Trauma and Stressor-Related Disorders 1: Acute Stress Disorder, Posttraumatic Stress Disorder

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Hoyle Leigh

Contents

16.1 Vignettes

1. An 18-year-old man was admitted to the intensive care unit following an automobile accident. He was a passenger in the car whose driver was killed in the crash. The patient had suffered 30 % second degree burn. On the fourth day of admission, a psychiatric consultation was requested for suspected depression. The patient admitted to some feelings of sadness, flashbacks, and interrupted sleep due to nightmares in spite of significant opiate analgesics. An acute stress disorder was diagnosed, and a regimen of Olanzapine 2.5 mg p.o. at bedtime for 2 weeks was initiated. The patient's nightmares and flashbacks subsided within 24 h. He was subsequently discharged without any psychotropic medications.
2. A 32-year-old woman with a history of repeated suicide attempts was referred to the Psychiatric Consultation Service following another acetaminophen overdose for evaluation of "suicidal gesture." On interview, the patient admitted to feeling depressed, paranoid, and abusing methamphetamines. History revealed that the patient had repeated traumatic rapes when she was involved with a motorcycle gang in her teens, and she had severe flashbacks, startle reactions, and almost daily nightmares. The patient was diagnosed with major depression, posttraumatic stress disorder, and methamphetamine abuse. Prazosin 1 mg h.s. was prescribed for the

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nightmare as well as sertraline 50 mg per day for depression and PTSD once the liver function returned to normal, and she was referred for outpatient treatment.

16.2 Introduction: Stress, Trauma, Reactions, and Results

Stress is an adaptational demand on an entity, be it an organism, an organ, a tissue, or a molecule, and conversely, a family, a nation, or a planet. It may be in the form of matter-energy, as in excessive or insufficient ambient heat, environmental toxins, or in the form of information, as in an unwelcome (or welcome) news, an approaching exam, or an inundation by internet connection demands.

Stress is obviously necessary for any change to take place, and optimal physical, intellectual, and emotional development is contingent on a steady dose of optimal stress.

When an organism encounters an excessive amount of stress, then homeostasis may fail, and the initial distortion exerted by the stress on the organism, called strain, may remain as the new baseline and the organism may have to carry on further adaptation with the preexisting load (*allostatic load*). This results in a distorted developmental path, which, if combined with a constitutional/genetic vulnerability, may lead to the development of disease. (For further discussion on this topic, see Chap. 7.)

What constitutes excessive stress? The answer must always be an equation of the interaction: gene × meme × stressor × environment as discussed in Chap. 7. Thus, the same stress (e.g., rape) may have different outcome just as the same genes (i.e., monozygous twins) may fare very differently depending on experience (of trauma or nurturance).

In Trauma and Stressor-Related Disorders, there is a presumption that a person experiences a very strong stressor, and the outcome is classified in DSM-5 on the basis of age of the individual and the type and severity of symptoms. The disorders in children are Reactive Attachment Disorder and Disinhibited Social Engagement Disorder, which are discussed in this chapter. The disorders that are not exclusively seen in children are: Posttraumatic Stress Disorder (PTSD), Acute Stress Disorder (ASD), Adjustment Disorders (AD), Other Specified Trauma- and Stressor-Related Disorders, and Unspecified Trauma- and Stressor-Related disorders. The latter three disorders are discussed in Chap. 17.

16.3 Posttraumatic Stress Disorder (PTSD) and Acute Stress Disorder (ASD)

Though classified as a primary psychiatric disorder, this syndrome is secondary to or the sequelae of major identifiable stresses. In fact, until the term, PTSD, was introduced in 1970s and formalized in DSM III in 1980, combat neurosis, combat fatigue, and shell shock were the terms used to denote the psychiatric sequelae of exposure to the extreme stress of combat (1916; Crocq and Crocq 2000; Earlam 1998; Hayman 1946; Milligan 1916; Wadsworth et al. 1946).

Now it is recognized that posttraumatic stress disorder is not confined to combats or wars, but *any major trauma*, either directly experienced or witnessing such trauma to others, as well as learning about trauma to family or close friend, or experiencing repeated or extreme exposure to details of traumatic events, may cause PTSD (DSM-5).

About 8–9 % of the general population will have PTSD during their lifetime (Hidalgo and Davidson 2000; Yule 2001). In the CL setting, PTSD is often found in trauma, burn, and rape victims. Patients with acute coronary syndrome, and patients admitted to the intensive care unit, often develop PTSD-like symptoms (see Chap. 26.)

Others may have an existing posttraumatic stress disorder diagnosis from combat experience and may be hospitalized for an unrelated medical condition. The prevalence of PTSD in combat veterans is considered to be about 25 %, and in other traumatized groups, 3–60 %.

