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Chapter 15

Current State of the Art in Treatment of Posttraumatic Stress Disorder

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Additional information is available at the end of the chapter

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1. Introduction

Posttraumatic stress disorder (PTSD) is the most common mental health problem among people exposed to traumatic events. Since its introduction into the psychiatric classification system in the 1980s various treatments have been tested for PTSD. Meta-analyses based on randomized controlled trials (RCTs) concluded that trauma-focused psychotherapies are most effective treatments for PTSD [1-3]. The most widely used trauma-focused psychotherapies are exposure treatment, cognitive therapy, cognitive behavioural treatment (CBT) involving a combination of exposure and cognitive interventions, and Eye Movement Desensitization and Reprocessing (EMDR). In this chapter we briefly review these treatments in terms of their theoretical background, application, efficacy, tolerability, and length of delivery.

2. Trauma-focused psychotherapies

2.1. Exposure treatment

Exposure based interventions have the largest evidence base and received the strongest empirical support for efficacy in treatment of PTSD as well as other anxiety disorders [4, 5]. Exposure treatment has its theoretical foundation in learning theory of fear acquisition and extinction. Basically, learning theory holds that fear is learned through classical conditioning and systematic exposure to feared stimulus without any adverse consequence results in progressive reduction in the fear response (i.e. extinction or habituation of fear response). The mechanism of exposure treatment is now explained with the concept of habituation and corrective learning in the widely known *emotional processing theory* developed by Foa and colleagues [6, 7]. According to this theory, fear is represented in memory as a structure consisting of informa-

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tion about (a) the feared stimulus, (b) verbal, physiological, and motor responses, and (c) their interpreted meaning [8, 9]. Exposure therapy exerts its effect through activation of the 'fear structure' and integration of corrective information that is incompatible with it (e.g. disconfirmation of overestimated probability of harm) [6]. Successful exposure therapy does not abolish pathological associations in the fear structure, but rather establishes new, non-pathological ones [7]. In other words, fear reduction implies new learning, not unlearning. Three indicators of emotional processing determine successful learning and thus outcome of exposure therapy: (a) initial fear activation (i.e. physiological arousal in response to feared stimulus), (b) within-session habituation of anxiety (i.e. fear reduction during exposure to feared stimulus), and (c) between-session habituation (i.e. reduction in initial fear response across sessions) [6]. Within-session habituation helps dissociating the stimulus from fear response and between-session habituation forms the basis for long-term learning by providing opportunities of change in the meaning of the association between stimulus and fear response (i.e. lowered expectation of harm and lessened valence, negativity, of the stimulus). Within-session habituation is a necessary prerequisite for between-session habituation.

Although the contemporary learning theory provides the most validated, comprehensive, and plausible theory of anxiety disorders [10, 11], the emotional-processing theory has received partial support. In an extensive review of clinical studies that examined the contribution of three indicators of learning to treatment outcome, Craske and colleagues found only weak support for the premises of emotional processing theory [12]. The authors found no consistent evidence to support or refute the role of initial fear activation. While within session-habituation often occurs, the amount by which fear declines or the level of fear on which a given exposure trial ends does not predict overall improvement. Hence, within session-habituation appears to be mediated by mechanisms that are different than the mechanisms responsible for long-term outcomes. Although some studies show that the amount by which fear is reduced across occasions of exposure (between-session habituation) predicts treatment outcome, other studies indicate that improvement occurs despite lack of significant reductions in parameters of fear (e.g. heart rate or skin conductance) between exposure sessions. Finally, the authors found no evidence for the premise that within session-habituation is a necessary precursor to between-session habituation. On the basis of these findings and the literature documenting the context-specific nature of fear extinction [13], it has been suggested that that there is a need to shift away from an emphasis on fear reduction during exposure therapy to a new exposure paradigm which emphasizes attenuating avoidance behaviour and strengthening anxiety and fear tolerance [12, 14]. This is consistent with experimental work with animals which show that unpredictable and uncontrollable stressors play an important role in the development of anxiety and fear responses [15, 16] and the evidence from research with trauma survivors suggesting that lack of sense of control over traumatic stressors is the critical mediating factor in PTSD [11, 17-20]. Thus, helping the person regain control over traumatic stressors might therefore reduce traumatic stress [15, 21].

The goal of classic exposure therapy in PTSD as practised today is to promote anxiety reduction through habituation and emotional processing of trauma memory [22]. This is achieved by imaginal exposure to trauma memory and live exposure to trauma reminders. In imaginal exposure the survivor recounts anxiety evoking memories about the traumatic event in a

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systematic, prolonged and repetitive manner, while in live exposure s/he confronts anxiety evoking reminders of the traumatic event. Most treatment protocols combine imaginal and live exposure, while a few incorporate only imaginal exposure [23-25]. The way imaginal and live exposure is implemented shows great variability across programmes. For instance, in the widely used *Prolonged Exposure* programme developed by Foa and colleagues [26], live exposure is introduced simultaneously with imaginal exposure and imaginal exposure is followed by a discussion of emotional responses to trauma memory. In the *Exposure Therapy* protocol of Marks and colleagues [27], on the other hand, live exposure is introduced midway in the treatment following 5 sessions of imaginal exposure and emotional responses to trauma memory are not discussed at any stage. Many treatment programmes that are largely based on these two protocols also employed additional interventions such as anxiety management techniques (e.g. relaxation training, coping skills training, breathing training, thought stopping, and guided self-dialogue) [28, 29], cognitive restructuring [30-33], supportive counselling [23] and imagery rescripting (i.e. developing a positive alternative visual representation of oneself coping more effectively with the trauma during and / or after its occurrence) [34, 35]. Relatively little research has been conducted to examine the contribution of these techniques to improvement. While some evidence suggests that adding cognitive restructuring to exposure enhances treatment effects [23], other studies show that cognitive interventions [27, 36, 37] or various anxiety management techniques [38] do not confer additional benefits when used in combination with exposure.

