CHAPTER 11.

POSTTRAUMATIC STRESS DISORDER

The most recent edition (5th) of the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association includes a new chapter: Trauma and Stress-Related Disorders.

Exposure to a traumatic or stressful event is the trigger of all the listed disorders. Posttraumatic stress disorder (PTSD) is the most prominent and will be discussed in detail. Others include Acute stress disorder and Adjustment disorder, but these will not be discussed.

Reactions to stress

Immediately following traumatic events, most (95%) exposed survivors experience some mental distress (Norris et al, 2003). Thus, in the early stages, some psychological distress is "normal".

ICD-10 describes "a mixed and usually changing picture" including, "daze, depression, anxiety, anger, despair, over-activity, and withdrawal may be seen, but no one type of symptom predominates for long".

In the following days, these initial responses may be replaced by symptoms resembling PTSD.

On the spectrum of responses to trauma, on which "normal" or non-pathological distress is at one end and PTSD is at the other, two other conditions can also be located: Acute stress disorder and Adjustment disorder.

Views of PTSD

PTSD is an accepted as a psychiatric disorder. It 'makes sense,' and 'treatment' is an expectation of the general public.

An opposing view held by some social commentators and health professionals is that PTSD is greatly over diagnosed and that most treatments are unnecessary and ineffective.

The majority view will be given in detail. Brief mention will then be made of some dissenting views.

THE MAJORITY VIEW

Introduction

Plato described melancholia (major depressive disorder), mania, and dementia more than 2000 years ago. There is debate about when schizophrenia was first described, but it was probably more than two centuries ago. It is surprising then, that PTSD was first accepted as a legitimate mental disorder only a few decades ago.

The current author (Pridmore, 2011, 2014) has identified ancient proverbs (some perhaps 1000 years old) which describe the triggering of memories and the re-experiencing of trauma. One states that, the individual having been bitten by a snake, is afraid of a rope laying on the ground. They suggest PTSD has a long human history.

Dr. Jacob Da Costa described veterans who developed a rapid heart rate, having participated in the American Civil War (1861-1865). This condition was attributed to war service, and was known as "Da Costa's heart" - the role of the brain/psychology was not recognized. In World War One (1914-1918) what would now be called PTSD was known as "Shell shock". The brain was thought to be involved, and one theory was that powerful explosions propelled metal fragments so small that they could not be seen, into the head. In World War Two (1939-1945) this disorder was called "War neurosis", and psychological factors were recognized. In the Vietnam War (1965-1973), PTSD was described in Western veterans, and it was first included in the DSM-III in 1980.

PTSD has been described in many cultures: Kalahari Tribesmen, Cambodian, Kosovo, Bosnian, Iraqi and Kurdish refugees, Ugandan child soldiers, Mexican bus accident survivors, Singaporean victims of child sexual abuse, Japanese cancer survivors, and Bam (Iran) earthquake survivors, among many others.

The prevalence of PTSD varies form one country to another; from 3.3% in Australia (McLennan, 1997) to 11% in Mexico (Norris et al, 2003). This may reflect different research methodology, differences in risk of exposure to trauma, or cultural factors.

How a disorder with a prevalence of 3.3% remained unrecognized until 1980 is a mystery. Part of the answer is probably that in earlier times, PTSD was subsumed under different disorders, predominantly anxiety, major depression, and substance abuse. Another part of the answer is probably recent changes in societal attitudes. Until the change to the "caring society", of the present time, individuals anticipated adversity and were expected to shoulder their difficulties without complaint.

The diagnosis

In summary, the individual must have been exposed to a **severe event** (life threatening or similar) and there must be **intrusive symptoms**, **avoidance** of reminders, negative **alterations in cognitions and mood**, and alterations in the **level of arousal**.

DSM-5 PTSD criteria

A) Exposure to actual or threatened death, serious injury or sexual violence in one of the following ways:
   1) Directly experiencing the traumatic event
   2) Witnessing, in person, the event as it occurred to others
   3) Learning that the event occurred to a close family member or close friend
   4) Experiencing repeated or extreme exposure to aversive details of the events (e.g., first responders collecting human remains)

B) Presence of one or more of the following intrusion symptoms associated with the event:
   1) recurrent and intrusive distressing memories of the event
   2) recurrent distressing dreams of the event
   3) dissociative reactions (e.g., flashbacks) in which the individuals feels or acts as if the traumatic event was recurring
   4) intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
   5) physiological reactions to internal or external cues that symbolize or resemble and aspect of the traumatic event

C) Persistent avoidance of stimuli associated with the trauma:
   1) efforts to avoid thoughts, feelings, or conversations associated with the trauma
   2) efforts to avoid external reminders (activities, places, or people) that arouse distressing memories, feeling etc. associated with the trauma