PTSD is characterized by three classes of symptoms and signs: (1) intrusion symptoms, including intrusive thoughts, nightmares, and

dissociative symptoms such as flashbacks; (2) arousal symptoms, including hypervigilance, hyperarousal, and startle reactions; (3) avoidance of situations and stimuli that may remind the person of the trauma, and (4) negative alterations in cognitions and mood associated with the traumatic event, such as inability to remember aspects of the trauma, persistent negative belief or expectations, persistent negative emotional state, inability to experience positive emotions, markedly diminished interest, feelings of detachment and estrangement. In addition to these symptoms, any number of psychiatric symptoms may be associated with PTSD, including brief psychotic episodes with hallucinations and delusions, depression, panic, substance abuse, and suicidal behavior. Memory impairment and learning disability may be prominent. In fact, PTSD may be called the SLE (systemic lupus erythematosus) of psychiatry in the protean symptomatology. A traumatic childhood may predispose an individual to adult stress disorders.

Therefore, PTSD should be included in the differential diagnosis of any psychiatric symptom.

16.4 Pathophysiology

The pathophysiology of PTSD involves the limbic system, particularly the amygdala, hippocampus, the locus ceruleus, and the prefrontal cortex. A reduced volume of the hippocampus has been consistently reported in PTSD (Bremner et al. 1995; Karl et al. 2006). Hypercortisolemia associated with acute stress has been postulated to underlie the learning disability and memory impairment associated with PTSD (Munhoz et al. 2010; Rodrigues et al. 2009; Sapolsky 1996). In addition to dysfunctions of the limbic system and hippocampus, there is dysfunction of contextualization by medial prefrontal cortex in PTSD (Liberzon and Sripada 2008; Zovkic and Sweatt 2013).

Charney and colleagues postulated that the primary symptoms of PTSD, the persistent reexperiencing of the traumatic event, avoidance of stimuli associated with the trauma, and the symptoms of increased arousal, are related to the neural mechanisms involved in fear conditioning, experimental extinction, and behavioral sensitization as well as the altered function of specific brain regions and neurochemical systems (Charney et al. 1993; Southwick et al. 1994).

In addition to stress inducing the secretion of norepinephrine, dopamine, and opioids, long term potentiation through NMDA receptors in the amygdala may be involved in the encoding of traumatic memories vividly in PTSD (Ledoux et al. 1989).

An intriguing area of research is the role of the protein, Stathmin, which is known to be involved in fear memory formation. In one study, adult male rats were exposed to repetitive blast injury while under anesthesia. Blast exposure induced a variety of PTSD-related behavioral traits that were present many months after the blast exposure, including increased anxiety, enhanced contextual fear conditioning, and an altered response in a predator scent assay. The authors also found elevation in the amygdala of the protein stathmin 1. Because the blast overpressure injuries occurred while animals were under general anesthesia, their results suggest that a blast-related traumatic brain exposure can, in the absence of any psychological stressor, induce PTSD-related traits that are chronic and persistent (Elder et al. 2012).

There is evidence that the balance between neuronal activities of the amygdala and prefrontal cortex defines an impairment or facilitation of extinction to the cue while the hippocampus is involved in the context-specificity of extinction (Martel et al. 2012).

In memetic terms, PTSD results from an overwhelming infusion or activation of stress memes that take over the function of the brain (Leigh 2010, 2012). The stress reaction involves the activation of the hypothalamo-pituitary-adrenocortical axis and massive production of glucocorticoids which are neurotoxic to the hippocampus, and may result in a smaller volume and difficulty in processing memory. With PTSD, there may be a permanent damage to the meme-processing ability of the brain, setting the stage for a labile equilibrium among conflicting memes and susceptibility to be overwhelmed with new incoming memes or an inability to process new and useful memes. The stress memes that

overwhelmed the brain are likely to reside in the brain and proliferate at every opportunity. Note that strong emotions may enhance long-term potentiation and thus memory formation through dopaminergic and serotonergic mechanisms ("flashbulb memory"). Persons who have no memory of a traumatic event in 24 h were shown to be less likely to develop PTSD in 6 months than those who had memories of the trauma (Gil et al. 2005). This finding supports the notion that the ability to inhibit the traumatic meme proliferation (memory) prevents PTSD.

Once PTSD has been established, reservoirs of traumatic memes may proliferate unpredictably and uncontrollably as in flashbacks and nightmares.

16.5 Treatment

16.5.1 Psychotherapy

Remembering the traumatic event within 24 h after it occurred has been shown to be a predictor of future PTSD, whereas amnesia concerning the event is a predictor of not developing PTSD (Gil et al. 2006). Thus, when a patient who suffered an acute stress, such as a motor vehicle accident or assault, has no memory of the incident, it is prudent for the medical staff not to encourage the patient to remember it. Psychological debriefing and critical incident debriefing, in which the individual relives in detail the traumatic experience in a group situation, have been shown to be ineffective or even detrimental and more likely to result in PTSD (Mayor 2005). In contrast to this type of acute reliving of trauma in group situations, individualized, planned psychotherapy seems to be the most effective treatment for PTSD.

Among the various modalities of psychotherapy, *Cognitive behavioral therapy* (*CBT*) and *Prolonged exposure therapy* (*PE*) have strongest evidence base for PTSD, and are probably far more effective than extant pharmacotherapy (Cukor et al. 2010).

