Chapter 20: Posttraumatic Stress Disorder

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Introduction

The capacity for people to develop psychopathological stress reactions has been recognised for over 100 years, however it is only in the wake of the Vietnam war that the definition of posttraumatic stress disorder (PTSD) was formally introduced. The current definition by the American Psychiatric Association's DSM-5-TR (American Psychiatric Association, 2022) stipulates that for a person to be considered for a diagnosis of PTSD, they must experience or witness a marked threat to themself or others; this form of threat needs to be severe, such as war, disaster, assault, or severe accident. Although harassment or bullying can be very stressful, these types of events do not involve threat to safety or life and so tend not to trigger PTSD. If a person has experienced a traumatic event, then they need to experience four different clusters of symptoms. First, a person needs to experience a group of symptoms that comprise re-experiencing of the trauma, including intrusive memories, flashbacks, nightmares, and distress to reminders of the trauma. Second, one is required to display active avoidance of internal reminders of the trauma (e.g. thoughts, memories) or external reminders (e.g. situations, conversations). Third, the person needs to have a range of symptoms involving mood and thoughts, such as exaggerated negative thoughts (e.g. "no one can be trusted", "everything is ruined"), excessive blame, pervasive negative emotions (e.g. horror, fear, guilt or shame), diminished interest, feeling detached or estranged from others, or psychogenic amnesia. The final cluster comprises hyperarousal symptoms, such as exaggerated startle response, reckless behaviour, insomnia, aggressive behaviour, and sleeping or concentration difficulties.

Diagnostic systems have always recognised that most people will have stress reactions in the acute phase after a traumatic event. Many of these responses should not be pathologized because evidence indicates that most of these reactions will

remit in the following weeks (Bryant, 2003). Accordingly, DSM-5-TR (American Psychiatric Association, 2022) stipulates that PTSD can only be diagnosed one month after trauma. There is a provision for diagnosing people in the acute phase in DSM-5-TR in the form of acute stress disorder, which describes posttraumatic stress reactions that occur in the first month after trauma exposure. This diagnosis was initially introduced in DSM-IV as a means of describing severely distressed people who could benefit from treatment, as in many healthcare systems in the USA it can be difficult to access treatment without a diagnosis. It was also initially constructed as a potential means to identify people in the acute phase who are high risk for developing subsequent PTSD. Longitudinal studies have shown that the acute stress disorder diagnosis is only a modest predictor of PTSD because at least half of people who develop PTSD do not initially meet the acute stress disorder criteria (Bryant, 2010). In DSM-5-TR the acute stress disorder diagnosis does not require specific symptoms clusters to be satisfied but rather requires that at least 9 of 14 potential acute stress reactions be present (Bryant et al., 2011). This diagnosis is not intended to predict subsequent PTSD but instead aims to identify people who could benefit from treatment in the initial month after trauma (Bryant et al., 2011).

Prevalence of PTSD

Epidemiological studies indicate that most people will experience a traumatic event at some point in their lives, however these studies also suggest most people are resilient and do not develop a psychiatric disorder (Bonanno et al., 2015). Lifetime prevalence rates of PTSD are between 13%-20.4% for women and between 6.2%-8.2% for men (Breslau et al., 1991; Kessler et al., 2013). There is variability depending on the type of traumatic event, with interpersonal violence resulting in higher rates of PTSD (Forbes et al., 2011; Forbes et al., 2013). Consistent with this conclusion, the World Mental Health Survey found that organized, physical, or sexual violence increased the risk for PTSD (Liu et al., 2017). It is important to note that there are high rates of comorbidity between PTSD and other psychiatric disorders, including depression, anxiety disorders, and substance use disorder (Breslau et al., 1997; Kessler et al., 2013; Rytwinski et al., 2013).

The Course of PTSD

Many longitudinal studies have tracked trauma over time, and this has allowed understanding of how traumatic stress develops and maintains over time. We now know that rather than being a static condition, it actually fluctuates over time (Bryant et al., 2013). Further, modelling shows that there are four major trajectories of traumatic stress response: (a) a resilient class with few PTSD symptoms, (b) a recovery class with initial distress then gradual remission, (c) a delayed reaction class with initial low symptom levels but increased symptoms over

time, and (d) a chronic distress class with consistently high PTSD levels (Bonanno et al., 2008; Bryant et al., 2015; deRoon-Cassini et al., 2010; Galatzer-Levy et al., 2018). This pattern has resulted in a major challenge to early intervention following trauma exposure because we do not have robust metrics to predict in the acute phase who will subsequently develop PTSD. Although people with more severe psychological distress in the weeks after trauma are more likely to develop PTSD (Blanchard et al., 1997; Frommberger et al., 1998; Jehel et al., 2003; Karstoft et al., 2015; Shalev and Freedman, 2005), this association does not allow us to definitively identify who will and will not develop PTSD.