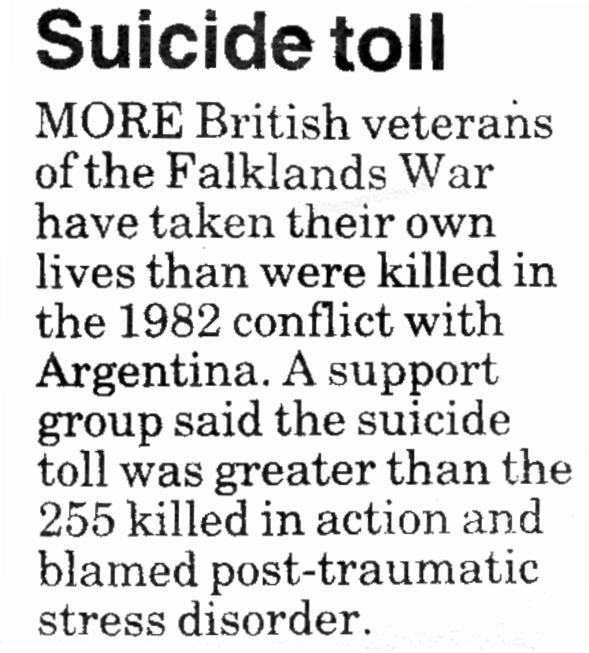
D) Negative alterations in cognitions and mood associated with the trauma
   1) inability to recall an important aspect of the trauma
   2) negative beliefs or expectations about oneself, others, or the world
   3) distorted cognitions about the cause or consequence of the trauma
   4) persistent negative emotional state (fear, horror, anger, guilt, or shame)
   5) diminished interest or participation in significant activities
   6) feelings of detachment or estrangement from others
   7) inability to experience positive emotions (happiness, satisfaction, loving feelings)

E) Marked alterations in arousal and reactivity associated with the event
   1) irritable behavior and angry outbursts with little provocation
   2) reckless or self-destructive behavior
   3) hypervigilance
   4) exaggerated startle response
   5) problems with concentration
   6) sleep disturbance

F) Duration of disturbance (B-E) more than 1 month
G) Disturbance causes significant distress and impaired function

Suicide

PTSD is associated with suicidal behavior, but the relationship is not simple. The elevated suicide rate among war veterans may reflect protracted PTSD, life stressors, alienation and alcohol use.



Suicide toll

MORE British veterans of the Falklands War have taken their own lives than were killed in the 1982 conflict with Argentina. A support group said the suicide toll was greater than the 255 killed in action and blamed post-traumatic stress disorder.

Illustration. The term PTSD is loosely applied by lay people and pressure groups. It is unlikely that all the suicides of the British Falklands War veterans can be attributed to PTSD, but it was doubtless a factor in some.

Risk and natural history

More than 70% of adults worldwide experience trauma (Benjet et al, 2016), however, the overall lifetime prevalence for PTSD is 7-12%. This indicates there are individual differences in susceptibility to the disorder (Mehta and Binder, 2011).

Women are at greater risk. Breslau, et al (1999) found the risk of developing PTSD after any kind of trauma is 13% for women and 6% for men. Younger people, the socially disadvantaged and those with a history of childhood trauma are also at greater risk (Shalev et al, 2017). The intensity of trauma is also an important factor.

Family and twin studies show a genetic vulnerability for PTSD, and 30-40% of the variance is related to a heritable component (Almili et al, 2014).

Among soldiers (Seifert et al, 2011) and civilians (Breslau et al, 2013), a history of childhood abuse is a risk factor for developing PTSD.

Various studies show around 50% of cases remit by 6 months, and about 75% remit by one year. One year after severe trauma, PTSD will be present in 10-15% of survivors.

There have been claims that some individuals do not develop PTSD until years after the trauma. One study (North et al, 2003) found 98% presented in the first month. The ICD-10 states that, in general, the condition should not be diagnosed if the onset is more than 6 months after a traumatic event. However, delayed onset PTSD is reported (Andrews et al, 2007).

While the symptoms of PTSD frequently resolve over time, established, chronic PTSD, is a serious disorder, causing much suffering for the individual, destroying marriages, and sometimes ending in suicide. PTSD may result in large financial compensations.

Cultural factors may impact on risk. The rate of PTSD for soldiers who served in Iraq and Afghanistan is 1.6-6% for UK forces and two to three times higher in the US forces (Sundin et al 2011).

In a study of cultural factors in Hainan (China), the severity of PTSD symptoms and serum cytokine and cortisol levels in 30 PTSD patients of Li ethnicity and 30 PTSD patients from Han ethnicity (Tao et al, 2014). Li is a disadvantaged ethnic group with low income and education, exposed to discrimination. Their cultural beliefs and practices result in great distress being caused by sudden events. Hainan was hit by a major earthquake in 2008.

Subsequently, patients of Li ethnicity scored significantly higher than patients of Han ethnicity on PTSD symptoms. They also scored significantly higher than patients on Han ethnicity on serum levels of interleukin 2 (IL-2), IL-6, IL-8, tumor necrosis factor alpha (TNF-a) and cortisol.

Prediction

Risk factors are listed above.

It was thought that the severity of the acute stress reactions, and perhaps certain early symptoms, might predict PTSD - studies have not supported these ideas (Bryant, 2003).

Surprisingly, there is some evidence suggesting that most of those who develop PTSD have not had severe acute reactions (Wolfe et al, 2003).

There is some evidence to indicate that the belief (at the time of the trauma) that one is about to die, may predict PTSD (Voges & Romney, 2003).

The severity of the traumatic event has some value as a predictor, with events such as torture and sexual assault having higher potency than motor vehicle accidents and severe illness. However, there is no standardized means of grading the severity trauma. Also,

some people survive what appears to be very severe trauma without developing symptoms, while others have developed convincing PTSD following much less severe episodes. Thus, individual factors influence vulnerability.

Contrary to expectations, soldiers who were attacked but did not shot at the enemy, have less severe symptoms than those who have returned fire (McLay et al, 2014)

With respect to soldiers, nightmares before deployment indicate and increase risk for PTSD (Van Liempt, et al, 2013).

Also – pre-trauma immune hyperactivation may be a predictor or risk (Eraly et al, 2014).

