Early life trauma in war veterans with PTSD and Complex PTSD

Ivandić, Marijeta

UNIVERSITY OF SPLIT
SCHOOL OF MEDICINE

MARIJETA IVANDIĆ

EARLY LIFE TRAUMA IN WAR VETERANS WITH PTSD AND COMPLEX PTSD

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Prof. Dolores Britvić, MD, PhD

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1. INTRODUCTION

1.1. Posttraumatic stress disorder (PTSD)

1.1.1 Definition

Posttraumatic stress disorder (PTSD) is a psychiatric disorder that can be developed after experiencing or witnessing a traumatic event such as physical assault, sexual violence, war, torture, natural or human-made disasters, and severe motor vehicle accidents (1). Exposure to such overwhelming, traumatic events has a wide range of psychopathological consequences, but PTSD has shown to be the most common one (2). Individuals affected by the disorder experience intrusive recollections of the event, actively avoid stimuli associated with the event and have various alterations in cognition, mood, arousal, and reactivity, all leading to significant impairment in many areas of functioning (3). It was first introduced as a diagnosis in 1980 in the DSM-III (Diagnostic and Statistical Manual of Mental Disorders) by the American Psychiatric Association, following an epidemic of "post-Vietnam" syndrome diagnosis in veterans in the United States (4).

1.1.2 Epidemiology

Lifetime and 1-year prevalence of PTSD vary in different countries, ranging from 1.3 to 12.2% and 0.2 to 3.8%, respectively (5). Compared to the general population, rates of PTSD are higher among military personnel and first responders (e.g., police, firefighters, emergency medical personnel) (2). With regards to sex differences, studies have consistently shown that PTSD is more common in women, in whom the prevalence is about twice the one in men (6). Although PTSD can appear at any age, most cases are diagnosed before the age of 40 (7).

1.1.3 Etiology

Exposure to a traumatic event is necessary for PTSD to develop, but interestingly, most people will not develop the condition after being exposed to trauma (3). The susceptibility of an individual likely depends on personal history and specificities of the trauma experienced (2). Personal factors identified as risks for PTSD development are female sex, early life trauma, exposure to interpersonal violence, exposure to more traumatic events, fewer years of schooling, and prior mental disorders (8). Some meta-analyses suggest that factors relating to the traumatic event itself such as the severity or the magnitude of trauma, the perceived life threat, and the peritraumatic dissociation (depersonalization, derealization, dissociative

amnesia, out-of-body experiences, emotional numbness, and altered time perception) are stronger predictors of PTSD development, especially the peritraumatic dissociation (8,9).

When it comes to military personnel, they have an elevated risk of developing PTSD due to the many traumatic events that can be experienced in war zones (10). It is estimated that up to 30% of combat soldiers will be diagnosed with PTSD (11). Research has shown how soldiers pre- and post-combat differ in the PTSD symptom dynamics, showing consolidation of intrusive and avoidance symptoms after exposure to war (12).

There has been substantive research into the neurobiological mechanisms of PTSD, although there is debate as to whether the biological abnormalities preceded PTSD or are a consequence of trauma (13).

Increased sympathetic nervous system and decreased hypothalamic-pituitary-adrenal functioning have been largely proposed to influence PTSD onset and course, but neither has been shown to be reliable markers of disease development (14,15). Evidence of alterations of these two major stress response mechanisms in individuals with PTSD are raised catecholamines, elevated heart rate, elevated blood pressure, and low cortisol levels (16). Low cortisol level, a marker of reduced adrenal output, has been proposed as a pre-existing risk factor for PTSD and a possible consequence of adverse early experiences (17) The relative excess of catecholamines compared to cortisol is postulated to drive the memory formation around the traumatic event, leading to over-consolidation and resulting in a persistent hyper-aroused state (18).

Genetic susceptibility has been shown to account for about 30% of the risk of developing PTSD (19). This is in accordance with twin studies that showed how the risk of PTSD is moderately heritable (20). Binder *et al.* have shown an association between polymorphisms in the FKBP5 gene caused by childhood abuse and the development of PTSD (21). FKB5 is a chaperone protein to the glucocorticoid-glucocorticoid receptor complex, and impaired glucocorticoid signaling could explain the observed HPA axis dysfunction in PTSD (22).

Epigenetic studies looked at methylation patterns of several genes involved in synaptic plasticity and the HPA axis has found lower levels of methylation in veterans with PTSD compared to veterans without the disorder, which could be an early marker or a consequence of the disease (23).

1.1.4 Clinical features and diagnostic criteria

According to the DSM-V, there are 20 symptoms of PTSD categorized into four clusters: intrusion/re-experiencing symptoms, avoidance symptoms, negative alterations in cognition and mood, and symptoms of hyperarousal (1). A summarized version of the diagnosis would be that a person suffers from PTSD if they have been exposed to an identified stressor and have at least one intrusion symptom, one avoidance symptom, two symptoms of negative alterations in cognition and mood, and two symptoms of arousal and hyperactivity persisting for at least one month, accompanied by a significant functional impairment (24).

