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EARLY INTERVENTIONS FOR PTSD: A REVIEW

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Abstract

The high prevalence of trauma exposure and subsequent negative consequences for both survivors and society as a whole emphasize the need for secondary prevention of posttraumatic stress disorder. However, clinicians and relief workers remain limited in their ability to intervene effectively in the aftermath of trauma and alleviate traumatic stress reactions that can lead to chronic PTSD. The scientific literature on early intervention for PTSD is reviewed, including early studies on psychological debriefing, pharmacological, and psychosocial interventions aimed at preventing chronic PTSD. Studies on fear extinction and memory consolidation are discussed in relation to PTSD prevention and the potential importance of immediate versus delayed intervention approaches and genetic predictors are briefly reviewed. Preliminary results from a modified prolonged exposure intervention applied within hours of trauma exposure in an emergency room setting are discussed, along with considerations related to intervention reach and overall population impact. Suggestions for future research are included. Prevention of PTSD, although currently not yet a reality, remains an exciting and hopeful possibility with current research approaches translating work from the laboratory to the clinic.

Keywords

secondary prevention; early intervention; PTSD; ASD

Exposure to traumatic events is unfortunately a common experience, with prospective studies indicating that PTSD symptoms are almost universal in the immediate aftermath of trauma. The majority of individuals will have symptoms of reexperiencing, avoidance, and hyperarousal initially following the trauma that will extinguish over time.[1] For some individuals, however, their symptoms persist and cause impairment in functioning, which leads to a diagnosis of PTSD. Unfortunately, little progress has been made in identifying interventions that prevent trauma survivors from developing PTSD. Clinicians and relief workers still need a treatment strategy that can alleviate normal trauma reactions and decrease rates of PTSD, especially in high-risk individuals.

The lack of such an established early intervention has negative consequences for both trauma survivors and greater society. An estimated 37–92% of all people will be exposed to a traumatic event during their lifetime,[2] and surveys suggest that 6.8% of adult Americans currently have PTSD.[3] The prevalence is significantly higher in military personnel as 13.8% of veterans of the war in Iraq and Afghanistan met DSM-IV criteria for PTSD.[4]

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PTSD often exhibits a chronic course, with as many as 40% continuing to exhibit significant symptoms of the disorder 10 years after its onset.[5] Psychiatric comorbidity is between two and six times more likely to occur in individuals with PTSD.[6,7] Increased risk for physical health problems and visits to the doctor are observed as well, with PTSD often associated with significant functional impairment across a variety of domains.[8–14] With respect to the financial costs associated with this disorder, Greenberg et al.[15] found that through work impairment, hospitalization, and health visits, PTSD was responsible for higher costs than any of the other anxiety disorders. These considerations underscore the devastating impact of PTSD and illustrate the urgent need for interventions that may prevent the development of the disorder.

PREDICTORS OF PTSD

Research has been devoted to the study of potential predictors of PTSD to identify those most vulnerable following exposure to a traumatic event. Meta-analyses have identified prior trauma histories, family psychiatric history, perceived life threat, poor social support, and peritraumatic emotional responses as risk factors for PTSD.[16,17] Approximately one-third of the vulnerability to develop PTSD is genetically heritable and the remaining risk is primarily environmentally determined.[18,19] Thus, research that can identify potential candidate genes that predict the development of PTSD may offer a more efficient way of identifying at risk trauma survivors and determining who is most likely to require and to benefit from early intervention. For example, it was recently demonstrated that polymorphisms within the FKBP5 gene (which regulates HPA axis reactivity) interact with a history of child abuse to predict adult PTSD symptoms.[20–24] Other alterations of the HPA axis, including hyperactivity of corticotropin-releasing hormone receptor (CRHR1) in neurons,[25] have been demonstrated to be a prominent feature of PTSD. Specific CRHR1 polymorphisms moderate the effect of child abuse on the risk of adult depressive symptoms[26] and PTSD.[27] To the extent that CRHR1 polymorphisms function as a marker of CNS stress reactivity, variants may be valuable as vulnerability factors that interact with stress exposure to impact PTSD and may define a PTSD-depression phenotype.

