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CLINICAL REVIEW

Randomized controlled trials of psychological and pharmacological treatments for nightmares: A meta-analysis

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SUMMARY

A meta-analysis of treatments for nightmares is reported. The studies were identified by database searches and by an inspection of relevant reference lists. The inclusion criteria were: nightmares as a target problem, studies published in English, use of a randomized controlled trials and reporting of nightmare-relevant outcomes. A total of 19 studies, published between 1978 and 2012 were identified, which included 1285 participants. Effect sizes were calculated as Cohen's d. A statistically significant improvement for all studies combined ($d = 0.47$, 95% CI = 0.33–0.60, fixed effects model; $d = 0.49$, 95% CI = 0.32–0.66, random effects model) and for psychological treatments alone ($d = 0.48$, 95% CI = 0.36–0.60, random) and for prazosin alone ($d = 0.50$, 95% CI = 0.03–0.96, random) was found. Individual therapy format yielded a higher effect size than a self-help format ($p = 0.03$). Minimal interventions (relaxation, recording) yielded lower overall effect size than studies offering more extensive interventions ($p = 0.02$). It is concluded that there are both psychological and pharmacological interventions which have documented effects for the treatment of nightmares.

Background

The treatment of nightmares was not given much attention until the 1960–70s when various single case studies first appeared.[1–4] Since the 1980s, larger, randomized and controlled studies have been conducted on both the psychological and pharmacological treatment approaches for nightmares.[5,6] The International classification of sleep disorders, 2nd ed. (ICSD-2)[7] defines nightmares as "coherent dream sequences that seem real and become increasingly more disturbing as they unfold. Emotions usually involve anxiety, fear or terror, but also frequently involve anger, rage, embarrassment, disgust and other negative feelings. The dream content most often focuses on imminent physical danger to the individual, but may also involve other distressing themes".[7] Most nightmares occur during rapid eye movement (REM) sleep and usually awaken the sleeper.[8] However, nightmares may also occur during non-REM sleep,[9] and may not always awaken the sleeper.[10,11] As REM-sleep predominantly occurs during the latter half of the main sleep episode, most people experience nightmares late in the night or during the early morning hours,[12] and most are able to provide a detailed account of their dreams upon awakening from a nightmare.[13]

Nightmares may be caused by several factors. One study suggests that genetics plays a role.[14] Nightmares are also often a consequence of trauma.[15] According to Hartmann,[16] persons with "thin boundaries" (e.g., those who are open, sensitive and vulnerable to intrusions) more often experience nightmares than those with "thick boundaries", hence personality factors may play a role. Other studies have indicated that sleep disordered breathing may be responsible for nightmares in some individuals.[17] Drugs such as cholinergic agonists, beta blockers, selective serotonin reuptake inhibitors, dopamine agonists, amphetamine-like agents and GABA agonists may induce nightmares in some patients,[18] whereas in some cases withdrawal from barbiturates and alcohol can elicit nightmares due to REM-sleep rebound.[19] Moreover, nightmares are associated with several different psychiatric disorders, a topic discussed in more detail below.[20]

Nightmare disorder is diagnosed when the patient suffers from recurrent awakenings accompanied by dysphoric feelings. Upon awakening the patient experiences full alertness and recalls the dream content. The unpleasant dream causes delayed return to sleep and/or occur mainly in the latter half of the main sleep period.[7] Different diagnostic manuals emphasize similar

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criteria for nightmare disorders. The diagnostic criteria for nightmare disorders according to the ICSD-2[7] are shown in Appendix A.

Occasional nightmares are quite common in normal populations. In large community-based studies, between 57% and 83% of adolescents and adults report having nightmares with a yearly frequency,[14,21,22] while 9%–30% report experiencing at least one nightmare per month.[14,22–24] Between 2.0% and 5.1% report having one nightmare per week or more often.[14,22,25–28] It is also estimated that 10%–50% of children between the ages of three to five have nightmares that disturb their parents,[7] and that children and adolescents in general are more affected than the adult population.[20] Findings from both Zadra and Donderi[29] and Wood and Bootzin[30] indicate that prospective logged dreams seem to reveal higher nightmare frequency ratings than retrospective measures, although the opposite was reported in one study.[31]

A community-based study[27] of 8558 Hong Kong Chinese individuals revealed that the risk of psychiatric disorders was 5.7 times greater for individuals with frequent nightmares compared with those without nightmares. It is further estimated that 80% of PTSD patients experience nightmares.[32] The occurrence of nightmares is also associated with substance abuse, stress and anxiety, borderline personality and schizophrenia-spectrum disorders.[20] In a prospective study, Sjöström and colleagues[33] found that frequent nightmares were associated with a three-fold risk for repeated suicide attempts. Nightmares may therefore constitute an indicator for an increased risk of suicidal behaviour.[34]

