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REVIEW

Posttraumatic stress disorder – an overview in new diagnosis and treatment approaches

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Summary

Posttraumatic stress disorder (PTSD) is a complex condition, a common and disabling psychiatric disorder that causes immense suffering for millions of people. It is associated with a high rate of functional impairment, somatic complaints, a risk of suicide and comorbid psychiatric disorders, as well as extraordinary costs for health care system. The diagnosis of PTSD requires evidence of exposure to trauma, and is characterized by symptoms of re-experiencing, avoidance, and changes in arousal and reactivity. The American classification system added another cluster of symptoms related to negative changes in cognition and mood related to trauma, while the European classification system added complex PTSD as a new diagnosis. No evidence supported any particular intervention as a universal prevention strategy. CBT-TF, CBT and EMDR treatment had positive effects. Psychotherapy is the first line of choice in the treatment of PTSD. Trauma-focus interventions are recommended: CBT-TF, PE and EMDR, as well as stress management therapy. Pharmacotherapy approaches should start with one of the first-line options that include an SSRI such as fluoxetine, paroxetine, or sertraline, or the SNRI venlafaxine. Research evaluating combined psychological and pharmacological treatments for PTSD is limited and requires further study, but certain forms of PTSD require an integrative and multidisciplinary approach. Prevention, early detection, and clear treatment guidelines could be the best choice for every traumatized person as well as for the health care system.

Key words: posttraumatic stress disorder, traumatic experiences, diagnosis, pharmacotherapy, psychotherapy

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INTRODUCTION

The earliest records of humanity mention traumatic events and their consequences. In Gilgamesh (The Epic of Gilgamesh), the first great epic in the history of the human race, a vivid description of post-traumatic symptoms is given, suggesting that they are part of the fundamental human experience. Freud linked neurosis to trauma, describing the concept of traumatic neurosis in his early works (1). In the First and Second World War, disorders caused by stress, i.e., trauma, were described as "battle fatigue," "shock from shelling," "soldier's heart," and "survival guilt" (2). Contrary to literature, psychiatry has long had an ambivalent attitude towards the idea that reality can profoundly and permanently change human biology and psychology (3).

Post-traumatic stress disorder (PTSD) first appeared as a separate entity and was introduced as a diagnosable psychiatric disorder in the third edition of the Diagnostic and Statistical Manual of Mental Disorders - DSM-III (4) classification, following the knowledge of profound psychological effects of the Vietnam War (5) and concurrent studies on rape victims. It belonged to the group of anxiety disorders. In the International Classification of Disease (ICD-10) (6), it was introduced in the group of "Neurotic, stress-related, and somatoform disorders," in the category of "Reactions to severe stress and adjustment disorders." PTSD continues to attract debate, and it has experienced significant changes through the latest revisions.

Different kinds of traumas are unfortunately inevitable and frequently occurring in the contemporary world, with potentially devastating psychosocial consequences (7). Around the world, more than 50% of the general population experiences a traumatic event in their lifetime with the potential to develop PTSD, but most people experience multiple potentially traumatic events (8). About 3-7% of the adult population develops PTSD at least once in their lifetime (9). The lifetime prevalence of this disorder ranges between 1.9% (10) and 8.8% (11), but these rates are higher in post-conflict regions (12, 13). The incidence of PTSD after a traumatic experience is highly variable and can range from 0% to 100% (14). Therefore, not all individuals develop PTSD after facing trauma; a large number of people show a huge capacity and psychological resilience to recover after being exposed to trauma (15). Nevertheless, individuals also differ in flexible adaptation and effective coping with stress and trauma (16). A great number of potential risk and recovery factors are described, but determining why some individuals exposed to traumatic events develop PTSD and others do not is still a challenge (17). Comorbidity of PTSD and other mental disorders is almost a rule, but patients with PTSD have an increased risk of somatic disease (18, 19). Comorbid PTSD and depression are prevalent and are characterized by more psychological distress, with a high level of suicidality and poorer quality of life (20). PTSD is extraordinarily costly; it is one of the top psychiatric disorders that make sufferers use services of healthcare system, and its economic costs are among the highest (21).

