

Early interventions for the prevention of PTSD in adults: a systematic literature review

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Abstract

Background: Secondary interventions are implemented within a short interval following the occurrence of traumatic events with the purpose of preventing the onset of PTSD. **Objective:** Analyze the results of studies that assessed post-trauma interventions in adults aimed at preventing the onset of PTSD or symptoms related to PTSD. **Methods:** We performed literature searches using the search expression [(Early intervention OR secondary prevention) AND (Post traumatic stress disorder OR PTSD)] for articles published until October 2016. Among the references found, 29 fulfilled the selection criteria established for the review. Data were divided and analyzed according to the type of intervention: pharmacological or psychological. **Results:** Psychological measures used in the studies lack homogeneity regarding the type of intervention and the assessment of intervention outcomes. Pharmacological interventions were less frequent and findings require replication, together with an expansion in the types of substances investigated. In general, many of the studies reviewed suggest that both pharmacological and psychological interventions are effective in the prevention of PTSD. **Discussion:** Future trials should be focused on determining the best interventions for the secondary prevention of PTSD. The combination of psychological and pharmacological interventions for post-trauma patients poses opportunities and challenges that remain unexplored.

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Keywords: Early intervention, post-traumatic stress disorder, literature review.

Introduction

According to the DSM-IV, post-traumatic stress disorder (PTSD) is characterized by a set of responses triggered by exposure to a significant traumatic event. The condition generally involves four groups of symptoms consisting of persistent re-experiencing of the traumatic event in one or more forms (e.g., in nightmares or through feelings similar to those experienced in the traumatic event), constant avoidance of stimuli associated with the trauma, recurrent arousal responses, and cognition or mood alterations associated with the traumatic event. These symptoms should last more than a month and be followed by significant impairment or distress for the individual¹.

Interventions implemented shortly after the occurrence of the trauma are aimed at the secondary prevention of PTSD, that is, they are attempts to avoid the development of the disorder in individuals who have already been exposed to the traumatic event and reduce occasional harms resulting from the experience. Secondary interventions have received increasing attention because of the high prevalence of PTSD in the population (6.8% in the American population according to Kessler² and the protective action of post-trauma interventions³. In addition, the World Health Organization has listed important impacts of PTSD: economical and on social, interpersonal, and occupational functioning, adding that prevention strategies should be broadly promoted⁴.

In this article, we present the results of a systematic literature review on post-trauma interventions for adults aimed at preventing the onset of PTSD or symptoms related to the disorder. We were unable to use a quantitative approach such as a meta-analysis because (a) the information required for the calculation of effect sizes was not always available, which could restrict the analysis to a small subset of studies; (b) there were important differences regarding secondary

variables in the studies (e.g., gender, type of trauma, medication, comorbid conditions); (c) different methods were used to analyze data obtained through different forms of investigation; and (d) meta-analysis have intrinsic limitations related to the estimates of unpublished negative results (the “file drawer problem”⁵). The review was also limited to studies involving adult participants, since current models show that the development of PTSD in children is different from that of adults in terms of biological, psychological, and social aspects and the interactions between them⁶.

Methods

We made a search using the search expression [(Early intervention OR secondary prevention) AND (Post traumatic stress disorder OR PTSD)] on the electronic databases MEDLINE, Web of Knowledge, SciELO, PsycINFO, and LILACS. Articles published until October 2016 were included, with no previous time limit. The reference lists of the selected articles were manually checked for additional references relevant to the topic of the review.

The articles included in the review were published in English, Spanish or Portuguese. We included studies involving humans aged 18 or above who had suffered any type of trauma and which presented results of interventions effected up to one month after the traumatic event (this criterion was based on DSM-5, where PTSD is characterized by disturbances lasting more than one month after the trauma). In respect to the type of intervention, we included articles that assessed the effects of pharmacological or psychological trials.

Review articles, letters to the editor, editorials, abstracts published in the annals of scientific events, case reports, and articles dealing with other disorders different from PTSD or its prevention were not included in this review.