In terms of treatment for nightmares, several cognitive behavioural techniques (CBT) have been suggested: 1) Imagery rehearsal therapy (IRT) is among the most studied psychological approaches.[5,35] In IRT, the patient is instructed to modify a recurrent nightmare in an awaken state by verbal and/or written rehearsal of a new, self-made script in which the unpleasant ending or other parts from the nightmare are replaced with a more pleasant one. The rationale is that when the new dream is rehearsed, the new script will become more cognitively dominant than the nightmare, and eventually the unpleasant dreams will diminish or disappear, 2) Exposure techniques are based on the principle of reciprocal inhibition[36]; the patient is gradually exposed to the source of anxiety, i.e., the frightening aspects of the nightmare in safe surroundings such as when awake in a comfortable state, 3) Lucid dreaming therapy (LDT) is another cognitive restructuring technique in which the patient selects a salient part of the nightmare during which he or she can conduct a specific task. The patient imagines performing the task while saying that he or she is dreaming. Later, the action will cue that the experience is a dream, and at this point the patients can dream lucidly and thus decide the further events in the dream,[37] 4) Exposure, relaxation and rescripting therapy (ERRT) is an approach in which psychoeducation, sleep hygiene, progressive muscle relaxation training, rescripting the nightmare as well as exposure procedures are integrated.[38] More recently multi-component treatments, combing different therapeutic techniques against nightmares as well as basic techniques aimed at combating insomnia, have been introduced.[39] As for the pharmacological approaches, the only drugs studied in adequate randomized controlled trials (RCT) for nightmares are prazosin and cyproheptadine. Prazosin is a generic, non-sedating α_1- adrenergic antagonist,[40] and it is argued to be the most promising pharmacological treatment approach for posttraumatic nightmares.[5,41] Cyproheptadine is an antihistamine that produces sedation and enhances serotonergic activity.[41] It has shown promising effects in the treatment of nightmares in some uncontrolled studies.[42,43] A review by van Liempt et al.[6] concluded that there was a need for supplementary controlled studies to formulate evidence-based guidelines for the pharmacological treatment of nightmares. Some new studies have emerged since then and a guide to treatment has recently been proposed by the Standards of Practice Committee of the American Academy of Sleep Medicine.[20] Prazosin is the only drug recommended as a treatment for PTSD-associated nightmares, whereas IRT is the only recommended CBT for nightmare disorders.[20] A range of suggestions or possible considerations for other psychological and pharmacological approaches are also listed.[20]

Nightmares are typically assessed in terms of frequency, distress and intensity. The most commonly used measure for the assessment of nightmare frequency is the nightmare frequency questionnaire (NFQ),[44] which is a retrospective survey that estimates both the number of nights with nightmares and the number of nightmares for different time intervals.[45] Nightmare distress refers to the waking-life experience of distress that is associated with having nightmares and is most commonly assessed by the nightmare distress questionnaire (NDQ),[46] which comprises 13 items. This should be distinguished from nightmare intensity which reflects the levels of unpleasant emotions experienced during nightmares.[47]

Nightmare diaries and logs, in contrast, are prospective and seem to represent a more accurate measure of most nightmare parameters.[29,30]

Over the past few decades, we have witnessed a vast increase of research addressing the treatment of nightmares. Unfortunately, the majority of these studies are case studies that are uncontrolled or nonrandomized investigations, most of which are well described in previous qualitative reviews.[6,20,41] To date, no quantitative review or meta-analysis of treatment effects of nightmares has been reported. In order to provide the effect estimations of different treatments for nightmares, the goal of this paper is to report on a meta-analysis including all randomized controlled trials for nightmares published before February 1, 2012. In addition to providing an effect size estimation for each different treatment and each single study, as well as an overall effect size, the following a priori contrasts were investigated: 1) pharmacological treatment versus psychotherapeutic treatment, 2) individual versus group versus a self-help format, 3) distress versus frequency versus intensity outcomes, 4) active versus passive control groups, 5) PTSD diagnosis versus non-PTSD diagnosis versus no diagnosis provided, 6) IRT versus multi-component (MC) interventions versus other psychological treatments, and 7) minimal versus extensive interventions.

Methods

Literature search

Articles published in scientific journals before February 1, 2012 were identified in PubMed, PsychINFO and ISI Web Of Knowledge using two search terms: “nightmare” and “nightmares”. In addition, reference lists of primary and review articles were also inspected for relevant studies. A total of 14,829 studies were screened, and the following inclusion and exclusion criteria were employed: 1) The study had to include treatments (pharmacological and/or psychological) specifically addressing nightmares, 2) Only randomized controlled studies were allowed (randomization to at least two different conditions; one passive or active control group compared to at least one active treatment group), 3) The study had to be comprised of at least two participants; hence, single case studies were excluded (e.g.,[45–49]) 4) The study had to provide outcome data relevant to nightmares (i.e., the frequency, distress or intensity of nightmares), 5) The publication had to contain sufficient statistical information to warrant the calculation of effect sizes and, 6) The publication had to be written in English.