DIAGNOSIS AND CLASSIFICATION

Diagnostic criteria for PTSD have some divergence between DSM-5 (22), ICD-10 (6) and ICD-11 (23), but for all three versions of classification systems, key inclusion criteria are exposure to a major traumatic event and characteristic symptoms including re-experiencing, avoidance, and an increased sense of threat. DSM-5 has broadened the definition of PTSD and classified it in the group of "Trauma and stressor-related disorders", which also contains Acute Stress Disorder (ASD), Adjustment disorder, Reactive attachment disorder (RAD) (applied only in children), Disinhibited social engagement disorder (DSED) (applied only in children), Other specified trauma and stressor-related disorder and Unspecified trauma and stressor-related disorder. Furthermore, DSM-5 does not divide into acute and chronic PTSD anymore and it incorporates a new symptom cluster of "altered cognitions and mood associated with a traumatic event". DSM-5 classification lists 20 symptoms, out of which there have to be at least six from four clusters (re-experiencing, avoidance, negative alterations in cognition and mood, and altered arousal) **(Table 1)**.

ICD-11 classification defines PTSD as primarily fear-based and classifies it in the group of "Disorders Specifically Associated with Stress" and its diagnosis requires three symptoms which include re-experiencing, avoidance and persistent perception of heightened threat (Table 1). Main differences between ICD-11 and ICD-10 include the fact that Acute Stress Reaction is not a mental disorder anymore and the fact that ICD-11 has included a new diagnosis, complex post-traumatic stress disorder (CPTSD). Complex PTSD is related to individuals who experienced one or more events that are extremely threatening or horrific in nature, which re difficult or impossible to escape from (24). The diagnosis of complex PTSD requires the presence of all three main symptoms of PTSD – re-expe-

Table 1. Comparison of diagnostic criteria DSM-5 and ICD-11 for post-traumatic stress disorder (PTSD)

DSM-5 criteria (APA, 2013)	*ICD-11 criteria (WHO, 2018)*
Intrusion symptoms	**Intrusion symptoms**
Avoidance	**Avoidance**
Negative alterations in cognition and mood	*Not applicable*
Alterations in arousal and reactivity	**Alterations in arousal and reactivity**
Not applicable	**Additional criteria for complex PTSD**

riencing, avoidance, sense of threat, as well as functional impairment. In addition, complex PTSD is characterized by severe and persistent problems in affect regulation, a negative self-concept which includes believing oneself to be diminished, defeated or worthless, and disturbed relationships, i.e., difficulties in sustaining relationships and in feeling close to others (25, 26). The type of trauma is a risk factor, not a requirement for the diagnosis of CPTSD. The need for a complex PTSD diagnosis has arisen from the existence of clinical presentations of symptomatology that extend beyond those described by the ICD-10 diagnosis of PTSD, particularly among individuals who experienced extreme, prolonged or multiple forms of trauma, and which have been reported by clinicians and researchers over several decades (27). CPTSD acknowledges pervasive symptoms that may result from experiencing chronic, prolonged traumatic events and finally, CPTSD is a distinct diagnosis and not a subtype of PTSD (23).

PREVENTION AND TREATMENT

A universal prevention strategy that would be applied to the entire population and used for individual prevention is under consideration. A variety of public health approaches to preventing traumatic events and providing psychoeducational messages through media to unselected populations both pre- and post-incident to anyone exposed to a particular traumatic event would be an example of a universal approach (28). Individual prevention strategies should be designed to prevent the onset of PTSD in individuals who do not meet ICD or DSM criteria but exhibit early symptoms. A various range of psychosocial approaches have been evaluated to prevent the development of PTSD. The latest evidence confirms and emphasizes the effectiveness of trauma-focused cognitive-behavioral therapy (CBT-TF), cognitive therapy and rapid eye movement desensitization and reprocessing therapy (EMDR), for the early treatment of people with PTSD symptoms in the first three months after the traumatic event (29-31). It has been concluded that it is more important to detect and treat people with significant symptoms than to prepare a package of general preventive measures (28). Debriefing trauma victims is strongly discouraged, both in individual and group sessions (30, 32, 33). The evidence of early pharmacological interventions in the prevention of PTSD is limited (34). Available data are inconsistent with the effectiveness of different pharmacological agents, including hydrocortisone, benzodiazepines, beta-blocker propranolol or selective serotonin reuptake inhibitor (SSRI) therapy (35-38). The evidence to support routine intervention after traumatic events involving many people (for example, terrorist attacks and natural disasters) is lacking. Consensus guidelines recommend supportive, practical, and pragmatic input but the avoidance of formal clinical interventions unless indicated.