Risk Factors

What predisposes some trauma survivors to developing PTSD? Many of the risk factors are similar to risk factors observed across many psychiatric disorders, including female gender, low socio-demographic background, prior psychological disorder, family history of psychological disorders, and traumatic childhoods (Brewin et al., 2000). Risk also increases in relation to factors associated with the traumatic events, including more prolonged trauma, grotesque or interpersonal trauma, as well as the number of traumatic events that a person has experienced (Ozer et al., 2003). There is also considerable evidence that how a person responds to the trauma is also predictive of later PTSD, including dissociative reactions that comprise altered sense of reality or oneself after the trauma (Murray et al., 2002; Shalev et al., 1998) and catastrophic appraisals (Dunmore et al., 2001; Kleim et al., 2007; Wikman et al., 2011). There is also much evidence that poor social support and ongoing stressors contribute to the risk of the development of PTSD (Brewin et al., 2000).

Theories of PTSD

Neurobiological Models

Arguably the most influential theory of PTSD involves the concept of fear conditioning. In this theory it is proposed that stress hormones released at the time of trauma in association with the extreme fear experienced by a person leads to a strong learning response that associates the cues present at the time of trauma with the fear responses (Shalev et al., 2017). This learning leads to people reacting to these, and similar, cues in their environment as though the trauma is occurring again. A hallmark symptom of PTSD is the sense that memories of the trauma are very real and a sense that the trauma is recurring. For example, a firefighter may develop PTSD after pulling a dead baby out of a burning building. In the process the stimuli present at the time, such as the smell of smoke and burnt skin, may be strongly associated with the fear response. Subsequent to the trauma, each time the firefighter

smells burnt meat (e.g., at a barbeque), he may experience intrusive memories and extreme distress because the memories of the trauma are readily activated and he feels it is recurring. These models also propose that most people recover from initial stress reactions through a process called extinction learning, in which one is repeatedly exposed to reminders of the trauma but because there are no harmful outcomes, they learn that these stimuli are not indicative of threat but rather that they signal safety (Rauch and Drevets, 2009).

There is considerable evidence for fear conditioning models explaining PTSD. People with PTSD have dysfunction in neural circuits that are involved in fear conditioning, including the amygdala, prefrontal cortex, and hippocampus (Ressler et al., 2022). There is also much evidence of reduced activity of the medial prefrontal cortex, which is key for extinction learning (Kitayama et al., 2006).

There is also much evidence of neuroendocrinological abnormalities in PTSD, including noradrenergic and glucocorticoid abnormalities (Hendrickson and Raskind, 2016). Noradrenergic release interacts with cortisol to facilitate traumatic memories (McGaugh, 2000), and these abnormalities are well-documented in PTSD (Southwick et al., 1999; Southwick et al., 1997), and may explain the intrusive re-experiencing of trauma memories. Further support is from evidence that administration of propranolol, a beta-blocker that reduces noradrenergic activity, in the hours after trauma exposure limits subsequent reactivity to reminders (Pitman et al., 2002). In the context of the noradrenergic system, it is also worth noting that there is a potentially protective role for morphine in the acute phase after trauma. The locus coeruleus, which produces norepinephrine, is inhibited by morphine, and animal work indicates that morphine injections into the amygdala impairs memory for fear conditioning in rats (McNally and Westbrook, 2003). Numerous studies of traumatized populations indicate that greater morphine dose in the initial days after trauma exposure is associated with reduced PTSD at follow-up. Importantly, these studies are not randomized controlled trials, and so they do not allow us to conclude that morphine can limit subsequent PTSD.