Study characteristics

We identified a total of 19 RCTs on the treatment of nightmares,[10,38,48–64] all summarized in Table 1. Of these, there are four pharmacological trials,[53,59,60,63] 14 psychological trails,[10,38,48–51,54–58,61,62,64] and one study comprising both a pharmacological and a psychological intervention,[52] with a total N of 1285. All studies were published between 1978 and 2012.

In nine of the psychological intervention studies,[38,48,51,54–57,62,64] the control groups were offered treatment after completion of their waiting list period. Seven studies[10,49,52,53,58,59,61] did not provide details as to whether treatment was offered to the control group, and the duration of the waiting list period lasted from two[51] to 24 weeks.[54] For four studies, the randomization to the control condition was maintained beyond post-treatment, thus providing group comparisons at follow-up comprising of one,[48] four,[52] six,[50] and 30[58] months respectively. However, nightmare-relevant data were not provided at follow-up for one of these studies.[52]

In two of the pharmacological interventions[59,63] a crossover design was used. In the Raskind et al. study,[59] the participants entered a two-week washout period before crossing to the other treatment condition, and each treatment period lasted for 20 weeks. Participants in the Taylor et al. study[63] completed a three-week treatment followed by a one-week washout period before crossing over.

A total of six studies investigated military veterans with combat-related PTSD[50,53,59,60,64] or PTSD-symptoms.[52] One study[54] included sexually assaulted women with PTSD, and one study

Table 1
Randomized controlled studies examining the effectiveness of psychotherapeutic and pharmacological treatments for nightmares.

Study	Comparison (*n*)	*n* random.	Dose/Sessions	Measurements/comparison	Format	Age	Attrition %	% Women
Burgess et al.[48]	EXP ($n = 28$) REL ($n = 30$) Control (P) ($n = 41$)	206	0	S-Rep: NN, DI	S-H	44.0 (EXP) 46.0 (REL)	51.9	76.6
Cellucci & Lawrence[49]	DESENS ($n = 10$) REC ($n = 9$) Control (A) ($n = 10$)	29	5 × 40–60 min	DSQ: NN	I	–	0.0	–
Cook et al.[50]	IRT ($n = 39$) Control (A) ($n = 51$)	124	6 × 90 min	NFQ:NN, NNN NES: DI	G	59.4	23.4	0.0
Davis et al.[51]	ERRT ($n = 17$) Control (P) ($n = 18$)	47	3 × 120 min	TRNS: NN, NNN, IN	I(?)	47.0	25.5	75.0
Davis & Wright[38]	ERRT ($n = 17$) Control (P) ($n = 15$)	43	3 × 120 min	TRNS: NN, NNN, TRNS: IN	G	40.0	25.6	–
Germain et al.[52]	Prazosin ($n = 18$) BSI ($n = 17$) Placebo (A) ($n = 15$)	57	8.9 mg (5.7 mg) 8 × 45 min (BSI) 10.4 mg (5.7 mg)	S-Rep: NN	I	40.9	12.3	10.0
Jacobs-Rebhun et al.[53]	Cyproheptadine ($n = 31$) Placebo (A) ($n = 29$)	60	8.0 mg (–) range 4.0–16.0 mg	PSQI + CAPS: IN	I	–	–	0.0
Krakow et al.[10]	IRT ($n = 39$) Control (P) ($n = 19$	58	1 × 150 min	S-Rep: NN, NNN	G	40.9	0.0	22.4
Krakow et al.[54]	IRT ($n = 54$) Control (P) ($n = 60$)	168	2 × 180 min, 1 × 60 min	NFQ: NN, NNN NDQ: DI	G	40.0	33.9	100.0
Lancee et al.[56]	IRT ($n = 29$) IRT+ ($n = 42$) LDT + IRT ($n = 34$) Control (P) ($n = 46$)	278	–	SLEEP-50: DI, NN, NNN	S-H	36.17	45.7	73.5
Lancee et al.[55]	IRT ($n = 103$) EXP ($n = 95$) REC ($n = 106$) Control (P) ($n = 95$)	399	0	SLEEP-50: NN, NNN, DI	S-H	38.7	29.3	76.9
Miller & DiPilato[57]	DESENS ($n = 10$) REL ($n = 11$) Control (P) ($n = 11$)	32	6 × 45–75 min	S-Rep: NN, IN	I	36.0	–	–
Neidhardt et al.[58]	IRT ($n = 10$) Control (A) ($n = 10$)	20	1 session	S-Rep: NN	G	39.2	–	75.0
Raskind et al.[60]	Prasozin ($n = 10$) Placebo (A) ($n = 10$) *Cross- over design*	10	9.5 mg (0.5)	CAPS: IN	I	53	0.0	0.0
Raskind et al.[59]	Prasozin ($n = 14$) Placebo (A) ($n = 15$)	40	13.0 mg (3.0)	CAPS: IN NFQ: NN, NNN	I	56	–	5.0
Spoormaker & Bout[61]	LDTgr ($n = 8$) LDTind ($n = 8$) Control (P) ($n = 7$)	23	1 × 120min	SLEEP-50: NN (gr, ind)	I + G	28.4	0.0	73.9
St-Onge et al.[62]	IRT ($n = 9$) Control (P) ($n = 11$)	20	3 meetings	S-Rep: NN NDQ: DI	I	10.2	–	45.0
Taylor et al.[63]	Prasozin ($n = 13$) Placebo (A) ($n = 13$) *Cross- over design*	13	3.1 mg (1.3) range 2.0–6.0 mg	CAPS: IN	I	49	0.0	84.6
Ulmer et al.[64]	MC ($n = 12$) Control (P) ($n = 9$)	22	6 × 60min 2 nd week	S-Rep: NN	I	46.0	18.2	31.8