The electronic searches returned 22 articles that fulfilled the inclusion criteria for the review. Seven additional articles were included after hand-search of the reference lists of those articles. Figure 1 illustrates the process of article search, selection, and exclusion.

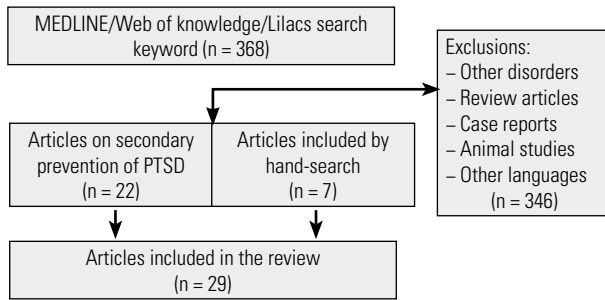


Figure 1. Flowchart showing the process of search and selection of articles included in the review.

Results and discussion

Table 1 presents the clinical and demographic data of the participants included in the 29 articles reviewed, whereas Table 2 describes the methodological aspects of the studies. Results were divided according to the type of intervention (pharmacological or psychological). From the 29 articles reviewed, 16 reported significant effects of interventions for the prevention of PTSD or symptoms related to the disorder⁷⁻²². Of these, 22 studies used psychological interventions and 7 used pharmacological interventions (Table 2).

Psychological interventions

We considered as psychological interventions those approaches that were not based on the administration of pharmacological substances. The main psychological approaches used in the studies were cognitive behavioral therapy (CBT) and debriefing, followed by other approaches described below.

Table 1. Clinical and demographic data of samples included in the studies reviewed

Reference	Subjects	N (M/F)	Mean age ± SD (years)	Type of trauma	Psychological measure
Amir <i>et al.</i> , 1998 ²⁵	15	0/15	28 ± 8	Terrorist attack	IES, PDS, SCL
Sijbrandij <i>et al.</i> , 2006 ⁷	236	121/115	41.7 ± 12.3	Assault, accidents	HADS, PSS
Bisson <i>et al.</i> , 2004 ⁹	152	65/87	Not informed	Physical injury	CAPS, HADS, IES
Brom <i>et al.</i> , 1993 ³⁴	151	89/62	39 ± 17	Traffic accident	IES
Bryant <i>et al.</i> , 1999 ¹⁰	45	22/23	32.5 ± 10.9	Civilian trauma survivors	BDI, Event scale, STAI
Bryant <i>et al.</i> , 2009 ³⁰	156	101/54	37.17 ± 13.27	Traumatic injury	CAPS, MINI
Deahl <i>et al.</i> , 2000 ¹¹	106	106/0	24	War	CAPS, CAGE, HADS, PTSS, SCL
Delahanty <i>et al.</i> , 2013 ¹²	64	42/32	30.6 ± 10.7	Traumatic injury	CAPS, CES-D, PDI, PDEQ, SF-36