A number of studies have examined the serotonin transporter variable length polymorphism (5HTTLPR) as a potential risk mediator of PTSD.[28–30] Related to predictive risk for who may develop PTSD in the immediate aftermath of trauma, one recent study prospectively analyzed a cohort of college students who all experienced a campus shooting in 2008. The short allele version of 5HTTLPR (which has been associated with decreased functioning relative to the functional long allele) was associated with increased PTSD symptoms in the weeks following the shooting in this prospective sample.[31]

Finally, a recent study suggests that PTSD is associated with differential regulation of the PACAP receptor (ADCYAP1R1) in females as a function of estrogen and stress interaction.[32] If replicated, this could help explain the higher prevalence of PTSD in women. Identifying genetic biomarkers for PTSD could streamline intervention approaches by focusing valuable clinical resources on those most in need of intervention.

Despite the above findings, there is a large variability in response to traumatic events that remains unexplained by these identified psychological, biological, or genetic factors. Currently, there have been no prospective studies validating any predictor of PTSD as specific and sensitive enough to determine who requires intervention and who will recover on their own. In this article, we review the literature on early interventions for PTSD.

PREVENTION APPROACHES TO PTSD

PSYCHOLOGICAL DEBRIEFING

Attempting to intervene in the immediate aftermath of trauma in an effort to assist coping and reduce further distress is not a new idea by any means. Psychological debriefing (PD) has its roots in World War I when commanders would meet with their men following a major battle to debrief them.[33] incident stress debrief-ing (CISD) is a specific form of PD that has been widely disseminated.[34] A CISD session typically lasts 3–4 hr, is conducted 2–10 days after the critical incident, is typically delivered in groups and has seven defined phases.

However, controlled studies of the efficacy of PD have called its efficacy. Mayou et al.[35] con-ducted a randomized controlled trial of PD for mo-tor vehicle crash (MVC) survivors and found that at a 3-year follow-up, patients who received the intervention remained symptomatic for PTSD and had significantly more physical health problems, travel anxiety, and general psychiatric symptoms than patients who received no intervention. Thus, the authors concluded that patients at risk for chronic PTSD are not helped by debriefing interventions and may actually be harmed by their participation. Bisson et al.[36] documented similar findings in a sample of acute burn victims, where higher rates of PTSD were observed among those who received PD versus a control group. A dismantling study by Sijbrandij et al.[37] randomized 236 recently traumatized (<2 weeks posttrauma) civilian adults to receive a single session of either emotional ventilation debriefing, educational debriefing, or no debriefing. Participants in the emotional debriefing group with higher baseline hyperarousal symptoms exhibited significantly more PTSD symptoms at 6 weeks than controls. The results of this study suggest that emotional debriefing, as opposed to the more neutral psychoeducational debriefing, may be associated with worse outcomes in individuals with significant symptoms of hyperarousal.

Several excellent critical reviews[38,39] have concluded from controlled studies that PD does not prevent PTSD. In fact, these reviews suggest that it may actually interfere with the natural recovery process and lead to an *increased* rate of PTSD in those debriefed. In the strongest position to date, the prestigious Cochrane Review (p. 1)[39] explicitly states, “Compulsory debriefing of victims of trauma should cease.”

PHARMACOLOGICAL TREATMENTS

Several pharmacological treatments have been proposed as possible preventative strategies that may be able to ameliorate the impact of trauma exposure. Early research in this area focused on benzodiazepine anxiolytics, which did not prove useful and may even lead to higher rates of PTSD.[40]

Based on evidence that propranolol abolishes the epinephrine enhancement of conditioning,[41] a pilot study attempted to prevent PTSD by administering propranolol (a β-adrenergic blocker) within 6 hr of trauma exposure.[42] Results indicated that although propranolol did not result in reduced PTSD relative to a placebo, patients receiving propranolol displayed less physiological reactivity on one measure to trauma reminders 3 months later. Another study found that propranolol administered immediately after trauma reduced PTSD severity 2 months later,[43] suggesting that administration of propranolol shortly after trauma exposure may limit fear conditioning that may contribute to subsequent PTSD development. Hurlemann et al.[44] indicated that propranolol reduces neural reactivity in the amygdala, which could reduce traumatic stress reactions. Despite these findings, more recent studies have failed to replicate their results. Stein et al.[45] found no differences in PTSD rates in a double-blind, randomized controlled trial of propranolol administered within 48 hr of trauma exposure. Another randomized controlled trial compared propranolol

to placebo and failed to identify any decrease in PTSD diagnoses or severity 3 months after the initial trauma.[46] These negative findings on propranolol are likely to lead researchers to look toward other preventative strategies in future work.

