Prevention and Early Intervention: PTSD Following Traumatic Events

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CLINICAL SYNTHESIS

Abstract: Posttraumatic stress disorder (PTSD) is often a chronic condition that has a significant impact on the individual and society. In attempts to prevent the disorder for those at risk, researchers have explored predictors of PTSD with limited success. As an alternative, early treatment options have been developed and are reviewed here, including pharmacological approaches and psychosocial interventions. While few early interventions or predictors have been shown to be consistently efficacious, recommendations are provided for future research building on recent promising findings in biomarkers, pharmacotherapy, and exposure-based psychotherapy interventions.

Posttraumatic stress disorder (PTSD) is a painful and often chronic condition (1) that occurs in approximately 6.8% of adults (2) and 13.8% of military personnel (3) in the United States. Researchers have attempted to identify predictors of those at risk and early interventions for PTSD, since approximately 37%−92% of people will be exposed to a traumatic event during their lifetime (4). Symptoms of PTSD are almost universal following DSM criterion A traumatic events but, for the majority of individuals, these symptoms will diminish over time (5). Minimal progress has been made toward identifying which individuals will develop PTSD, although there are some promising interventions that may prevent PTSD among trauma survivors. Clinicians who work with trauma survivors are in need of instructions for minimizing distressing trauma reactions or preventing the development of PTSD.

Clinical context

The psychological, physical, economic, and societal impact of chronic PTSD demonstrates the tremendous need for effective early interventions. Individuals with PTSD often report long-term symptoms (1) with emotional distress frequently above and beyond diagnostic criteria. For example, Cougle and colleagues (6) found in a national study among individuals with PTSD that 18.8% had attempted suicide and 40.3% endorsed suicidal ideation. PTSD has a high rate of comorbidity with other psychiatric disorders (7, 8). Cougle et al. also reported that comorbid PTSD and MDD was associated with prevalence rates of suicidal ideation among women that were nearly twice as high as having either diagnosis alone (9). In their national household probability sample, comorbid diagnosis and PTSD-only groups displayed greater prevalence of suicidal attempts than those with MDD only. Significant health problems are commonly found among individuals with PTSD (10–14) leading to frequent expensive hospitalizations, work impairments, and doctor visits (15). Miller et al. (16) noted that the mental health costs associated with criminal violence linked to PTSD reached $166 billion. While the widespread costs of a disorder can be

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Table 1. Proposed Matrix of Risk Domains and Measures of PTSD for Further Research[a]

Variables to Consider After Trauma Exposure
Sleep quality before and after trauma
Trauma type (intentional or not)
Peri-traumatic tonic immobility
Perceived sense of threat
Perceived self efficacy
Cognitive flexibility
Perceived/anticipated support/help
Social support before during and after
Family/social unit cohesion
Initial PTSD symptoms: psychological and physiological distress
Post trauma cognitive factors: how one remembers and thinks about it
Heritable risk: personal and family history of psychiatric, alcohol and drug problems
Childhood adversity/trauma
Predictors of future trauma: personality, alcohol, drug use, patterns of services use
Meaning attached to trauma experience
Parental stress related to child wellbeing
Prior perceived trauma (not exposure to potentially traumatic events)
Sense of control: over especially grotesque events and perceived threat
Negative emotionality
Cognitive appraisal style
Exposure characteristics
Personality factors
Difference score on a 0–10 scale of distress at emergency department (ED) admission versus leaving the ED/ discharge
Difference score on a measure of how upset a patient was in the ED assessed 24 hours later, and how they feel several days or weeks later

[a] Adapted from "Post-Traumatic Stress Disorder (PTSD) Risk Prediction," National Institute of Mental Health, 2011 (http://www.nimh.nih.gov/research-funding/scientific-meetings/2011/post-traumatic-stress-disorder-ptsd-risk-prediction/index.shtml).

difficult to assess accurately, previous research strongly demonstrates the potential benefit of intervening after a traumatic event.

The first step in the prevention of PTSD is to identify who requires intervention. Potential predictors can be grouped into three categories: pretrauma factors, trauma characteristics, and posttrauma variables. Meta-analyses have reported potential predictors of PTSD across the three categories including prior trauma history, family psychiatric history, perceived life threat, poor social support, and peritraumatic emotional responses (17, 18).

