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Abstract

Post-traumatic stress disorder (PTSD) is a complex mental disorder with psychological and emotional components, caused by exposure to single or repeated extreme traumatic events found in war, terrorist attacks, natural or man-caused disasters, and by violent personal assaults and accidents. In recent years, armed conflicts in the Middle East have resulted in high rates of exposure to traumatic events. Despite the increasing demand of mental health care provision, ongoing violence limits conventional approaches of mental health care provision. Internet-based interventions for post traumatic stress disorder (PTSD) have proved feasible and effective in Western countries, but their applicability and efficacy in war and conflict regions remains unknown. Despite clinical studies and improved understanding of the mechanisms of cellular damage, prevention and treatment strategies for patients with PTSD remain unsatisfactory. Post traumatic stress disorder is a prevalent mental health problem associated with substantial psychiatric morbidity. To develop an improved plan for treating and impeding progression of PTSD, it is important to identify underlying biochemical changes that may play key role in the initiation and progression of these disorders.

Keywords: Post-Traumatic Stress Disorder (PTSD); Epidemiology; Diagnosis; CBT; EMDR.

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Introduction

During the last 30 years, there has been a substantial increase in the study of post traumatic stress disorder (PTSD). Post-traumatic stress disorder (PTSD) is a complex disorder which is caused by exposure to single or repeated traumatic events such as those found in war, terrorism, in natural or human-caused disasters, and in violent personal assaults, such as rape, mugging, domestic violence and accidents [1]. Individuals with PTSD have persistent fear memory and often feel emotionally numb. If left untreated, PTSD can be life-threatening, as it is often linked with substance abuse and severe depression. In recent decades, war and human rights violations in the Middle East have led to high rates of exposure to traumatic events and to a correspondingly high incidence of post traumatic stress disorder (PTSD) in the region [2]. With

the invasion of Iraq by the US-led coalition forces in 2002, exposure to traumatizing events increased dramatically, with suicide bombers killing significantly more civilians than coalition soldiers [3]. A study of 289,328 Iraq and Afghanistan veterans who were first-time users of Veterans Affairs (VA) health care between 2002 and 2008 showed that 22% of veterans were diagnosed with PTSD and 17% were diagnosed with depression [4, 5]. People with post-traumatic stress disorder (PTSD) often suffer from memory disturbances. In particular, previous studies suggest that PTSD patients perform atypically on tests of directed forgetting, which may be mediated by an altered emotional appraisal of the presented material [6]. PTSD process has emerged from recent studies of the “freeze” response or tonic immobility. Briefly, tonic immobility is an involuntary, reflexive state, characterized by apparent physical paralysis, muscular rigidity, and inability to vocalize. The freeze response is more complex in humans, however, as it may be triggered by symbolic events such as the perception that a situation is inescapable [7, 8]. Traumatic events, PTSD and psychosis appear to have several interactions. The presence of a comorbid PTSD has been found to have a negative impact on the course and prognosis of the psychotic disorder and the combination of psychosis and PTSD appears to be associated with poorer social functioning and greater risk of relapsing in psychosis [9-11]. Considering these findings and being aware that PTSD in general is associated with forms of non-effective coping, more abuse of alcohol and drugs, negative self esteem, negative expectations of other people, and a greater risk of exposure to future potentially traumatic events [12], it becomes clear that trauma exposure is associated with impairment and major health problems in patients with psychosis, creating a burden for both patients and society [13, 14]. Providing medical or mental health care in regions of war and ongoing violent conflict often puts mental health professionals at great risk. Very few studies have reported

on mental health care services provided for survivors of war in developing countries. Although their results have been encouraging, these approaches are available to only small numbers of people, are relatively costly, and require health professionals to be located on site [15, 16]. Internet-based delivery of psychotherapeutic interventions has become increasingly established in the Western world. In particular, interventions developed for patients with PTSD have been shown to produce significant reductions in PTSD symptoms and in associated psychopathology, such as depression and anxiety [17-22].

