Pharmacotherapy for posttraumatic stress disorder: empirical review and clinical recommendations

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Objective: Growing awareness of the psychological effects of trauma has emphasized the need for clinicians across a range of practice settings to be aware of evidence-based treatment options for posttraumatic stress disorder (PTSD). The purpose of this article is to review the available empirical data on pharmacological approaches to PTSD and to provide recommendations for clinical practice.
Method: Although a comprehensive search of PsychInfo and Medline databases revealed a multitude of case reports and open-label trials, this paper focuses primarily on evidence obtained from randomized controlled trials to determine the most effective pharmacological treatments for PTSD.
Results: The research data overwhelmingly supports antidepressant medication as the first-line pharmacotherapy for PTSD, with selective serotonin re-uptake inhibitors having the strongest body of empirical support. Other medications, and with care, combination pharmacotherapy, may also have a role in the management of certain presentations. Cautions for clinicians in treating this complex disorder are provided.
Conclusions: Despite a substantial increase in the amount and quality of research into pharmacological treatments for PTSD in recent years, there is still a pressing need for more data to guide routine clinical practice. In particular, future research regarding the psychobiological basis of PTSD may guide the development of a PTSD-specific drug, designed to treat the unique characteristics of this disorder.
Key words: drug therapy, review, stress disorders, traumatic.

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The potential for adverse psychological effects following trauma has long been recognized, with epidemiological studies reporting lifetime prevalence rates of posttraumatic stress disorder (PTSD) in the general community of approximately 8% [1] and 12-month rates between 1.3% in Australia [2] and 3.9% in the US [3]. The disorder affects significant numbers of individuals and the search for effective interventions is a high priority. The purpose of this paper is to review the empirical literature regarding pharmacological approaches to the treatment of PTSD and to raise issues for consideration by clinicians working with these complex conditions. This review focuses primarily on data from randomized controlled trials (RCTs), which is generally considered to be the highest standard of evidence to inform best clinical practice. A comprehensive list of pharmacological studies in PTSD (including case reports and open trials) up to the time of writing is available from the senior author.

Posttraumatic stress disorder is characterized by three symptom clusters: re-experiencing, avoidance and numbing and hyperarousal. The first challenge for pharmacotherapy is to find an agent that will show efficacy across

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all three clusters. Further complicating the picture is the fact that chronic PTSD is frequently associated with comorbid psychiatric diagnoses such as substance abuse and depression, as well as social and occupational impairment [1,2,4]. Thus, pharmacotherapy ideally needs to have a broad spectrum of effect beyond the core symptoms of PTSD and a multimodal approach to treatment is often indicated, with a combination of pharmacological, psychotherapeutic and psychosocial approaches commonly providing the best solution.

Three sources of information underpin the use of pharmacotherapy for PTSD. First, there is an increasingly sophisticated elaboration of the biological alterations associated with PTSD. Although a comprehensive review of the area is beyond the scope of this paper, preclinical and clinical studies have implicated many entities and systems, including noradrenaline/locus coeruleus, serotonin, dopamine, glutamate, opioids, hypothalamic–pituitary–adrenocortical (HPA) dysregulation, corticotropin releasing factor (CRF), neuronal excitability and neuronal degeneration [5]. In short, the biological changes associated with PTSD suggest that pharmacotherapy may have an important place in treatment for the condition. Second, a growing body of data attests to the efficacy of pharmacological treatments of PTSD, with RCTs showing benefits for several medication types. Finally, examination of clinical practice, including case reports and expert consensus statements, reveals widespread use of pharmacotherapy in the treatment of PTSD.

Methodological issues

Several methodological issues require consideration when interpreting results from pharmacological intervention studies. One of the more important is the placebo response, an effect that has received considerable attention in the depression literature. It has been estimated that, in the treatment of depression, 50–75% of the apparent efficacy of antidepressant medication actually represents the placebo effect [6]. Many of the studies reported also show sizeable effects for placebo in pharmacological treatments for PTSD. A comprehensive discussion of this complex phenomenon is beyond the scope of this review and readers are referred to specialized texts on the subject [7]. Nevertheless, it should be emphasized that the placebo effect is very real; recent research suggests that placebo treatment induces measurable changes in the brain function that are distinct from those associated with antidepressant medication [6]. Valuable insights may be gained in our understanding of PTSD if specific research were designed to examine the placebo response in pharmacological treatments of the disorder.