Considering the problems associated with the habituation model and the findings on the importance of sense of control in trauma survivors (reviewed above), Basoglu and colleagues [21, 39-41] modified exposure treatment by: (a) focusing on only behavioural avoidance in treatment (i.e. live exposure to trauma cues), thereby eliminating treatment ingredients that rely on heavy therapist input and pose challenges of practicability in different post-disaster and cross-cultural settings; and (b) shifting treatment focus from habituation to feared stimuli to enhancement of 'sense of control' over them. The underlying principle of the new *Control-Focused Behavioural Treatment* is to enhance a person's resilience against traumatic stressors by helping them to develop sense of control over them. This can be achieved by exposure to either (a) unconditioned stimuli in a safe and controlled environment (i.e. the original traumatic stressor in simulated form or in virtual reality settings) or (b) conditioned stimuli (e.g. trauma reminders) that possess the distress-evoking characteristic of the unconditioned stimuli until the person is able tolerate and control associated distress [42]. To this end treatment targets behavioural avoidance of trauma reminders and mainly involves therapist-delivered instructions for self-exposure to feared and avoided situations until the survivor is able to tolerate and feel in control of anxiety or fear (rather than until 'fear is reduced'). The findings from clinical trials (reviewed below) showed that *Control Focused Behavioural Treatment* has promise in treatment of mass trauma survivors.

2.2. Cognitive therapy

Cognitive therapy of anxiety disorders is based on the understanding that anxiety occurs due to selective processing of information in the environment perceived as signalling threat or

danger to the individual and such cognitive biases can be corrected through conscious reasoning [43, 44]. The cognitive model of PTSD views anxiety as an outcome of maladaptive appraisals about trauma and its consequences and attributions centring on danger and threat [45]. In addition, traumatic events are believed to shatter people's basic beliefs and assumptions about themselves, the world, and others [46]. Therapy is thus designed to restructure or correct dysfunctional ways of thinking that cause distress, anxiety, or fear. The survivor is taught to challenge dysfunctional thoughts or beliefs through Socratic reasoning, test their accuracy through behavioural experiments in situations perceived threatening or dangerous, and replace them with alternative ones that better reflect reality.

Empirical support for cognitive theory of PTSD is rather weak. No prospective study with pre- to post-trauma assessments tested whether traumatic events shatter basic beliefs and assumptions. Although survivors with PTSD tend to report more negative beliefs [47-49] or information processing biases [50-52], there is not sufficient evidence to refute the argument that these may be epiphenomena of traumatic stress problems, rather than being a cause of them. Research on this issue that employed statistical controls to examine the role of all possible contributing factors to the disorder (e.g. demographic, personal history, trauma exposure characteristics etc.) did not indeed find a strong association between beliefs and PTSD [18, 20]. Furthermore, exposure, though referred to as *behavioural experiment*, is considered a necessary component of cognitive therapy for successful treatment because it allows better processing of threat [43, 44]. As exposure's efficacy is already established in anxiety disorders, it is difficult to attribute successful treatment outcome in cognitive therapy to cognitive change. Furthermore, even when treatment protocols do not directly involve an exposure component, they may indirectly trigger it. Similarly, exposure therapy alone may provide an opportunity to test dysfunctional appraisals about trauma and thereby lead to cognitive change. Comparative studies found cognitive therapy as effective as exposure [27, 53, 54]. However, the fact that no study examined whether cognitive therapy instigated self-exposure in between sessions among treated cases preclude a definitive conclusions about the importance of cognitive change in treatment. On the other hand, there is evidence showing that exposure treatment without cognitive restructuring produce as much cognitive change as exposure with cognitive restructuring [37, 55, 56]. Reductions in negative cognitions were significantly related to reductions in PTSD symptoms in these studies, suggesting that cognitive change occurs as a response to improvement in PTSD and not vice versa. These findings support the view that cognitive responses to trauma are epiphenomena of traumatic stress.

As exposure protocols, cognitive therapy programmes for PTSD differ in their specifics. The *Cognitive Therapy* programme developed by Ehlers and colleagues [57, 58] and *Cognitive Processing Therapy* developed by Resick and colleagues [53] involve imaginal exposure to the traumatic memory, but this is limited to only a few sessions and the focus of imaginal reliving is to teach the survivor modify their beliefs about the meaning of the traumatic event. The Ehlers et al programme also involves some unsystematic live exposure (e.g. visiting the site where the trauma happened). Other cognitive therapy protocols do not involve any exposure elements [24, 27].