Detailed DSM-V criteria of PTSD are presented in the text below (25).

Criterion A (exposure to the stressor):

- Direct exposure
- Witnessing trauma
- Learning of a trauma
- Repeated or extreme indirect exposure to aversive details.

Criterion B (intrusion symptoms):

- Recurrent memories
- Traumatic nightmares
- Dissociative reactions – flashbacks
- Psychological distress at traumatic reminders
- Marked physiological reactivity to reminders.

Criterion C (persistent avoidance):

- Avoidance of trauma-related thoughts or feelings
- Avoidance of trauma-related external reminders such as people, places, or activities.

Criterion D (negative alterations in cognitions and mood):

- Dissociative amnesia
- Persistent negative beliefs and expectations
- Persistent distorted blame of self or others for causing trauma.
- Negative trauma-related emotions: fear, horror, guilt, shame, and anger
- Diminished interest in activities

- Detachment or estrangement from others
- Inability to experience positive emotions.

Criterion E (alterations in arousal and reactivity):

- Irritable and aggressive behavior
- Self-destructive and reckless behavior
- Hypervigilance
- Exaggerated startle
- Problems concentrating
- Sleep disturbance.

Criterion F (duration)

- Must experience criteria for at least one month, prior to that a diagnosis of acute stress disorder is more suitable.

Criterion G (functional significance)

- Impairment in social, occupational, or other domains.

Criterion H (exclusion)

- The disorder is not attributable to medication, substance use, or other illness.

There are also two subtypes of PTSD, the first one being the dissociative subtype in whom symptoms of detachment, depersonalization, and derealization prevail (26). The second subtype of PTSD is called the delayed subtype, in which the PTSD diagnosis is made at least 6 months from the traumatic experience (27).

Patients with PTSD also have a high rate of co-occurring psychiatric disorders, most commonly depressive disorders, substance use, and anxiety disorders (28).

Additionally, they have a greater prevalence of somatic diseases like cardiometabolic disorders, which results in higher mortality than the general population (29,30). This is further confirmed by findings of elevated markers of inflammation in patients with PTSD such as CRP, IL-6, IL-1, and TNF-α (31).

1.1.5 Treatment

The recommended first-line treatment for PTSD is psychological therapy, with the most clinical effect being produced by cognitive-behavioral therapy with a trauma focus, cognitive therapy, cognitive processing therapy, prolonged exposure therapy, and eye-movement desensitization and reprocessing (EMDR) (32).

Trauma-focused therapies help to change unhelpful beliefs about the trauma and its consequences, which then likely drives the change in symptoms (33). EDMR psychotherapy is thought to enable access to traumatic memories so that they can be adequately processed by the brain and resolved (34).

What can attenuate the effect of trauma-focused psychotherapy is the co-occurrence of depression with PTSD, which is very common (35). Also, it has been shown that the military population shows poorer treatment outcomes when compared to civilians (36).

The recommendations for pharmacological treatment vary across guidelines. There is support in meta-analyses for the use of SSRIs (fluoxetine, sertraline, paroxetine), SNRIs (venlafaxine), atypical antipsychotics (risperidone, quetiapine), an anti-epileptic (topiramate), with fluoxetine having the greatest efficacy when compared to placebo (37).

In the newest attempt to find a treatment for chronic PTSD, clinical trials are investigating MDMA-assisted psychotherapy, the rationale being that MDMA can increase the tolerability and effectiveness of psychotherapy by modulating the mental and emotional state of the patient (38).

1.2. Complex PTSD

1.2.1. History of the complex PTSD diagnosis

The diagnosis of complex PTSD was developed during the making of the 11th version of the International Classification of Diseases (ICD-11), published in 2018. It is distinct from PTSD, although they are considered 'sibling' disorders, meaning that they belong to the same parent category of traumatic stress disorders (39).

This diagnosis was already proposed in 1992. by Harvard University's Dr. Judith Herman in her seminal book 'Trauma and recovery: The aftermath of violence - from domestic abuse to political terror' (40). From her research with victims of sexual and domestic violence, she concluded that chronic experience of trauma led to the development of specific symptoms that deserved a separate diagnosis from PTSD. These symptoms were as she noted: disturbances of affect regulation, alterations of consciousness, disturbed self-perception, disturbed perception of the offender, relationship problems, and changes in a person's value system.