Epidemiology and Risk Factors

The wars in Iraq and Afghanistan have renewed attention to the mental health effects of deployment, including PTSD, and, as a result, there is a large amount of research on the prevalence of PTSD in service personnel who were deployed to these countries [23]. Ahmadi et al. studied 150 cases of CIVs and 156 healthy men in 2002. They showed that in the veteran group 30 cases (20%) had severe stress disorders, 87 cases (58%) moderate and 3 mild stress disorders [24]. Hashemian et al. conducted a cross sectional study on 153 habitants of three cities in the West Azarbaijan province of Iran in 2004. The characteristics of locations were as follows: Sardasht as a high intensity of both chemically and conventional warfare exposed town, Rabat as a non-chemically attached town and Oshnavieh, a town with lower intensity conventional warfare [25]. Posttraumatic stress disorder (PTSD) occurs in an estimated 8% of men and 20% of women who are exposed to traumatic events. PTSD is a trauma- and stress-related disorder associated with significant psychosocial morbidity, substance abuse, and other negative physical health outcomes [26]. Between 1986 and 2005, none of the 10,000 participants in randomized clinical trials for major mental disorders were American Indians and Alaska Natives [27]. Risk factors associated with progression to chronic PTSD are not well understood. Although there may be a genetic component in a small percentage of cases, environmental and biologic factors (e.g., poor psychosocial support, history of trauma, history of mental health problems) are also important risk factors [28]. Resiliency development and positive psychology programs have been emphasized for persons with high-risk professions, but there is no evidence that these programs prevent PTSD [29].

Clinical Features and Symptoms

The symptoms of PTSD include unwanted re-experiencing of the traumatic memory (flashbacks, nightmares, triggered emotional responses), passive and active avoidance of the experience (emotional numbing, avoidance of discussions about the traumatic event) [1]. Many of the other symptoms of PTSD, such as hyperarousal, avoidance, and numbing, overlap with other mental disorders, such as generalized anxiety disorder, panic disorder, and depression. Thus it is important to delineate whether the person is re-experiencing symptoms in relation to a traumatic event [30, 31]. When patients are repeatedly confronted with their feared memories and at the same time experience a feeling of safety, over time this procedure can lead to reduced anxiety and aversive behavior associated with the fear memory. This process is called fear extinction and substantial progress has been made to understand the underlying molecular mechanisms [32].

Etiology

PTSD is conceptualized as a failure of recovery caused in part by altered fear learning; i.e., the failure to extinguish behavioral responses to stimuli associated with the trauma [33]. Following a trauma, the symptoms of PTSD are almost universal; however, many people are able to eventually confront fearful stimuli such as memories, reminders, or visual cues with a gradual decrease of fear [34, 35]. When this decrease does not occur, people tend to develop cognitive and avoidance strategies in an attempt to avoid distressing emotions. Subsequently, these strategies interfere with the extinction of fear by limiting exposure to safe reminders. Alterations in fear learning involve the hippocampus, amygdala, and prefrontal cortex. The hippocampus appears to be involved in the ability to recall safe episodes when faced with fearful stimuli. Research has shown that hippocampal volumes are decreased in patients with PTSD, but this may be a risk factor rather than a sequella [36, 37].

Causes

Genes: Currently, many scientists are focusing on genes that play a role in creating fear memories. Understanding how fear memories are created may help to refine or find new interventions for reducing the symptoms of PTSD [38]. For example, PTSD researchers have pinpointed genes that make: Stathmin, a protein needed to form fear memories. In one study, mice that did not make stathmin were less likely than normal mice to “freeze,” a natural, protective response to danger, after being exposed to a fearful experience. They also showed less innate fear by exploring open spaces more willingly than normal mice. GRP (gastrin releasing peptide) a signaling chemical in the brain released during emotional events. In mice, GRP seems to help control the fear response, and lack of GRP may lead to the creation of greater and more lasting memories of fear. Researchers have also found a version of the 5HTTLPR gene, which controls levels of serotonin—a brain chemical related to mood that appears to fuel the fear response. Like other mental disorders, it is likely that many genes with small effects are at work in PTSD [39, 40].