Gamble <i>et al.</i> , 2005 ¹³	103	0/103	28 ± 6.04	Experienced a distressing or traumatic birth	DASS, EPDS, MINI
Gidron <i>et al.</i> , 2001 ¹⁴	17	09/08	36.2	Motor vehicle accidents	CAPS, SCI
Gidron <i>et al.</i> , 2007 ²⁹	34	18/16	28.3 ± 10.0	Traffic accident	PTDS
Holmes <i>et al.</i> , 2007 ³⁵	90	63/27	39.9 ± 15.8	Physical trauma	AUDIT, HADS, IPC, PCL
Marchand <i>et al.</i> , 2006 ²⁶	75	36/39	22.4 years ± 7.3	Armed robbery	CAPS, IES
Matsuoka <i>et al.</i> , 2015 ⁴⁶	110	90/20	38.1 ± 13.5	Accident-injured	CD-RISC, CAPS, HADS, IES-R, MADRS
Miller <i>et al.</i> , 2015 ¹⁵	164	0/164	26.62 ± 9.32	Sexual assault	BDI, BAI, PSS
Mouthaan <i>et al.</i> , 2013 ²⁴	300	89/62	43.8 ± 15.9	Traumatic injury	CAPS, GCS, HADS, ISS
Pitman <i>et al.</i> , 2002 ³¹	41	20/21	34.3 ± 11.1	Psychologically traumatic event	CAPS
Price <i>et al.</i> , 2014 ²⁷	137	47/89	31.4 ± 11.65	Criterion A trauma according to the DSM-IV	CTQ, ISRC, PSS, STI
Resnick <i>et al.</i> , 2007 ¹⁶	140	0/140	25.82 ± 10.32	Sexual assault	BDI, BAI, PSS
Rothbaum <i>et al.</i> , 2008 ¹⁷	145	88/57	39.4 ± 16	Motor vehicle collision, unspecified trauma, physical assault	CGI, BDI, STAI
Rothbaum <i>et al.</i> , 2012 ¹⁸	137	69/68	30.17 ± 12.08/ 32.78 ± 11.12	Sexual assault, physical assault and transportation	BDI, ISRC, CTQ, PTSR, PSS
Rothbaum <i>et al.</i> , 2014 ¹⁹	65	25/40	33 ± 11.6	Rape, nonsexual assault, vehicle accident	CTQ, PSS, PDS
Ryding <i>et al.</i> , 2004 ³²	50	0/50	30	Emergency cesarean section	DEQ, IES
Scholes <i>et al.</i> , 2007 ²⁰	347	191/151	38.55 ± 14.97	Patients attending accident/emergency	ASDS, HADS, PDS
Suliman <i>et al.</i> , 2015 ⁸	29	19/10	29.52 ± 8.17	Vehicle collision or other accident, physical or sexual assault	ASD, MADRS, CAPS, CGI-S, CGI-I, MADRS, SDS, PDS, VAS-D, VAS-A
Stein <i>et al.</i> , 2007 ²¹	48	Not stated	29.4 ± 10.10	Physical trauma	CIDI, CES-D, PCL-C
Vaiva <i>et al.</i> , 2003 ²²	20	11/08	23.90 ± 10.59	Motor vehicle accidents, physical assault	MINI, PDI, PDS, TS, TO
Zatzick <i>et al.</i> , 2001 ³⁶	152	Not stated	38 ± 14.7	Physical injury	PCL-C
Zoellner <i>et al.</i> , 2011 ²³	90	0/90	33.7	Assault survivors	BDI, PSS, PBRS