One of the major mechanisms in the stress response is the glucocorticoid system. Interestingly, although increased cortisol is typically associated with chronic stress, PTSD is often associated with lower cortisol levels (Yehuda et al., 1990). It has also been shown that lower cortisol levels shortly after trauma predict subsequent PTSD severity (Delahanty et al., 2000). This paradoxical finding is interpreted in terms of cortisol binding to the glucocorticoid receptors in a negative feedback loop that promotes homeostasis of the stress response (Yehuda and McFarlane, 1997). It is proposed that lower cortisol in PTSD may result in elevated ongoing HPA activity, resulting in exaggerated catecholamine response and

consequent over-consolidation of trauma memories. This proposition has received some initial support from early intervention studies that administration of hydrocortisone shortly after trauma limits subsequent PTSD symptoms (Zohar et al., 2011b).

There is also much evidence of strong psychophysiological reactivity to reminders of the trauma in people with PTSD, which supports fear conditioning models. When given reminders of the trauma, people with PTSD display greater heart rate, skin conductance response, or facial electromyogram measurements than those without PTSD (Orr et al., 1993). Further, elevated resting heart rate in the days after trauma is predictive of later developing PTSD (Bryant et al., 2000).

Genetic Factors

Genetic factors play an important role in susceptibility to PTSD, accounting for 30%-72% of risk for developing PTSD (Sartor et al., 2011; True et al., 1993). Studies suggest that genes associated with PTSD are also linked with other common psychiatric disorders, including major depression, generalized anxiety disorder, panic disorder, and substance use (Koenen et al., 2008). For example, studies have indicated a role of the functional polymorphism in the promoter region of the serotonin transporter gene (SLC6A4) across many disorders, and this pattern extends to PTSD. The short allele (5-HTTLPR S), which reduces serotonergic expression and uptake by nearly 50% (Lesch et al., 1996), has been linked with impaired extinction learning (Galatzer-Levy et al., 2017), and gene x environment association studies indicate that *FKBP5* alleles increase risk for PTSD (Binder et al., 2008). Currently over 50 gene variants have been linked with PTSD, including HPA axis functions, noradrenergic, dopaminergic and 5-HT systems, and neurotrophins (Sheerin et al., 2017). To sum up this work, there is no single gene that represents a significant risk distinctively for PTSD, it appears that polygenetic approaches are more appropriate. One attempt to address this problem is the Psychiatric Genomics Consortium – Posttraumatic Stress Disorder Group, which has reported a genome-wide analysis of 20,730 people. Although no single-nucleotide polymorphism was found to be significantly associated with PTSD, this study did find a polygenetic risk profile that overlapped with risk for schizophrenia (Duncan et al., 2018).

Cognitive Behavioural Models

Cognitive behavioural models typically acknowledge that fear conditioning is instrumental in the development of PTSD, however they put much more emphasis on the influence of cognitive appraisals about the traumatic event, the person's responses to it, and their perceptions of future likelihood of harm. By engaging in excessively negative appraisals about the sense of threat or pessimism of recovery,

these cognitive styles tend to maintain PTSD (Foa et al., 1999). Evidence indicates that engaging in negative appraisals prior to trauma is a risk factor for developing PTSD (Bryant and Guthrie, 2007), and that the presence of these appraisals shortly after trauma predicts development and maintenance of PTSD (Dunmore et al., 1999; Kleim et al., 2007), as well as their decline after successful therapy (Kleim et al., 2013). This exaggerated sense of threat in PTSD can lead to strong avoidance of potential threats, which in turn deprives the person of learning that normal daily events (including those that are reminders of the trauma) are not threatening, and this impedes extinction learning (Foa et al., 1989).

Prevention of PTSD

Prevention

Programs have been initiated to prevent people developing PTSD by teaching them strategies that are intended to 'inoculate' them against the aversive elements of a traumatic experience. There is evidence that some prevention programs can mitigate the degree of mental health problems that emerge after trauma (Bisson et al., 2021). One example of attempting to limit PTSD focused on correcting attentional problems that have been observed in PTSD. Although most anxiety disorders are characterised by a bias to attend towards threat, PTSD is distinguished by having a bias to attend both towards (Bryant and Harvey, 1997; Buckley et al., 2000) and away from threat (Bar-Haim et al., 2010; Wald et al., 2011), resulting in greater attentional variability in PTSD (Naim et al., 2015). A large trial built on this evidence to test a prevention program in soldiers involved training them to control their attentional biases by using a brief computer task administered prior to deployment to combat. This trial found that soldiers receiving this program had fewer subsequent PTSD symptoms than those in a control condition and this result was mediated by a reduction in attentional variability, a finding that was subsequently replicated in a cohort of US troops (Badura-Brack et al., 2015). Apart from these isolated studies, however, the overall evidence for prevention of PTSD is very limited.