Several studies have suggested that high-dose glucocorticoid activation may be beneficial in the immediate aftermath of trauma. Schelling et al.[47] examined the effects of stress doses of hydrocortisone in preventing PTSD symptoms following critical illness and surgery in intensive care units. They found that glucocorticoid administration during ICU treatment results in a significant reduction of PTSD symptoms in long-term survivors as well as improvements in quality-of-life outcomes. In a more recent study,[48] veterans with combat-related PTSD were exposed to a memory reactivation task using well-established imagery and psychophysiological assessments followed by administration of either glucocorticoid or placebo. They found that 1 week after glucocorticoid administration, patients showed symptom improvement compared with control participants. However, reduction of symptoms degraded at a 1-month postadministration assessment. Zohar et al.[49] reported that high-dose hydrocortisone treatment given in the first few hours after a traumatic experience was associated with significant favorable changes in the trajectory of exposure to trauma. From this study and animal studies, they propose that there is a “window of opportunity” in the early aftermath of trauma to help those who are vulnerable to the development of chronic PTSD. Regarding potential mechanisms, two recent studies demonstrated that treatment with either hydrocorticosterone or dexamethasone prior to fear potentiated startle and discriminant conditioning decreases the hyperactive fear response in subjects with PTSD.[50,51] Thus, it is possible that glucocorticoid treatment following trauma exposure decreases the hyperactive fear response and thus the enhanced consolidation that is hypothesized to contribute to the development of PTSD.

Other preliminary studies have been conducted examining medications such as morphine and ketamine. Naturalistic studies of morphine administration following a trauma injury have suggested that morphine may provide some protective benefit against later development of PTSD.[52,53] Ketamine, an anesthetic often used in emergency settings, has also been associated with lower rates of PTSD,[54] but contradictory findings have been documented as well.[55] Of note, intravenous low-dose ketamine has recently been broadly examined as a potential acute treatment for depression symptoms and suicidality.[56,57] Whether the same neural mechanisms underlie these findings and the potential effects for PTSD are not yet clear. At this stage, it is premature to point to morphine or ketamine administration as an early intervention for PTSD. Randomized controlled trials are needed to prospectively test the relationship between these pharmacological approaches and subsequent PTSD severity.

Recent commentary by clinical epidemiologists has suggested expanding the notion of translational research to include bidirectional bedside to bench translational epidemiology in order to inform more tractable intervention approaches.[58,59] As an example, Zatzick and Roy-Byrne used epidemiologic methods to determine which medications with strong theoretical support in animal models for the secondary prevention of PTSD, were already in widespread use in trauma center settings.[60] The authors reasoned that medications already in widespread use may have the greatest potential breadth of applicability to populations of injured trauma survivors admitted to acute care medical settings. Both β-adrenergic blockers and opiate analgesic medications may prevent traumatic memory consolidation through a β-adrenergic mechanism. However, in random samples trauma center adult and adolescent patients, opiate analgesic medications were prescribed to 82–88% of patients, whereas β-adrenergic blockers were prescribed to less than 5% of patients. Beta-blockers are often contraindicated in the early hours after injury in acute care medical settings as patients frequently present with hypovolemia and associated cardiovascular instability.

Clinically, these epidemiologic observations regarding rates and patterns of psychotropic and analgesic use in real-world practice may be extremely useful in identifying which agents may be more feasibly tested in acute care medical early PTSD prevention trials. Clinically, it is easier to test a medication that is already in widespread use than one that may have contraindications in a postinjury, trauma center/emergency department context.