Educational and organising preventive programs and interventions for traumatized people at the individual level, as well as at the collective level are necessary (39). It has been suggested that intervention right after the exposure to a traumatic event could be most efficient in preventing or attenuating a pathological response to stress-response disorders such as PTSD (16). Early interventions following traumatic events represent a heterogeneous group of approaches which include pharmacological interventions applied within a few hours of the traumatic event as well as early psychosocial assistance such as a single session psychological intervention for everybody involved within a month after traumatic events (40). Post-traumatic therapy is initially aimed at self-regulation and establishing control, the sense of security and predictability, and at taking engagement in an adaptive situation. Furthermore, it is aimed at controlling and managing physiological and biological stress reactions and finally at re-establishing secure social bonds and interpersonal effectiveness (41). The intervention focuses on improving coping skills, developing new coping strategies, considering changing the appraisal, improving personal resiliency, and obtaining social support from others, which can result in a reduction in negative consequences of stress such as PTSD (7).

Psychotherapy is the first line of choice in the treatment of PTSD, which has shown its unequivocal effectiveness, although some meta-analyses suggest that it is less effective than pharmacotherapy, especially in comorbidity with depression (42). According to the guidelines of the American Psychiatric Association (43), as well as the guidelines of the British Association for Psychopharmacology (44), pharmacotherapy and psychotherapy are the first line of choice. On the other hand, the National Institute for Clinical Excellence (30), the International Society for Traumatic Stress (29), as well as the Department of Defense for Veterans Affairs (45) claim that trauma-focus psychotherapy is more effective than pharmacotherapy.

Clinical guidelines based on evidence from systematic reviews and meta-analyses recommend trauma-focused psychological therapies (33, 46-48). Individual CBT with a focus on trauma, eye movement desensitization and reprocessing, as well as exposure therapy have been efficient **(Table 2)**.

Table 2. Psychotherapy approaches to posttraumatic stress disorder (PTSD)

Trauma-focused psychological therapies
Exposure therapy
Trauma focused cognitive therapy
Eye movement desensitization and reprocessing (EMDR)
Non-trauma-focused psychological therapies
Relaxation
Stress inoculation therapy
Interpersonal therapy

All trauma-focused psychotherapies have common components and common goals. They include imagined re-exposure to the event and exposure to real-life triggering cues typically avoided and all of them promote re-exposure to avoided memories, process emotional responses and correct cognitive distortions. Non-trauma-focus CBT – including relaxation training, stress inoculation therapy, self-regulation, interpersonal therapy, positive thinking – has been shown to have similar efficacy to trauma-focused CBT and EMDR immediately after treatment, but it does not remain so during follow-up (49). Non-trauma-focus CBT could be a valid substitution to trauma-focus therapy if trauma-focus is contraindicated or unavailable. Evidence suggests that phased approaches may be useful for more complex presentations of PTSD, but there is not enough research evidence (27). Stage-based approaches target specific problems such as dysregulation, dissociation, somatic symptoms to promote adaptive coping, a sense of safety and stabilization before undertaking any trauma-focused intervention (50).

Despite current guideline recommendations for first-line psychotherapy, pharmacotherapy is still often used as first-line treatment for PTSD. There is strong research evidence to support pharmacological treatment of post-traumatic stress disorder (PTSD) as a second line of trauma-focused psychological interventions. Results of meta-analyses as well as various guidelines recommend selective serotonin reuptake inhibitors (SSRIs) as a group and venlafaxine as first-line pharmacological treatments for PTSD (29,30,48,51,52) **(Table 3)**.

Table 3. Pharmacotherapy for posttraumatic stress disorder (PTSD)

First line
Fluoxetine, Paroxetine, Sertraline, Venlafaxine
Second line
Antipsychotics as a monotherapy (if antidepressant is not tolerated)
SSRI/SNRI + Antipsychotics (risperidone, olanzapine, quetiapine)
Mirtazapine – Augmentation for specific presentations, e.g., insomnia
SSRI/SNRI + Prazosin – The evidence is for augmentation versus monotherapy
Third line
Amitriptyline and Phenelzine
Mood stabilizers: carbamazepine, lamotrigine, gabapentin, topiramate, tiagabine, levetiracetam