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2.3. Eye Movement Desensitization and Reprocessing (EMDR)

The field of PTSD treatment witnessed a rapid growth of new treatment protocols, the most studied of which is undoubtedly EMDR. EMDR is an information processing therapy during which the patient recounts trauma story with its cognitive, affective, and physiological features while simultaneously focusing visually on bilateral movements of an external stimulus until the distress evoked by traumatic memory subsides [59]. The EMDR theorists maintain that the eye movements reduce the distress associated with trauma memories and help cognitive and emotional reprocessing of the traumatic event. EMDR combines multiple theoretical perspectives and techniques, most pronouncedly imaginal exposure and cognitive restructuring. Proponents of EMDR hold that the very brief and interrupted nature of imaginal exposure in EMDR sessions is at stark contrast with the behaviour therapists' requirement of prolonged and uninterrupted exposure to achieve habituation and disconfirmation of fear-expectancies [5, 6]. However, research on the processes of change in exposure treatment has not been conclusive regarding these requirements [12, 60]. EMDR proponents also contend that the use of directed eye movements distinguishes this form of therapy from other cognitive behavioural approaches. However, the role of eye movements in treatment has not been theoretically clarified and the findings of dismantling studies (reviewed in a meta-analysis) suggest that the eye movements are neither necessary nor sufficient to treatment outcome [61].

2.4. Other trauma focused interventions

Some treatment programmes for PTSD combined different components of existing treatment protocols under a different name (e.g. *Cognitive-Behaviour Trauma Treatment Protocol* [62], *Trauma Focused Group Psychotherapy* [32], *Direct Therapeutic Exposure* [33]. Some other new protocols, on the other hand, mainly embodied some form of exposure and cognitive restructuring, but these were presented with a different rationale for efficacy and they varied in the procedures of implementation (e.g. *Narrative Exposure Therapy* [63], *Imagery Rehearsal Therapy* [64], *Image Habituation Training* [65, 66], etc.). Although they look like new treatment approaches, these are mainly modified forms of existing treatments for PTSD. Also, few are grounded in theories of aetiology of PTSD and related empirical support.

2.5. Evidence base of trauma-focused psychotherapies

As noted earlier, several meta-analyses of randomised controlled trials showed comparable efficacies for various trauma-focused psychotherapies [1-3]. These meta-analyses, however, did not examine the efficacy of various treatment packages with respect to their main components. Such examination is important in clarifying the ingredients that are most useful for achieving maximum efficacy. Such knowledge also has important implications for refining theories of PTSD. To identify the contribution of each component to treatment efficacy we conducted a comprehensive literature review of randomized controlled trauma-focused treatment studies of PTSD. These studies were selected through a literature search of randomized controlled trials of CBT in PsycInfo (1806 – 2009), PILOTS (1960 – 2009), and PubMed (1966 – 2009) databases. To be included in the meta-analysis the study must have (a) tested the efficacy of a treatment for PTSD against a control group, waitlist or placebo

treatment or alternative intervention, or combination of any of these, using a randomized controlled trial design, (b) included adults who met diagnostic criteria for acute (1 to 3 months post-trauma) or chronic (more than 6 months post trauma) PTSD as defined by DSM-III, DSM-IIIR, DSM-IV, or DSM-IVTR, (c) used valid structured interview forms and / or self-rated instruments for the assessment of PTSD, (d) its sample size was large enough to allow sufficient power in analyses (i.e. at least 8 patients in each group), (e) provided sufficient data in the article for calculation of effect sizes or through contact with authors, and (f) has been published in English. This search revealed 41 studies that met the inclusion criteria. We analysed them meta-analytically by combining their findings using the standardised effect size statistic. Effect size is a measure of the strength or magnitude of a treatment effect and one way to calculate it is by computing the difference between pre- and post-treatment means on outcome measures and dividing this by the pooled standard deviation of those means [67]. This method can also be used to calculate the effect size between two treatment conditions. Effect size values of 0.20 indicate small, 0.50 moderate, and 0.80 large treatment effects. Larger effect sizes indicate more symptom reduction and less residual symptoms at the end of treatment. As various clinician-rated and / or self-rated instruments were used to assess PTSD we computed an aggregate effect size over all PTSD measures employed in a study. Data were analysed using SPSS 14.

Table 1 shows the number of participants, attrition rates, treatment duration (number of sessions and total hours spent), and effect sizes for PTSD and depression from baseline to post-treatment for main treatment components of 41 randomized controlled trials. Studies involving *Control-Focused Behavioural Treatment* [21] are excluded from this meta-analysis due to its theoretical difference from other treatment protocols and brevity (i.e. single-session application). These studies are reviewed separately in Section 2.6. Treatments in Table 1 were tested with survivors from a wide range of trauma events, including war veterans, rape victims and survivors of childhood abuse, survivors of civilian trauma (e.g. physical assault, crime, traffic accident, etc.), and refugees. Exposure-based interventions were tested with all these trauma survivors, whereas cognitive treatments and EMDR were mainly tested with survivors of rape and civilian trauma. Control conditions involved waiting list and non-specific treatments such as relaxation, supportive counselling, and present-centred therapy (i.e. coping and problem solving skills training).