A second methodological issue is that, with a few notable exceptions, sample sizes are small and selection of patients (even within RCTs) cannot always be described as random. This is important since the nature of the sample may be crucial in understanding the treatment effects and great care must be taken in generalizing to other populations. Many of the larger selective serotonin re-uptake inhibitor (SSRI) studies have comprised predominantly female participants and it appears that females may be more responsive to SSRI treatment for PTSD and depression than males [8]. However, while preliminary evidence suggests that women may show a superior treatment response, the impact of gender is frequently confounded by differences in trauma-type.

Most PTSD research samples comprise either male combat veterans or female sexual assault survivors and several RCTs have reported reduced efficacy for SSRIs in veterans when compared to civilian samples. For example, Van der Kolk *et al*. [9] found that, regardless of gender, a 5-week fluoxetine treatment was associated with significant symptom reductions in civilians, whereas veteran participants did not significantly improve. Hertzberg *et al*. [10] reported a lack of efficacy for fluoxetine with combat veterans and, similarly, Zohar *et al*. [11] reported only small, non-significant improvements for veterans randomized to sertraline compared to placebo. Baseline PTSD scores were also higher for the veteran group, suggesting that differential efficacy may be related, at least in part, to the severe nature of combat-related PTSD. It is notable that improvements in anger (a common problem for veterans with PTSD) were observed in the study for sertraline completers. Davidson *et al*. [12] found that anger reduction during sertraline treatment partly mediated subsequent PTSD symptom improvement. Thus, it may be speculated that longer treatment trials may produce better outcomes for veteran populations treated with the SSRIs. All these methodological concerns point to the need for very large long-duration trials, with mixed populations in terms of gender and trauma-type. Such trials would require coordinated multisite (and probably multinational) studies with sufficient numbers to allow elucidation of these complex questions.

A further cautionary note concerns the exclusion from virtually all the pharmacotherapy trials of PTSD patients with current comorbid substance abuse. Substance abuse is common in PTSD and, while admission of these patients may decrease the magnitude of treatment effects, their exclusion decreases the clinical generalizability of findings. Controlled trials designed to investigate the impact of substance abuse may provide an insight into the degree to which such comorbidity affects the efficacy of drug treatments for PTSD.

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Finally, it is important to consider the quality of individual studies when determining how much weight to place on the results. Small open-label trials, while important in providing pilot data and suggesting avenues for future research, do not carry the same weight as RCTs. Thus, this review uses RCT data wherever possible.

Review of the empirical research

Search strategy

A literature search was conducted using the electronic databases PsychInfo and Medline. Descriptors included drug types (e.g. antidepressant or anxiolytic), class labels (e.g. SSRI or benzodiazepine) and generic drug names (e.g. sertraline or alprazolam) combined with the text words 'PTSD or posttraumatic stress disorder or acute stress disorder'. Case studies, clinical reports and open trials located in the search are mentioned in this review only if they are of special relevance. Studies selected for more detailed discussion are predominantly RCTs examining the pharmacological treatment of PTSD using medications available within Australia.

The clinical effectiveness of pharmacotherapy

It should be emphasized that pharmacotherapy of PTSD is not generally considered to be curative. Withdrawal of medication, more often than not, leads to a return of the original symptoms, particularly if psychological interventions have not occurred concurrently. Although many studies cite 'significant improvements' compared to placebo, by no means do all patients respond to pharmacotherapy; and changes, when they do occur, are not always large. Stein *et al*. [13], for example, noted that response rates to SSRIs rarely exceed 60% and only 20–30% of the patients improve to the point of remission. Thus, pharmacotherapy should be considered as one aspect of a broader management plan for PTSD, in combination with attention to psychological and psychosocial aspects of the disorder.

Relative treatment effects across various classes of antidepressants do not vary substantially. Although the recent American Psychiatric Association guidelines for the treatment of PTSD (available at www.psych.org/psych_pract/treatg/pg/prac_guide.cfm) suggest a marginal superiority for SSRIs over other classes, a more comprehensive systematic review of the literature conducted by the National Institute for Clinical Excellence (NICE) in the UK (see www.nice.org.uk) found no such difference.