While much of the risk for developing PTSD appears to be environmentally determined, approximately one-third of the vulnerability is genetically heritable (19, 20). Researchers have been exploring the role of genes as moderators and mediators of PTSD with many promising results. Genes that regulate HPA axis reactivity, specifically FKBP5 polymorphisms, have been shown to predict PTSD symptoms in individuals with histories of child abuse (21–25). Similarly, specific CRHR1 polymorphisms, which may indicate CNS stress reactivity, have been found to moderate the effect of child abuse on the risk of adult depressive symptoms (26) and PTSD (27). The short allele version of 5HTTLPR has been associated with decreased functioning and increased PTSD severity in a prospective sample (28). Differential regulation of the PACAP receptor (ADCYAP1R1) in females as a function of estrogen and stress interaction has been associated with PTSD (29). More work is needed, but the use of biomarker predictors of PTSD has great potential in identifying high-risk trauma survivors who may require clinical intervention.

While there have been promising group findings, no validated predictors have been discovered that can inform providers as to who will develop PTSD on an individual basis. At an NIMH-sponsored meeting of researchers examining early interventions and predictors of PTSD (30), it was recommended to examine the potential predictors listed in Table 1. Researchers are continuing to investigate predictors and developing early interventions to prevent the development of PTSD. In the meantime, patients who report these potential predictors following a traumatic event may benefit from prevention strategies or early intervention.

Treatment strategies and evidence

Pharmacological treatments

In recent years, researchers have attempted to identify pharmacological treatments that prevent PTSD. While some findings have been promising, other results indicate that some pharmacological approaches may worsen the impact of trauma. For example, propranolol has been researched extensively with mildly positive initial results (31–33) but more recent findings have indicated no difference from placebo (34, 35). Initial research on benzodiazepine anxiolytics did not show the approach to be

effective and indicated the medication may have resulted in elevated symptoms of PTSD (36). Preliminary naturalistic studies indicate that morphine may provide some protective benefit against the development of PTSD (37, 38), while other research on the use of ketamine (an anesthetic) with trauma patients has been inconsistent (39, 40).

While there are currently no recommended pharmacological approaches to prevent PTSD, recent studies have explored high dose glucocorticoid activation and suggested that it may be helpful as a preventative strategy. Schelling et al. (41) indicated that glucocorticoid administration during treatment in an intensive care unit (ICU) resulted in significantly fewer long-term symptoms of PTSD. Similar results were found in a study of veterans with combat-related PTSD in which they were given glucocorticoid or placebo following a memory reactivation task (42). While patients who received glucocorticoid as opposed to the placebo showed symptom improvement, these results diminished at 1-month postadministration. Zohar and colleagues (43) proposed a "window of opportunity" in administering glucocorticoids as they reported that a high dose of hydrocortisone treatment given in the first few hours after a trauma was associated with favorable changes in those susceptible to chronic PTSD. Further research suggests it is possible that glucocorticoid treatment following trauma exposure decreases the hyperactive fear response as well as enhanced consolidation which is hypothesized to contribute to the development of PTSD (44, 45). There is growing evidence of an inflammation hypothesis in depression that may be active in PTSD as well and may be counteracted with high dose glucocorticoids, which we refer to as the inflammation hypothesis in PTSD (46–48). These seem to be the most promising candidates of the pharmaceutical agents tested for early intervention: benzodiazepines and beta-blockers have essentially been eliminated, and it is unlikely that civilians exposed to a traumatic event without physical injury will be administered morphine routinely.

Other researchers of pharmacological approaches to PTSD prevention have argued for the study of medications that are already commonly prescribed to acutely injured trauma survivors in emergency settings. Using pharmacoepidemiologic methods, for example, Zatzick and Roy-Byrne (49) found that 80% of trauma patients are prescribed opiate analgesics, as compared with less than 10% of patients being prescribed medications studied for PTSD prevention (e.g., propranolol, gabapentin) which may be contraindicated in many cases. Thus, the greater breadth of applicability of medications that are already in widespread use with injured trauma survivors may enhance the population impact of potential pharmacological approaches (50). Regardless, randomized controlled trials are greatly needed to establish the efficacy of promising pharmacological strategies for preventing PTSD.

PSYCHOLOGICAL DEBRIEFING

The earliest psychological interventions following traumatic events were documented in World War I (51) and were eventually described as crisis interventions that are brief, delivered within days of a trauma, and that fall under the generic term psychological debriefing. The general aim of psychological debriefing is to reduce distress and mitigate long-term problems, such as PTSD, by discussing emotions and reactions to a trauma while providing psychoeducation and normalization of reactions (52). However, the specific components of psychological debriefing have generally lacked specificity. The most widely used crisis intervention method is Critical Incident Stress Debriefing (CISD), which consists of one session that lasts 3–4 hours and is delivered typically in a group format that occurs 2–10 days after the traumatic event (53). While the goal of preventing PTSD at the earliest possible point is ideal, extensive research on psychological debriefing as a prevention method for PTSD has resulted in significant doubt in its efficacy (54). In a recent dismantling study on CISD (55), emotional debriefing, as compared with psychoeducation, was associated with worsening symptoms 6 months after a trauma for those with early hyperarousal symptoms.

