



## NATIONAL MENTAL HEALTH RESEARCH STRATEGY

### BACKGROUND PAPER: Trauma and stressor-related disorders (Session 7B)

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#### **Introduction**

The scope of this review will focus primarily on Post-Traumatic Stress Disorder (PTSD), although it is recognised that stressors can trigger many conditions, including adjustment disorder, Prolonged Grief Disorder and other conditions. PTSD is commonly defined by DSM-5 as a condition that develops at least a month after exposure to a threatening event, characterised by reliving symptoms in the forms of memories, avoidance of reminders, negative mood and cognitive appraisals, and hyperarousal. ICD-11 has a similar, but simpler definition. The other common stress-related condition that has received considerable attention in recent years is Prolonged Grief Disorder, which ICD-11 defines as persistent yearning for a deceased person, associated with emotional pain, difficulty accepting the death, a sense of meaninglessness, bitterness about the death, loss of identity and difficulty engaging in new activities.

#### **Background**

##### ***Epidemiology***

Epidemiological studies have reported lifetime prevalence rates of PTSD of 3.9% across nations,<sup>1</sup> and the Australian 12-month prevalence is estimated at 4.4%.<sup>2</sup> Most PTSD cases have comorbid disorders, most commonly depression, anxiety disorders, and substance use disorder.<sup>3</sup> The high rates of comorbidity may be attributed to psychiatric disorders predisposing people to experience traumatic events or to PTSD triggering the development of other psychiatric disorders, such as depression or substance use disorder. In terms of other stress-related disorders, it is also worth noting that recent studies indicate that approximately 7% of bereaved people suffer Prolonged Grief Disorder.<sup>4</sup>

##### ***Course of PTSD***

Although earlier studies indicated PTSD followed a linear course over time, more recent studies have used latent growth mixture modelling to map the trajectories of the course of PTSD. These studies have reliably demonstrated: (a) approximately 75% of trauma survivors comprise a resilient class which consistently shows 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.<sup>5</sup> Network analyses suggest that, whereas PTSD symptoms form as a distinct syndrome over the initial months after trauma exposure,<sup>6</sup> PTSD then typically follows a dynamic course, with symptoms changing over time depending on current stressors.<sup>7</sup>

## **Risks**

Many of the risk factors are in fact the same risk factors observed across many other psychiatric disorders: female gender, low socio-demographic background, prior psychological disorder, family history of psychological disorders and traumatic childhoods.<sup>8</sup> In terms of vulnerability factors more specific to PTSD, the disorder is more likely after more prolonged trauma, and grotesque or interpersonal traumatic events.<sup>9</sup> The post-trauma environment is also important, with low social support and ongoing stressors contributing to risk for PTSD development.<sup>8</sup>

## **Models**

Most theories of PTSD invoke processes involving fear conditioning. This model posits that at the time of trauma, the surge of stress hormones released in association with the fear experienced by the individual results in strong associative learning between cues present at the time of trauma and fear responses. This fear response is predicated on the notion that the associated cues assume properties of predicting future threat, thereby resulting in re-experiencing symptoms and fear when exposed to internal and external reminders of the trauma.<sup>10</sup> These models also posit that recovery from initial stress reactions involve extinction learning, in which one is repeatedly exposed to reminders of the trauma but on these occasions there is no adverse consequence; accordingly, there is new learning that the previously conditioned cues now signal safety.

There is evidence of changes in neural circuitry in people with PTSD that is consistent with circuitry known to be implicated in fear conditioning: the amygdala, prefrontal cortex and hippocampus.<sup>10</sup> Many studies indicate that PTSD is characterised by smaller hippocampus, with meta-analyses indicating this effect is observed bilaterally.<sup>11</sup> Many studies have used fear provocation tasks to elicit the threat network in PTSD patients. Arguably the most replicated finding is evidence of under-activation of medial prefrontal cortex regions, consistent with the proposal of impoverished regulatory processes in PTSD that promote extinction.<sup>12</sup> It is worth noting that over the past 15 years there has been a concerted effort to identify a biological marker for PTSD – despite enormous efforts, these attempts have resulted in no biomarker.