Comparison: EXP = exposure, REL = relaxation, (P) = passive, DESENS = desensitization, REC = recording, (A) = active, IRT = image rehearsal therapy, IRT+ = image rehersal therapy with sleep hygiene, ERRT = exposure, relaxation & rescripting therapy, DI = distress, LTD = lucid dreaming therapy, NN = number of nightmares, NNN = number of nights with nightmare, LDTgr = lucid dreaming therapy group, LDTind = lucid dreaming therapy individual, MC = multi-component therapy (cognitive therapy and imagery rehersal therapy). *Measurements/comparison*: S-Rep = self-report, NN = number of nightmares, IN = intensity, DI = distress, DSQ = daily sleep questionnaire, NFQ = nightmare frequency questionnaire, NES = nightmare effects survey, TRNS = the trauma related nightmare survey, NNN = number of nights with nightmare, NDQ = nightmare distress questionnaire, SLEEP-50 = sleep complaints, gr = group, ind = individual, PSQI = Pittsburgh sleep quality index, CAPS = clinical administered PTSD scale.
Format: G = group, I=individual, S-H=self-help.

consisted of participants suffering from civilian trauma PTSD.[63] One study comprised children, aged 9–11, only.[62] Eight of the other studies included participants defined as chronic[10,58] nightmare sufferers,[48,49,55–57,61] while two studies focused on nightmares in trauma-exposed adults.[38,51]

12 of the 19 studies recruited participants through media advertisements,[10,38,48,52,54–58,61,62,64] one study[49] recruited undergraduate students enrolled in a psychology course, and another study[50] recruited participants through the Philadelphia VA Medical Center who were screened for eligibility, and had combat-related nightmares for at least one time a week. In the Taylor et al. study,[63] eligible participants were recruited by a clinic of family-based therapy, and four studies[51,53,59,60] did not report how they recruited their participants.

In terms of the nightmare characteristics required for inclusion in the trial, most studies[10,38,48,50,51,55,57,58,61,62] adhered to a frequency cut-off of a minimum of one weekly nightmare or an average of two or more nightmares per week.[49] Inclusion criteria used in other studies were self-reported nightmares and post-traumatic stress symptoms according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV)[65] criterion A for PTSD,[54] or endorsing nightmares[56] on the SLEEP-50.[66] Patients with PTSD and trauma-related nightmares were included based on their scores on the clinical administered PTSD scale (CAPS),[67] the PTSD checklist-military version,[68] the Pittsburgh sleep quality index (PSQI)[69] and/or according to the DSM-IV[65] criteria.[52,53,59,60,63,64]

General exclusion criteria employed in the included studies were alcohol or drug abuse,[10,38,48,50–54,57,58,60,63,64] medication use known to affect sleep,[50,62] mental retardation,[48,51] psychosis or schizophrenia, or other psychiatric illness,[10,38,48,50–57,59,62] in addition to suicidal or parasuicidal ideation.[38,51,55,56,59] Two studies did not report any specific exclusion criteria.[49,61]

Five studies[10,49,60,61,63] did not have any dropout, whereas another five studies[53,57–59,62] did not report their dropout rate, and the dropout rate for all the other studies[38,48,50–52,54–56,64] ranged between 23.4%[50] and 51.9%.[48] For those studies reporting dropouts, the following reasons were stated: the nightmare frequency had reduced,[48,55] lack of time,[48] a loss of interest,[50] work conflict and travelling distance to treatment center,[64] and personal reasons.[50,55]

Seven studies[10,50,54–56,58,62] assessed IRT as a treatment intervention, two studies[49,57] used desensitization, two studies[38,51] investigated the effects of ERRT, two used exposure,[48,55] one used LDT,[61] two used relaxation,[48,57] one used recording[55] and three studies investigated the effects of MC.[52,56,64] Among the pharmacological intervention, four studies[52,59,60,63] used prazosin and one employed cyproheptadine.[53]

Most of the psychological studies used participants on a waiting-list as the control group.[10,38,48,51,54–57,61,62,64] Three of the psychotherapeutic studies used an active control group; nightmare discussion placebo,[49] sleep and nightmare management,[50] nightmare recordings.[58] All the pharmacological studies[52,53,59,60,63] used placebo as a control condition.