From a theoretical perspective, these observations highlight the importance of considering the potential population impact of early PTSD interventions.[59] The overall population impact of an intervention is a function of both the intervention treatment effects and the breadth of applicability of the intervention.[61] Even if opiate analgesic agents and β-adrenergic blockers had equivalent treatment effectiveness in the early prevention of PTSD, the greater breadth of applicability of analgesic agents in acute care medical settings would suggest a greater overall population or "public health" impact for analgesic medications.

BRIEF PSYCHOSOCIAL INTERVENTIONS

In addition to PD, there are a number of other brief psychosocial interventions that have been developed with the aim of preventing PTSD. A memory-structuring intervention aimed at helping trauma survivors organize their memory of the traumatic event was developed by Gidron et al.[62] A small randomized controlled study of traffic accident victims indicated lower PTSD symptoms among participants who received the memory-structuring intervention. A follow-up study aimed at replicating these findings found a gender-specific effect, where female participants experienced reduced PTSD symptoms in the intervention group, but male participants did not.[63] These inconsistent findings point to the need for further replication, especially as both studies utilized small sample sizes.

Other studies have examined the utility of self-help information or psychoeducation as a way to prevent PTSD following a traumatic experience, but initial results suggest that these approaches are ineffective. Providing trauma survivors with self-help booklets that outline common trauma reactions and suggested coping strategies has not been associated with lower subsequent rates of PTSD and depression.[64,65] A study by Bugg et al.[66] compared a self-help booklet with a structured writing intervention and found no differences between the two types of intervention. Based on these findings, the authors concluded that neither format could be recommended as an early intervention for trauma.

Other approaches have been developed that target-specific trauma populations. For example, Battlemind PD is a group-based intervention designed for a military population exposed to combat trauma. In contrast to PD, this program does not emphasize recounting the traumatic event, and instead focuses on normalizing trauma reactions and educating participants on common problems (e.g., sleep, anger difficulties) that they may experience or see in their fellow unit members as a result of the identified trauma.[67] Adler et al.[68] documented some preliminary support suggesting that postdeployment participation in the Battlemind program was associated with fewer PTSD and depression symptoms compared to a stress education group, particularly among soldiers with high-combat trauma exposure.

An innovative prevention approach designed specifically for sexual assault survivors is a video-based intervention implemented prior to a forensic rape exam. Resnick et al.[69] developed a 17-min video presenting a variety of information related to the forensic exam, traumatic stress reactions, and coping strategies that can reduce subsequent anxiety and avoidance. Reductions in postrape psychopathology, including PTSD symptoms and marijuana abuse, were observed in women who received the video intervention in a randomized design.[70] This study also suggested an increased benefit for women with prior assault histories, which was replicated in a follow-up study.[71] Although specific to sexual

assault traumas, this brief video-based approach has potential as an easily disseminated prevention strategy. However, more research and replication is needed.

Finally, two investigations have tested a stepped collaborative care approach for acutely injured trauma survivors who are provided with case management initiated during inpatient treatment, and supplemented with pharmacotherapy, cognitive-behavioral therapy (CBT), and motivational interviewing as needed in the weeks and months following trauma exposure.[72] A smaller scale ($N = 120$) initial investigation demonstrated feasibility and reduced alcohol problems in those receiving the intervention, although the effect on PTSD symptoms was small.[72] A second larger early PTSD prevention trial that included 207 highly symptomatic injured trauma survivors demonstrated statistically and clinically significant reductions in PTSD symptom levels over the course of the year after injury. Intervention patients' physical function as assessed with the Medical Outcomes Study Short Form 36 Physical Function Subscale improved significantly relative to controls.[73]

Using translational clinical epidemiologic methods, the breadth of applicability, treatment effects, and overall population impact indices from two trials were compared, a cognitive-behavioral psychotherapy efficacy trial of behavioral activation and smaller scale ($N = 120$) stepped collaborative care effectiveness trial.[72,74]

The behavioral activation intervention involved multiple (i.e., four to six) office-based psychotherapy sessions. Exclusion criteria included a history of substance abuse or dependence, alcohol dependence, pre-injury PTSD or depression, ongoing intimate partner violence, ongoing lawsuits, or patients with extended intensive care unit stays. Screening procedures required patients to be diagnosed with PTSD in order to be included. Of particular note, the intervention focused exclusively on behavioral activation, and did not address competing demands that might serve as barriers to participation in intervention activities. Intervention patients in the collaborative care trial received stepped care. Stepped collaborative care combined care management and motivational interviewing targeting treatment retention and engagement with psychopharmacological and exposure-based CBT interventions specifically targeting PTSD symptom reduction. Treatment began with each injured intervention patient being met at bedside in the surgical ward by a masters in social work (MSW) care manager. Treatment delivery occurred in acute care settings (e.g., surgical outpatient clinic follow-up appointments), in the community, or over the telephone. There were few intervention specific exclusions and all patients with active alcohol or drug abuse/dependence were included. In both trials, patients assigned to the control condition received care as usual.