The cluster of symptoms Herman wrote about was described in the DSM-IV as DESNOS, disorders of extreme stress not otherwise specified (41). This was not made a separate diagnosis, but rather an associated feature of PTSD due to the finding that 92% of individuals with DESNOS meet the diagnostic criteria for PTSD (42). The DSM-V still does not include complex PTSD as a separate diagnosis.

A similar diagnosis called EPCACE (Enduring personality change after catastrophic experience) appeared in the ICD-10 in the chapter of 'Disorders of adult personality and behavior' but it did not gain much attention in the literature (43).

In the new ICD-11, EPCACE was replaced by the complex PTSD diagnosis (44).

1.2.2. Clinical features and diagnostic criteria

To be diagnosed with complex PTSD a person needs to meet all the PTSD criteria first: at least one traumatic event identified and at least one symptom from the categories of re-experiencing the trauma, avoidance of trauma reminders, and heightened sense of threat.

Further diagnostic requirements are what distinguishes complex PTSD from PTSD - the presence of at least one symptom from each of the three disturbances of self-organization

(DSO) clusters: affect dysregulation, interpersonal difficulties, and negative self-concept (45). Affect dysregulation is evident in emotional dysregulation displayed as increased emotional reactivity, violent outbursts, reckless or self-destructive behavior, dissociation under stress, and emotional numbing. Interpersonal difficulties are reflected by constant difficulties in sustaining relationships, difficulty in feeling close to others, and avoidance of social events. Negative self-concept is evident in the belief one is worthless and in the feelings of shame or guilt (44). CPTSD is also associated with a worse functional impairment than PTSD (46).

When it comes to war and CPTSD, high rates of CPTSD among treatment-seeking veterans have been shown (47). This goes in hand with the knowledge of how prolonged and repeated interpersonal trauma is a risk for this disorder, and the experience of war surely falls within this trauma category (48).

Complex PTSD is most often diagnostically confused for borderline personality disorder (BPD), as they both share the presence of DSO symptoms and BPD is commonly associated with PTSD (49). Although their symptoms overlap, they are still two separate diagnostic entities. A useful tool to establish the diagnosis of CPTSD is the International Trauma Questionnaire (ITQ) (50), which was developed according to the ICD-11 diagnostic criteria and was also used for this purpose in our study.

1.2.3. Treatment

PTSD is a relatively new diagnosis, and clinical trials evaluating the best treatment options are still greatly lacking. Existing PTSD treatment guidelines cannot simply be translated to this population as data shows that CPTSD is more severe and may require more treatment interventions of longer duration (51). It is theorized that a 'flexible modular approach' might be most helpful in patients with CTPSD (52). According to this approach, the patient and the therapist agree on which interventions to choose from based on the problems that are creating the greatest concern for the patient.

To conclude, PTSD and complex PTSD have different symptom profiles, levels of impairment, risk factors, are associated with different subgroups of individuals, and require distinct therapeutic approaches, all of which support their separation as two distinct disorders (44).

2. OBJECTIVES

2.1. Aim

This study aimed to investigate the correlation between early life trauma and symptoms of PTSD and complex PTSD in Croatian war veterans.

2.2. Hypothesis

1. PTSD and C-PTSD symptoms in war veterans will not have a positive correlation with early life trauma.

2. C-PTSD symptoms will not have a greater correlation with early life trauma as compared to PTSD symptoms in war veterans.

3. MATERIALS AND METHODS

3.1. Study design

This study is a part of an ongoing research project titled "Lifelong exposure to stress, inflammation and health outcomes in patients with posttraumatic stress disorder" done in collaboration with the Mediterranean Institute for Life Sciences (MedILS) and the Laboratory for Stress Assessment and Research, Cousins Center for Psychoneuroimmunology, University of California, Los Angeles (UCLA). The research was conducted at the Department of Psychiatry, University Hospital of Split, and the Regional Center for Psychotrauma during the day hospital in 2018 for a total duration of three months.

The measurement instruments were four questionnaires: the Clinician-Administered PTSD Scale for DSM-V (CAPS-V) used to confirm the diagnosis of PTSD, the International Trauma Questionnaire (ITQ) used to establish the diagnosis of CPTSD, the Stress and Adversity Inventory (STRAIN) used to gain information on early childhood trauma, and a sociodemographic questionnaire used for demographic variable analysis and exclusion/inclusion criteria. The Clinician-Administered PTSD Scale for DSM-V and the International Trauma Questionnaire were conducted as an interview, whereas the Stress and Adversity Inventory was implemented entirely online.

This research was approved by the Ethics Committee of the University Hospital Centre Split (500-03/20-01/11).