PATHOPHYSIOLOGY

The pathophysiology of PTSD is not fully understood. Various systems/structures are involved, including but not limited to: 1) stress/endocrine factors, 2) brain structure factors, 3) genetic factors, 4) epigenetic factors, 5) immunological factors, 6) other factors. How these influence each other is also incompletely understood.

Stress/endocrine factors

The hypothalamic-pituitary-adrenal (HPA) axis is of central importance in homeostasis. Stress triggers release of corticotrophin-releasing factor (CRF) from the hypothalamus; ACTH released from the pituitary, in turn, triggers the release of cortisol from the adrenal glands. In a negative feed-back loop, elevated levels of cortisol act on the brain to reduce the release of ACTH and cortisol. CRF plays a key role in modulating the autonomic, immune and behavioral effects of stress.

Cortisol prepares the individual to respond to sudden stress. Additionally, activation of the glucocorticoid receptor (GR) regulates availability of brain derived neurotropic factor (BDNF) – a crucial factor for neural plasticity. Hence, stress induces neuroplastic changes, which include the formation of long-lasting memories (Deppermann et al, 2014).

Negative feed-back (to reduce cortisol levels) activates GRs in the hippocampus and medial prefrontal cortex. However, high levels of cortisol over sustained periods may damage these structures, in which case positive-feedback is established and chronic high cortisol levels cause progressive damage the CNS.

In animal studies, stress is associated with reduced length and complexity of the dendrites of the pyramidal cells of region CA3 of the hippocampus (McKittrick et al, 2000), and the medial prefrontal cortex (Radley et al, 2004). In people with PTSD, structural abnormalities have been demonstrated in both of these regions (Nutt et al, 2004). The

startle reaction and flashbacks of PTSD may be related to failure of these regions to dampen an overactive amygdala.

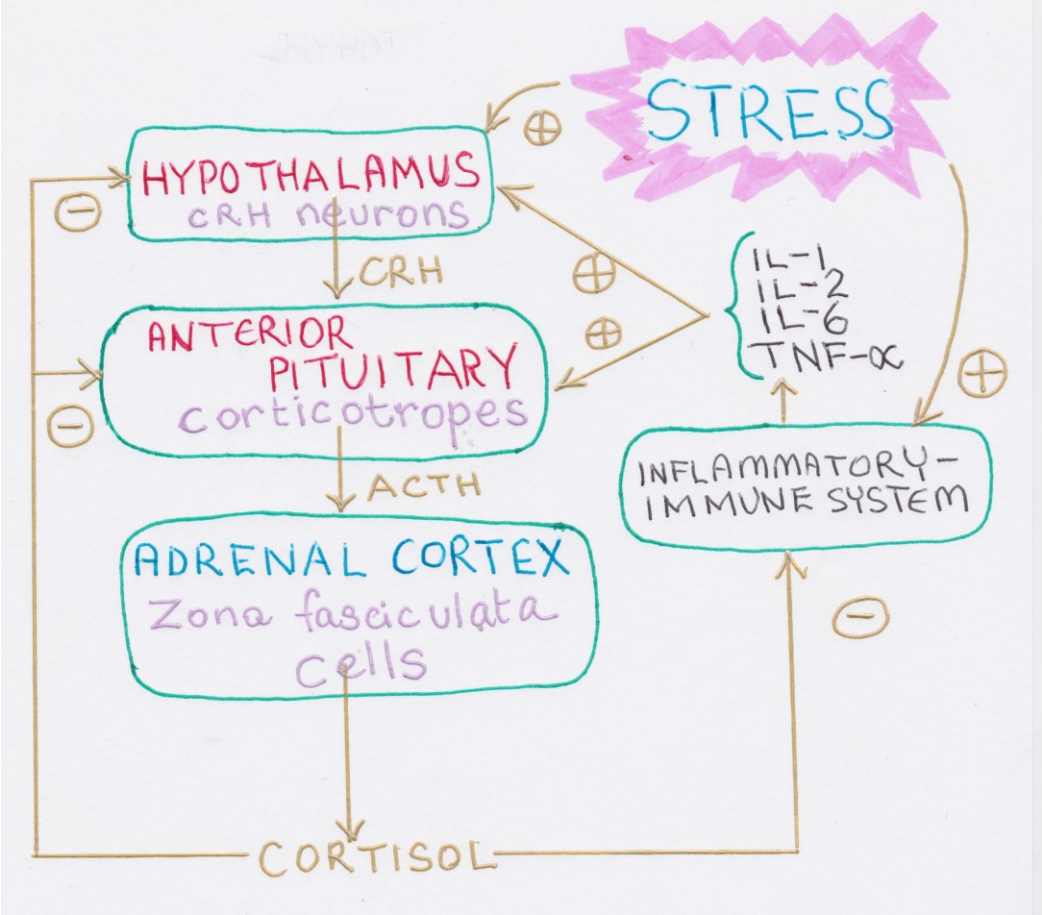


Illustration. Hypothalamic-pituitary-adrenal (HPA) axis and its relationship to stress and the inflammatory-immune system. Cortisol exerts a negative feedback control on the secretion of corticotropin-releasing hormone *(CRH)* and adrenocorticotropic hormone *(ACTH)*. Physiologic or psychological stress increases cortisol secretion directly through neural mechanisms or by activation of the inflammatory-immune system and production of cytokines, including interleukin-1 *(IL-1)*, interleukin-2 *(IL-2)*, interleukin-6 *(IL-6)*, and tumor necrosis factor-α *(TNF-α)*.

Immunological factors

Immunological factors are part of an interacted system. The above illustration provides information.

