbidity compared to PTSD patients without psychiatric comorbidity, in univariate and multiple logistic regression models (N = 501).

	Univariate		Adjusted		Logistic regression model*	
	OR	95% CI	P	OR	95% CI	P
Diseases of the Gastrointestinal Tract	0.905	0.583-1.405	.656	0.918	0.585-1.441	.711
Cardiological Diseases	0.537	0.361-0.800	.002	0.607	0.402-0.916	.017
Dermatological Diseases	0.487	0.270-0.877	.016	0.510	0.280-0.929	.028
Diseases of the Locomotor Apparatus	0.778	0.542-1.116	.172	0.840	0.579-1.217	.357
Neurological Diseases	0.878	0.552-1.396	.582	0.914	0.568-1.470	.711
Metabolic Diseases	0.978	0.555-1.723	.938	1.117	0.624-1.999	.710
Pulmonary Diseases	0.758	0.347-1.657	.488	0.834	0.347-1.858	.657
Malignant Diseases	0.364	0.086-1.539	.169	0.516	0.116-2.241	.377
Other	1.008	0.614-1.653	.976	1.023	0.616-1.696	.931
					χ^2 (df)	P
					12.64 (9)	.180
					18.13 (9)	.034
					17.35 (9)	.044
					13.35 (9)	.147
					12.64 (9)	.180
					12.64 (9)	.180
					12.67 (9)	.177
					13.31 (9)	.149
					12.51 (9)	.186

Note. *Including the specific diagnosis and confounding variables age, education, marital status and employment. CI = 95% confidence intervals; OR = odds ratio for negative change; Univariate = univariate binary logistic regression; Adjusted = adjusted or multivariate binary logistic regression controlling for age, education, marital status and employment status.

influences on veterans to suffer from physical illnesses than the length of time being exposed to combat trauma. In fact, the meta-analysis of PTSD in the general population demonstrated that the majority of studies found a greater incidence of arthritis, while the data on the incidence of coronary disease, diabetes and stroke are inconsistent (Qureshi et al., 2009). In contrast to our study where we compared veterans suffered from PTSD with control group that was not exposed to combat experience, in these studies comorbid physical disorders were evaluated between veterans with or without PTSD (O'Toole & Catts, 2008; Vasterling et al., 2008), indicating that exposure to trauma might have affected physical health, regardless of the PTSD diagnosis.

Although ulcerative colitis was recorded in three veterans with PTSD, but not in control subjects, a surprising finding from our study was that ulcer disease occurred more often in general population, while gastritis was more common among veterans. This observation is in contrast with data from Fink (2011), suggesting the greater significance of stress in the incidence of functional disorders than for ulcer disease.

In line with increased ECG abnormalities (Boscarino, 2004), we have found the higher incidences of myocardial infarction and cardiac arrhythmia in veterans, indicating the significant impact of traumatic experiences as well as PTSD diagnosis on coronary cardiac diseases. These disorders might also be associated with disturbances in the hypothalamic-pituitary adrenal (HPA) and the sympathetic-adrenal-medullary (SAM) stress axes occurring in PTSD, that result in consequent increases in circulating catecholamines and diminished levels of cortisol (Radley et al., 2011). Exposure to stress also leads to suppression of lymphocyte function, impaired proliferation of T lymphocytes and NK-cell activity, which are all associated with impaired immune response (Raison, Capuron, & Miller, 2006). In our study veterans had more dermatological diseases than control subjects. This might be explained by the altered inflammation responsiveness and aberrant allergic mechanisms, that are associated with the significantly larger number of patients with alopecia, allergic reactions and other skin diseases (eczema, dermatitis) (Gupta & Gupta, 2012). We observed a higher incidence of psoriasis in the general population than in PTSD veterans, a finding in contrast with data obtained from U.S. veterans (Boscarino, 2004). The explanation for this finding is at present unclear. Impaired immune response is related to an increased incidence of diseases of the musculoskeletal system and joints, rheumatoid arthritis and back problems, which is consistent with findings from our and other (Boscarino, Forsberg, & Goldberg, 2010; O'Toole & Catts, 2008) studies. The possible disturbances of the immune system were presumably associated with more frequent findings of asthma and other pulmonary diseases among veterans with PTSD compared to control subjects (Boscarino, 2004).