3.2. Subjects

This research initially included 100 war veterans from the Homeland war in Croatia that have been treated for PTSD at the Regional Center for Psychotrauma and the Department of Psychiatry at the University Hospital of Split. They have volunteered to be a part of this study and have given their informed consent in writing. All research participants were men. Inclusion criteria were PTSD developed during the participation in the Homeland war and age from 45 to 70 at the time of the study. Exclusion criteria were the following: diagnosis of severe psychotic diseases including bipolar affective disorder, drug or alcohol dependency, autoimmune diseases including diabetes mellitus type one, HIV, acute bacterial or viral infection, intellectual disability, and individuals deprived of legal capacity.

Out of 100 initial research participants, 88 have fulfilled the criteria for PTSD or CPTSD. A total of 40 participants have fulfilled the criteria for PTSD and 48 participants have fulfilled the criteria for CPTSD.

3.3. Measurement instruments

3.3.1. The Clinician-Administered PTSD Scale for DSM-V (CAPS-V)

The Clinician-Administered PTSD Scale (CAPS) is a 30-item structured diagnostic interview developed in 1989 at the National Centre for PTSD by Blake *et al* (53). It has been a gold standard for diagnosing and assessing the symptoms of PTSD since (54). The Clinician-Administered PTSD Scale for DSM-V is the most recent version of the interview, updated according to the diagnostic criteria for PTSD in the DSM-V (55). It can be used to make current and lifetime diagnoses of PTSD, as well as to assess the symptoms of PTSD over the past week. (53).

To conduct this interview, it is necessary to identify the main (index) traumatic event which will be used for further symptom inquiry. All 20 PTSD symptoms listed in the DSM-V are inquired for as well as overall response validity, subjective distress, improvement in symptoms since a previous questionnaire administration and overall PTSD severity. Specific questions on depersonalization and derealization are included for the dissociative subtype of PTSD. The assessor combines symptoms reported in terms of frequency and intensity into a single severity score for an item ranging from 0-4. The severity scores are interpreted in the following way:

0. Absent: The respondent denied the problem or the respondent's report doesn't fit the DSM-5 symptom criterion.

1. Mild/subthreshold: The respondent described a problem that is consistent with the symptom criterion but isn't severe enough to be considered clinically significant. The problem doesn't satisfy the DSM-5 symptom criterion and thus doesn't count toward a PTSD diagnosis.

2. Moderate/threshold: The respondent described a clinically significant problem. The problem satisfies the DSM-5 symptom criterion and thus counts toward a PTSD diagnosis. The problem would be a target for intervention. This rating requires a minimum frequency of 2 x month or some of the time (20-30%) plus a minimum intensity of *Clearly Present*.

3. Severe/markedly elevated: The respondent described a problem that is above the threshold. The problem is difficult to manage and at times overwhelming and would be a prominent target for intervention. This rating requires a minimum frequency of 2 x week or much of the time (50-60%) plus a minimum intensity of *Pronounced*.

4. Extreme/incapacitating: The respondent described a dramatic symptom, far above the threshold. The problem is pervasive, unmanageable, and overwhelming, and would be a high-priority target for intervention.

The total severity score of the Clinician-Administered PTSD Scale for DSM-V is calculated by summing the severity scores for all 20 PTSD symptoms mentioned in the DSM-V. It is also possible to calculate the total severity score for each of the PTSD symptom clusters (56).

3.3.2. The International Trauma Questionnaire (ITQ)

The International Trauma Questionnaire (ITQ) is the first instrument made to diagnose and differentiate PTSD and CPTSD according to the criteria set forth by the ICD-11(50).

It's a self-report measure focused on the core features of PTSD and CPTSD. It is important to emphasize that one can be diagnosed with either PTSD or CPTSD, not both. This questionnaire includes 28 test items, 12 for PTSD and 16 for DSO (Disturbances in Self-Organization). All items in the questionnaire are answered on a five-point Likert scale: "Not at all" (0), "A little bit" (1), "Moderately" (2), "Quite a bit" (3), and "Extremely" (4). Scores of ≥ 2 (Moderately) are used to indicate the presence of a symptom. PTSD diagnosis requires having one of two symptoms from each of the three symptom clusters: re-experiencing in the here and now, avoidance of traumatic reminders, and sense of current threat. Additionally, these symptoms need to be associated with functional impairment.

CPTSD is diagnosed when the person meets the criteria for PTSD and has one of two symptoms from each of the three Disturbances in Self-Organization (DSO) clusters: affective dysregulation, negative self-concept, and disturbances in relationships, and these symptoms have to result in functional impairment (57).