Older antidepressants

Early controlled trials reported modest improvements in PTSD for the tricyclic antidepressants (TCAs) amitriptyline and imipramine [14–16]. Positive outcomes were also reported for the monoamine oxidase inhibitor (MAOI) phenelzine in two of these trials [15,16]. Both studies compared imipramine and phenelzine and both reported superior efficacy for the MAOI in reducing post-treatment PTSD. Conversely, Shestatzky *et al*. [17] did not find significant benefits for phenelzine over placebo following a 4-week within-subject cross-over trial. However, methodological problems such as small sample sizes and short trial lengths were notable in all the studies, making the results difficult to interpret. An important clinical issue also concerns the side-effects of these medications. Tricyclic antidepressants can be associated with hypotension, cardiac arrhythmias, anticholinergic side-effects and sedation, while the MAOIs can cause cardiovascular and hepatotoxic problems as well as requiring tyramine-minimizing dietary restrictions [18]. Moclobemide, a reversible inhibiter of MAO (RIMA), overcomes many of these problems, but only one 12-week open trial has been reported [19], albeit with encouraging results. Finally, a pilot study of child-burn victims found imipramine to be useful in treating acute stress disorder (ASD) symptoms in that population [20], a finding that may have implications for the prevention of subsequent PTSD.

Selective serotonin re-uptake inhibitor antidepressants

The newer SSRIs are better-tolerated and safer in overdose than either the MAOIs or TCAs. Two multisite, 12-week, double-blind RCTs containing 187 and 208 mixed trauma patients, respectively [21,22] provided support for sertraline across a range of clinician-assessed and self-report measures of global improvement, PTSD severity and associated morbidity. Both studies reported more treatment responders in the sertraline (53% and 60%, respectively) than the placebo group (32% and 38%, respectively). Subsequent analyses [23] indicated that the presence of comorbid anxiety or depression was associated with a small increase (10–20%) in side-effects and a small increase in mean response time (approximately 1 week). Although slightly higher doses were of greater therapeutic value for these patients, sertraline efficacy was not significantly compromised by comorbidity.

Sertraline was also examined in one of very few RCTs investigating discontinuation of pharmacotherapy in PTSD. Volunteer participants who had completed a

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12-week double-blind RCT were randomly allocated to either placebo or sertraline for a further 28 weeks. Greater relapse-rates were found for patients who discontinued sertraline (26%) than for those who continued (5%) [24]. Despite the association between discontinuation and relapse, a subsequent review of the entire 64 weeks of sertraline treatment indicated that symptom severity did not deteriorate to baseline levels for patients who discontinued its use [25].

Two similarly large 12-week double-blind RCTs have also reported positive treatment effects for another SSRI, paroxetine [26,27]. Compared with placebo, paroxetine was associated with improvements across all three PTSD clusters, depressive symptoms and functional outcomes in both studies. Moreover, Marshall *et al*. [26] reported similar outcomes for patients randomized to either 20 or 40 mg/day paroxetine, suggesting substantial benefits from relatively low drug dosage. Australia's Therapeutic Goods Administration advises that paroxetine is the only medication with a specific indication for the treatment of PTSD. A third SSRI, fluoxetine, has also been shown to reduce PTSD severity and associated morbidity in three double-blind RCTs [9,28,29]. Other SSRIs such as fluvoxamine and citalopram have shown promise in several open trials but have yet to be evaluated in RCTs.

Novel antidepressants

The serotonergic properties of third-generation non-SSRI antidepressants such as venlafaxine and mirtazapine also hold promise in the treatment of PTSD, although few RCTs have been published to provide a reliable evidence-base for their use. A recent small RCT [30] reported reductions in anxiety and some PTSD measures following an 8-week mirtazapine treatment, however, the NICE reviewers deemed its effect equivalent to that of paroxetine, phenelzine and amitriptyline (and superior to sertraline). Although encouraging results were found for nefazodone, this drug has recently been removed from the Australian market following reports of severe liver dysfunction.

The antidepressant bupropion, which has noradrenergic and dopaminergic properties, is marketed and indicated in Australia for smoking cessation, not for depression or PTSD. A single RCT indicated some benefits in treating smoking behaviour associated with chronic PTSD [31], but failed to find a reduction in symptoms of PTSD, anxiety or depression.