One study had three intervention groups,[56] five studies[48,49,52,55,57] had two intervention groups, while one study[61] had one intervention given in either an individual or group format and 12 studies[10,38,50,51,53,54,58–60,62–64] had one intervention group in which all patients received treatment in the same format.

In total, 16 of the 19 studies assessed nightmare frequency[10,38,48–52,54–59,61,62,64] whereas 13 of the 19 studies included measures of either nightmare intensity or distress.[38,48,50,51,53–57,59,60,62,63] In all, eight studies[38,48,49,51,55,57,58,62] used prospective measurements such as nightmare logs or diaries and 11 studies[10,50,52–54,56,59–61,63,64] administered retrospective measurements.

Coding

The following variables were extracted and coded from the studies meeting inclusion criteria: Author, publication year, comparisons, time-point of post-treatment measures, format (individual, group or self-help), type of control group (active or passive), pharmacological or psychotherapeutic intervention, mean age of the participants, diagnosis (PTSD, non-PTSD or non-defined diagnosis of the participants), treatment dosage (medication dosage or the number of therapy sessions), type of outcome (frequency or distress/intensity) and gender.

Statistical analyses

Data were entered and analysed by the comprehensive meta analysis software, version 2.2.057. Most effect sizes (Cohen's d) were calculated by subtracting the mean post-test score in the control group from the mean post-test score in the treatment group and dividing the result by the pooled standard deviations of both groups, which is the recommended approach when a control group has been employed.[70] Due to limited data, the effect sizes were calculated from *F*-values for the Jacobs-Rebhun et al. study,[53] for one comparison in the Krakow et al. study,[54] and for two comparisons in another Krakow et al. study.[10] Among the studies, heterogeneity was assessed by Q and I^2 statistics. The Q test examines whether there is more heterogeneity in the results than could be explained by chance alone, which would be indicated by a corresponding p-value lower than 0.05. The I^2 describes the proportion of total variation caused by heterogeneity, and is used as a descriptive supplement to Q. I^2 values $< 25\%$ are interpreted as small, $< 50\%$ as medium and $>75\%$ as a large heterogeneity.[71] The calculation of both fixed and random effects were conducted for the overall effect sizes. We calculated random effects only for the contrast analyses. The fixed effects model assumes that all variables which may influence effect size measures are identical for all the studies' populations, while the random effects model assumes that the studies are drawn from populations that differ from each other.[72] Analysis of publication bias is based on visual analysis of the funnel plots, by the Duval and Tweedie's[73] trim and fill procedure, and by the "fail-safe N test".[74] The funnel plot is a simple diagram of the effect estimates from each study measured against a measure of each study's size or precision, and a publication bias is indicated when the funnel plot is asymmetric.[75] The Duval and Tweedie's[73] trim and fill test provides an adjusted estimate of the combined effect size by including the expected values of theoretically missing studies which would have created a symmetrical funnel plot. The "fail-safe N" gives an estimation of how many comparisons with a mean effect of zero need to be incorporated in the analysis in order to yield a statistically non-significant overall effect.

Results

Overall effect sizes

Each study's individual post-treatment total effect sizes are presented in Fig. 1 and Fig. 2. The total overall effect size across all studies was 0.47 (95% CI = 0.33–0.60) for fixed effects and 0.49 (95% CI = 0.32–0.66) for random effects. The psychological treatments had an overall total fixed effect size of 0.47 (95% CI = 0.36–0.58) and 0.48 (95% CI = 0.36–0.60) (random). The pharmacological treatments' overall total fixed effect size was 0.15 (95% CI = −0.17–0.47) and 0.29 (95% CI = −0.24–0.83) (random), which was non-significant, as the confidence interval included 0.00. The overall effect size (random) for the strongest

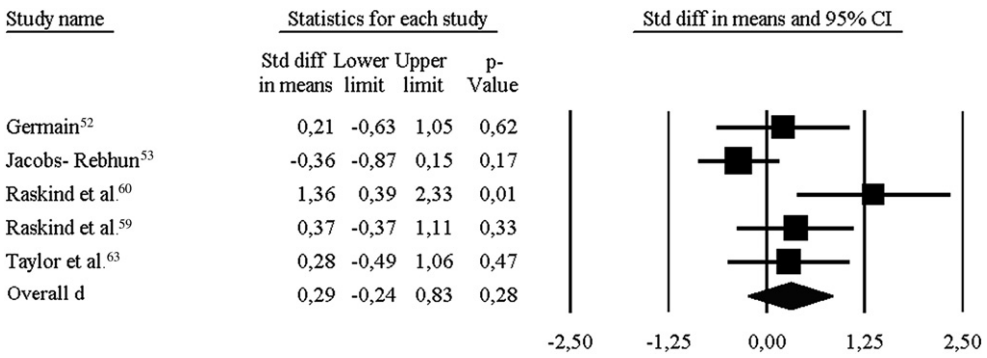

Fig. 1. Forest plot presenting the post-treatment total effect sizes and 95% confidence intervals (CI) for each pharmacological study individually and for all pharmacological studies combined, calculated with random effects model; Std diff = standard difference.