A reciprocal relationship between effect size and breadth of applicability was evident in a direct comparison of the two trials.[75] The CBT trial demonstrated a larger effect size (50% PTSD prevention), but limited breadth of applicability; in a target population of over 1,000 patients, less than 1% of potential subjects met study inclusion criteria and were randomized. The stepped collaborative care demonstrated a smaller effect size of 7% PTSD prevention, but markedly enhanced breadth of applicability to the target population for PTSD prevention relative to the efficacy trial. Modeling of the population impact suggested that a 9.5-fold greater cumulative reduction in the incidence of PTSD would result from implementation of the collaborative care early intervention. The investigation suggested that despite the greater effect size observed in the behavioral activation CBT trial, the enhanced breadth of applicability associated with the stepped collaborative care early intervention strategy would yield greater overall population impact as this intervention approach would be applied to a much larger proportion of the target population at risk for PTSD. The population impact estimation method also emphasized the importance of not only tracking

of treatment effects in early PTSD prevention trials but also the necessity of carefully assessing intervention reach to a pre-specified target population.[61,76]

COGNITIVE-BEHAVIORAL INTERVENTIONS

In the treatment of PTSD, CBT usually involves prolonged, imaginal exposure to the patient's memory of the trauma, and in vivo exposure to various reminders of the trauma, as well as cognitive restructuring and anxiety management techniques.[77] The efficacy of CBT in treating chronic PTSD has led researchers to question whether this approach may also be useful as an early intervention. Most of these studies have tested CBT in the first weeks or months of trauma exposure, consisting of approximately 4–5 sessions with patients who meet criteria for acute stress disorder. As one example, a study by Bryant et al.[78] examined the efficacy of CBT and anxiety management in the treatment of ASD. Civilian trauma survivors were given five sessions of either prolonged exposure (PE), a combination of exposure and anxiety management, or supportive counseling within 2 weeks of their trauma. Results indicated that fewer individuals in the exposure (14%) and exposure plus anxiety management (20%) conditions met the criteria for PTSD following treatment than those in the supportive counseling group (56%). Results of this study suggested that PTSD can be prevented by early provision of CBT and that exposure may be a critical component in the treatment of ASD.[78] Another study that applied cognitive-behavioral techniques to a sample of female assault survivors found that the intervention produced lower rates of PTSD and anxiety compared to supportive counseling at a 2-month follow-up.[79] Other studies have documented similar results for the efficacy of CBT applied in the first month after trauma exposure in preventing chronic PTSD,[80,81] or at accelerating recovery.[79] In addition to these early intervention studies, the use of exposure and other cognitive-behavioral techniques implemented several weeks or months after the initial trauma have also produced positive findings.[82–85] Bryant et al.[86] conducted a study that dismantled exposure versus cognitive restructuring approaches and found that those who received exposure therapy were less likely to meet criteria for PTSD and to have achieved full remission of symptoms at follow-up. In summary, interventions that were delivered individually, in multiple sessions, to patients with severe symptoms, in the early weeks of trauma exposure, have typically been effective at reducing the incidence of PTSD compared to no treatment or supportive counseling control groups, with exposure techniques potentially being key in producing these results. These intervention approaches highlight the potential benefit of CBT in recently traumatized individuals, especially exposure techniques.