Benzodiazepines

Despite anecdotal reports of widespread use, few controlled studies have investigated the efficacy of benzodiazepines (BDZs) in the treatment of PTSD. A small RCT of alprazolam with 10 PTSD patients failed to show improvements in PTSD, although reductions in anxiety were observed [32]. In an often-quoted study [33], 13 emergency room admissions were assessed within 2 days of the trauma as showing high levels of acute distress and were treated with high-potency BDZs (clonazepam and alprazolam). This group was then matched on gender and 1-week symptom scores to 13 other participants from the larger sample. Although there were no significant differences between the groups at 1 or 6 months on anxiety, PTSD, or depression severity, nine of the BDZ group met the criteria for a PTSD diagnosis at 6 months compared to only two of the comparison sample. Although those outcomes have been interpreted as indicating an adverse effect of BDZs in acute trauma [34], the original authors made no such interpretation. A small RCT of 22 patients with acute PTSD symptoms indicated that short-term temazepam treatment had little effect on subsequent PTSD severity [35].

The expert consensus guidelines [36] took a somewhat ambivalent stance toward the use of BDZs in PTSD, emphasizing the need for caution in patients with substance abuse problems. The Consensus Statement on PTSD from the International Consensus Group on Depression and Anxiety [37] was unequivocal in denying a role for BDZs, noting the absence of supporting evidence, asserting that some patients with PTSD deteriorate when treated with benzodiazepines because of 'impairment of learning' and withdrawal symptoms as reasons to avoid their use. This position was restated following the recent publication of updated guidelines [38]. The potentiation of alcohol is noted and advice is provided to avoid BDZs even for acute sleep disturbance.

The consistent message that emerges from the empirical literature, expert consensus and clinical practice is that BDZs do not specifically improve the symptoms of PTSD, although they may reduce the accompanying and pervasive generalized anxiety. Although there is little evidence to suggest that they actually make PTSD worse, there are well-known risks associated with their use, which require careful consideration. Tolerance with prolonged use and withdrawal symptoms need to be anticipated and managed, or avoided altogether in patients with relevant substance abuse problems. Rebound anxiety with the shorter-acting agents is also relevant in the treatment of PTSD. As in other anxiety disorders, if a decision is taken to prescribe BDZs for a patient with PTSD, longer-acting agents such as diazepam or clonazepam are preferable and, as a general rule, they should be used for as short a time as possible. This situation is reflected in Davidson's [39] conclusion that BDZs should not be used as monotherapy for PTSD but, rather, as an

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augmentation option and they should not be thought of as having a preventative effect.

Mood stabilizers/anticonvulsants

The purported antikindling properties of anticonvulsants have potential value in PTSD, particularly for symptoms of intrusion and hyperarousal. Preliminary evidence in the form of open trials with PTSD patients has suggested the therapeutic benefits of medications such as gabapentin, topiramate, carbamazepine and valproate, with a suggestion that they may be particularly useful for treating symptoms of sleep disturbance and nightmares, which are often refractory to the antidepressants. To date, however, only one small RCT has been published, examining a 12-week lamotrigine treatment for PTSD [40]. Response rates were approximately 50% for the treatment group compared to 25% of placebo. Lamotrigine appeared to be particularly effective for reducing symptoms of avoidance/numbing and intrusions. Case studies of the mood stabilizer, lithium, suggest that there may be some benefits for ameliorating anger, anxiety and insomnia associated with PTSD, although no RCTs have been conducted.

Adrenergic agents

Acute hyperarousal at the time of the trauma may predict subsequent PTSD [41,42], suggesting that the arousal reduction properties of adrenergic agents may have preventive value in acute trauma. Administration of the beta-blocker propranolol for 10 days, beginning within 6 hours of hospital admission, was associated with lowered reactivity to internal trauma cues 3 months after the event [43]. One-month PTSD symptom levels were also lower for the treatment group, although by 3 months post-trauma both placebo and control groups had improved to a similar level. In a similar study, lower PTSD rates and severity scores were observed at 2-month follow-up for patients who received propranolol for 7 days (followed by a taper period of 8–12 days), commencing within 20 hours of hospital admission, compared to matched non-randomized controls [44]. These data are hard to interpret, however, given the lack of randomization and the brief follow-up period, particularly as many individuals spontaneously recover from post-trauma symptoms within the initial 6 months following the event.

Alpha adrenergic agonists such as clonidine and prazosin have also been a focus of interest for some time, both as a preventive strategy in acute traumatic stress [45] and as a treatment for chronic PTSD. Although several case studies and open trials suggest some benefits, no RCTs have yet appeared and the potential benefits of this class of medication must be viewed cautiously.