There are still only 2 drugs approved by the US Food and Drug Administration for the treatment of PTSD: paroxetine and sertraline. The second line of pharmacological treatment of PTSD is represented by antipsychotics – risperidone, olanzapine, quetiapine (22, 33, 44, 52). Also, alpha-1 antagonist prazosin, as well as alpha-2A antagonist guanfacine, have been shown to be effective in the treatment of PTSD (53). Prazosin in combination with atypical antipsychotics has shown some efficacy in therapy-resistant patients with PTSD (54), while a growing number of recent studies show its efficacy in the treatment of nightmares (55, 56). Atypical antipsychotics as a second-line therapy can be given as monotherapy, if antidepressants are not tolerated, or as adjuvant therapy for refractory patients who have not had a favorable therapeutic response to SSRIs/SNRIs. These drugs are commonly prescribed to improve dissociation, hyperactivity, paranoia, psychosis, irritability, and aggression. The last step is to consider drugs from other classes with less evidence of effect, the occurrence of side effects, as well as insufficient clinical experience on their use. Thus, the third-line therapy could include amitriptyline or phenelzine, mood stabilizers such as carbamazepine, lamotrigine, gabapentin, topiramate, tiagabine, levetiracetam (48, 57). The increasing importance of the glutamatergic and GABA-ergic effects of anticonvulsants, as well as the discovery of abnormalities in these two systems among PTSD patients, has increased the level of interest in this class of drugs (58, 59). All anticonvulsants block sensitization and the so-called "kindling", although their mechanisms of action are different. From this class, medications that have shown their effectiveness are: carbamazepine, lamotrigine, gabapentin, topiramate, tiagabine, and levetiracetam (48). Benzodiazepines are strongly not recommended for the treatment of PTSD, as they showed not only ineffectiveness, but also worsening of symptoms in patients with PTSD (60).

There is some evidence that certain self-help programs, neurofeedback and yoga may be useful in alleviating PTSD symptoms (61-63). Acupuncture has been shown to be effective in patients who were waiting for CBT (64). Symptom-oriented hypnotherapy, transcendental meditation and breathing exercises have proven to be effective in a small number of cases (65). Australian guidelines support physical exercise in promoting general well-being (33).

CONCLUSION

Posttraumatic stress disorder (PTSD) is a complex condition, a multiclausal phenomenon that causes immense suffering for millions of people worldwide. This serious disorder does not strictly develop only in individuals affected by war or natural disasters; PTSD has been recognized as a much more pervasive problem that can affect literally any human being. The consequences could be devastating for individuals, as well as for healthcare systems, with significant costs. Understanding the nature of trauma, how and why the exposure to certain stressors causes psychological trauma, and how and in whom this leads to disabling disorder of PTSD, is an essential challenge. It is necessary to improve personal resilience, implement appropriate prevention, apply early diagnostics, as well as establish clear treatment guidelines with newer and novel therapeutic interventions.

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POSTTRAUMATSKI STRESNI POREMEĆAJ – PREGLED NOVINA U DIJAGNOSTIČKIM I TERAPIJSKIM PRISTUPIMA

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Sažetak

Posttraumatski stresni poremećaj (PTSP) je kompleksno stanje, uobičajen i onesposobljavajući psihijatrijski poremećaj koji uzrokuje neprocenjivu patnju milionima ljudi. Povezuje se sa visokom stopom funkcionalnih oštećenja, somatskim tegobama, rizikom od suicida i komorbidnih psihijatrijskih poremećaja, kao i sa dodatnim troškovima vezanim za zdravstveni sistem. Postavljanje dijagnoze PTSP-a zahteva dokaz o izloženosti traumi, a karakteriše se simptomima ponovnog doživljavanja traume, izbegavanja i promenama u pobuđenosti i reaktivnosti. Američki sistem klasifikacije dodao je još jedan klaster simptoma koji se odnose na promene u kogniciji i raspoloženju u vezi sa traumom, dok je u evropski sistem klasifikacije dodat složeni PTSP kao nova dijagnoza. Nema dokaza koji podržavaju bilo koju intervenciju kao univerzalnu strategiju prevencije. KBT-TF (usmeren na traumu), KBT i EMDR su pokazali pozitivan efekat. Psihoterapija je prva terapija izbora u lečenju izbora PTSP-a. Preporučuju se intervencije sa fokusom na traumu: KBT-TF, PE i EMDR, kao i terapija upravljanja stresom. Farmakoterapijski pristupi treba da počnu sa jednom od opcija prve linije koja uključuje SSRI kao što su fluoksetin, paroksetin ili sertralin, ili SNRI venlafaksin. Istraživanja koja procenjuju kombinovane psihološke i farmakološke tretmane PTSP-a su ograničena i zahtevaju dalje proučavanje, ali određeni oblici PTSP-a zahtevaju integrativni i multidisciplinarni pristup. Prevencija, rano otkivanje i jasne smernice za lečenje mogu biti najbolji izbor za svaku traumatizovanu osobu, kao i za zdravstveni sistem.

Ključne reči: posttraumatski stresni poremećaj, traumatska iskustva, dijagnoza, farmakoterapija, psihoterapija

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