3.3.3. The Stress and Adversity Inventory (STRAIN)

The Stress and Adversity Inventory (STRAIN) is the first online instrument that assesses a person's lifetime stress exposure (58). It was developed by George M. Slavich at UCLA's Cousins Center for Psychoneuroimmunology as a response to the difficulties faced when trying to measure stress over a person's life span. It is described as a combination of an interview-based system and a self-report instrument. It can be self- or interviewer-administered and it takes approximately 20 minutes to complete. The questions are presented one at a time and for each stressor, there are follow-up questions on the stressor's frequency, timing, duration as well as perceived severity. This allows for both the objective and subjective tell of the stress experience. It also automatically omits illogical questions (for example, questions about children to someone who doesn't have them). The respondent is questioned on about 55 different stressors, 26 acute life events, and 29 chronic difficulties over 12 major life domains (housing, education, work, treatment/health, marital/partner, reproduction, financial, legal/crime, other relationships, death, life-threatening situations, possessions) and 5 social-psychological characteristics (interpersonal loss, physical danger, humiliation, entrapment, role change/disruption). This questionnaire also categorizes two exposure indices (stressor count and severity) and two distinct timing categories (early life and adulthood).

We have focused on stressors reported during early life for the purpose of this study. These include, among others, childhood maltreatment and neglect, parental loss or separation from them, death of a family member, and bullying. These stressors were categorized as acute or chronic, and their count and severity were measured.

The use of the Stress and Adversity Inventory was authorized by George M. Slavich. It was also translated into Croatian for the first time as this is its first use in this language.

3.4. Statistical analysis

The data for this study were analyzed using SPSS Statistics 26 (IBM Corp. Armonk, N.Y., USA). Independent samples t-test was used for continuous variables, which were reported as means with standard deviation. Categorical data were reported as numbers and valid percentages and were compared using a chi-square test of independence. Statistical significance was set at $P < 0.05$.

4. RESULTS

Out of 100 initial research participants, 88 have fulfilled the criteria for PTSD according to the Clinician-Administered PTSD Scale for DSM-V. The International Trauma Questionnaire was further used to distinguish PTSD from C-PTSD, resulting in 40 veterans with PTSD and 48 veterans with C-PTSD.

4.1. Sociodemographic variables

War veterans with PTSD and C-PTSD were compared according to their age, marital status, having children, education, economic status, years of work experience, and work status. All our research participants were men, the majority of them married (80% in PTSD group and 81.3% in C-PTSD group), with children (90% in PTSD group and 87.5% in C-PTSD group) and a completed high school education (77.5% in PTSD group and 66.7% in C-PTSD group). There was no statistically significant difference in any of the sociodemographic variables investigated in war veterans with PTSD and C-PTSD (Table 1 and 2).

Table 1. Sociodemographic variables (age, economic status, and years of work experience) of war veterans with PTSD and C-PTSD

	PTSD (n=40)	**C-PTSD (n=48)**	***P****
Age	54.65±7.41	53.50±6.10	0.426
Economic status			
Significantly below average	4 (10%)	9 (19.1%)	0.295
Below average	12 (30%)	17 (36.2%)	
Average	24 (60%)	19 (40.4%)	
Above average	0 (0%)	1 (2.1%)	
Significantly above average	0 (0%)	1 (2.1%)	
Years of work experience	27.62±11.34	23.7±10.73	0.106

Data are presented as mean±standard deviation or as numbers (%)
* Independent samples t-test

Table 2. Sociodemographic variables (marital status, children, education, work status) of war veterans with PTSD and C-PTSD

	PTSD (n=40)	C-PTSD (n=48)	*P**	χ^2
Marital status				
Married	32 (80%)	39 (81.3%)		
Cohabitation	3 (7.5%)	1 (2.1%)	0.618	1.79
Divorced	2 (5%)	4 (8.3%)		
Single	3 (7.5%)	4 (8.3%)		
Children				
Yes	36 (90%)	42 (87.5%)	0.713	0.14
No	4 (10%)	6 (12.5%)		
Education				
Elementary school	6 (15%)	10 (20.8%)	0.522	1.3
High school	31 (77.5%)	32 (66.7%)		
Higher education	3 (7.5%)	6 (12.5%)		
Work status				
Employed	10 (25%)	10 (20.8%)		
Long term sick leave	3 (7.5%)	4 (8.3%)	0.709	1.39
Unemployed	9 (22.5%)	16 (33.3%)		
Retired	18 (45%)	18 (37.5%)		

Data are presented as numbers (%)
* Chi-square test of independence

4.2. The Clinician administered PTSD scale for DMS-V (CAPS-V)

The Clinician-Administered PTSD Scale for DSM-V was used to assess the symptoms of PTSD that veterans with PTSD and complex PTSD experience.

A statistically significant difference in symptoms was found between war veterans with PTSD and those with complex PTSD. Veterans with complex PTSD have scored significantly higher on the symptoms of avoidance (*P*=0.008), cognitive symptoms *(P*=0.014), arousal/irritability symptoms (*P*=0.004), social functioning problems (*P*=0.005), and subjective disturbance (*P*=0.005) (Table 3). There was no statistically significant difference between the two groups when it came to intrusive symptoms and dissociative symptoms. Veterans with complex PTSD have also shown a statistically greater overall Clinician-Administered PTSD Scale for DSM-V score (*P*=0.005).