	N conditions	Sample Size	Attrition rate	N sessions	Treatment duration		Effect size[a] Mean (SD)
Main treatment components			**%**	**Mean (range)**	**Hours Mean (SD)**	**Weeks Mean (Range)**	**PTSD**
Imaginal exposure[1]	6	105	20	8.5 (4-14)	11.8 (6.6)	9 (3-23)	0.86 (0.39)
Imaginal + live exposure[2]	11	317	25	10 (5-20)	16.5 (9.2)	9 (4.5-16)	1.98 (0.69)

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	N conditions	Sample Size	Attrition rate	N sessions	Treatment duration		Effect size[a] Mean (SD)
Main treatment components			**%**	**Mean (range)**	**Hours Mean (SD)**	**Weeks Mean (Range)**	**PTSD**
Imaginal exposure + cognitive restructuring[3]	4	165	20	17 (8-30)	29.6 (21.7)	17 (9-30)	1.29 (1.11)
Live exposure + cognitive restructuring[4]	2	64	16	11 (--)	16.5 (0.0)	5.5 (--)	3.80 (0.83)
Imaginal + live exposure + cognitive restructuring[5]	10	193	32	11 (4-20)	18.5 (9.9)	12 (4-18)	1.74 (0.48)
Cognitive therapy without exposure[6]	2	51	8	11 (10-12)	13.5 (2.1)	21 (16-26)	1.41 (0.35)
Cognitive therapy with limited imaginal / live exposure[7]	4	107	19	16 (12-27)	18.1 (11.6)	12 (6-17)	2.42 (0.67)
Imaginal & live exposure + anxiety management[8]	2	34	17	8 (7-9)	12.0 (2.1)	6 (5-7)	1.78 (0.30)
Imaginal exposure + skills training[9]	2	33	32	25 (16-34)	37.5 (19.1)	15 (12-17)	1.16 (0.87)
Imaginal exposure + imaginal rescripting[10]	2	76	31	6.5 (3-10)	11.0 (5.7)	7.5 (5-10)	1.09 (0.31)
EMDR[11]	12	199	16	6 (2-12)	8.5 (4.6)	6 (2-10)	1.66 (0.94)
Control Conditions							

	N conditions	Sample Size	Attrition rate	N sessions	Treatment duration		Effect size[a] Mean (SD)
Main treatment components			**%**	**Mean (range)**	**Hours Mean (SD)**	**Weeks Mean (Range)**	**PTSD**
Relaxation[12]	4	59	11	10 (8-12)	11.7 (3.5)	10 (6-16)	0.75 (0.61)
Supportive counseling[13]	4	66	18	8 (5-10)	11.4 (3.0)	6 (4-10)	0.60 (0.32)
Present centered therapy[14]	3	268	18	18 (9-30)	27.8 (15.8)	20 (10-30)	0.70 (0.48)
Treatment as usual[15]	2	47	7	--	--	--	0.69 (0.58)
Waitlist / minimal attention control[16]	25	516	11	--	--	--	0.27 (0.38)

[a] Calculated from the raw data reported in the articles. Where data were provided only in graphic form, raw data were obtained from the authors. For articles reporting effect sizes without reporting any data, effect sizes as reported in the published article were used.

1= [23, 25, 34, 54, 63, 65], 2 = [26, 27, 36-38, 53, 89, 107-110], 3 = [23, 32, 33, 111], 4 = [112, 113], 5 = [27, 30, 31, 36, 37, 62, 114-117], 6 = [27, 54], 7 = [53, 57, 118, 119], 8 = [29, 38], 9 = [28, 33], 10 = [34, 64], 11 = [29, 62, 65, 108, 110, 116, 120-125], 12 = [27, 65, 110, 120], 13 = [23, 26, 63, 114], 14 = [32, 115, 126], 15 = [31, 123], 16 = [25, 26, 28, 30, 33, 36, 38, 53, 57, 63, 64, 89, 108, 111-116, 118-122, 124]

Table 1. Evidence base for trauma-focused interventions

All active treatments yielded larger effects on PTSD than did control conditions. Although all treatments achieved clinically large effect sizes (over 0.80) in PTSD, they differed in their efficacy. Imaginal exposure and cognitive therapy had limited efficacy compared with other treatments when they were used alone. Although the addition of cognitive restructuring, skills training, and imagery rescripting enhanced the efficacy of imaginal exposure, treatment effects still remained limited. On the other hand, the efficacy of both imaginal exposure and cognitive therapy reached their maximum when they were combined with live exposure (1.98 and 3.80, respectively). These findings imply that live exposure is the critical ingredient in CBT packages. Cognitive therapy programmes involving an exposure component also performed significantly better than cognitive therapy alone, suggesting that cognitive interventions by themselves are not sufficient for successful treatment outcome. The addition of other interventions to full exposure programmes did not lead to better outcomes (they even compromised treatment gains). EMDR was also effective in PTSD, however it was associated with more residual symptoms than the potent forms of exposure based treatments with or without

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cognitive restructuring. It is also noteworthy that the evidence base for exposure treatments involves more methodologically rigorous studies than that of EMDR.

It is worth noting that the effect sizes reported in Table 1 are based on cases that completed a given programme during a RCT. As 8% to 32% of the patients dropped out of the studies, the composition of the experimental groups can no longer be considered random, which creates a selection bias reflecting the outcome of those who remain in the study or who respond to the specific treatment [68]. Findings based on more conservative intent-to-treat (or last observation carried forward) analyses, which include non-treated or non-treatment-responder cases, are more attenuated. For example, the effect sizes for imaginal and live exposure and cognitive therapy with limited exposure programmes in studies that reported intent-to-treat analyses were 1.23 (n = 4) and 1.80 (n = 3), respectively. We selected to report findings based on completers analyses because we were interested in seeing treatment outcome among those who received the full treatment. Also, intent-to-treat analyses were not consistently reported in all articles.

Tolerability of a treatment as indicated by attrition rates is an important parameter in evaluating treatment protocols. Attrition rates varied across treatment protocols but the differences were not statistically significant. When we grouped interventions, the average rate of dropout was 25% from treatment packages involving an exposure component (including cognitive therapy with limited exposure), 8% from cognitive therapy and, 16% from EMDR. Although it seemed that interventions involving exposure were less tolerable, this finding needs to be cautiously interpreted because they were examined in a total of 43 trial conditions compared with only 2 cognitive therapy and 12 EMDR conditions. In addition, the number of participants in exposure was 5.5 to 21 times higher than those in EMDR and cognitive therapy (1094 vs 199 and 51, respectively).