recommended[20] psychological (IRT) and pharmacological treatment (prazosin) was 0.58 (95% CI = 0.37–0.78) and 0.50 (95% CI = 0.03–0.96), respectively. Post-treatment effect sizes for each individual treatment are presented in Table 2.

Homogeneity analyses

The analysis of homogeneity between all studies demonstrated that Q was non-significant ($Q = 26.60$, $p = 0.09$). The heterogeneity analysis revealed medium heterogeneity between all studies ($I^2 = 32.34\%$). The same was the case within studies assessing psychological treatment ($Q = 12.57$, $p = 0.56$, $I^2 = 0.\%$). The analysis revealed that Q was significant for studies investigating pharmacological treatment ($Q = 10.22$, $p < 0.05$, $I^2 = 60.86\%$). The cyproheptadine study by Jacobs-Rebhun et al.[53] was the only study with a negative effect size (the effect favoured the control group). Excluding this study from the homogeneity analysis for the pharmacological studies yielded a non-significant Q ($Q = 3.87$, $p = 0.28$, $I^2 = 22.38\%$).

Contrast analyses

The results from the different contrast analyses are depicted in Table 3. The difference between the total effects of the pharmacological studies and the total effects of the psychological studies was not significant. The difference between the strongest recommended psychological intervention (IRT) and the strongest recommended pharmacological treatment (Prasozin) was also not significant.

The contrast analyses for different formats were only computed for the psychological studies. The individual therapy format exhibited the largest size, 0.74 (95% CI = 0.43–1.04), group therapy had an effect size of 0.63 (95% CI = 0.33–0.92), and the self-help format had an effect size of 0.36 (95% CI = 0.22–0.50). The

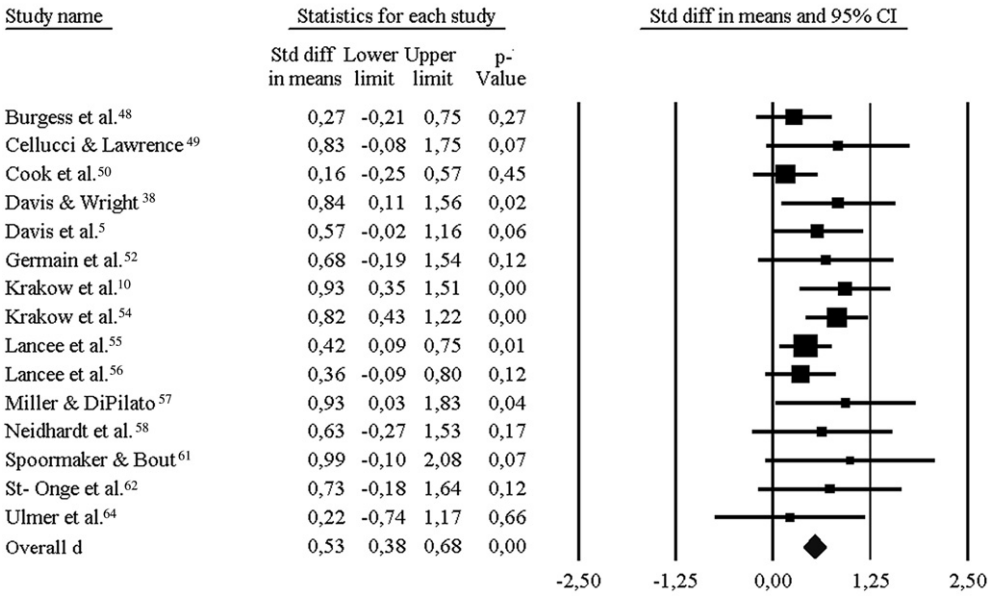

Fig. 2. Forest plot presenting the post-treatment total effect sizes and 95% confidence intervals (CI) for each psychological study individually and for all psychological studies combined, calculated with random effects model; Std diff = standard difference.

Table 2
Number of studies and participants in the analyses for each treatment comparison, post-treatment total effect sizes with 95% confidence intervals (CI).