Antipsychotics

Traditional antipsychotic medications are rarely considered appropriate for the treatment of PTSD unless psychotic symptoms are present. The newer atypical antipsychotics, however, are of interest with several small trials appearing in the literature. One 10-week double-blind study did not report significant differences in PTSD outcome following olanzapine treatment [46], although the sample size was small and placebo response was high. Three controlled studies investigating the adjunctive utility of low-dose risperidone and olanzapine for combat-related PTSD produced somewhat more positive results [13,47,48]. Stein *et al*. [13] reported significant reductions in PTSD, depressive and sleep disorder symptoms following the augmentation of SSRI treatment with olanzapine compared to those who continued their existing regimen. Hamner *et al*. [47] and Monnelly *et al*. [48] both reported small but significant benefits from 5- or 6-week adjunctive risperidone treatment for PTSD patients. Although there are currently no controlled trials of other atypical antipsychotic medications (such as quetiapine, amisulpride and aripiprazole), the evidence from open-labelled studies is encouraging.

Miscellaneous

Although beneficial effects have been suggested for the antihistamine cyproheptadine in treating nightmares and improving sleep in PTSD, the only controlled trial in the literature reported slightly worse outcomes for the treatment group on measures of PTSD, nightmares and sleep quality [49]. Although the trial was of short duration (2 weeks) and the differences not significant, the results provide an interesting counterbalance to the case reports and suggest caution in the use of this agent.

Combining pharmacotherapy and psychotherapy

Although little empirical data exist, clinical experience suggests that combination approaches may have a mutually synergistic effect. Amelioration of hyperarousal symptoms with medication, for example, may assist the psychotherapeutic process. In one of the few RCTs to examine this issue, Otto *et al*. [50] found greater efficacy for pharmacotherapy-refractory patients randomized to sertraline and cognitive behaviour therapy (CBT) compared to those randomized to sertraline alone. Conversely,

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a study of treatment outcome predictors indicated that benzodiazepine use was associated with reduced efficacy of prolonged exposure for PTSD [51]. The authors suggested that BDZs may reduce the level of fear activation required for effective exposure treatment. Interestingly, however, BDZ use was associated with lower dropout rates.

Psychological interventions may be particularly important in reducing relapse following discontinuation of medication. In one of few studies to directly compare pharmacological and psychological treatments in PTSD, Frommberger *et al*. [52] reported that both paroxetine and CBT significantly decreased PTSD and depression symptoms to a comparable extent at post-treatment. At 6-month follow-up, however, symptoms of PTSD had slightly increased in the paroxetine group and further decreased in the CBT group. Although an integrated pharmacotherapy and psychotherapy approach to the treatment of PTSD is recommended, controlled trials are urgently required.

Consensus statements

A comprehensive document on the treatment of PTSD was presented as a supplement to the *Journal of Clinical Psychiatry* in 1999 as part of the Expert Consensus Guideline Series [36]. In the section on medication, the guidelines commend SSRIs, venlafaxine and nefazodone, emphasizing these agents' broad spectrum effect. The more useful information in this document pertains to second line or 'also consider' options in which TCAs, mood stabilizers, anti-adrenergic agents and (with several caveats) benzodiazepines are recommended for consideration in different settings. These recommendations were reaffirmed by the updated Consensus Statement on PTSD from the International Consensus Group on Depression and Anxiety. As stated earlier, they do not recommend the use of benzodiazepines and, instead, suggest substituting an alternative new generation antidepressant such as venlafaxine or mirtazapine if a patient has not responded to SSRIs [38].

Implications and issues for clinical practice

Although empirical research in the area of pharmacological approaches to PTSD has increased dramatically in the last decade, many questions remain unanswered. Although data now exist to answer questions of whether drugs have a place in the treatment of PTSD, and which classes might represent the best initial options, the research findings are a long way from illuminating the more subtle questions that confront clinicians on a daily basis. The purpose of this section is to make several recommendations for routine clinical practice. Although empirically supported wherever possible, most of these are based on clinical experience and expert consensus.