The greater incidence of all the neurological diseases, including headaches, could be associated with tension headaches, frequently within the framework of somatization in PTSD (Ginzburg et al., 2010). Although our study included only a small number of patients with epilepsy (EPI) and cerebrovascular insult (CVI), significantly higher incidence of CVI in veterans may be associated with atherosclerotic events that lead to coronary cardiac diseases. The reason for higher

incidence may be a lifestyle (smoking eg), but unfortunately we have not explored in the study.

Consistent with recent findings of the increased incidence of diabetes in patients suffering from PTSD (Boyko et al., 2010), and disruptions in thyroid hormone levels, associated with disturbances of the hypothalamus-pituitary-thyroid (HPT) axis in subjects with civilian PTSD (Glaesmer et al., 2011; Olff, Güzelcan, de Vries, Assies, & Gersons, 2006), metabolic diseases (i.e. diabetes mellitus and diseases of the thyroid gland) were significantly more common among the veterans with PTSD than in control group.

The results suggesting that age was a predictor of morbidity in both groups were expected. The severity of morbidity was predicted by the length of time spent on the battlefield and being wounded, emphasizing the importance of the intensity and duration of the exposure to traumatic experience for the occurrence of physical illness. Employment status was a predictor of morbidity in control group, presumably due to the workplace stress, associated with the adverse working conditions in developing countries (Kortum, Leka, & Cox, 2010).

The high percentage of psychiatric comorbidity with PTSD and the large proportion of patients with Enduring Personality Change After Catastrophic Experience (EPCACE) and anxiety-depressive disorder are findings consistent with previous reports (Ginzburg et al., 2010; Nemčić-Moro, Frančišković, Britvić, Klarić, & Zečević, 2011), however our and other (McTeague et al., 2010) studies underscored the significance of the duration of trauma exposure on the occurrence of psychiatric comorbidities. The reason why veterans with PTSD complicated with various psychiatric comorbidities suffer less frequently from all cardiovascular diseases, except arrhythmia, and also dermatological diseases is unclear, but might be due to the process of psychiatric diagnosis and clinical evaluation of psychiatric comorbidity that may relieve anxiety, which consequently reduces the risk for other diseases. This finding remains unclear and requires further investigations.

The explanation for our findings of the increased morbidity from physical as well as psychiatric disorders may be sought in the current understanding of the neurobiology of response to traumatic experience, and its impact on the occurrence of depression and physical illnesses. The influence of trauma leads to abnormal, excessive activation of the HPA axis and inflammatory pathways. Activation of macrophages due to inflammatory challenges (infection, tissue damage or destruction) may cause the release of proinflammatory cytokines. These cytokines enter several areas of the afferent sensory systems and can lead to increased activity. Once in the brain, cytokines can cause altered metabolism of serotonin (5-HT) and dopamine (DA), activation of corticotrophin-releasing hormone (CRH) leading to increased serum cortisol levels, and disruption of synaptic plasticity through changes in growth factors such as brain-derived neurotrophic factor (BDNF) (Raison et al., 2006). These cellular disturbances might be correlated with disorders in the immune response, which reflects stress at both the psychological and physical levels. In patients with chronic PTSD, low cortisol levels and high HPA sensitivity are usually found (Yehuda, 1997). Unfortunately, these explanations are only speculations because indicators (cortisol, inflammatory cytokines) were not measured.

This study has some limitations: experimental group was studied 15 years after the end of the war. Presumably, because of that reason, about half of the veterans from this group, with PTSD diagnosis, also suffer from Enduring Personality Change After Catastrophic Experience (EPCACE). Due to afore mentioned, it can be supposed that these veterans suffer from more difficult form of PTSD, and as such they are not adequate representatives of the total veteran population from this area. Therefore, this group of veterans consisted of the most severely ill patients who required years of treatment. In addition, the use of hospital and clinic samples, as in the current study, is potentially open to Berkson's bias. Since the group of veterans was not evaluated for possible other kind of traumatic experience besides war induced trauma, we realized that any other trauma during lifetime can also affect the appearance of symptoms. Unfortunately, this has not been studied (Guerra, Cumsille, & Martinez, 2014). On the other hand, although the control group was formed from members of the general population who did not fought in the war; these subjects were also exposed to the stressful experience of living under wartime conditions, although the degree of their traumatization was certainly far lower. Also, it should be considered that most veterans did not work, opposed to the control group, which also may represent an additional stressor factor. Another limitation might be that psychiatrists did not examine each member of the control group, in order to rule out the diagnosis of PTSD. Smoking and body mass index (as well as physical training), pre-war medical history or health behavior were not evaluated, as these factors may also contribute to a higher incidence of physical illness, which is also a shortcoming of the study. Future research should focus on all veterans with PTSD, veterans without PTSD and corresponding control subjects from the general population, using objective laboratory and clinical measures.