Treatment	Studies	*N*	Statistics for each treatment	
			Cohen's d (95% CI)	*P*-value
Psychological				
Desensitization	2	41	0.97 (0.32–1.62)	0.00
ERRT	2	79	0.68 (0.22–1.13)	0.00
Exposure	2	208	0.52 (0.24–0.81)	0.00
IRT	7	510	0.58 (0.37–0.78)	0.00
LDT	1	30	0.96 (0.05–1.86)	0.04
Recording	1	163	0.20 (−0.11–0.51)	0.20
Relaxation	2	93	0.32 (−0.31–0.94)	0.32
MC	3	207	0.28 (0.01–0.56)	0.05
Pharmacological				
Cyproheptadine	1	60	−0.36 (−0.87–0.15)	0.17
Prazosin	4	97	0.50 (0.03–0.96)	0.04

ERRT = exposure, relaxation and rescripting therapy; IRT = image rehearsal therapy; LDT = lucid dreaming therapy; MC = multi-component therapy.

individual format yielded a better effect than the self-help format ($p = 0.03$). The difference between the individual format and the group format and between the group format and the self-help format was however not significant.

The contrast analyses concerning the different outcome measures revealed an overall effect size for nightmare distress of 0.39 (95% CI = 0.20–0.57). The corresponding overall random effect size for nightmare intensity was 0.54 (95% CI = 0.23–0.86), and for nightmare frequency 0.46 (95% CI = 0.36–0.57). None of the classes of outcome measures differed significantly from each other in terms of effect sizes.

The overall effect size for the IRT interventions was 0.58 (95% CI = 0.37–0.78), the multi-component treatments showed an overall effect size of 0.28 (95% CI = 0.01–0.56), while the other psychological treatments yielded an overall effect size of 0.49 (95% CI = 0.30–0.69). None of the differences between these interventions reached statistical significance.

Three interventions, two relaxation studies[48,57] and one recording study[55] were regarded as minimal interventions, whereas the other studies comprised more extensive treatments.

Table 3
Post-treatment effect sizes and 95% confidence intervals (CI) for different contrast analysis variables.

Contrasts	Cohen's d (95% CI)	Contrast analyses
Format		
Group	0.63 (0.33–0.92)	Group vs. individual: $P = 0.62$
Individual	0.74 (0.43–1.04)	Individual vs. self-help: $P = 0.03^*$
Self-help	0.36 (0.22–0.50)	Self-help vs. group: $P = 0.11$
Outcome		
Distress	0.39 (0.20–0.57)	Distress vs. frequency: $P = 0.47$
Frequency	0.46 (0.36–0.57)	Frequency vs. intensity: $P = 0.64$
Intensity	0.54 (0.23–0.86)	Intensity vs. distress: $P = 0.41$
Control		
Active	0.36 (−0.03–0.74)	Passive vs. active:
Passive	0.57 (0.41–0.73)	$P = 0.32$
Diagnosis		
ND PTSD	0.56 (0.37–0.75)	ND PTSD vs. PTSD: $P = 0.56$
Non-PTSD	0.37 (−0.06–0.79)	Non-PTSD vs. ND PTSD: $P = 0.35$
PTSD	0.37 (−0.03–0.77)	PTSD vs. Non-PTSD: $P = 0.88$
Psychological interventions		
IRT	0.57 (0.39–0.75)	IRT vs. MC: $P = 0.09$
MC	0.28 (0.01–0.56)	MC vs. other: $P = 0.22$
Other	0.49 (0.30–0.69)	Other vs. IRT: $P = 0.58$
Treatment magnitude		
Extensive	0.53 (0.41–0.66)	Minimal vs. extensive interventions
Minimal	0.22 (0.03–0.46)	$P = 0.02^*$

PTSD = posttraumatic stress disorder; ND PTSD = not defined status of post-traumatic stress disorder; IRT = image rehearsal therapy; MC = multi-component intervention; * = indicate significance.

The overall effect size based on the minimal interventions was 0.22 (95% CI = −0.03–0.46) whereas the more extensive studies yielded an overall effect size of 0.53 (95% CI = 0.41–0.66). This difference was statistically significant ($p = 0.02$). The overall effect size in the studies with a passive control group was 0.57 (95% CI = 0.41–0.73), which was not significantly higher than the overall effect size of the studies with an active control group, 0.36 (95% CI = −0.03–0.74).

Two studies[48,62] reported post-treatment data for non-PTSD participants, seven studies[50,53,54,59,60,63,64] reported post-treatment measures for PTSD participants and ten studies[10,38,49,51,52,55–58,61] did not report the PTSD status of their participants. The two non-PTSD studies had a combined effect size of 0.32 (95% CI = 0.06–0.64), the PTSD group showed an overall effect size of 0.36 (95% CI = −0.04–0.77), whereas the studies that did not report the PTSD status of their participants had an effect size of 0.49 (95% CI = 0.36–0.62). No differences in overall effect sizes were found based on PTSD status of study participants.