Table 3. Symptoms in war veterans with PTSD and complex PTSD evaluated with the Clinician-Administered PTSD Scale for DSM-V

	PTSD (n=40)	**C-PTSD (n=48)**	***P****
Intrusive symptoms	10.98±3.71	11.98±2.6	0.14
Avoidance	4.38±1.51	5.17±1.24	**0.008**
Cognitive symptoms	11.82±4.9	14.52±5.1	**0.014**
Arousal/irritability symptoms	11.9±3.57	14.23±3.82	**0.004**
Dissociative symptoms	0.35±0.48	0.38±0.53	0.819
Social functioning problems	1.88±1.04	2.47±0.86	**0.005**
Subjective disturbance	2.55±0.75	2.71±0.74	**0.005**
CAPS total score	39.23±11.32	45.9±10.26	**0.005**

Data are presented as mean±standard deviation.
* Independent samples t-test

4.3. The Stress and Adversity Inventory (STRAIN)

The Stress and Adversity Inventory (STRAIN) was used to assess traumatic early life experiences in war veterans with PTSD and complex PTSD.

The two groups were compared in terms of how many traumatic early life experiences they have had, whether these were acute or chronic and how severely did they perceive them to be. The prenatal category assessed the adversities that the mother of the participant might have experienced during pregnancy and around childbirth.

There were no statistically significant differences between the two groups of veterans in the early adversity categories. However, it is worth noting that when it came to chronic difficulties experienced in childhood, veterans with C-PTSD reported somewhat greater count and severity (*P*=0.141 and *P*=0.2, respectively) than veterans with PTSD (Table 4).

Table 4. Scores of war veterans with PTSD and C-PTSD on the Stress and Adversity Inventory (STRAIN)

	PTSD (n=40)	**C-PTSD (n=48)**	***P****
Prenatal (total count)	0.38±0.70	0.44±0.77	0.694
EARLY ADVERSITY			
Total count	2.08±2.03	2.10±1.87	0.944
Total threat	6.03±7.43	6.79±6.75	0.614
Count of acute life events	1.3±1.54	0.96±1.27	0.257
The severity of acute life events	3.4±4.64	2.85±3.43	0.528
Count of chronic difficulties	0.78±0.95	1.15±1.32	0.141
The severity of chronic difficulties	2.63±4.12	3.94±5.21	0.2

Data are presented as mean±standard deviation.
* Independent samples t-test

5. DISCUSSION

The main objective of our research was to investigate the relationship between early childhood trauma and PTSD and CPTSD symptoms. For this purpose, we have focused on parts of the Stress and Adversity Inventory that inquire on early adversity and have compared war veterans with these two distinct diagnoses in terms of count and severity of childhood difficulties, as well as their acuity or chronicity.

We have found no statistically significant differences between PTSD and CPTSD within categories of childhood adversity. The closest to statistical significance were categories of count and severity of chronic difficulties, veterans with CPTSD scoring somewhat higher on these (P= 0.14 and P=0.2, respectively). Although our findings were not statistically significant, the tendency shown goes along with what the body of research has found insofar: CPTSD is more strongly associated with chronic, early traumatic experiences than PTSD (46,59,60). In fact, the diagnosis of CPTSD came about as a result of PTSD diagnosis not being able to account for all the different symptoms patients with chronic exposure to trauma were experiencing (39).

Childhood adversities have been repeatedly shown to predict PTSD development in adults who are re-traumatized in adulthood, with four adversities showing the greatest association – physical and sexual abuse, neglect, and parent psychopathology (61). There is also genetic research backing this connection, with polymorphisms in FKB5 shown to interact with childhood abuse, increasing the risk for developing PTSD and having more severe symptoms of arousal (62). When it comes to war veterans with PTSD specifically, they report higher rates of childhood trauma compared to veterans that did not develop the disorder (63). Another potential mechanism behind this association is a heightened reactivity of the amygdala to threat, which has been demonstrated in maltreated children and patients with PTSD (61). New research is confirming this hypothesis by showing that patients with CPTSD and PTSD have different neural profiles during threat processing, with patients with CPTSD having increased insula and right amygdala activation, corresponding to more pronounced disturbances in emotion regulation and self-concept (64).

Looking at CPTSD through the prism of chronic childhood trauma makes even more sense when we look at the symptom cluster in which it differs from PTSD – the disturbance of self-organization (DSO) symptoms: affect dysregulation, interpersonal difficulties, and negative self-concept. Exposure to chronic traumas, especially in childhood results in difficulties with emotion regulation, relationships, and self-regulatory behaviors (65).

We have also compared our participants in terms of their socio-demographic background and symptom intensity.