In conclusion, 501 veterans with PTSD suffered more often from cardiovascular, dermatological, musculoskeletal, pulmonary and metabolic diseases than 825 corresponding control subjects who were not exposed to combat experience. The predictors of cardiovascular, musculoskeletal and malignant diseases in veterans were age, length of time spent in combat, and having been wounded. A longer period in the combat zone was associated with arrhythmias in veterans with PTSD complicated with other psychiatric comorbidities. PTSD as a result of exposure to war trauma increases the likelihood of developing somatic diseases.

Funding

This research was supported by Project 141-0000000-0068 of the Croatian Ministry of Science, Education and Sports.

References

- Beckham, J. C., Taft, C. T., Vrana, S. R., Feldman, M. E., Barefoot, J. C., Moore, S. D., Mozley, S. L., Butterfield, M. I., & Calhoun, P. S. (2003). Ambulatory monitoring and physical health report in Vietnam veterans with and without chronic posttraumatic stress disorder. *Journal of Traumatic Stress, 16*, 329–335. doi:10.1023/A:1024457700599
- Boscarino, J. A. (2004). Posttraumatic stress disorder and physical illness: Results from clinical and epidemiologic studies.

- Annals of New York Academy of Sciences*, 1032, 141–153. doi:10.1196/annals.1314.011
- Boscarino, J. A., Forsberg, C. W., & Goldberg, J. (2010). A twin study of association between PTSD symptoms and rheumatoid arthritis. *Psychosomatic Medicine*, 72, 481–486. doi:10.1097/PSY.0b013e3181d9a80c
- Boyko, E. J., Jacobson, I. G., Smith, B., Ryan, M. A., Hooper, T. I., Amoroso, P. J., Gackstetter, G. D., Barrett-Connor, E., & Smith, T. C. (2010). Risk of diabetes in U.S. military service members in relation to combat deployment and mental health. *Diabetes Care*, 33, 1771–1777. doi:10.1097/PSY.0b013e3181d9a80c
- Coughlin, S. S. (2011). Post-traumatic Stress Disorder and Cardiovascular Disease. *Open Cardiovascular Medicine Journal*, 5, 164–170. doi:10.2174/1874192401105010164
- Edmundson, D., & Cohen, B. E. (2013). Posttraumatic stress disorder and cardiovascular disease. *Progress in Cardiovascular Disease*, 55, 548–556. doi:10.1016/j.pcad.2013.03.004
- Fink, G. (2011). Stress controversies: Post-traumatic stress disorder, hippocampal volume, gastroduodenal ulceration. *Journal of Neuroendocrinology*, 23, 107–117. doi:10.1111/j.1365-2826.2010.02089.x
- First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2000). *Strukturirani klinički intervju za poremećaje s osi I iz DSM-IV-klinička verzija (SKID-KV)*. Jastrebarsko: Naklada Slap.
- Ginzburg, K., Ein-Dor, T., & Solomon, Z. (2010). Comorbidity of posttraumatic stress disorder, anxiety and depression: A 20-year longitudinal study of war veterans. *Journal of Affective Disorders*, 123, 249–257. doi:10.1016/j.jad.2009.08.006
- Ginzburg, K., & Solomon, Z. (2011). Trajectories of stress reactions and somatization symptoms among war veterans: A 20-year longitudinal study. *Psychological Medicine*, 41, 353–362. doi:10.1017/S0033291710000528
- Glaesmer, H., Brähler, E., Gündel, H., & Riedel-Heller, S. G. (2011). The association of traumatic experiences and posttraumatic stress disorder with physical morbidity in old age: A German population-based study. *Psychosomatic Medicine*, 73, 401–406. doi:10.1097/PSY.0b013e318121b47e8
- Guerra, C., Cumsille, P., & Martinez, M. L. (2014). Post-traumatic stress symptoms in adolescents exposed to an earthquake: Association with self-efficacy, perceived magnitude, and fear. *International Journal of Clinical and Health Psychology*, 14, 165–177. doi:10.1016/j.ijchp.2014.05.001