Psychological Treatments

Most international treatment guidelines recommend that the frontline treatment for PTSD is what may be termed "trauma-focused cognitive behaviour therapy" (Health, 2005). There are a range of treatments that can be described under this category, including Prolonged Exposure, Eye Movement Desensitization and Reprocessing, Cognitive Therapy, Cognitive Processing Therapy, and Imagery Rescripting Therapy. Although each treatment is somewhat different, they converge on two critical elements that are regarded as the core components of effective

treatment of PTSD. The treatments involve some form of emotional processing of the traumatic memory and changing maladaptive appraisals so people have a more realistic perspective of the experience and their future. This treatment has been shown to be effective for people PTSD after traumatic injury and assault, sexual assault, combat, terrorist attacks, refugees, and child sexual abuse (Bryant et al., 2008; Duffy et al., 2007; Foa et al., 1991; McDonagh et al., 2005; Neuner et al., 2004; Schnurr et al., 2003). A central strategy used in most treatments is exposure therapy in which the patient is assisted to 'relive' their trauma memory for approximately 10-30 minutes. Much evidence indicates that doing this over a series of therapy sessions results in less distress and fewer intrusive memories of the trauma, and accordingly is conceptualized as a form of extinction learning because the person learns that this trauma reminder is no longer threatening.

This approach has also been used shortly after trauma with patients who are more at risk of developing PTSD because they have high levels of acute stress. These programs employed a brief form of trauma-focused CBT (usually 5-6 sessions), and typically found that they were more efficacious than control conditions (Bryant, 2003; Bryant et al., 1998; Bryant et al., 2008; Bryant et al., 2005; Shalev et al., 2012). One trial even commenced trauma-focused CBT in the emergency department and provided subsequent sessions in the weeks after discharge, and this study also found that this approach can be beneficial (Rothbaum et al., 2014). Note that this approach is different from the universal prevention strategies described above because this 'secondary prevention' focused on patients with elevated stress responses and so more at risk of PTSD. The utility of early provision of trauma-focused CBT is supported by meta-analytic studies that suggest this intervention can limit later PTSD (Kornør et al., 2008; Roberts D Clin Psy et al., 2009). Although trauma-focused CBT has been shown to be effective in reducing PTSD, it is important to note that only two-thirds of patients respond adequately to this intervention (Bradley et al., 2005).

Pharmacological Treatments

PTSD is one of the psychiatric disorders in which psychological treatments are preferred over psychopharmacological interventions, which have only modest success. International treatment guidelines converge on the conclusion that stronger benefits from psychotherapy, potential adverse side-effects from pharmacotherapy, and possible relapse after medication discontinuation results in trauma-focused CBT being the first line of treatment. Despite this conclusion, the major psychotropic medications recommended for PTSD are selective serotonin reuptake inhibitors (SSRIs), which are the only medication approved by the US Food and Drug Administration for treatment of PTSD (sertraline and paroxetine). It should be noted that their effect sizes in PTSD is small (Thomas and Stein, 2017), underscoring

the need to prioritise trauma-focused CBT. One reason why SSRIs may be useful in treating PTSD is that they are effective in treating major depressive disorder, which is highly comorbid with PTSD.

Other medications have been used with PTSD, or rather specific symptoms of PTSD. For example, nightmares have been treated with prazosin (an α1-adrenergic antagonist), which has been found to be effective in reducing nightmares and hyperarousal (Singh et al., 2016). It is also worth noting that benzodiazepines have often been prescribed in the context of PTSD, and particularly in the acute phase after trauma, as a means of reducing arousal and improving sleep. They are generally contraindicated because of limited efficacy and high risk of addiction. Further, benzodiazepines can result in more subsequent PTSD (Gelpin et al., 1996; Mellman et al., 2002). Potentially it can interfere with the regulatory function of the HPA axis (Zohar et al., 2011a).

Conclusion

As one in ten people will develop PTSD at some point in their lives, it is likely that most medical professionals will encounter patients with this condition regularly. Fortunately, we have efficacious treatments that can benefit most PTSD patients. One of the challenges for treating PTSD is that most patients only receive evidence-based care years after the onset of PTSD, which risks the development of chronic patterns of illness and entrenched psychiatric comorbidities. Medical and health practitioners can play a key role in promoting early help-seeking to stop PTSD from becoming chronic and debilitating.

Further Reading

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