Psychotropic medication should normally be considered as part of a comprehensive management plan for chronic PTSD, particularly in more severe cases and in those with significant comorbidity. Clinical experience, as well as some research data [24,53], suggests the importance of maintenance in reducing the risk of relapse. An initial trial of 12 months, with longer subsequent courses if required, is recommended for chronic PTSD. Equally, in the absence of solid empirical data on this question, clinical judgement will always play an important role. The use of adjunct psychological therapies, changes in life circumstances and, indeed, the simple passage of time may lead to varying needs for antidepressant medication, both in terms of dosage (up or down) and, at times, different agents.

Although evidence exists for the safety profile of SSRIs, patients with PSTD may be sensitive to the paradoxical anxiety and akathisia that can sometimes occur as an acute side-effect. Clinicians should forewarn patients of this possibility and should use low-dose starting regimens to minimize this risk. Use of agents like amitriptyline can have the additional benefit of pain-relieving properties, which may be useful in cases where the PTSD is associated with pain from physical injuries sustained from the same trauma. In addition, the non-specific benefits for sleep and anxiety from TCAs are worth considering. Indeed, given that outcomes probably do not differ greatly across the classes of antidepressants in the treatment of PTSD, factors such as side-effect profile, toxicity and drug interactions, as well as past and family histories, can help to determine the choice of agent. In the absence of solid empirical data, it seems reasonable to adopt similar algorithms to those used in the treatment of depression as relevant guides in this process.

When a first-line intervention fails or is not tolerated, careful consideration may be given to combination therapy and augmentation strategies. More complex multipharmacotherapy regimens may be designed to enhance the effectiveness of the primary agent on an overall PTSD symptom profile or to target-specific symptoms that are more severe or have failed to respond to the initial medication. As always, these strategies bring with them greater risks of drug interactions and side-effects. Some reactions, like the serotonin syndrome, can be potentially serious. Consequently, more complicated treatment regimens will be reserved for patients whose PTSD is more severe, complicated with comorbid conditions, or resistant to conventional psychological and pharmacological interventions.

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Although the following examples are provided for consideration by clinicians, it must be emphasized that no empirical data are available to guide prescribing decisions in such cases. Rather, careful consideration of the potential risks and benefits is required, with close monitoring of effects (both positive and negative), especially in the early stages of combination pharmacotherapy regimens. Nevertheless, in cases of high severity PTSD combined with depression that has not responded to a new generation antidepressant, for example, it may be reasonable to trial the concurrent use of a second antidepressant. Where insomnia remains as a residual symptom, the use of a hypnotic in addition to the antidepressant may be indicated, while the addition of an anxiolytic or an atypical antipsychotic may be useful in cases of high arousal or psychosis, respectively. Anticonvulsants may be useful additions in cases of excessive anger, while the anti-adrenergics are worth considering in patients with residual problems of excessive arousal. Although such combination pharmacotherapy may prove useful in some severe cases, psychological and psychosocial interventions to address these non-responsive symptoms should always be given careful consideration.

Similarly, little data are available to inform on the use of pharmacotherapy in the immediate aftermath of trauma. Although clinical pragmatism may demand that clinicians attend to distressing symptoms such as sleep disturbance, intrusive symptoms and hyperarousal, in the vast majority of cases these symptoms will settle with time and some simple psychosocial interventions. Rest, physical comfort, family support, arousal and stress reduction strategies and brief psychological interventions that include support, education and sleep hygiene measures should always be offered to traumatized patients. As noted earlier, two preliminary trials have suggested possible benefits of adrenergic agents in the immediate post-trauma period but, in the absence of more consistent empirical support, we recommend that clinicians do not automatically adopt a pharmacological approach in the first few days. Simple advice and reassurance, with re-assessment a few days later, may be an appropriate first step, with medication reserved for those who do not begin to show a normal recovery pattern.

Conclusions

Despite a substantial increase in the number and quality of RCTs examining pharmacological treatments for PTSD in recent years, there is still a pressing need for more research. In particular, such research needs to focus on combination therapies (multipharmacotherapy as well as psychological and pharmacological combinations), as well as examining the effects of medication on patients who more closely resemble those presenting in routine clinical practice. Future research regarding the psychobiological basis of PTSD may guide the development of a PTSD-specific drug, designed to treat the unique characteristics of this disorder. Such knowledge would enhance not only our understanding of how and why PTSD develops, but would also provide a rationale for the future development of effective treatment approaches to reduce the considerable pathology and distress caused by this disorder.

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