Brain Areas: Studying parts of the brain involved in dealing with fear and stress also helps researchers to better understand possible causes of PTSD. One such brain structure is the amygdala, known for its role in emotion, learning, and memory. The amygdala appears to be active in fear acquisition, or learning to fear an event (such as touching a hot stove), as well as in the early stages of fear extinction, or learning not to fear [41]. Storing extinction memories and dampening the original fear response appears to involve the prefrontal cortex (PFC) area of the brain, involved in tasks such as decision making, problem solving, and judgment. Certain areas of the PFC play slightly different roles. For example, when it deems a source of stress controllable, the medial PFC suppresses the amygdala an alarm center deep in the brainstem and controls the stress response [42-44]. The ventromedial PFC helps sustain long term extinction of fearful memories, and the size of this brain area may affect its ability to do so [45]. Individual differences in these genes or brain areas may only set the stage for PTSD without actually causing symptoms. Environmental factors, such as childhood trauma, head injury, or a history of mental illness, may further increase a person's risk by affecting the early growth of the brain. Also, personality and cognitive factors, such as optimism and the tendency to view challenges in a

positive or negative way, as well as social factors, such as the availability and use of social support, appear to influence how people adjust to trauma. More research may show what combinations of these or perhaps other factors could be used someday to predict who will develop PTSD following a traumatic event [46].

Diagnosis

Assessment

The diagnosis of post traumatic stress disorder (PTSD), from its introduction into the psychiatric nosology in DSM-III to the latest edition DSM-IV, attests to the centrality of the stressor criterion in the definition of this disorder. The DSM-IV definition of the PTSD stressor is a clear departure from previous versions [47]. Various scales to measure the severity and frequency of PTSD symptoms exist. The Clinician-Administered PTSD Scale (CAPS-1) appears to satisfy these standards most uniformly [48]. Standardized screening tools such as Trauma Screening Questionnaire [49] and PTSD Symptom Scale [50] can be used to detect possible symptoms of post traumatic stress disorder and suggest the need for a formal diagnostic assessment.

DSM-5 Criteria for PTSD diagnosis

"A" stressor criterion specifies that a person has been exposed to a catastrophic event involving actual or threatened death or injury, or a threat to the physical integrity of him/herself or others (such as sexual violence). Indirect exposure includes learning about the violent or accidental death or perpetration of sexual violence to a loved one. Exposure through electronic media (e.g. televised images of the 9/11 attacks on the World Trade Center) is not considered a traumatic event. It is important to understand that one new feature of DSM-5 is that all of these symptoms must have had their onset or been significantly exacerbated after exposure to the traumatic event [51]. Specifies criteria for the diagnosis of post-traumatic stress disorder. These include [52]:

- Exposure to a traumatic event that involved actual or threatened death or injury (to self or others) or a threat to physical integrity,
- The person's response to the traumatic life event must have involved intense fear, helplessness, or horror,
- Persistent re-experiencing of the event (criteria specify that the person must have one or more of the re-experiencing symptoms),
- Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (three or more avoidance symptoms),
- Two or more persistent symptoms of arousal,
- Duration of symptoms must last more than one month, and
- Symptoms must cause clinically significant distress or impaired functioning.

Prevention

The first generation of research on PTSD prevention focused primarily on universal prevention (i.e., the delivery of interventions to all people exposed to trauma, regardless of symptoms or risk of developing PTSD). However, based on evidence that 1) debriefing interventions for all people exposed to particular traumas did not reduce PTSD and 2) most people exposed to trauma experience symptoms of PTSD but do not develop PTSD and its

attendant functional impairment, a new model of PTSD prevention, targeted prevention, has generated a second generation of PTSD prevention research. The goal of targeted prevention is to identify, from among all people exposed to trauma, those individuals who are at high risk of developing the disorder of PTSD and then intervene only with those at high risk [53].