COMPARISON OF PSYCHOSOCIAL AND PHARMACOLOGICAL INTERVENTIONS

A recent randomized early intervention trial found that CBT administered about a month following exposure to a traumatic event was effective in reducing PTSD posttreatment but no more effective than wait list 9 months later, and that SSRI treatment was no more effective than placebo. Patients (n = 240) who met PTSD criteria after experiencing a traumatic event were randomized to receive PE, cognitive therapy, or a waiting list (WL) control, or escitalopram or pill placebo.[87] An equipoise-stratified randomization strategy allowed patients to refuse randomization to up to two treatment arms: 42.6% declined the SSRI versus placebo arms, 5% declined wait list, 3.3% declined cognitive therapy, and 1.2% declined PE. PTSD rates after 5 months were lower in active conditions as compared to WL: 21.6% PTSD in PE versus 57.1% WL, and 20.0% cognitive therapy versus 58.7% WL. No difference in the rate of PTSD was seen between patients who received escitalopram or pill placebo (61.9 versus 55.6 percent). At 9 months, there were no differences in rates of PTSD between patients who received PE (20.8%) or wait list (21.4%). A limitation of the trial included small sample sizes of patients who received escitalopram or placebo (46 patients).

PTSD AS A DISORDER OF EXTINCTION: EXTINCTION AND HABITUATION

As we have said, most trauma victims show fear and other reactions following the traumatic event, which extinguish over time. We believe the development of chronic PTSD in those who do not recover represents a failure of extinction, due to a variety of factors such as genetics, early life stress, intensity of the trauma, and other factors. Foa and Kozak[88] theorized that in order to reduce pathological anxiety, two conditions are necessary for emotional processing to occur: activation of the fear memory and the incorporation of corrective information (e.g., that the feared consequence does not occur). These two conditions are met in exposure therapy when the patient confronts actual fear-related stimuli (in vivo exposure) or intentionally retrieves a memory of the traumatic experience (imaginal exposure) and experiences the associated fear reactions, but in the absence of the feared consequence (being assaulted).

This is, in fact, basically the same process that occurs in extinction training that can be studied directly in animals. Thus, repeated presentations of the conditioned stimulus (CS; in vivo exposure—extinction training) typically elicits the fear response (activation), which then diminishes over the course of repeated trials within an extinction session as well as over the course of successive extinction sessions. Another similarity across exposure therapy and extinction training is a partial return of the conditioned response following exposure/extinction training at the beginning of the next session, referred to as the return of fear[89] in the clinical literature and spontaneous recovery in the extinction literature. In addition, fear often returns in patients that undergo a subsequent major life stress (reinstatement) or even a change in context (renewal). Research that targets the three primary causes of relapse, namely spontaneous recovery, renewal and reinstatement in patients with current PTSD symptoms is extremely important, and ideally, the most effective way of avoiding relapse is to prevent the development of PTSD in the first place.

There is emerging evidence that early extinction immediately after fear conditioning may prevent fear consolidation, which is relevant to research on early prevention of disorders such as PTSD. One particularly surprising piece of information that emerged from this research[90] is that extinction may be mediated by either the prevention of consolidation or new learning depending on the time after fear conditioning when extinction training is initiated. In this study, different groups of rats were fear conditioned and then given extinction training either 10 min, 1 hr, 24 hr, or 72 hr after acquisition and their susceptibility to recovery of fear through reinstatement, renewal, and spontaneous recovery was evaluated. Animals extinguished at the typical 72 hr exhibited robust recovery of fear in all cases, whereas animals extinguished at 10 min exhibited no recovery of fear—they remained fully extinguished. Animals extinguished at intermediate intervals exhibited intermediate recovery of fear. In many cases, extinction at the shortest time point was less complete than that at the longest timepoint,[91,92] but this did not seem to explain the lack of fear recovery in the 10-min group. Because memory recovery effects have served as the impetus for new learning accounts of extinction, the lack of fear recovery in the short-interval group would seem to be explained most parsimoniously in terms of erasure of conditioned fear and/or prevention of consolidation of the fear memory. Consistent evidence is emerging for a neurobiological difference between short- and long-interval extinction as well. Cain et al.[91] reported that immediate extinction is not affected by the L-type voltage-gated calcium channel (L-VGCC) inhibitor nifedipine, and Mao et al.[93] found that fear extinction initiated 1 hr after fear acquisition reversed a fear conditioning induced change in a particular glutamate receptor (the GluR1 subunit of the AMPA receptor) within the amygdala. This reversal did not occur when extinction was initiated 24 hr after acquisition. Together these data suggest that appropriate intervention shortly after a trauma memory has been encoded may have unique properties affecting the long-term fear memory of the trauma.