There was no statistically significant difference in the sociodemographic variables between the two groups of veterans. However, research has shown that patients with CPTSD are more commonly younger, unemployed, not married, living alone, have lower education, and lower socioeconomic status (47). Croatian veterans with PTSD have been shown to have a lower quality of life and health, as well as a perceived lack of social support, compared to veterans without PTSD (66).

We have found a statistically significant difference in symptoms between war veterans with PTSD and complex PTSD, as measured by the Clinician-Administered PTSD Scale for DSM-V questionnaire. Veterans with CPTSD have scored significantly higher on the symptoms of avoidance, cognitive symptoms, arousal/irritability symptoms, social functioning problems, and subjective disturbance. Intrusive symptoms and dissociative symptoms showed no significant difference in the two groups. CPTSD veterans also had a greater overall Clinician-Administered PTSD Scale for DSM-V score.

Findings from some previous studies have found that patients with CPTSD tend to have stronger PTSD symptoms (67). It has also been found that symptoms of intrusion, avoidance, and hyperarousal best represent CPTSD, in the civilian and combat-exposed population (67,68). However, a study on Croatian veterans by Letica-Crepulja *et al.* found no difference in symptom intensity among veterans with PTSD and CPTSD but did similarly find a greater functional impairment in veterans with CPTSD (47). Murphy *et al.* have shown that veterans with CPTSD experience high levels of anger, dissociation, and greater impairment than veterans with PTSD (48).

Patients with CPTSD tend to have higher dissociation scores, which was not replicated in our study (69). Greater social functioning problems and subjective disturbances in CPTSD veterans were in accordance with other findings (60).

The symptom severity in CPTSD has been linked to childhood adverse experiences, especially emotional neglect and sexual abuse (70). Although our results were not statistically significant, the severity and count of chronic childhood difficulties were more reported in veterans with CPTSD, who did show significantly higher PTSD symptoms, and this could be a potential explanation. A study done on Croatian veterans by Jaksic *et al.* looked at types of childhood trauma and symptom severity in veterans with PTSD. They did not find a significant

correlation between the total score on the childhood trauma questionnaire and PTSD symptoms, but they did find a significant correlation between emotional abuse and the clinical picture of PTSD (71).

The main limitations of our study were the small sample size, exclusively male participants, use of an online, retrospective self-report questionnaire for collecting data on childhood trauma, and having a convenient sample of veterans who are already in psychiatric treatment.

To our knowledge, this is the first time the Stress and Adversity Inventory has been used to assess the relationship of childhood adversity with PTSD and CPTSD symptoms in war veterans. This questionnaire is very valuable in terms of quantifying adverse experiences across a lifetime, which some other measures of childhood trauma like the Life Events Checklist for DSM-V and the Childhood Trauma Questionnaire lack. We have not been able to show a statistically significant difference between veterans with PTSD and CPTSD in terms of childhood trauma, but in the light of findings from other authors, it would be valuable to use further analyses on our data to show exactly which childhood adversities were more reported in veterans with CPTSD. Also, repeating the use of the Stress and Adversity Inventory on a greater sample of veterans would be worth doing.

It has already been shown that patients with PTSD with more childhood traumas tend to have a diminished response to some therapy modalities, and we know from research insofar that patients with CPTSD tend to report more chronic childhood traumas (72). Therefore, it is not surprising that patients with CPTSD on average require more and longer treatment interventions (52). Identifying and quantifying childhood trauma in patients with PTSD and CPTSD at the start of treatment using a method like the Stress and Adversity Inventory could help set better therapy goals. Also, the guidelines for CPTSD treatment are constantly evolving and in need of research on treatment efficacy in patients with CPTSD with complex trauma history (73). Identifying these patients, following them up, and studying their treatment response can therefore add to the body research.

6. CONCLUSIONS

Veterans with CPTSD reported a somewhat greater count and severity of chronic traumatic childhood experiences than veterans with PTSD, but the difference was not statistically significant.

There was no statistically significant difference in sociodemographic variables between veterans with PTSD and CPTSD.

Veterans with CPTSD reported significantly greater symptoms of avoidance, cognitive symptoms, arousal/irritability symptoms, social functioning problems, and subjective disturbance than veterans with PTSD.

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8. SUMMARY

Objectives: The main objective of this research was to investigate the relationship between early childhood trauma, PTSD, and complex PTSD in war veterans.

Materials and methods: Research participants were 88 male war veterans, 40 diagnosed with PTSD and 48 diagnosed with CPTSD. This research was conducted at the Department of Psychiatry, University Hospital Split, and the Regional Center for Psychotrauma. The measurement instruments were four questionnaires: the Clinician-Administered PTSD Scale for DSM-V (CAPS-V) used to confirm the diagnosis of PTSD, the International Trauma Questionnaire (ITQ) used to establish the diagnosis of CPTSD, the Stress and Adversity Inventory (STRAIN) used to gain information on early childhood trauma, and a sociodemographic questionnaire used for demographic variable analysis and exclusion/inclusion criteria.