Treatments showed great variability with respect to number of sessions and time to recovery they required. Interventions involving exposure and cognitive therapy were delivered in a mean 12 sessions, while EMDR was administered in an average of 6 sessions. Treatment lasted an average of 16 hours (SD = 11) in exposure, 20 (SD = 12) hours in exposure with cognitive interventions, 13.5 (SD = 2.1) in cognitive therapy, and 8.5 (SD = 4.6) in EMDR. Treatment delivery in these interventions took a mean of 9 (SD = 5), 12 (SD = 6), 21 (SD = 7), and 6 (SD = 3) weeks, respectively. Although delivered in about the same number of sessions, cognitive interventions required more time in treatment than did exposure alone. Cognitive therapy alone achieved relatively limited effects in a longer period of time than did all other treatments. EMDR appeared to be the briefest treatment.

Treatment programmes reported in Table 1 vary in their complexity for training. Although practice varies, more complex treatment programmes require more time for training and supervision and they are therefore more difficult to disseminate. There is not much information on the duration of various training programmes. The most common exposure protocol used with trauma survivors, prolonged exposure [26] and cognitive therapy [58] require 5 days of training each [36]. Combined treatments take longer time for training. EMDR Institute's website states that EMDR basic training is completed in 40 hours and 2-day workshops are held for advanced training. The complex procedures involved in conduct-

ing imaginal exposure and cognitive restructuring pose challenges in training of lay therapists. All these treatments also require continuous supervision. Furthermore, they rely on heavy therapist input and as such they are not suitable for dissemination on a self-help basis.

The cross-cultural applicability of these interventions is largely unknown as they were mostly tested in western countries. As exposure therapy targets universals of human behaviour (fear and avoidance) it would be expected to have promise in different cultural settings. On the other hand, it is difficult to make predictions about cognitive interventions, because cross-cultural validity of the so called maladaptive / faulty thinking patterns about trauma and its sequelae is not known. Furthermore, requirements of keeping homework sheets [26, 53] and heavy writing tasks involved in some treatment protocols [53] may complicate their practicability among survivors with low level of education that characterize populations of developing countries. They also pose challenges of use under difficult post-disaster or post-war settings, where survivors deal with day-to-day survival problems. Finally, the efficacy of these treatments has rarely been examined in survivors of natural disasters and war.

2.6. Control-focused behavioural treatment

Control-Focused Behavioural Treatment was tested in two open and two randomized clinical trials involving 331 earthquake survivors with chronic PTSD. In an open trial [39], among survivors with a PTSD diagnosis, the probability of clinically significant improvement was 76% after one session and 88% after two sessions, reaching 100% after four sessions. This improvement corresponded to a mean 57% reduction in PTSD symptoms, 69% in fear and avoidance behaviours, and 50% in depression. The mean number of sessions required for improvement was 1.7. In a subsequent randomized controlled trial *Control-Focused Behavioural Treatment* achieved improvement in 80% of survivors when delivered in a *single session* [40]. In the latter study, behavioural avoidance was the first symptom to improve early in treatment (6 weeks), followed by improvement in re-experiencing and hyperarousal symptoms [69]. Thus, reduction in avoidance appeared to be the critical factor that initiated the process of improvement in other symptoms. Further studies showed that treatment effect could be enhanced by 20% by an additional session involving therapist aided exposure to simulated earthquake tremors in an earthquake simulator [41, 70]. Improvement was maintained in the long-term in all studies, despite further exposure to numerous aftershocks and expectations of another major earthquake. An average of 6 sessions of *Control-Focused Behavioural Treatment* achieved similar improvement rates in asylum-seekers and refugees in Turkey, despite adverse psychosocial and economic circumstances [21, 71]. These findings suggested that *Control-Focused Behavioural Treatment* has promise in treatment of mass trauma survivors in non-western settings. The single-session application of *Control-Focused Behavioural Treatment*, which emphasizes self-conducted exposure in survivors' daily routine, has promise of easy distribution to large number of survivors in mass disaster settings. Further studies are needed to confirm these findings in different trauma populations living in different cross-cultural settings.

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3. Pharmacotherapy of PTSD

According to pathophysiological theories, PTSD symptoms occur as an outcome of excessive activation of the amygdala by stimuli that are perceived to be threatening. The key psychobiological systems that are believed to be altered in PTSD are adrenergic, hypothalamic-pituitary-adrenocortical (HPA), glutametergic, serotenergic, and dopaminergic systems. Various pharmacological agents therefore aim to intervene disruptions in these systems. Before 2000 a handful of randomized controlled trials reported some beneficial effects of tricyclic antidepressants. With the introduction of *Selective Serotonin Reuptake Inhibitors* (SSRI) in the treatment of anxiety disorders, researchers lost interest in studying these medications because SSRIs had more tolerable side effects and pharmaceutical companies are more eager to provide funding for research on these medications [72]. SSRIs are now indicated as the pharmacotherapy of choice in several clinical practice guidelines for PTSD [72-74]. Recently, the efficacy of newer antidepressants, including serotonin-norepinephrine reuptake inhibitors (SNRIs, venlafaxine) and noradregenic and specific serotonergic agents (NaSSA, mirtazaine) has also been examined. In addition, some atypic antipsychotic medications (risperidone and olanzapine) have been tested as adjunctive agents for refractory patients who have failed to respond to antidepressants. In this section we review the evidence from double-blind placebo controlled randomized clinical trials of SSRIs, SNRIs, NaSSa, and atypical antipsychotics. These agents are selected for the review because other drugs (e.g. anticonvulsant / antikindling agents, monoamine oxidase inhibitors, etc.) have been mostly tested in case studies or open label trials. Benzodiazepines are not included in the review because they were not found to be effective in PTSD [72]. The same methodology described above for trauma-focused therapy protocols was followed.