AIS: Abbreviated Injury Scale; BDI: Beck Depression Inventory; CAPS: Clinician Administered PTSD Scale; CGI: Clinical Global Improvement Scale; CIDI: Comprehensive International Diagnostic Interview; CTQ: Childhood Trauma Questionnaire; DASS: Depression Anxiety and Stress Scale; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders; EPDS: Edinburgh Postnatal Depression Scale; HADS: Hospital Anxiety and Depression Scale; IES: Impact of Event Scale; IPC: interpersonal counseling; ISRC: Immediate Stress Reaction Checklist; MINI: Mini International Neuropsychiatric Interview; MSS: Maternity Social Support Scale; PCL: post-trauma stress disorder checklist; PDS: PTSD Diagnostic Scale; PDI: Peritraumatic Distress Inventory; PDEQ: Peritraumatic Dissociative Experiences Questionnaire; PSS: PTSD Symptom Scale-I; STAI: State-Trait Anxiety Inventory; SDS: Sheehan Disability Scale; STI: Standardized Trauma Interview; TS: Trauma Score; TO: Treatment Outcome; TSI: Trauma Symptom Inventory.

Table 2. Methodological aspects and results of the articles included in the review

Reference	Type of intervention	Time up to intervention	Follow-up	Results	Result + or -
Psychological					
Amir <i>et al.</i> , 1998 ²⁵	Debriefing (6 sessions)	2 days after trauma	2 and 6 months	27% diagnosed with PTSD	+/-
Sijbrandij <i>et al.</i> , 2006 ⁷	Debriefing (1 session)	15 days after trauma	2 and 6 weeks and 6 months	Symptom decrease in all 3 groups/ emotional debriefing had an adverse effect in participants with early hyperarousal symptoms	+
Bisson <i>et al.</i> , 2004 ⁹	CBT (4 sessions)	1-3 weeks post-injury	3 and 13 months	IES reduced in the intervention group	+
Brom <i>et al.</i> , 1993 ³⁴	Preventive counseling program	Not informed	1 and 6 months	10% of the victims suffered from PTSD	-
Bryant <i>et al.</i> , 1999 ¹⁰	5 sessions of (1) prolonged exposure; (2) a combination of prolonged exposure; and (3) anxiety management supportive counseling	2 weeks	6 months	Fewer patients with prolonged exposure/ prolonged exposure + anxiety management met criteria for PTSD after treatment	+
Deahl <i>et al.</i> , 2000 ¹¹	Operational Stress Training Package pre and post trauma	Not informed	3 and 6 months and 1 year	CAGE scores decreased in the debriefed group by the end of the follow-up	+
Gamble <i>et al.</i> , 2005 ¹³	Counseling 72h after birth and at 4 to 6 weeks postpartum	72 hours and 4/6 weeks after birth	3 months	Decreased trauma symptoms, low relative risk of depression, low relative risk of stress, and low feelings of self-blame	+
Gidron <i>et al.</i> , 2001 ¹⁴	Memory structuring intervention	24 hours after trauma	3 months	Patients reported significantly less frequent intrusive, arousal, and total PTSD symptoms than controls	+
Gidron <i>et al.</i> , 2007 ²⁹	Memory structuring intervention or supportive listening	24 to 48 hours after trauma	3 months	No overall group differences were found	-
Holmes <i>et al.</i> , 2007 ³⁵	Interpersonal counseling (6 sessions)	Within 2 weeks after trauma	3 and 6 months	Level of depressive, anxiety and post-traumatic symptoms and prevalence of psychiatric disorders did not differ	-
Marchand <i>et al.</i> , 2006 ²⁶	Critical Incident Stress Debriefing (2 sessions)	2 to 22 days after trauma	40 and 110 days	No differences between the CISD-A and the control group in preventing PTSD	+
Miller <i>et al.</i> , 2015 ¹⁵	Video intervention	72 hours after trauma	2 weeks and 2 months	Significantly fewer anxiety symptoms at the follow-up assessments	+
Mouthaan <i>et al.</i> , 2013 ²⁴	Self-guided Internet-based intervention based on CBT	1 week after trauma	1, 3, 6 and 12 months	No support for the efficacy of the Trauma TIPS in the prevention of PTSD symptoms	-
Price <i>et al.</i> , 2014 ²⁷	Prolonged exposure intervention or assessment-only condition (3 sessions)	In the emergency department after the patient was medically stable	4 and 12 weeks posttrauma	Dissociation at the time at which treatment starts may indicate poorer response to early intervention. Those with reduced dissociation at the start of treatment benefited most from early treatment	+/-
Resnick <i>et al.</i> , 2007 ¹⁶	Video intervention	72 hours after trauma	6 weeks and 6 months	Time 1: intervention associated with lower PTSD and depression scores among women with a prior rape history relative to women in the standard care condition. Time 2: depression scores were lower among those with a prior rape history who were in the video intervention	+
Rothbaum <i>et al.</i> , 2008 ¹⁷	Individualized exposure-based therapy (CBT, 1 session)	24 hours after trauma	1 week	Patients: slightly decrease in depression and lower scores in clinician-rated global severity of symptoms than patients in the assessment-condition	+
Rothbaum <i>et al.</i> , 2012 ¹⁸	Early intervention CBT (3 sessions)	12 hours after trauma	1 and 3 months	Intervention participants reported significantly lower PTSR than the assessment group at 4 and 12 weeks post injury	+
Rothbaum <i>et al.</i> , 2014 ¹⁹	Exposure intervention (3 sessions)	Emergency department shortly after trauma	4 and 12 weeks	Combined genetic variants may serve to predict those most at risk for developing PTSD following trauma. Psychotherapeutic intervention may mitigate this risk	+
Ryding <i>et al.</i> , 2004 ³²	Counseling (2 sessions) conducted about 2 months postpartum	1/2 month after trauma	6 months	No difference between the groups was found	-
Scholes <i>et al.</i> , 2007 ²⁰	Self-help information	Within 1 month after trauma	3 months	No group differences	-

cont.