Cognitive models propose that trauma memories are encoded in a distinctive manner that is characterised by fragmented and disorganised sequencing as a result of the elevated arousal at the time of trauma. Much emphasis is also placed on the extent to which people appraise the traumatic event, their responses to it and their future likelihood of harm. There is abundant evidence of the predictive role of catastrophic appraisals in the development and maintenance of PTSD, as well as their decline after successful therapy.<sup>13</sup>

## **Treatment**

The treatment of choice for PTSD is trauma-focused cognitive behaviour therapy (TF-CBT), and most treatment guidelines support this conclusion.<sup>14,15</sup> There are numerous variants of TF-CBT, including Prolonged Exposure, Eye Movement Desensitization and Reprocessing, Cognitive Therapy, Cognitive Processing Therapy and Imagery Rescripting Therapy. Although each of these treatments posit that they are distinctive, in one way or another, they essentially each comprise emotional processing of the traumatic memory and integration of new, corrective information. This form of therapy has been shown to be effective with many populations, including survivors of traumatic injury and assault, sexual assault, combat, terrorist attacks, refugee experiences and child sexual abuse. The core component of this treatment typically involves exposure therapy in which the patient is directed to engage with the trauma memory for a prolonged period. This strategy is commonly conceptualised as a form of extinction learning, insofar as the person learns that the trauma reminder is no longer a signal of threat. Although TF-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.<sup>16,17</sup> Although selective serotonin reuptake inhibitors (SSRIs) have been approved as a frontline treatment for PTSD, there is no strong evidence that psychopharmacological approaches should be the first line treatment for PTSD.

### ***Consensus of knowledge***

- PTSD affects approximately 10-15% of trauma survivors (most people are resilient)
- PTSD is a dynamic disorder that fluctuates over time, depending largely on current stressors
- Rates and severity of PTSD are dependent on nature of trauma, especially interpersonal trauma
- Females are at twice the risk of PTSD as males
- Childhood trauma is a major risk for PTSD
- Although genetic factors account for much of the variance of PTSD, there are no known genes or polygenetic risk scores strongly associated with PTSD
- Trauma-focused psychotherapies are the treatment of choice for PTSD in adults and children; however, only 50% of people are likely to respond to this treatment

### **Gaps and uncertainties**

#### ***Complex trauma***

Over the past 10 years there has been an explosion in research into Complex PTSD. Although DSM-5 rejected this as a subtype of PTSD, ICD-11 has recognised Complex PTSD as a form of PTSD: it is defined as PTSD that can occur in association with significant disturbances in emotional regulation, social relationships and self-identity.<sup>18</sup> Although typically seen in adults in the aftermath of prolonged childhood abuse, it can also occur in adults following prolonged trauma, such as in refugee populations. Despite the surge of attention into this topic in recent years, there is much we do not understand about this condition, including (a) its qualitative distinctions from PTSD and other stressor-related disorders, (b) longitudinal analysis of the onset and course of the disorder, and (c) treatment options.

#### ***Onset and long-term course of stress-related disorders***

Although many longitudinal studies have been conducted on the course of PTSD, these are typically restricted to a salient onset (disaster, assault, accident). We know much less about the course of trauma-related disorders after prolonged trauma. For instance, although prolonged childhood trauma is a major risk factor for PTSD later in life, there is insufficient data regarding how exposure to ongoing adversity during childhood leads to trauma-related disorders. Inherent to this issue is identification of key developmental stages at which one may be most susceptible to the effects of trauma. Initial work has proposed key stages in which neuronal integrity in young people may be impacted by different types of trauma.<sup>19</sup> There is scant evidence regarding how childhood sexual/physical abuse, neglect and witnessing violence can impact on development of disorders over time.

### ***Course of grief***

The study of grief is years behind that of PTSD, and there is a great need to understand the course of grief reactions. Prospective studies of families, commencing when patients are dying and continuing for years after the death, will inform the field about psychopathological risk factors and open opportunities for prevention and early intervention.

### ***Non-response to treatment***

A robust finding from systematic reviews is that up to 50% of PTSD patients will not respond to trauma-focused psychotherapies.<sup>16</sup> This has resulted in many attempts over the past 20 years to augment existing treatments. Most of these attempts have been based on augmenting extinction learning as the key mechanism that underpins exposure therapy for PTSD.<sup>20</sup> Despite the many pharmacological, psychological, and stimulation approaches, none of these attempts have resulted in major improvements in treatment response. There remains an outstanding need for evidence-based approaches to tackling treatment non-response. This situation equally applies to treatment of Prolonged Grief Disorder, in which studies indicate that at least 1 in 3 patients will not respond to treatment.