De Oliveira et al (2017) studied people at presentation with PTSD (and no depression). They found significant elevation of serumIL-6 and IL-10, and concluded there was early activation of the immune system, which could lead to neuroinflammation.

Other immunological system observations in PTSD:

1. Combat veterans with PTSD have a significantly increased risk for autoimmune disorders (O'Donovan et al, 2014).
2. Evidence of disorder associated low-grade inflammation (Gola et al, 2013)
3. Lower than normal levels of C-reactive protein (Spitzer et al, 2014).
4. Methylation of the promoter regions of the IL-18 gene (Rusiecki et al, 2013).
5. Methylation of the FKBP5 gene (FKBP5 is a protein with a role in immunoregulation) in combat veterans with PTSD decreases with psychotherapy induced recovery (Yehuda et al, 2013).
6. For a review see Wang et al (2017).

Genetics

30-40% of the risk for PTSD is heritable. As yet, not particular genes have been identified (Almili et al, 2014).

Epigenetics

Chapter 37 provides a detailed account of this subject. Epigenetics refers to the molecular mechanism by which environmental circumstances modify gene expression (without influencing the DNA sequence) to produce different phenotypes. Traumatic stress is a major environmental circumstance. Thus, there is a role for epigenetics in understanding, diagnosing and potentially even the treating PTSD.

The functional state of genes (whether they are physically available for transcription) is dictated by the tightness of the chromatin. Chromatin is DNA wound around histones 9 (protein) cores. The tightness of chromatin is influenced in particular by the attachment of methyl groups to DNA, and methyl, acetyl and other molecules to the tails of the histone proteins.

The influence of experience on gene expression is observed in the offspring of high quality nurturing rat mothers - their pups display significantly reduced levels of DNA methylation (Weaver et al, 2004). In a spectacular human study, McGowen et al (2009) demonstrated that DNA methylation led to decreased glucocorticoids receptors in the hippocampus of people who had been victims of childhood abuse.

As mentioned above under "Immunological factors", PTSD in combat veterans is associated with an increase in the methylation of the promoter regions of the IL-18 gene (Rusiecki et al, 2013) and the FKBP5 gene (Yehuda et al, 2013).

Imaging studies

In the largest-to-date meta-analysis of spontaneous neural activity in PTSD (Disner, et al, 2017) 5 regions of interest were identified: 1) left golbus pallidus, 2) left inferior parietal

lobule, 3) right lingual gyrus, 4) left amygdala, and 5) right caudate head. Thus, widespread pathology in PTSD is suggested by neuroimaging studies. The following paragraphs provide an account of findings as they developed over the life of the Download of Psychiatry.

Smaller hippocampal volumes predispose to PTSD (Gilbertson et al, 2002), and PTSD then causes further (secondary) hippocampal volume reductions (Felmingham et al, 2009).

A similar process (smaller structure predisposing to PTSD, followed by secondary size reductions) may also apply to the anterior cingulate (Kasai et al 2008).

PET studies (Shin et al, 2009) suggest an increased metabolic rate in the anterior cingulate may precede the onset of PTSD, which increases further, as a consequence of the disorder.

Geuze et al (2008) found that people with PTSD had reduced frontal and temporal cortical thickness and performed significantly less well on memory tasks. There was a correlation between cortical thickness and memory performance.

Sailer et al (2008) found people with PTSD displayed lower activation in the nucleus accumbens and medial PFC, which are both critical structures in the reward pathway. This suggested that people with PTSD may not experience the same intensity of reward as others, and this could be expected to impact on responses and behavior.

Falconer et al (2008) studied inhibition in PTSD. They found people with PTSD made more errors than a matched healthy sample on tests of inhibition, and the number of errors was directly related to the PTSD severity. Using fMRI, they also found that, in contrast with the healthy sample, which predominantly activated right brain structures during inhibitory tasks, people with PTSD predominantly activated left brain structures.

Zhang et al (2011) found people with PTSD had significantly decreased gray matter volume in left anterior hippocampus, left parahippocampal gyrus and bilateral calcarine cortex. And, PTSD severity was associated with gray matter density in the hippocampus and calcarine cortex.

Structural MRI studies of adults and children have evaluated volumetric alterations in PTSD. In adults hippocampal volumetric reduction has been repeatedly demonstrated, while in children and adolescents, the main finding is smaller medial and posterior portions of the corpus callosum. This may indicate that the neurobiological effects of stress vary with developmental stage (Jackowski et al, 2009).

Resting-state fMRI has demonstrated reduced functional connectivity between the middle prefrontal cortex, amygdala and hippocampus, and between the inferior orbitofrontal cortex and the hippocampus (Jin et al, 2013).

Sullivan et al (2013), using PET, demonstrated higher brainstem and forebrain serotonin-IA binding in PTSD.

Thus, exposure to severe stress results in structural and functional brain changes. In adults, there is evidence of reduced hippocampal volume, and thinning of frontal temporal and occipital cortex, and reduced functional connectivity between the frontal cortex and limbic structures. These changes have been associated with reduced cognition, altered inhibitory and reward functions, and PTSD symptoms in general.

Treatment of established PTSD

World Federation of Societies of Biological Psychiatry guidelines for the pharmacological treatment of PTSD (Bandelow et al, 2008) list the first line treatments as the SSRIs, the serotonin and noradrenalin reuptake inhibitors (SNRIs), and the calcium channel modulator pregabalin. But, positive findings are not universal. Drugs may not help the individual with all symptoms (they are often more helpful with intrusive thoughts). However, they frequently enable patients to participate in treatment plans and get on with their lives. Benzodiazepines and antipsychotic medications may have a place for non-specific symptoms.