Table 2 lists 21 studies that tested the efficacy of antidepressants and antipsychotics combined with antidepressants in double-blind placebo controlled randomized controlled design. Treatment duration varied between 4 to 16 weeks. The attrition rates for drug and placebo were 31% (SD = 7%, range 13-47%) and 29% (SD = 14%, range 0-59%), respectively. These figures were slightly higher than those reported in psychotherapy trials. Mean reduction in PTSD symptoms was 38% (SD = 16.5) in cases treated with active drugs, while it was 28% (SD = 14.1) in cases given pill placebo. Thus, drug-placebo difference was only 10%. This pattern of improvement was also noted in effect sizes (these were calculated using change scores as described by Kazis et al. [75], because drug trials did not always report post-treatment scores). Although the majority of the drugs achieved large pre- to post-treatment effects, so did the pill placebo. Indeed, the between-treatment effect sizes rarely exceeded the threshold (i.e. 0.50) necessary to detect a clinically significant difference between an active drug and placebo. This is in contrast with exposure-based treatments which yielded much larger effect sizes. It is worth noting, however, drug trials based their findings on all cases that completed at least one assessment after baseline, thus including the cases that dropped-out from treatment by carrying their last observation forward in the data set. Even though this conservative analysis strategy may counteracted drug efficacy compared to trauma-focused psychological treatments, evidence shows that treatment effects are more stable in the latter. There are no studies that examined relapse rates in drug-free follow-ups. Few double-blind placebo controlled

		Drug			Placebo			Drug vs Placebo
	N studies	n	% Change[b]	Effect Size Mean (SD)	n	% Change[b]	Effect Size Mean (SD)	Effect Size Mean (SD)
Sertraline[1]	5	*471*	36	1.54 (0.69)	*474*	29	1.30 (0.63)	0.31 (0.20)
Fluoxetine[2]	5	*464*	44	2.35 (0.38)[c]	*245*	32	1.83 (0.39)[c]	0.62 (0.37)[d]
Paroxetine[3]	3	*541*	44	1.77 (0.69)	*363*	30	1.22 (0.41)	0.57 (0.31)
Venlafaxine[4]	2	*340*	57	3.16 (0.54)	*347*	48	2.61 (0.40)	0.48 (0.04)
Mirtazapine[5]	1	*17*	35	1.06 (--)	*9*	17	0.86 (--)	0.60 (--)
Risperidone augmentation[6]	4	*67*	26	0.99 (0.60)	*63*	21	0.87 (0.44)	0.26 (0.53)
Olanzapine augmentation[7]	1	*10*	17	0.67 (--)	*9*	3	0.16 (--)	0.75 (--)

[a] Effect sizes calculated from the raw data reported in the articles. Within group effect sizes calculated as mean change score divided by the standard deviation of the baseline score. Between-groups effect sizes were calculated as mean change score between drug and pill placebo groups divided by standard deviation of the baseline score for placebo group.

[b] Percent reductions in PTSD symptoms pre- to post-treatment

[c] Within treatment effect sizes for one study (van der Kolk et al, 1994) were not available and thus excluded.

[d] Drug vs placebo effect size for one study (van der Kolk et al, 1994) taken from [127]

1 = [128-132], 2 = [125, 133-136], 3 = [137-139], 4 = [132, 140], 5 = [141], 6 = [142-145], 7 = [146]

Table 2. Effect sizes in double-blind randomized controlled trials of pharmacotherapy for PTSD[a]

maintenance studies involving survivors treated with SSRIs found that discontinuation of drug treatment is associated with return of PTSD symptoms [76-78].

The augmentation of antidepressant treatments with atypical antipsychotics in treatment refractory patients did not also result in better outcomes, except for one study which involved only a small number of survivors. Antidepressant treatment (paroxetine) did not also augment treatment effects in patients who remained symptomatic after 12 weeks of exposure treatment [79](not listed in Table 2). On the other hand, adding exposure treatment to SSRI treatment conferred additional benefits in patients who did not respond to previous pharmacotherapy [80, 81].

A problem concerning pharmacotherapy clinical trials in PTSD is that the findings have limited generalizability because most studies involved middle-aged females sexually abused as children or Vietnam Veterans [72]. There is also less evidence on the efficacy of medications in different age groups, because concerns about increased suicides among children and adolescents treated with SSRIs for depression and concerns about safety, age-related pharmacokinetic capacity, drug-drug interactions, and comorbid medical conditions in elderly people,

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pose obstacles to pharmacotherapy research in these populations [72]. Finally, when used in combination with exposure-based treatments, drugs may undermine the efficacy of the latter by facilitating attributions of improvement to the tablets rather than to personal efforts. In view of these findings, use of antidepressants as a first-line intervention in treatment of trauma survivors could hardly be justified.