Reference	Type of intervention	Time up to intervention	Follow-up	Results	Result + or -
Zatzick <i>et al.</i> , 2001 ³⁶	Collaborative care intervention (4 months)	Newly admitted patients	1, 4 months	First month: decreased PTSD and depressive symptoms/4 months: no significant improvements in PTSD and depressive symptoms	+/-
Zoellner <i>et al.</i> , 2011 ²³	Brief cognitive behavioral intervention (4 weeks)	20 days after trauma	2, 3, 6, 9 and 12 months	Brief cognitive-behavioral intervention caused changes in perceptions of self and changes in trauma-related symptom	+
Pharmacological					
Bryant <i>et al.</i> , 2009 ³⁰	Single dose of morphine	Between 48 hours and 7 days after trauma	3 months	14% met criteria for PTSD at 3 months. Patients who developed PTSD received less morphine than those without PTSD. Morphine administered in the initial 48 hours was apparently more protective than the dose administered over the initial week	+
Delahanty <i>et al.</i> , 2013 ¹²	10 days of hydrocortisone (20 mg) or placebo	12 hours after trauma	1 and 3 months	Hydrocortisone recipients reported fewer PTSD and depression symptoms than placebo recipients	+
Matsuoka <i>et al.</i> 2015 ⁴⁶	1,470 mg/d of DHA plus 147 mg/d of eicosapentaenoic acid or placebo for 12 weeks	3 days after trauma	3 months	11.1% of the DHA group and 5.5% of the placebo group developed PTSD	-
Pitman <i>et al.</i> , 2002 ³¹	10 days of propranolol 40 mg or placebo (4 times daily)	6 hours after trauma	1 and 3 months	Non significant trend for propranolol group CAPS scores did not differ in the propranolol and placebo groups	-
Stein <i>et al.</i> , 2007 ²¹	14 days: propranolol, anxiolytic anticonvulsant gabapentin or placebo	48 hours after trauma	1, 4 and 8 months	None of the study drugs showed a significant benefit over placebo on depressive or post-traumatic stress symptoms	-
Suliman <i>et al.</i> , 2015 ⁸	10-20 mg of escitalopram or placebo daily for 24 weeks	Within 1 month after trauma	Weeks 0, 4, 12, 24, 32, 40, 48 and 56	Significant reduction in CAPS scores over the course of treatment in both the escitalopram and placebo groups	-
Vaiva <i>et al.</i> , 2003 ²²	3 times daily for 7 days: 40 mg of propranolol	2-20 hours after trauma	2 months	PTSD rates were higher in the group that refused propranolol when compared to the group who received propranolol	+

CBT: Cognitive Behavior Therapy; CAPS: Clinician Administered PTSD Scale; CISD-A: Critical Incident Stress Debriefing; DHA: docosahexaenoic acid; PTRS: posttraumatic stress reactions; PTSD: post-traumatic stress disorder; + positive result; - negative result; +/- indefinite r.

Cognitive behavioral therapy (CBT)

Four of the six studies that used CBT or related techniques reported results compatible with reduced occurrence of PTSD or PTSD-related symptoms in groups who underwent interventions in relation to control groups^{9,17-19}. In the study by Mouthaan *et al.*²⁴, which did not report reductions in the occurrence of PTSD, the authors discuss the fact that one-fifth of the volunteers failed to adhere to the intervention program. Another possible explanation for these results could be related to the low level of PTSD symptoms in the sample, which may have hampered the detection of improvements in the group that received the intervention.

In respect to the methodological aspects of these studies, the duration of treatment varied between 1-12 weeks and follow-up assessments were made in all the investigations. Regarding the type of intervention, there was no homogeneity in respect to the techniques described in the articles. Despite the positive results, additional studies involving larger and more homogeneous samples and longer follow-up periods are desirable to clarify the effects of such interventions.