Cognitive-behavior therapy (CBT) has been found helpful (Harvey & Bryant, 1998; Bandelow et al, 2008). Such treatment involves relaxation and stress management techniques, education and cognitive restructuring. The optimal length of a course of treatment is not yet clear; research studies usually involve 10 to 18 sessions. CBT needs to be tailored to the individual as there may be various complicating symptoms such as depression and survivor guilt.

Eye movement desensitization and reprocessing (EMDR) is a form of psychotherapy which has been extensively used in PTSD. While it has been available for decades, some debate continues regarding its usefulness. Pagani et al (2017) describe EMDR as of proven value.

Future treatments will almost certainly include using agents in the attempt to influence chromatin function – that is, to alter the epigenetic status of the individual.

Taking this thinking further, newly acquired memories are unstable initially, and then become ‘consolidated’. Retrieval of memories results in another period of instability, until they are ‘re-consolidated’. It is proposed that the periods of instability provide an opportunity for a therapeutic agent to treat persistent, unhelpful memories, as are found in PTSD and drug addiction. Such agents may target the epigenetic processes.

Maddox et al (2013) have shown that systemic administration of garcinol disrupts fear conditioning in mice, and suggest it may have a place in the treatment of PTSD in humans. Garcinol is a naturally-occurring agent which interferes with epigenetic modifications.

Prevention – "debriefing"

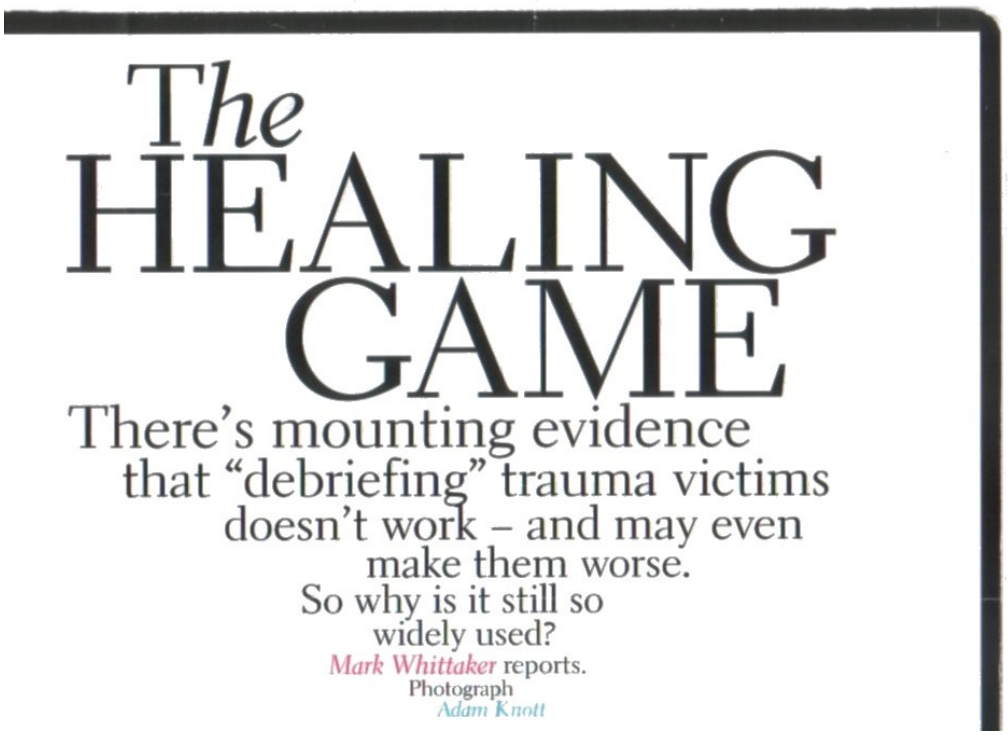


Illustration. Headline in the Weekend Australian Magazine, June 28-29, 2008. The story was critical of the popular (at the time) form of acute psychological treatment of people who have experienced traumatic events.

In 1983, the concept of "critical incident stress debriefing" was proposed as a method of preventing the adverse psychological consequences of trauma (Mitchell, 1983). In this approach, a single session of "debriefing" was provided, immediately after exposure to trauma. A central feature was ventilation, or unrestrained talking about the individual's experience. Debriefing was promoted as a simple and economical preventative technique. It became very popular and many mental health professionals, and even volunteers with no mental health training, were eager to be involved in this dramatic and apparently important work.

Debriefing grew in importance in public opinion. In some workplaces, employers provided compulsory debriefing (to prevent being sued at a later date, for having failed to take preventive action).

Some mental health professionals, however, believed single session debriefing, focusing on the reliving and verbalization about traumatic events to be a questionable "therapy".

In the period immediately after trauma, victims may experience a range of reactions. Some do not want to be involved in discussions, while for others, there is an irresistible outpouring of words and emotion. People seeking to assist victims must be well trained to recognize the different reactions. They must also be assisting for the benefit of the traumatized individuals, and not to gratify their own psychological needs.

Opponents of the debriefing industry have drawn an analogy with physical trauma. The argument is that if trauma results in a gash, the doctor does not keep poking his/her finger into the wound, asking if it still hurts. The doubters conclude that the debriefing industry has the potential to disturb the healing process. No metaphor is perfect and this one is perhaps less perfect than most. Nevertheless, some people do not want to talk about their trauma, they want to forget, and there is concern that compulsory debriefing could lead to unnecessary psychological scars (Zohar et al, 2009).