### ***Tailored interventions***

All evidence to date regarding treatments relies on standard treatments that apply to all patients with PTSD. This standard is in contradiction to much evidence that people present for treatment with varied symptoms, crossing diagnostic boundaries. There is a scarcity of evidence related to how treatment approaches should be matched to different varieties of post-traumatic clinical disorders. For example, patients presenting with primarily fear-based anxiety may need different strategies relative to those with dysphoric presentations.<sup>21</sup>

### ***Implementation research***

Despite the well-documented research that trauma-focused psychotherapies are the treatment of choice, there remain worrying statistics that many mental health practitioners are insufficiently skilled in these strategies, and many patients seeking care will receive non-evidence-based treatments. There is a strong need to bridge for implementation research that addresses how efficacy evidence for treating PTSD and its comorbid conditions can be translated to implementation research involving uptake of evidence-based strategies in normal clinical practice. This gap in the research literature extends to health economics, where more work is needed to document the relative costs and savings that can be made by implementing evidence-based care.

### ***Social/community factors***

One curious gap in the research literature is that nearly all research is focused on individual factors. Many cases of trauma-related disorders occur on a large scale, however, including natural and human-made disasters, war and humanitarian crises. These events by definition affect entire communities, or even countries, and there is a need to understand how trauma and adversity affects recovery of communities. Although many commentators have pointed to the importance of community factors in mental health after disasters, it is rarely studied. Highlighting the relevance of this issue is recent evidence from the Black Saturday fires that used social network analysis to indicate that mental health is 'transmitted' across communities and needs to be understood at communal, as well as individual, levels.<sup>22</sup>

### ***Prevention in high-risk groups***

One of the persistent uncertainties in the field is the extent to which PTSD and related disorders can be prevented. Most of this research has focused on high-risk groups, such as the military and first responders, because these people are more likely to be exposed to trauma and so evaluating preventative programs is more realistic. One meta-analysis of resilience training in high-risk occupations found that programs based on cognitive behavioural and mindfulness strategies have a moderate impact on enhancing subsequent mental health.<sup>23</sup> Despite this, these effects are modest and there remains a need for more research at both an individual and systemic level on how to limit PTSD development.

### ***Barriers to accessing care***

Most people with trauma-related disorders do not access care. There is a need to understand factors that impede accessing care, including stigma, social barriers, health system factors and (especially in the case of regional Australia) the role of access to appropriately trained professionals. In recent years, digital programs have flourished with the ambition of overcoming traditional barriers to care, however the retention in these programs and the extent to which they have translated to the implementation phase is disappointing.

### ***Novel treatments***

There are numerous treatments emerging for trauma-related disorders with very tentative evidence, ranging from repetitive transcranial magnetic stimulation as a stand-alone treatment to MDMA ('ecstasy') as a means to augment existing therapy. As noted above, there are numerous small pilot studies that also suggest some evidence for pharmacological interventions. These interventions need to be evaluated relative to our best available treatments (i.e. trauma-focused psychotherapy) because if novel treatments are to be evaluated, they need to be assessed against the best treatments currently accessible.

### ***Refugee and multicultural trauma***

Most people affected by trauma live in non-western settings. Despite this, the vast majority of research on traumatic stress is focused on western populations from high income countries. This represents a marked gap in the literature because there is evidence from neural, psychological and social domains that people from collectivist backgrounds process life experiences distinctly from those with individualistic viewpoints. This is particularly an issue for Australia because of the high proportion of our population from varied ethnic backgrounds. Moreover, with over 70 million people forcibly displaced in the world, and Australia's own refugee intake, there is a need to understand how to better manage the traumatic stress experienced by these individuals and groups.

### ***Social and emotional wellbeing in Indigenous Australians***

In the context of Australia, arguably one of the most urgent issues for trauma-related stress research is the development of understanding and programs for Indigenous Australians. Although the prevalence of trauma-related disorders has been very well documented over the years, there has not been sufficient advances in key areas. Specifically, in the context of Indigenous Australians there are very significant gaps in conceptualising trauma-related stress, psychometrically valid assessment tools that are culturally appropriate, and evaluated programs to enhance social and emotional wellbeing in individuals and communities.