Preclinical considerations suggest that treatment with a beta-adrenergic blocker following an acute psychologically traumatic event may reduce subsequent post traumatic stress disorder (PTSD) symptoms. Modest benefits have been seen from early access to cognitive behavioral therapy, as well as from some medications such as propranolol [54]. Critical incident stress management has been suggested as a means of preventing PTSD, but subsequent studies suggest the likelihood of its producing iatrogenic outcomes [55]. The World Health Organization recommends against the use of benzodiazepines and antidepressants in those having experienced trauma. Common practices in the aftermath of trauma such as debriefing and benzodiazepines need to be carefully considered, taking into account their potential harm to the spontaneous recovery process, and the trajectory of PTSD, and not only judging them according to their immediate (comforting) effects [56].

Treatments

The main treatments for post traumatic stress disorder (PTSD) are psychotherapy and medication. Traumatic events can be very difficult to come to terms with, but confronting your feelings and seeking professional help is often the only way of effectively treating PTSD. It is possible for PTSD to be successfully treated many years after the traumatic event occurred, which means it is never too late to seek help [46, 51, 57].

Assessment

Before having treatment for PTSD, a detailed assessment of your symptoms will be carried out to ensure treatment is tailored to your individual needs. Your GP will often carry out an initial assessment, but you will be referred to a mental health specialist for further assessment and treatment if you have had symptoms of PTSD for more than four weeks or your symptoms are severe [57]. There are a number of mental health specialists you may see if you have PTSD, such as: a psychologist an expert in how the mind works, a community psychiatric nurse a nurse who specializes in mental healthcare, a psychiatrist a mental health specialist who diagnosis and treats mental health conditions [46, 57].

Watchful waiting

If you have mild symptoms of PTSD, or you have had symptoms for less than four weeks, an approach called watchful waiting may be recommended. Watchful waiting involves carefully monitoring your symptoms to see whether they improve or get worse. It is sometimes recommended because 2 in every 3 people who develop problems after a traumatic experience will get better without treatment within a few weeks. If watchful waiting is recommended, you should have a follow up appointment within one month [46, 57].

Psychotherapy

If you have PTSD that requires treatment, psychotherapy is usu-

ally recommended first. A combination of psychotherapy and medication may be recommended If you have severe or persistent PTSD. Psychotherapy is a type of therapy often used to treat emotional problems and mental health conditions such as PTSD, depression, anxiety and obsessive compulsive disorder. The treatment is carried out by trained mental health professionals who will listen to you and help you come up with effective strategies to resolve your problems. The two main types of psychotherapy used to treat people with PTSD are described below [46, 52, 57].

Cognitive behavioural therapy (CBT)

Cognitive behavioural therapy (CBT) is a type of therapy that aims to help you manage your problems by changing how you think and act. Trauma focused CBT uses a range of psychological treatment techniques to help you come to terms with the traumatic event. For example, your therapist may ask you to confront your traumatic memories by thinking about your experience in detail. During this process your therapist will help you cope with any distress you feel, while identifying any unhelpful thoughts or misrepresentations you have about the experience. By doing this, your therapist can help you gain control of your fear and distress by changing the negative way you think about your experience, such as feeling that you are to blame for what happened or fear that it may happen again. You may also be encouraged to gradually restart any activities you have avoided since your experience, such as driving a car if you had an accident. You will usually have 812 weekly sessions of trauma focused CBT, although fewer may be needed if the treatment starts within one month of the traumatic event. Sessions where the trauma is discussed will last for around 90 minutes [46, 52, 57, 58].

Eye movement desensitization and reprocessing (EMDR)

Eye movement desensitization and reprocessing (EMDR) is a relatively new treatment (Figure: 1) that has been found to reduce the symptoms of PTSD. EMDR involves making side to side eye movements, usually by following the movement of your therapist's finger, while recalling the traumatic incident. It is not clear exactly how EMDR works, but it may help the malfunctioning part of the brain (the hippocampus) to process distressing memories and flashbacks so that their influence over your mind is reduced [46, 52, 57].