Controlled trials of debriefing indicate that debriefing was of no benefit (Sijbrandij et al, 2006) and may actually harm patients (Bisson et al, 1997; Mayou et al, 2000). Consequently, authorities have strongly recommended that debriefing should cease and that intervention should not be provided to unscreened populations (McFarlane, 2003).

Attention has been drawn to "social referencing" (Klinnert et al, 1986), the concept that the meaning children attach to events is greatly influenced by the reactions of those around them. Drawing attention to the frightening nature of traumatic events can be expected to inadvertently increase the risk of ongoing distress in children. This would be even more likely if conducted in group settings, which is one method by which debriefing was delivered.

"Caution is required in the immediate response to avoid revisiting the traumatic events through 'debriefing' as this may compound the trauma. Attention is directed instead to assisting people to recover with appropriate support and acknowledgement of loss and grief."

Australian and New Zealand College of Psychiatrists

Illustration. This media release of February 9, 2009, followed devastating bush-fires in Victoria (Australia) which cost 200 lives and great loss of property.

Prevention – preferred action

In the immediate aftermath of trauma, the most necessary and suitable assistance is social and practical support (Ehlers & Clark, 2000). Helpers should reinforce to survivors that they are now safe and the situation is under control. Survivors should be provided with food, shelter, transport and emotional support.

Education is recommended. People may benefit from being informed about the "normal reaction" to trauma. For example, visual flashbacks may be misunderstood, by victims, as evidence of psychosis or moral weakness. Some may be distressed by their own reactions, particularly when these have involved loss of control, freezing, or surrender.

However, a randomized controlled trial has failed to show any advantage for education compared to debriefing and no-treatment (Sijbrandij et al, 2006). Further work is necessary.

Initiation of active treatment

Treatment should be available when needed. But, it is important not to impair the spontaneous adjustment/recovery which occurs in the majority of survivors. It is unclear when active/intrusive treatment should commence. Initial post trauma screening should be to be done by a trained mental health professional and not left to teachers, police or employers. There is some evidence that screening at 10 days post trauma can identify individuals at risk of PTSD (Ehlers & Clark, 2000). Treatment should be provided when there is delayed adjustment or clear evidence of significant symptoms.

THE MINORITY VIEW

A minority of mental health professionals and social scientists have complaints about the status of PTSD.

This is an area in the region of the cross roads of pathology and normality. A sense of the arguments (Brenner et al, 2017): “Currently we are further isolating soldiers with trauma symptoms by treating them as if they are diseased persons suffering from a pathogen inside their brains. Instead, we need to cultivate genuine empathic curiosity about what most soldiers suffer from, which is an altered way of being in the world”.

The leading complaints are that PTSD is “over diagnosed” and “over treated”, and that unnecessary treatment may do harm rather than good. This introduces the term “medicalization” by which is meant, non-medical problems are wrongly managed using medical concepts and resources, as though they are medical issues (Summerfield, 2001; Pupavac, 2001; Lerner and Micale, 2001; see in Chapter 32).

Ethan Watters, in his 2010 book, “Crazy like us: the globalization of the American psyche”, has a chapter, ‘The wave that brought PTSD to Sri Lanka’, in which he tells of the aftermath of the tsunami which hit Sri Lanka in 2004. It makes upsetting (not quite PTSD level) reading, describing how Western trauma experts invaded the country and applied Western “treatments” where they were unnecessary, and culturally damaging.

Social scientists Horwitz and Wakefield (2011) drew attention to earlier versions of the DSM and state that “trauma has moved from the battlefield into the realm of everyday life”.

The treatments of PTSD have received criticism. “At this time, we can make no judgment about the effectiveness of most psychotherapies or about any medications in helping

patients with PTSD" (Institute of Medicine, 2007). Some reports state that traumatized soldiers who did not enter treatment had better outcomes than those who received treatment (Milikan et al, 2007). There are also reports that treatment can worsen symptoms and interpersonal problems (McHugh, 2008). This may be because messages are given that normally painful emotions are 'evidence' of sickness/disorder which require treatment. In this way there may be focusing on and retention of symptoms which may otherwise have dissipated (Horwitz and Wakefield, 2011).

Many of the arguments raised by critics of PTSD diagnosis and treatment are persuasive. However, clinical experience is that PTSD is a distinct disorder which can have serious effects on the individual, family and community. Separating normal from pathological reactions remains a challenge. More work is needed to ensure accurate diagnosis and appropriate management can be provided.

References

Almli L, et al. Genetic approaches to understanding post-traumatic stress disorder. International Journal of Neuropsychopharmacology 2014; 17: 355-370.

Andrews B, et al. Delayed-onset posttraumatic stress disorder. American Journal of Psychiatry 2007; 164: 1319-1326.

Bisson J, Jenkins P, Alexander J, et al. A randomized controlled trial of psychological debriefing for victims of acute burn trauma. British Journal Psychiatry 1997; 171:78-81.

Bandelow B, Zohar J, Hollander E, et al. World Federation of Societies of Biological Psychiatry (WFBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders – first revision. World Journal Biological Psychiatry 2008; 9:248-312.

Benjet C, et al. The epidemiology of traumatic event exposure worldwide. Psychological Medicine 2016; 46: 327-343.

Breslau N, Chilcoat H, Kessler R, et al. Vulnerability to assaultive violence: further specification of the sex difference in post-traumatic stress disorder. Psychological Medicine 1999; 29:813-821.