Debriefing

Four articles described the use of interventions based on a techniques know as debriefing^{7,11,25,26}. Debriefing involves different forms of brief counseling and is aimed at allowing victims of psychological trauma to process their experiences cognitively and emotionally. The technique is generally applied hours after

the occurrence of a traumatic event²⁸. The results obtained with this technique are convergent in respect to the poor efficacy of the method in the prevention of PTSD and, in some cases, there were reports of symptom worsening. The authors of the studies that used this technique discuss that the poor effectiveness of the interventions performed may be due to the long interval between the occurrence of the traumatic event and the beginning of debriefing²⁶.

Other types of psychological intervention

Thirteen studies used different types of intervention including, for example, video-based interventions, counseling, and self help programs (*e.g.*, psychoeducational and motivational techniques). Six of these studies suggest that the interventions resulted in a decrease in PTSD symptoms when compared to groups that did not receive the intervention. Despite these results, in one of the studies participants received training for stress management before the occurrence of the traumatic event (war combat), as well as psychological interventions after the trauma. Therefore, it is still a matter of debate whether the results obtained stem from the primary or the secondary intervention, that is, if they come from the intervention that preceded or the one that followed the trauma¹¹.

In respect to the studies that found no significant changes in PTSD and PTSD-related symptoms, some contradictions should be mentioned. For example, a study by Gidron²⁹ reported that women participating in a given intervention had a lower frequency of PTSD

symptoms than men taking part in the same intervention²⁹, which contrasts with previous results from the same group¹⁴.

Pharmacological interventions

As shown in Table 2, drugs used in the selected studies included propranolol, escitalopram, docosahexaenoic and eicosapentaenoic acid, hydrocortisone, and morphine. Among the five trials using pharmacological interventions, only one used a single dose of the test medication³⁰. On average, test medications were administered for seven days in the remaining studies.

Two articles reported results compatible with a lower occurrence of PTSD and related symptoms^{12,22}. These results were based mainly on scales applied after the intervention and at follow-up assessments.

In the studies that found no statistically significant effects of pharmacological interventions in the prevention of PTSD, the authors described variables that may have interfered in their results, such as poor adherence to treatment, and suggest that it may be preferable to recruit individuals at increased risk of developing PTSD, such as individuals with high stress levels²¹.

The article by Bryant *et al.*³⁰ reported that, although no significant results were found in terms of PTSD symptoms, the acute administration of morphine had a protective effect related to the severity of PTSD. Another study reported that, despite their weak results, propranolol may be useful in the prevention of PTSD because the results of psychophysiological tests suggest that the drug reduces the arousal elicited by exposure to stimuli resembling the traumatic event³¹.

In addition to the results described above, methodological aspects including sample size, gender and age of participants, type of trauma, assessment scales, randomization procedures, intervention starting time, and follow-up duration also deserve attention, as they can have a direct impact on the results obtained.

Other relevant aspects

In respect to the sample size, we highlight the discrepancy in the number of participants across the studies. Some authors have underscored the need for further investigations involving larger samples in order to confirm the data obtained to date^{14,22,25}.

Regarding the gender of participants, two of the articles reviewed had discrepancies in the number of female and male participants^{20,39}. Both studies included a higher number of men in the groups of patients undergoing the intervention compared to the other groups. It should also be noted that, in some studies, samples were formed exclusively by women^{13,16,17,23,25,32} or men¹¹. Although the authors make no mention to the discrepancies in the numbers of male and female participants, evidence points to a higher vulnerability to PTSD in females³³. Therefore, studies with unbalanced gender distributions may not be as representative as studies with gender-balanced samples in what concerns the prevalence of the disorder. This can be, however, a limitation that is difficult to overcome in populations that are more vulnerable to certain types of trauma and with a high predominance of one gender, as in the case of soldiers (mainly men) or victims of sexual abuse (mainly women).

Only one of the articles reviewed did not inform the mean age of participants⁸. This is highly relevant because, although the onset of PTSD may occur at any age, it is more common in young adults since they are more prone to have the type of experiences that trigger the disorder³³. Still in respect to the age of study participants, there was less homogeneity in the data presented by some authors^{7,17,34-36}. These articles do not discuss the age discrepancies in their samples, as well as the possible influence of this factor on their results.