PE is based on the learning theory model, and views PTSD as a disorder of extinction, whereby the individual's response to crisis does not diminish sufficiently, and the association between the memory of the event and a message of danger has not been extinguished even when the danger has passed. The main components of PE, imaginal exposure and in vivo exposure, entail the revisiting of trauma memories and triggers to extinguish this response, by facilitating habituation to the memory, decreasing avoidance, and eliminating associations with danger by providing corrective information about safety (Foa et al. 2007). During imaginal exposure, patients are instructed to relate their trauma experience in detail with their eyes closed, while trying to engage emotionally in the memory. The patient retells his/her trauma experience repeatedly over the course of a number of sessions, thereby allowing the processing of the trauma experience. In vivo exposure entails approaching activities, people, and/or places the patient may have been avoiding to allow habituation to the environment, and the assimilation of the corrective information regarding safety.

Within CBT for PTSD, prolonged imaginal exposure may be used as a specific therapeutic technique in various populations including sexual assault and motor vehicle accidents (Cukor et al. 2010).

Cognitive processing therapy (CPT) is another exposure-based protocol with a strong emphasis on increasing the cognitive components and decreasing the amount of exposure necessary for treatment, which some believe will be more palatable to individuals with PTSD. CPT consists of a 12-session protocol comprising of two integrated elements. The cognitive therapy component focuses on deconstructing assimilated distorted beliefs, such as guilt, and more global beliefs about the world and self, and generating more balanced statements. The exposure component entails having the patient write the trauma memory and read it to their therapist and to themselves and then examine the writing for "stuck points"(Resick et al. 2002; Rizvi et al. 2009).

Initial case studies and clinical trials were promising and led to a randomized controlled trial comparing CPT to PE and a minimal attention waitlist control for the treatment of PTSD in a sample of chronically distressed rape victims.

Results found that both PE and CPT were highly successful in treating PTSD and comorbid depressive symptomatology.

Stress management and relaxation therapy, may be effective.

Couples and family therapy may also be helpful in treating PTSD patients.

16.5.2 Pharmacotherapy

The SSRIs are considered to be the first line of treatment. For many patients who experience insomnia, nightmares, flashbacks, and hypervigilance shortly after severe trauma, antipsychotic mood stabilizers such as olanzapine in small doses (e.g., 2.5–5 mg) hs for 2 weeks to 1 month may be particularly helpful (Labbate and Douglas 2000; Stein et al. 2002). For nightmares associated with PTSD, the α-adrenergic blocker prazosin (1 mg h.s. po gradually increased up to 6 mg) has been shown to be useful. Benzodiazepines may also be used for reducing anxiety. For PTSD, the treatment is always symptomatic, as the symptoms may range from depression, to impulsivity, to psychotic symptoms, to panic. Thus, in addition to SSRIs and antipsychotics, mood stabilizers such as valproic acid and lithium may be indicated. Beta-blockers such as propranolol and alpha-2 agonists like clonidine, as well as drugs that act on NMDA and MDMA receptors may be helpful in modifying the fear conditioning process in PTSD (Kerbage and Richa 2013).

Only two pharmacologic agents are FDA approved for the treatment of PTSD: sertraline and paroxetine. These selective serotonin reuptake inhibitors (SSRIs) have response rates rarely over 60 % with less than 30 % achieving full remission (Berger et al. 2009). Overall, less than 50 % of PTSD patients improve on SSRIs. Nevertheless, practice guidelines endorse SSRIs as first line pharmacotherapy for PTSD (Ipser and Stein 2012). Antipsychotics such as risperidone or olanzapine may be useful for some symptoms such as insomnia, and anticonvulsants seem helpful when used as an augmentation to other therapeutic regimens (Berger et al. 2009). Benzodiazepines are generally not recommended in PTSD because of its potentially addictive nature and the question of whether it may contribute to the development of PTSD, but in practice, it is frequently used to target more isolated symptoms such as insomnia and anxiety (Cukor et al. 2010).

Prazosin is an alpha-1 adrenergic receptor blocker which is efficacious in treating sleep-related PTSD symptoms. These symptoms are believed to be moderated by increased central nervous system adrenergic activity, resulting in greater release of norepinephrine and increased sensitivity to norepinephrine at receptor sites. Prazosin's effectiveness for the treating nightmares has been reported in various studies, with reports of 50 % decrease in nightmares after 8 weeks of treatment at 1–6 mg h.s. dosing (Ipser and Stein 2012).

D-*Cycloserine* (*DCS*, *Seromycin*) is a cognitive enhancer that shows promise among pharmacologic agents for PTSD for its potential to facilitate extinction learning. Originally developed as an antituberculosis antibiotic, DCS is a partial agonist for the *N*-methyl-D-aspartate (NMDA) glutamate receptor, which has a crucial role in learning and memory functions. DCS has been shown to facilitate extinction learning in animal models of conditioned fear and in some human trials of other types of learning including social phobia and shows a potential role of DCS in facilitating fear extinction and reducing post-treatment relapse (Cukor et al. 2010)

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