Results: Veterans with CPTSD reported a somewhat greater count and severity of chronic traumatic childhood experiences than veterans with PTSD, but the difference was not statistically significant (P= 0.14 and P=0.2, respectively). Veterans with CPTSD and PTSD did not differ significantly in sociodemographic characteristics. Veterans with CPTSD reported significantly greater symptoms of avoidance, cognitive symptoms, arousal/irritability symptoms, social functioning problems, and subjective disturbance than veterans with PTSD.

Conclusions: Although veterans with CPTSD and PTSD did not show a statistically significant difference in early childhood trauma, veterans with CPTSD did report a somewhat greater count and severity of chronic childhood adversities, which is in accordance with the literature. Veterans with CPTSD showed significantly greater symptoms of avoidance, cognitive symptoms, arousal/irritability symptoms, social functioning problems, and subjective disturbance compared to veterans with CPTSD. There was no statistically significant difference in the sociodemographic variables of veterans with CPTSD and PTSD.

9. SAŽETAK

Naslov: Rana traumatizacija u ratnih veterana sa PTSP-om i kompleks PTSP-om

Ciljevi: Glavni cilj ovog istraživanja je bio ispitati povezanost rane traumatizacije i nastanka posttraumatskog stresnog poremećaja i kompleks posttraumatskog stresnog poremećaja u ratnih veterana.

Materijali i metode: Ispitanici su bili 88 ratnih veterana, 40 njih dijagnosticirano s PTSP-om i 48 s kompleks PTSP-om. Istraživanje je provedeno pri Klinici za psihijatriju KBC-a Split i Regionalnom centru za psihotraumu. U ovom istraživanju su kao mjerni instrumenti korištena četiri upitnika: Clinician-Administered PTSD Scale for DSM-V (CAPS-V) korišten za dijagnosticiranje PTSP-a, International Trauma Questionnaire (ITQ) korišten za dijagnosticiranje kompleks PTSP-a, Stress and Adversity Inventory (STRAIN) korišten za prikupljanje informacija o ranoj životnoj traumi i sociodemografski upitnik koji je korišten za analizu demografskih varijabli te kao mjerilo kriterija uključivanja i isključivanja.

Rezultati: Veterani s kompleks PTSP-om su iskazivali donekle veći broj i težinu kroničnih traumatskih iskustava u djetinjstvu od veterana s PTSP-om, iako razlika nije statistički značajna (P= 0.14 i P=0.2). Nije bilo statistički značajne razlike između sociodemografskih karakteristika veterana s PTSP-om i kompleks PTSP-om. Veterani s kompleks PTSP-om su iskazali značajno više simptoma izbjegavanja, kognitivnih simptoma, simptoma iritabilnosti, problema sa socijalnim funkcioniranjem i subjektivne procjene uznemirenosti od veterana s PTSP-om.

Zaključak: Iako veterani s kompleks PTSP-om nisu pokazali statistički značajnu razliku u ranoj traumatizaciji od veterana s PTSP-om, iskazali su donekle veći broj i težinu kroničnih traumatskih iskustava u djetinjstvu, što je u skladu s dosadašnjom literaturom. Veterani s kompleks PTSP-om su pokazali statistički više simptoma izbjegavanja, kognitivnih simptoma, simptoma iritabilnosti, problema sa socijalnim funkcioniranjem i subjektivne procjene uznemirenosti od veterana s PTSP-om. Nije bilo statistički značajne razlike u sociodemografskim karakteristikama između veterana s PTSP-om i kompleks PTSP-om.

10. CURRICULUM VITAE

Personal data

Marijeta Ivandić

Born on 7th of October 1995 in Split, Croatia

Trg Hrvatske bratske zajednice 3, 21000 Split

marijetaivandic@gmail.com

Education

2002 - 2010 Elementary school 'Skalice'

2010 - 2014 'II jezična gimnazija' high school

2014 - 2021 University of Split School of Medicine, Medical studies in English

Languages

English - C2 Proficiency (CPE)

German - A2

Publications

Delić, I., Kostić, S., Filipović, N., Gudelj Ensor, L., Ivandić, M., Dukić Josipa Jozefina, Vitlov Uljević, M., Ferhatović Hamzić, L., Puljak, L. & Vukojević, K. (2018) Changes in expression of special AT-rich sequence binding protein 1 and phosphatase and tensin homologue in kidneys of diabetic rats during ageing. Nephrology, dialysis, transplantation, 33 (10), 1734-1741 doi:10.1093/ndt/gfy003.