Brenner P, et al. Beyond pathologizing harm: understanding PTSD in the context of war experience. Journal Med Humanit 2017; [Epub ahead of print]

Breslau N, Koenen K, Lou Z et al. Childhood maltreatment, juvenile disorders and adult post-traumatic stress disorder: a prospective investigation. Psychol Med 2013 Oct 29 [Epub ahead of print]

Bryant R. Early predictors of posttraumatic stress disorder. Biological Psychiatry 2003; 53: 789-95.

De Oliveira J, et al. Serum levels of interleukins IL-6 and IL-10 in individuals with PTSD. Psychiatry Research 2017; 260: 111-115.

Deppermann S, Storchak H, Fallgatter A, Ehlis A. Stress-induced neuroplasticity: (mal)adaption to adverse life events in patients with PTSD – a critical overview. Neuroscience 2014; 283: 166-177.

Disner S, et al. Spontaneous neural activity differences in PTSD. Human Brain Mapping 2017; 2017; [Epub ahead of print].
Ehlers A, Clark D. A cognitive model of posttraumatic stress disorder. Behavior Research Therapy 2000; 38:319-345.
Eraly S, et al. Assessment of plasma C-reactive protein as a biomarker of PTSD risk. JAMA Psychiatry 2014; 71: 423-431.
Falconer E, Bryant R, Felmingham K, et al. The neural networks of inhibitory control in posttraumatic stress disorder. Journal Psychiatry and Neuroscience 2008; 33:413-422.
Felmingham K, Williams L, Whitford T, et al. Duration of posttraumatic stress disorder predicts hippocampal grey matter loss. Neuroreport 2009; 20:1402-1406.
Geuze E, Westenberg H, Heinecke A, et al. Thinner prefrontal cortex in veterans with posttraumatic stress disorder. Neuroimage 2008; 41:675-681.
Gilbertson M, Shenton M, Ciszewski A, et al. Smaller hippocampal volume predicts pathological vulnerability to psychological trauma. Nature Neuroscience 2002; 5:1242-1247.
Gola H, Engler H, Sommershof A, et al. Posttraumatic stress disorder is associated with and enhanced spontaneous production of pro-inflammatory cytokines by peripheral blood mononuclear cells. BMC Psychiatry 2013; 13:40.
Harvey A, Bryant R. Relationship of acute stress disorder and posttraumatic stress disorder following motor vehicle accidents. Journal Consulting Clinical Psychology 1998; 66: 507-512.
Horwitz A, Wakefield J. The expansion of post-traumatic stress disorder: some issues regarding diagnosis and treatment. MDADVISOR 2011, Winter, 6-10.
Institute of Medicine. Treatment of PTSD: An assessment of the evidence. Washington, DC: National Academic Press. 2007.
Jackowski A, Araujo C, de Lacerda A, et al. Neurostructural imaging findings in children with post-traumatic stress disorder. Psychiatry and Clinical Neurosciences 2009; 63:1-8.
Jin C, Qi R, Yin Y et al. Abnormalities in whole-brain functional connectivity observed in treatment-naïve post-traumatic stress disorder patients following an earthquake. Psychol Med 2013 Oct 29. [Epub ahead of print]
Kasai K, Yamasue H, Gilbertson M, et al. Evidence for acquired pregenual anterior cingulate gray matter loss from a twin study of combat-related posttraumatic stress disorder. Biological Psychiatry 2008; 63:550-556.
Klinnert M, Emde R, Butterfield P, et al. Social referencing: The infant's use of emotional signals from a friendly adult with mother present. Developmental Psychology 1986; 22:427-432.
Lerner P, Micale M. Trauma, psychiatry, and history: a conceptual and historiographical introduction. In P Lerner and P Micale (Eds.), Traumatic pasts: history, psychiatry, and trauma in the modern age (p.3). New York: Cambridge University Press. 2001.
McFarlane A. Debriefing: care and sympathy are not enough. Medical Journal of Australia 2003; 178:533-534.

Maddox S, Watts C, Doyere V, Schafe G. A naturally-occurring histone acetyltransferase inhibitor derived from *garcinia indica* impairs newly acquired and reactivated fear memories. PLOS ONE 2013; 8:e54463.
Mayou R, Ehlers A, Hobbs M. Psychological debriefing for road traffic accidents. British Journal of Psychiatry 2000; 176:589-593.
McKittrick C, Magarinos A, Blanchard D, Blandchard R, McEwen B, Sakai R. Chronic social stress reduces dendritic arbors in CA3 of hippocampus and decreases binding to serotonin transporter sites. Synapse 2000; 36:85-94.
Mehta D, Binder E. Gene X environment vulnerability factors for PTSD: the HPA axis. Neuropharmacology 2011 March 23 [Epub ahead of print]
Mitchell J. When disaster strikes: the critical incident stress debriefing process. Journal Emergency Medical Services 1983; 8: 36-39.
McGowen P, Sasaki A, D'Alessio A et al. Epigenetic regulation of the gluicocortioid receptor in human brain associates with childhood abuse. Nat Neuroscience 2009; 12:342-348.
McHugh P. Try to remember: Psychiatry's clash over meaning, memory, and mind. New York: Dana Press. 2008.
McLay R, Mantanona C, Ram V, et al. Risk of PTSD in service members who were fired upon by the enemy is higher in those who also returned fire. Military Medicine 2014; 179:986-989.
McLennan W. Mental Health and Wellbeing: Profile of Adults, Australia. ABS Catalogue No. 4326.0. Canberra: Australian Bureau of Statistics 1997: 18.
Milikan C, Auchterlonie J, Hoge C. Longitudinal assessment of mental health problems among active and reserve component soldiers returning from the Iraq war. Journal of the American Medical Association 2007; 298:2141-2148.
Norris F, Murphy A, Baker C, et al. Severity, timing, and duration of reactions to trauma in the population: An example in Mexico. Biological Psychiatry 2003; 53: 769-778.
Nutt D, Malizia A. Structural and functional brain changes in post-traumatic stress disorder. J Clin Psychiatry 2004; 65 Suppl 1:11-17.
O'Donovan A, Cohen B, Seal K, et al. Elevated risk for autoimmune disorders in Iraq and Afghanistan veterans with posttraumatic stress disorder 2014; [Epub ahead of print].
Pagani M, et al. Eye movement desensitization and reprocessing and slow wave sleep. Fronta Psychol 2017; [Epub ahead of print]
Pridmore S. PTSD criterion in proverbs. Australian and New Zealand Journal of Psychiatry 2011; 45:1094-1095.
Pridmore S. An African PTSD proverb? Australian and New Zealand Journal of Psychiatry 2014; 48:1094-1095.
Pupavac V. Therapeutic governance: psycho-social intervention and trauma risk management. Disasters 2001: 25:198.
Radley J, Sisti H, Hao J, Rocher A, McCall T, Hof P, McEwen B, Morrison J. Chronic behavioral stress induces apical dendritic reorganization in pyramidal neurons of the medial prefrontal cortex. Neuroscience 2004; 125:1-6.