4. Other psychological treatments

There are various other interventions used with trauma survivors, which vary greatly in their emphasis in treatment. Some of these treatments aim to increase general well-being of survivors (e.g. psychosocial support, psychoeducation, normalisation, art therapy or other expressive recreational activities, etc.) or alleviate general psychological distress (e.g. coping skills training, affect management, counselling, family therapy, etc.), while others target specific psychopathology such as PTSD and depression (e.g., interpersonal psychotherapy, school based intervention for children, brief eclectic psychotherapy, etc.). Most of these treatments involve a mixture of diverse interventions without a well-defined theoretical framework. This is an important problem because a treatment could only achieve partial effects unless its mechanisms of action match the causal processes that underlie a mental health problem [82]. Furthermore, as they do not specifically target trauma induced anxiety and fear reactions, many treatments achieve low improvement rates. One example of such treatments is school-based intervention programme developed for children. This treatment mainly involves psychoeducation, normalisation of trauma reactions through creative-expressive activities (e.g. play, art therapy), and skills training. Two RCTs that tested the efficacy of this intervention in child survivors of war in Bosnia [83] and political violence in Indonesia [84] found only small to moderate treatment effects in PTSD symptoms compared to waitlist controls (effect sizes = 0.22 and 0.51, respectively). Similar moderate treatment effects were obtained in other RCTs of a psychosocial intervention program for female survivors of war in Bosnia [85] and an affect management treatment in child sexual abuse survivors [86].

A misplaced focus in treatment also occurs when specific psychiatric disorders other than PTSD are targeted. The findings of two RCTs are cases in point. In one of the studies [87], depressive symptoms were targeted with group interpersonal psychotherapy and creative play in Ugandan adolescent war survivors. Creative play showed no effect on depression severity, while interpersonal group psychotherapy reduced depression in girls but not in boys. Neither treatment resulted in significant improvement in anxiety, conduct problems, and psychosocial functioning. Targeting depression with a self-management treatment also failed to reduce depression, PTSD, and psychosocial functioning in adult male veterans [88]. These limited treatment effects could be explained by a misplaced focus in treatment.

There is some evidence suggesting that trauma focused psychodynamic therapy and brief eclectic psychotherapy combining psychodynamic therapy with cognitive restructuring and imaginal exposure are effective in PTSD. In three RCTs, compared to waitlist controls, these treatments achieved medium to large treatment effects in PTSD symptoms (range 0.66-0.94)

[89-91]. Methodological problems preclude definitive conclusions about the effects of these treatments. It is also worth noting that treatment was delivered in 16 to 20 sessions. Considering that exposure based treatments achieve higher treatment effects when delivered in a mean of 12 sessions, the usefulness of psychodynamic or eclectic approaches become questionable.

A widely used treatment approach for refugees and survivors of torture in rehabilitation centres around the world is multi-disciplinary treatment, including social, legal, medical, and psychological aid for survivors. An open outcome evaluation study based on 55 persons admitted to the Research Centre for Torture Victims in Denmark in 2001 and 2002 showed no improvement in PTSD, depression, anxiety or health-related quality of life after 9 months of treatment, leading the authors to conclude that future studies are needed to explore effective interventions for traumatised refugees [92]. In a more recent non-random quasi experimental study of torture survivors in Nepal, multi-disciplinary treatment reduced non-specific somatic problems related to torture, but not more severe specific mental health problems, including PTSD and depression, and associated disability [93]. The authors concluded that evidence-based treatments that are able to address specific mental health problems and associated disability need to be investigated for torture survivors.

5. Interventions to prevent the development of PTSD

5.1. Critical incident stress debriefing

Critical Incident Stress Debriefing has been a widely used psychological intervention after mass trauma events. In this approach survivors exposed to similar traumatic experiences participate in a structured session where they talk about the traumatic event in detail. This session, which takes place soon after the trauma, is said to allow venting of survivors' emotions about the traumatic incident within the context of psychosocial support from others and attenuate the intensity of acute stress reactions, thereby reducing the risk of developing PTSD [94]. Two RCTs with individual trauma survivors [95, 96] and one RCT with deployed soldiers [97] did not find beneficial effects of debriefing in preventing or improving PTSD symptoms. These findings led major clinical guidelines for Acute Stress Disorder (ASD) and PTSD not to recommend the use of debriefing following traumatic events [73, 98].

5.2. Brief CBT

Condensed forms of treatment based on cognitive-behavioural principles have been tested in survivors with ASD (i.e. within 1-month post-trauma) or acute PTSD (i.e. within 3 months post-trauma). Treatment packages, usually delivered in 4 to 5 sessions, involved psychoeducation; breathing, relaxation, anxiety management training; cognitive restructuring; imaginal and live exposure. A meta-analysis of the efficacy of these interventions in ASD with respect to control groups is reported in Table 3. The latter included repeated assessment (1 study), supportive counselling (5 studies), and waiting list (1 study). As the outcome was similar across all controls they were pooled for the meta-analysis. Brief CBT and prolonged exposure

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(imaginal + live exposure) achieved large treatment effects in PTSD severity and moderate effects in depression both at post-treatment and 6-months post-trauma. More survivors in the control groups met diagnostic criteria for PTSD at post-treatment and follow up. It is worth noting that the effect sizes in Table 3 are based on those who completed treatment and more conservative intent-to-treat analyses do not always yield favourable outcome for treatment [99]. Also, between-groups differences disappeared at follow-up in some studies [100]. The generalizability of these findings is limited because they are mainly based on survivors of assault and traffic accident. Furthermore, although treatment is relatively brief, the applicability of a 5-session treatment following mass trauma events is questionable. Nevertheless, these findings suggest that brief exposure-based interventions delivered early after the trauma accelerate recovery process in survivors and prove effective in preventing chronic PTSD.