## Challenges

The main challenges that limit advances in research identified above include:

- Funding opportunities are limited.
- Most people with trauma-related disorders do not present for treatment or research studies.
- Adequate population-level studies are impeded because of privacy laws that prevent contacting people affected by disaster (e.g. bushfires).
- Parents/caregivers are commonly very reluctant to have their children participate in treatment or research.
- Clinical trials networks are lacking that promote recruitment of large-scale multi-site studies of trauma survivors in adults and children.
- Too much research is focused on disorder-specific conditions. PTSD is only one condition arising after trauma/adversity, and research funding needs to accommodate the complex and broad sequelae of trauma.
- There has been a myopic approach to augmenting trauma-focused therapies by attempting to increase extinction mechanisms. This has occurred despite the fact that many factors predicting treatment resistance are not related to extinction. There is a need for evidence-informed broader approaches to improving current treatments.
- Research with high-risk groups (military, first responders) suffers because there is often research fatigue in these populations.
- The major challenge of research with refugees and multicultural groups is translation obstacles. The cost of interpreting is very high and research grants do not recognise this massive barrier. Accordingly, research with these groups is typically not done because it is too difficult and costly.
- Research with Indigenous Australians is highly challenging because of community/systematic issues. Further, research with these communities cannot be achieved in timeframes expected in other populations, which results in many funded projects failing their goals and the Indigenous communities with whom they collaborate. Longer timeframes would also allow better quality collaborations and mentoring with Indigenous partners.

## Opportunities

Trauma-related disorders present at many different health sectors, and so there are often not clear sectors that are focused on trauma-related disorders. One exception to this in the public and private health systems is the treatment of Complex PTSD because increasingly agencies are offering specialist services to these patients. Research initiatives could usefully align with these services, which would increase access to research participants and improve research outcomes to clinical implementation.

Select agencies are highly invested in research on trauma-related disorders because their employees are regularly exposed to trauma, including the Australian Defence Force, Department of Veterans' Affairs and emergency service agencies (police, fire and rescue, ambulance). There is an opportunity for greater coordination between these agencies (who conduct their own research) and mainstream health funding agencies (e.g. NHMRC).

Other agencies are not highly invested in trauma-related research, however, many of the people under their charge do have strong trauma histories. Agencies responsible for prisons, juvenile justice, drug and alcohol services and refugee services deal with people with significant trauma backgrounds. Stronger links with these services could enable greater opportunities for research. In this sense, national or state initiatives akin to clinical trials networks that give research access to individuals exposed to trauma or adversity, could be formed to readily facilitate research opportunities.

A major enabler of future research in prolonged grief are palliative care and oncology units. Although there are many such units around Australia, there is little co-ordination between units to encourage research on mental health factors. A major obstacle in this regard is that the patient is the enrolled individual in the relevant health system, and so privacy laws limit access to families. Greater access to families via these units would facilitate research.

Many funding initiatives are disorder-specific. Trauma-related disorders, however, are highly complex and comorbid, and therefore encompass more than single diagnoses. Targeted calls, such as those from the Medical Research Future Fund, could focus on trauma-related disorders (encompassing PTSD, adjustment disorders, traumatic grief and post-traumatic depression).

### ***Potential research priorities***

There are many possible research priorities in this domain. This list is not exhaustive but should be regarded as indicative of some of the key areas requiring attention:

- Indigenous social and emotional wellbeing
- Refugee and multicultural studies
- Treatment resistant populations with trauma-related stress disorders
- Complex PTSD
- Disadvantaged populations (homeless, prisoners, juvenile justice)
- Implementation research
- Child developmental trauma

### **Conclusion**

Trauma and adversity is a common trigger for many psychiatric disorders. However, trauma-related disorders can be limited to those whose specific symptoms can be tied to the event, such as PTSD and prolonged grief disorder. These disorders contribute to major disability worldwide, and because of Australia's unfortunate history with natural disasters, wars, institutional abuse and maltreatment of Indigenous Australians, we have a strong interest in the mental health effects of trauma and adversity.

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