Rusiecki J, Byrne C, Galdzicki Z et al. PTSD and DNA methylation in select immune function gene promoter regions: a repeated measures case-control study of US Military service members. Frontiers in Psychiatry 2013 Jun 24;4:56.
Sailer U, Robinson S, Fischmeister P et al. Altered reward processing in the nucleus accumbens and mesial prefrontal context of patients with posttraumatic stress disorder. Neuopsychologia 2008; 46:2836-2844.
Seifert A, Polusny M, Murdoch M. The association between childhood physical and sexual abuse and functioning and psychiatry symptoms in a sample of US Army soldiers. Military Medicine 2011; 176:176-181.
Shalev A, et al. Post-traumatic stress disorder. New England Journal of Medicine 2017; 376: 2459-2469.
Shin L, Lasko N, Macklin M, et al. Resting metabolic activity in the cingulate cortex and vulnerability to posttraumatic stress disorder. Archives of General Psychiatry 2009; 66:1099-1107.
Sijbrandij M, Olff M, Reitsma J, Carlier I, Gersons B. Emotional or educational debriefing after psychological trauma. A Randomized trial. British Journal of Psychiatry 2006; 189:150-155.
Spitzer C, Wibisono D, Terfehr K et al. C-reactive protein, pre- and postdexamethasone cortisol levels in post-traumatic stress disorder. Nordic Journal of Psychiatry 2014; 68: 296-299.
Sundin J, Forbes H, Fear N et al. The impact of the conflicts of Iraq and Afghanistan: a UK perspective. International Review of Psychiatry 2011; 23:153-159.
Sullivan G, Ogden R, Huang Y-Y, et al. Higher in vivo serotonin-1A binding in posttraumatic stress disorder: a PET study. Depression and Anxiety 2013, in press.
Summerfield D. The intention of post-traumatic stress disorder and the social usefulness of a psychiatric category. British Medical Journal 2001: 322:95-98.
Tao C, Min G, Yunsuo G et al. A comparative study on the levels of serum cytokines and cortisol among post-traumatic stress disorder patients of Li and Han ethnicities in Hainan. Chinese Medical Journal 2014; 127:2771-2774.
Tso C, Min G, Yunsuo G et al. A comparative study on the levels of serum cytokines and cortisol among post-traumatic stress disorder patients of Li and Han ethnicities in Hainan. Chinese Medical Journal 2014; 127:2771-2774.
Van Liempt S, van Zuiden M, Westenberg H, et al. Impact of impaired sleep on the development of PTSD symptoms in combat veterans: a prospective longitudinal cohort study. Depress Anxiety 2013; in press.
Voges M, Romney D. Risk and resiliency factors in posttraumatic stress disorder. Annals of General Hospital Psychiatry 2003; 2: 4.
Wang Z, et al. Posttraumatic stress disorder: an immunological disorder? Front Psychiatry2017; 8: 222.
Watters E. Crazy like us. The Globalization of the American Psyche. Melbourne: Scribe, 2010.
Weaver I, Cervoni N, Champagne F et al. Epigenetic programming by maternal behavior. Nature Neuroscience 2004; 7:847-854.
Wolfe J, Erickson D, Sharkansky E. Course and predictors of posttraumatic stress disorder among Gulf War veterans: a prospective analysis. Journal Consulting and Clinical Psychology 1999; 67: 520-528.

Yehuda R, Daskalakis N, Desamaud F, et al. Epigenetic biomarkers as predictors and correlates of symptom impromvement following psychotherapy in combat veterans with PTSD. Frontiers in Psychiatry 2013 Sep 27; 4:118
Zhang J, Tan Q, Yin H, et al. Decreased gray matter volume in the left hippocampus and bilateral calcarine cortex in coal mine flood disaster survivors with recent onset PTSD. Psychiatry Research 2011; April 16 [Epub ahead of print]
Zohar J, Sonnino R, Juven-Wetzler A, Cohen H. Can post traumatic stress disorder be prevented. CNS Spectrums 2009; 14:44-51.