From the 29 articles reviewed, four had no uniform samples in terms of the type of trauma experienced, that is, these studies assessed more than one type of trauma^{17,18,22,28}. There is evidence in the literature of correlations between the type of trauma experienced and gender-related vulnerability³⁷. In this sense, variations in the

types of trauma assessed in a same study can be seen as a limitation that hinders the reproducibility of its results.

The most frequently used scale in the studies included in this review was the Clinician Administered PTSD Scale (CAPS³⁸), designed to assess PTSD symptoms. Despite that, there was no standard in what concerns the instruments used in the articles reviewed. In general, the studies included scales to assess symptoms of depression and anxiety. The lack of homogeneity in the types of instruments used in the studies also hampers the comparison of results available to date, as well as the generalization of findings.

The randomization and blinding strategies used in the trials were also examined in this review. Only one of the articles included informed that the study sample had not been randomized²². Four of the studies were described by their authors as single-blind^{13,14,18,22}, five did not include information about whether they were double-blind trials or not^{7,18,27,32,34}, and one informed that the trial was "not double-blind". In respect to the study design, only two articles did not describe the inclusion of comparison groups^{25,30}. The remaining articles included one or more comparison groups. Still regarding the study design, the trial by Bryant *et al.*³⁰ used an observational design, assessing the use of morphine after the trauma and the development of PTSD-related symptoms in the follow-up.

The time between the occurrence of the trauma and the beginning of the intervention varied greatly across studies, from 6 hours³¹ to 10 weeks⁹. It has been argued that the shorter the interval between the traumatic event and the beginning of the intervention, the more likely is the blockade of the consolidation of aversive memories¹⁷ with a consequent reduction in the possible negative emotional consequences of the trauma. Regarding follow-up assessments, all the studies reviewed included this type of analysis; however, the frequency and the interval between assessments varied.

Some limitations related to follow-up assessments were pointed in the studies reviewed, such as excessively short intervals between assessments¹⁷ and poor treatment adherence by participants during long follow-up periods²⁴. Finally, one limitation described in some studies refers to the intrinsic difficulties of proving the efficacy of early interventions, since a significant part of volunteers may not be vulnerable to the development of PTSD. Future research should seek to determine reliable criteria for the identification of trauma victims at risk of developing PTSD, which would allow improved assessments of the interventions performed. As an example, psychological and biological factors are known to influence the vulnerability to PTSD, including internalizing behavioral problems, psychiatric comorbidities, alterations in the hypothalamic-pituitary adrenal axis, brain abnormalities, and genetic factors^{39,40}.

Conclusion

The main difficulty in the analysis of the 29 articles included in this review rose from the significant methodological variations across the studies, as discussed above. In general terms, we conclude that studies using psychological interventions lack homogeneity in respect to the type of intervention and measures used to assess intervention outcomes. Pharmacological trials were less frequent in the area of PTSD prevention and should have their findings replicated, in addition to expanding the range of drugs tested. Possible investigation targets for future research include cannabinoid compounds, and especially cannabidiol (CBD), since this compound seems to play an important role in the blockade of the reconsolidation of aversive memories⁴¹. In addition, preclinical studies provide support for the test of oxytocin as a promising strategy in the prevention of PTSD-like manifestations⁴².

Despite the methodological issues described above, the studies reviewed further our understanding about PTSD and interventions aimed at preventing the disorder or minimizing post-trauma symptoms⁴³⁻⁴⁸. Importantly, many of the articles reviewed suggest that pharmacological and psychological interventions are effective in this regard. However, we were unable to find studies that combined pharmacological and psychological interventions. Since

this association has proved useful in the management of other psychiatric conditions (e.g., OCD, panic disorder, depression, alcohol dependence), the use of combined interventions in post-trauma volunteers could bring important contributions to the field.

Conflict of interest

The authors have no conflict of interest related to the topic of this article. The funding agency had no role in the study design or in the decision to submit the paper for publication.

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