BRIEF PSYCHOSOCIAL INTERVENTIONS

With the questionable effectiveness of psychological debriefing, researchers have increasingly studied other brief psychosocial interventions aimed at preventing PTSD. Psychoeducation has been explored as a possible prevention method, but initial results indicate that this early intervention strategy is not associated with reductions in PTSD or depression symptoms (56–58). Gidron and colleagues (59) developed a memory structuring intervention that was initially associated with lower PTSD symptoms but, in a follow-up study, found to be more effective with women than men (60).

Other researchers have developed more specialized approaches that address the needs of populations that have experienced specific types of trauma. The high trauma exposure and PTSD rates among military service members led to the development of the Battlemind Psychological Debriefing, which is a group-based intervention that focuses on

normalizing trauma reactions and providing psychoeducation to combat veterans (58). Adler and colleagues (61) noted some initial findings of fewer PTSD and depression symptoms among those who participated in the Battlemind program postdeployment as compared with a stress education group, especially among soldiers with high combat exposure. Another high risk group is sexual assault victims for whom Resnick and colleagues (62) developed a novel video-based intervention that was viewed before forensic rape exams. Information was provided about the exam and PTSD as well as coping strategies to reduce symptoms. Results suggest women, especially those with prior assault histories, benefitted from the intervention by reporting reductions in postrape pathology including PTSD symptoms (63). Finally, for acutely injured trauma survivors, a stepped care collaborative approach was investigated which provided extensive support including case management, pharmacotherapy, and cognitive-behavioral therapy for months following the trauma (64). This approach showed reductions in alcohol problems but minimal impact on PTSD symptoms. However, a follow-up study of this stepped care intervention with 207 acutely injured hospitalized trauma survivors did suggest that compared with usual care, the intervention significantly reduced PTSD symptoms at 6, 9, and 12 month follow-up assessments (65). These commendable interventions may be reaching vulnerable high-risk populations, but more research is needed to determine their effectiveness and feasibility in the wider community.

COGNITIVE BEHAVIORAL INTERVENTIONS

Studies have suggested that cognitive-behavioral therapy (CBT) is a promising early intervention method. CBT approaches for PTSD, such as prolonged exposure, generally include elements such as exposure to the trauma memory and trauma reminders, cognitive restructuring and breathing retraining (66). Researchers have targeted patients who meet criteria for acute stress disorder (ASD) for early intervention since it has been hypothesized that ASD predicts PTSD in some individuals (67). As one example, Bryant and colleagues (67) examined the efficacy of CBT and anxiety management in the treatment of ASD in civilian trauma survivors and found that fewer participants who received exposure (14%) or exposure and anxiety management (20%) met criteria for PTSD posttreatment than participants who received supportive counseling (56%). Other studies have documented similar results demonstrating that CBT techniques applied shortly after a trauma lead to reduced rates of PTSD (68), sometimes preventing chronic PTSD in the longer term (69, 70).

While multiple studies have reported promising findings on utilizing CBT as an early intervention strategy (71–74), other studies have reported mixed results. In a recent randomized intervention trial (75), CBT, prolonged exposure, and escitalopram were compared with placebo or wait list control conditions among patients 1-month posttrauma. Patients receiving prolonged exposure or CBT were less likely to have PTSD as compared with patients in the wait list group. However, there were no differences in rates of PTSD when comparing patients who received the medication to patients who received the placebo. At 9 months posttreatment, there was no difference in rates of PTSD between patients who received prolonged exposure and wait list controls. An equipoise-stratified randomization strategy allowed patients to refuse treatment arms: 42.6% declined the SSRI versus placebo arms, 5% declined wait list, 3.3% declined cognitive therapy, and 1.2% declined prolonged exposure. Sijbrandij and colleagues (76) also reported mixed findings when they assigned patients with acute PTSD to receive either four sessions of CBT or be assigned to a wait list. Among those who received the brief early CBT, there was an accelerated rate of recovery from symptoms of acute PTSD with particular benefit for those with comorbid PTSD and depression. Yet, at the 4-month follow-up assessment, there were no significant differences for PTSD, depression, or anxiety symptoms between groups. The authors suggested this finding may be associated with the need for additional sessions or for the intervention to occur sooner after the traumatic event. More research is needed to determine which elements of a CBT intervention, such as the timing or length, are critical. Bryant and colleagues (74) began this in their dismantling study in which they found fewer PTSD symptoms and more frequent full remission at follow up of participants who received exposure, as compared with cognitive restructuring. Overall, the most promising results were from studies in which patients with severe symptoms met individually with a clinician within weeks after a trauma as opposed to psychological debriefing group sessions for all exposed meeting just once.