- Gupta, M. A., & Gupta, A. K. (2012). Chronic idiopathic urticaria and post-traumatic stress disorder (PTSD): An under-recognized comorbidity. *Clinics in Dermatology*, 30, 351–354. doi:10.1016/j.clindermatol.2012.01.012
- Keane, T. M., Cadell, J. M., & Taylor, K. L. (1988). *Mississippi Scale for Combat-Related Posttraumatic Stress Disorder: Three studies in reliability and validity*. *Journal of Consulting Clinical Psychology*, 56, 85–90.
- Kortum, E., Leka, S., & Cox, T. (2010). Psychosocial risks and work-related stress in developing countries: Health impact, priorities, barriers and solutions. *International Journal of Occupational Medicine and Environmental Health*, 23, 225–238. doi:10.2478/v10001-010-0024-5
- Kulka, A., Schlenger, W. E., Fairbank, J. A., Jordan, B. K., Hough, R. L., Marmar, C. R., & Weiss, D. S. (1991). Assessment of posttraumatic stress disorder in the community: Prospects and pitfalls from recent studies of Vietnam veterans. *Journal of Consulting Clinical Psychology*, 3, 547–560. doi:10.1037/1040-3590.3.4.547
- McTeague, L. M., Lang, P. J., Laplante, M. C., Cuthbert, B. N., Shumen, J. R., & Bradley, M. M. (2010). Aversive imagery in posttraumatic stress disorder: Trauma recurrence, comorbidity, and physiological reactivity. *Biological Psychiatry*, 67, 346–356. doi:10.1016/j.biopsych.2009.08.023
- Nemčić-Moro, I., Frančišković, T., Britvić, D., Klarić, M., & Zečević, I. (2011). Disorder of extreme stress not otherwise specified (DESNOS) in Croatian war veterans with posttraumatic stress disorder: Case–control study. *Croatian Medical Journal*, 52, 505–512. doi:10.3325/cmj.2011.52.505
- Olf, M., Güzelcan, Y., de Vries, G. J., Assies, J., & Gersons, B. P. (2006). HPA- and HPT-axis alterations in chronic posttraumatic stress disorder. *Psychoneuroendocrinology*, 31, 1220–1230. doi:10.1016/j.psyneuen.2006.09.003
- O'Toole, B. I., & Catts, S. V. (2008). Trauma, PTSD, and physical health: An epidemiological study of Australian Vietnam veterans. *Journal of Psychosomatic Research*, 64, 33–40. doi:10.1016/j.jpsychores.2007.07.006
- Qureshi, S. U., Pyne, J. M., Magruder, K. M., Schultz, P. E., & Kunik, M. E. (2009). The link between post-traumatic stress disorder and physical comorbidities: A systematic review. *Psychiatric Quarterly*, 80, 87–97. doi:10.1007/s11126-009-9096-4
- Radley, J. J., Kabbaj, M., Jacobson, L., Heydendael, W., Yehuda, R., & Herman, J. P. (2011). Stress risk factors and stress-related pathology: Neuroplasticity, epigenetics and endophenotypes. *Stress*, 14, 481–497. doi:10.3109/10253890.2011.604751
- Raison, C. L., Capuron, L., & Miller, A. H. (2006). Cytokines sing the blues: Inflammation and the pathogenesis of depression. *Trends in Immunology*, 27, 24–31. doi:10.1016/j.it.2005.11.006
- Vasterling, J. J., Schumm, J., Proctor, S. P., Gentry, E., King, D. W., & King, L. A. (2008). Posttraumatic stress disorder and health functioning in a non-treatment seeking sample of Iraq war veterans: A prospective analysis. *Journal of Rehabilitation Research and Development*, 45, 347–358. doi:10.1682/JRRD.2007.05.0077
- World Health Organization. (1992). *International Statistical Classification of Diseases and Related Health Problems (ICD-10)*. Geneva: WHO.
- Yehuda, R. (1997). Sensitization of the Hypothalamic-Pituitary-Adrenal Axis in Posttraumatic Stress Disorder. *Psychobiology of Posttraumatic Stress Disorder (Annals of the New York Academy of Sciences)*, 821, 57–75. doi:10.1111/j.1749-6632.1997.tb48269.x
- Zen, A. L., Whooley, M. A., Zhao, S., & Cohen, B. E. (2012). Post-traumatic stress disorder is associated with poor health behaviors: Findings from the heart and soul study. *Health Psychology*, 31, 194–201. doi:10.1037/a0025989