				Post-Treatment		Follow-up	
	N conditions	n Treatment	n Control	Effect Size	PTSD diagnosis (Tx vs control)	Effect Size	PTSD diagnosis (Tx vs control)
Acute Stress Disorder							
Brief CBT[1]	4	58	56	1.21	8-13% vs 46-83%	0.83	10-22% vs 22-67%
Imaginal + live exposure[2]	3	54	53	1.13	12-14% vs 56-71%	1.15	15% vs 67%
Cognitive restructuring[3]	1	23	21	0.59	52% vs 71%	--	--
Acute PTSD							
Brief CBT[a, 4]	--	76	76	0.30	30% vs 30%	0.61	10% vs 15%
Brief CBT[5]	--	61	52	0.63	38% vs 61%	0.34	26% vs 44%
Cognitive restructuring + coping skills training[6]	--	10	10	0.82	20% vs 50%	1.03	0 vs 20%

Effect Size = between-groups Cohen's d effect size index

[a] Effect sizes reflect outcome in intent-to-treat analyses.

1 = [99-102], 2 = [23, 103, 147], 3 = [147], 4 = [104], 5 = [148], 6 = [149]

Table 3. Efficacy of brief cognitive-behavioural treatment programmes in ASD and Acute PTSD in randomised controlled trials

Treatment outcome in early intervention studies of acute PTSD was not as good as that obtained in studies of ASD. Table 3 also shows findings from 3 RCTs. These studies are examined separately because their findings were not consistent, probably due to the fact that one study reported only intent-to-treat data. Compared to waiting list groups two studies of brief CBT found only small to moderate treatment effects in PTSD and small effect in depression at both post-treatment and follow-up (conducted about 6 to 13 months post-trauma). More favourable treatment effects were obtained with cognitive restructuring combined with coping

skills training relative to relaxation control, however this study was based on a very small sample.

Interestingly, early interventions produced greater reductions in avoidance behaviour and, whereas significant improvement occurred in reexperiencing and arousal symptoms, negligible reductions occurred on avoidance symptoms in control groups [99, 101-104]. These findings points to the important role played by avoidance symptoms in the maintenance of PTSD. More studies need to be conducted on diverse survivor populations and different cultural settings.

5.3. Propranolol

It has been proposed that the beta-adrenergic antagonist propranolol may have promise in preventing the later development of PTSD by reducing enhancement of traumatic memories. Two RCTs that tested this hypothesis yielded inconsistent results. In one of these studies [105] 41 emergency department patients who had experienced a trauma likely to precipitate PTSD were treated orally with 40 mg of propranolol within six hours of the occurrence of the traumatic event. The drug dose was repeated four times daily for 10 days, with a nine-day taper period. After one month, 18% (2 / 11) of propranolol completers met diagnostic criteria for PTSD, in contrast to 30% (6 / 20) of placebo completers. The drop-out rate from propranolol and placebo was 39% and 13%, respectively. In the other study [106] 48 acute physical injury patients admitted to a surgical trauma centre were randomised to receive propranolol, the anxiolytic anticonvulsant gabapentin, or placebo within 48 hours of trauma. Although well tolerated, neither drug showed a significant benefit over placebo on posttraumatic stress symptoms or depressive symptoms. It is worth noting that 92% of the acutely injured patients refused to participate in the study, in part reflecting their reluctance to receive medication. These inconsistent findings on treatment efficacy considered together with high drop-out rate and refusal to take the medication suggest that medication is not a viable preventative option for PTSD.

6. Conclusion

In this chapter we reviewed critically current treatment approaches for PTSD. The evidence in the literature clearly shows that trauma-focused psychotherapies are the first line of choice in the treatment of PTSD. The question remains as to which trauma-focused treatment protocol is the best option. Exposure therapy involving live exposure and cognitive therapies incorporating an exposure component are the more efficacious treatments for PTSD. Exposure therapy has several advantages over cognitive therapy. Its theoretical background is more robust and experimentally validated than cognitive therapy. It also has larger evidence base, was tested with a wider range of trauma survivors, and has more promise in cross-cultural applicability. Furthermore, cognitive therapy involves elaborate procedures that require substantial training in its administration. Finally, exposure therapy requires relatively less time for observable improvement.

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Despite these advantages exposure therapy is not without problems. About 40% to 50% of patients fail to achieve clinically significant improvement after exposure therapy. These modest improvement rates could be explained by a strong focus on anxiety reduction, rather than anxiety tolerance, which may be counterproductive in treatment. Indeed, the evidence indicates that the degree by which fear reduces or the level of fear following exposure is not related to treatment outcome. Furthermore, exposure therapy is not sufficiently brief for use in mass disaster settings. Although the procedures involved in exposure do not require lengthy and costly training compared to other treatments, they are not suitable for delivery on a self-help basis. There is thus need for a simple and brief intervention that emphasises anxiety / fear tolerance and that can be easily delivered to masses. *Control-Focused Behavioural Treatment* has promise in meeting this need. This short and effective treatment, which emphasizes self-conducted exposure in survivors' daily routine with an aim to increase anxiety tolerance and promote resilience, is suitable for easy distribution to large number of survivors in mass disaster settings.

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