EARLY INTERVENTION FOR TRAUMA-EXPOSED INDIVIDUALS IN THE EMERGENCY DEPARTMENT

Preliminary animal data and consolidation theory support intervening early after a trauma to prevent PTSD. Previous animal research (77) demonstrated that the consolidation of a fear memory appears to be interrupted when extinction training is

administered 10 minutes after fear conditioning as opposed to 72 hours after fear conditioning (78). Consolidation theory holds that memories are first held in a short-term transient state and then, within a time-dependent process, they are transferred into a long-term permanent state (79). Translational studies have presented similar findings with human participants (80) who underwent extinction training 10 minutes, as compared with 72 hours, after fear conditioning. It appears that early extinction training may modify a conditioned fear and prevent it from entering long-term memory as an enduring fear memory.

Two recent studies have sought to test the hypothesis that an early exposure-focused intervention delivered within hours after a trauma will prevent memory consolidation which will then reduce or prevent PTSD symptoms. Rothbaum et al. (81) developed a novel, brief exposure-based intervention which they tested in the emergency department where they recruited participants immediately posttrauma. They discovered that the approach was not only safe and feasible, but also resulted in lower levels of depression and distress (81). Rothbaum and colleagues proceeded to expand upon this open-label pilot study by conducting a randomized controlled trial of 137 emergency room patients and utilized a modified prolonged exposure protocol (82). Results supported the earlier finding in that individuals who received the intervention, as compared with an assessment only, reported fewer depression and PTSD symptoms at 4 weeks and 12 weeks and reported half the rate of PTSD 12 weeks after their trauma. A subgroup analysis suggested that the intervention had a greater positive effect for rape victims, which is interesting given that rape represents a type of trauma exposure that is particularly high risk for subsequent development of PTSD. These findings are promising and indicate a need for more research to investigate exposure-based approaches that intervene within hours of trauma exposure. Even more exciting, this early intervention appeared to mitigate genetic risk for developing PTSD (unpublished study of Rothbaum et al.).

Questions and controversy

The largest question is what to do with survivors in the aftermath of trauma. The most controversial early intervention has been psychological debriefing. Some controlled studies comparing recipients of psychological debriefing with those who received no intervention concluded that patients at risk for developing PTSD do not derive benefit from psychological debriefing and may be harmed by the intervention (54, 83). Concerned about the negative impact of psychological debriefing, the Cochrane Review (36) recommended that survivors of trauma specifically not be debriefed. Moreover, recent reviews (84, 85) have suggested that groups using psychological debriefing either conduct research to demonstrate its effectiveness or cease using it.

Even if effective methods are identified, the next largest question is how to determine who is at risk and is likely to respond to an early intervention. Questions remain around many of the predictors of and early interventions for PTSD. Researchers are continuing to search for validated predictors of PTSD and inconsistent findings on early interventions for preventing PTSD point to the need for additional research and replication of these approaches. While results are promising for early CBT interventions, the research is preliminary and it is premature to indicate whether these will be consistently effective interventions for all trauma-exposed populations. Randomized controlled trials are needed to prospectively test the relationship between early treatment approaches and subsequent PTSD severity.

Recommendations from the authors

Unlike other psychiatric disorders, the precipitant for adult PTSD is a known event, allowing for immediate intervention, thus presenting the potential to prevent, and ultimately eliminate for many, the occurrence of this most serious condition. The safest approach to early intervention, and one that has been repeatedly recommended, is a "wait and see" policy with recent trauma survivors. However, this misses an opportunity for primary prevention. Regarding pharmacotherapy, the most promising results are from the glucocorticoids. Regarding psychotherapy, the most promising results in treating ASD is CBT, but even more exciting is the recent success of administering exposure therapy within hours of the traumatic event, resulting in half the rate of PTSD 12 weeks later. We recommend that clinicians utilize CBT psychotherapies that have demonstrated the most effectiveness thus far such as prolonged exposure and cognitive processing therapy or utilizing anxiety management techniques combined with exposure. The current state of knowledge offers no good predictors of response to trauma, but our hope is that soon we will have accurate biomarkers that, combined with a patient's history and current trauma characteristics (e.g., rape versus nonsexual assault), establishes useful predictors. In the absence of validated predictors, we think the best approach is to offer early interventions for those who endorse experiencing a criterion A event and conduct research to establish response.

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