The apparent difference in the mechanisms of short- and long-interval extinction may be understandable in the context of consolidation theory. This holds that memories, once acquired, undergo a time-dependent process by which they are converted from a short-term, labile state into a long-term, permanent state.[94] When extinction training is initiated 10 min after acquisition, fear memory has only just begun to consolidate, whereas when extinction training is initiated 72 hr after acquisition, consolidation probably is complete or close to it. This difference in the consolidation state of fear memory at the two time points may offer a different substrate for extinction to act upon, and thus may be a critical factor in determining the mechanism of extinction.[91,95] Translational studies with human subjects have documented similar findings, where lower levels of fear potentiated startle responses were noted in participants who underwent early extinction training (i.e., 10 min after fear conditioning) versus delayed extinction training (i.e., 72 hr after fear conditioning).[96] These findings highlight the potential importance of early prevention and the possibility that more immediate intervention could disrupt fear consolidation, resulting in less-pronounced trauma memories and thus a decreased risk for later PTSD.

EARLY INTERVENTION FOR TRAUMA-EXPOSED INDIVIDUALS IN THE EMERGENCY DEPARTMENT

The above scientific findings suggest that novel interventions that are applied in the hours immediately following trauma may have a more significant impact in reducing the prevalence of chronic PTSD compared to other interventions that have been tested weeks after the initial trauma exposure. Rothbaum et al.[97] have initiated testing of a brief exposure-based intervention delivered in the emergency department immediately posttrauma and determined that such an intervention is feasible and safe. In contrast to debriefing, this intervention includes individual versus group delivery, stress management components (breathing relaxation, attention to cognitions, self-care), and repeated imaginal exposure to the trauma memory to allow for extinction of fear within and between sessions. These are consistent with the components of successful early CBT interventions cited above, merely delivered earlier. This nonrandomized study indicated lower levels of depression and distress among individuals receiving the intervention.[97] A more recent randomized controlled trial of 137 emergency room patients evaluated a modified PE protocol.[98] Results indicated that participants in the intervention group had lower depression 1 month later and less severe PTSD symptoms 4 and 12 weeks after the initial trauma compared to an assessment-only condition that allowed for natural recovery. Implementing an intervention within hours of the trauma makes this a novel approach to preventing PTSD, and although results are preliminary, the findings are promising and should encourage more research on early intervention.

SUMMARY AND CONCLUSIONS

High rates of trauma exposure and the impact and cost of PTSD highlight the need for secondary prevention that can accelerate recovery and decrease the severity of traumatic stress reactions in order to prevent development of chronic PTSD. As this review suggests, progress has been made in identifying who is most at risk for developing PTSD and in developing effective interventions, but a considerable amount of research is still needed to replicate these preliminary findings and disseminate interventions to clinicians working with trauma survivors.

An important area for future research is resolving methodological differences in the design of early intervention studies, such as the timing of the intervention (immediate versus stepped), variability in follow-up length (weeks versus months), different screening methods (e.g., heart rate versus interview assessments), and selection of eligible patients (e.g., inclusive of all trauma-exposed individuals versus selecting individuals who are already

symptomatic). These methodological differences can and should be tested empirically in order to determine the most effective and efficient way of conducting research on PTSD prevention.

Along with assessments of treatment effects, early PTSD intervention studies could productively incorporate assessments of intervention breadth of applicability and overall population impact. Research that can clarify who needs intervention in the aftermath of trauma versus who will recover spontaneously could greatly enhance research on early intervention. In addition, identifying predictors that can pinpoint who will respond to what type of treatment and the dose of treatment needed will be increasingly important, as these findings can help target valuable resources and factor in the heterogeneity in response to trauma exposure. Finally, future research should attempt to disseminate empirically supported interventions more widely and test the effectiveness of these interventions when delivered by community providers and first line responders. Although much more work is needed, the benefits of finding an effective way to prevent chronic PTSD would be substantial to both individuals and society as a whole.

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