Medication

Antidepressants such as paroxetine, mirtazapine, amitriptyline or phenelzine are sometimes used to treat PTSD in adults. Of these medications, paroxetine is the only one licensed specifically for the treatment of PTSD. However, mirtazapine, amitriptyline and phenelzine have also been found to be effective and are often recommended as well [46, 52, 57]. However, these medications will only be used if:

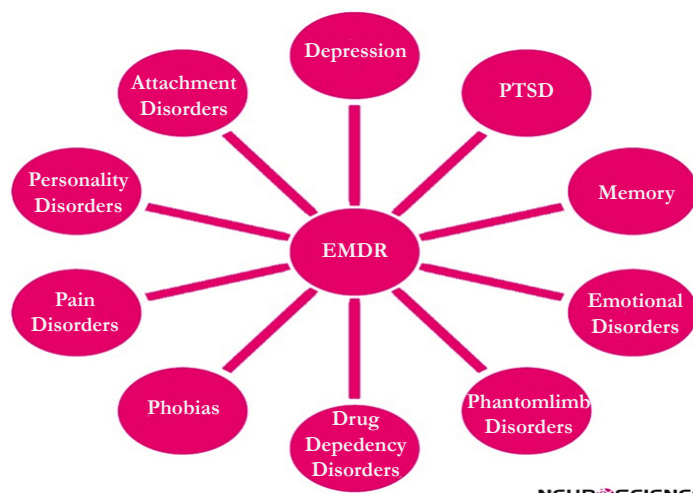
- You choose not to have trauma focused psychological treatment.
- Psychological treatment would not be effective because there is an ongoing threat of further trauma (such as domestic violence).
- You have gained little or no benefit from a course of trauma focused psychological treatment
- You have an underlying medical condition, such as severe depression, that significantly affects your ability to benefit from psychological treatment.

Amitriptyline or phenelzine will only be used under the supervision of a mental health specialist. Antidepressants can also be prescribed to reduce any associated symptoms of depression and anxiety and to help with sleeping problems. However, they are not usually prescribed for people younger than 18 unless recommended by a specialist. If medication for PTSD is effective, it will usually be continued for a minimum of 12 months before being gradually withdrawn over the course of four weeks or longer. If a medication is ineffective at reducing your symptoms, your dosage may be increased. Before prescribing a medication, your doctor should inform you about possible side effects that you may have while taking it, along with any possible withdrawal symptoms when the medication is withdrawn. For example, common side effects of paroxetine include feeling sick, blurred vision, constipation and diarrhoea. Possible withdrawal symptoms associated with paroxetine include sleep disturbances, intense dreams, anxiety and irritability [46, 52].

Children and young people

For children and young people with PTSD, trauma focused CBT is usually recommended. This will normally involve a course of 812 sessions that have been adapted to suit the child's age, circum-

Figure 1. Diseases treated by EMDR [59].



stances and level of development. Where appropriate, treatment will include consulting with and involving the child's family. Treatment with medication is not usually recommended for children and young people with PTSD [46]. Individual trauma-focused CBT is an effective treatment for PTSD in children and young people [60].

Discussion

The aim of this study was to investigate whether it is possible to produce significant and sustained reduction of post traumatic stress in participants living in an unstable conflict region using a brief Internet-delivered intervention. We observed significant reductions in post traumatic stress symptom severity in all symptom clusters, and the effect sizes were of a similar magnitude to those reported for Western samples using the same treatment protocol. In addition, the treatment had significant benefits with respect to symptoms of depression and anxiety and quality of life. Although many of the patients continued to experience difficulties in terms of exposure to life-threatening situations and severe human rights violations during the course of the treatment, they nevertheless benefited psychologically from the intervention.

Conclusions

The traumatized PTSD brain accumulates damage over time. Neurons in the hippocampus, amygdala and other parts of the brain are destroyed by glucocorticoids. Chemical imbalances and their corresponding effects (as well as the opposite effects) may occur. Adrenergics and glucocorticoids, along with serotonin and other moieties, affect immune, chemical and structural responses to produce short- and long-term effects that we recognize as sequelae of PTSD. In a naturalistic study we observed a significant reduction in PTSD scores and functional impairment following treatment. These improvements were maintained at 6 month follow-up. It may be helpful to take a closer look at combining individual trauma-focused cognitive behaviour therapy and group sessions when treating veterans with PTSD.

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