Follow-up studies

As previously mentioned, there were only three studies providing nightmare-related data for a follow-up analysis with a control group: Burgess et al.[48] showed a similar effect size, $d = 0.27$ (95% CI = −0.21–0.75) for the follow-up analysis four weeks after treatment termination as for the post-treatment. Cook et al.[50] showed a decrease of total effect size from 0.13 (post-treatment) to −0.05 (95% CI = −0.48–0.38) at the 24-week follow-up. For Krakow et al.,[76] based on the study population as reported by Neidhard et al.,[58] an effect size of 0.74 (95% CI = −0.31–1.79) was found at follow-up.

Publication bias

The funnel plot displayed some indications of publication bias. The smaller studies provided more positive results than the larger ones. The Duval and Tweedie's[73] trim and fill test revealed that five studies were theoretically missing in order to make the funnel plot symmetric. Recalculations by the trim and fill method gave an imputed overall total fixed effect size of 0.38 (95% CI = 0.25–0.51) and an overall total random effect size of 0.38 (95% CI = 0.20–0.56). The "fail-safe N" was equal to 222, meaning that 222 theoretical comparisons yielding null results had to be added to the analysis in order to bring the overall effect size to an insignificant level.

Discussion

Main results

The overall total effect in this meta-analysis demonstrates that the treatment of nightmares yields a moderate effect.[77] The results inform and extend the existing evidence provided by qualitative reviews with regard to the pharmacological treatment of PTSD,[78] CBT treatments for nightmares[5] and psychological treatment for chronic PTSD.[79]

The overall total effect for the psychological treatments indicated a significant improvement. This finding is in accordance with a systematic review of CBT for nightmares by Lancee et al.[5] In contrast, the overall effect was not significant for the pharmacological treatments. This seems to be attributable to the cyproheptadine study,[53] which yielded a negative result, as the four prazosin studies[52,59,60,63] all yielded favourable outcomes. Our findings showing an overall significant effect of prazosin for PTSD-related nightmares are in accordance with a previous review and current treatment recommendations.[20]

Based on Cohen's[77] effect size conventions (small-effect size = 0.20, medium-effect size = 0.50, large-effect size = 0.80), most of the effect sizes from the single studies fall in the range between small to moderate, although some large-effect sizes are noted. Compared to effects from other CBT interventions for conditions such as panic disorder, depression, generalized anxiety disorder and PTSD, the effect sizes found in the present meta-analysis are relatively small.[80] Thus, the room for future treatment development and refinement concerning nightmare treatment is most likely to be relatively large. There was a small discrepancy between the total effect sizes at post-analysis and follow-up for the three studies that provided nightmare-related follow-up data. This indicates that the treatment effects for nightmares may last beyond the active treatment period. Nevertheless, this interpretation should be undertaken with caution since the overall follow-up time was rather narrow and follow-up data were only available from three studies.[48,50,76] Still, there are several uncontrolled non-pharmacological nightmare treatment studies with at least one year follow-up which suggest that treatment response seems to be long-lasting.[81–83]

The overall heterogeneity analysis was not significant, thereby indicating lack of large variations among the effect sizes obtained from the various studies. This pertained also to the separate heterogeneity analysis conducted for the psychological studies. However, the heterogeneity analysis for the pharmacological intervention studies was significant, reflecting large variations among the effects sized based on these studies. When deleting the largest outlier,[53] the heterogeneity analysis became non-significant, thus the heterogeneity could be attributed to the outlier.

Publication bias

The extent to which publication bias may have influenced the results of the present meta-analysis is difficult to accurately estimate. Even so, we did investigate the potential presence of publication bias using a funnel plot, and conclude that publication bias seems to be unlikely based on the fact that the present funnel plot has a relatively inverted symmetrical shape. Smaller studies show more variability than larger ones, although there seems to be a tendency for small studies to report more positive effects. The Duval and Tweedie's[73] trim and fill procedure, which yields an estimate of the overall effect size after taking publication bias into account, documented that the adjusted overall effect size only diverged to a limited extent from the overall effect size obtained in the present study. The fail-safe N test suggested that 222 comparisons with non-significant results must be added to the included comparisons in order to yield an overall non-significant result. Consequently, we conclude that the results from the present meta-analysis seem stable and that the publication bias is largely negligible.

Contrast analyses

Regarding format of treatment delivery for the psychological interventions, treatment administered in an individual format demonstrated a significantly larger effect when compared to self-help, though not when compared to the group format. There was no significant difference between the group format and self-help. These findings are in accordance with results from the treatment of panic disorder[84] and exposure therapy for PTSD.[85] Nonetheless, self-help treatment has shown results similar to those for the face-to-face treatment of disorders such as depression and anxiety disorders,[86] bulimia nervosa[87] and nightmare frequency and sleep quality.[88]

Treatment complexity could be a possible mediating variable when comparing self-help treatment with face-to-face treatment. Lancee et al.[56] reasoned that the use of many treatment components could be more confusing in self-help than in face-to-face treatments. Findings from Andersson et al.[89] reporting that signs of personality disorder might have a negative impact on internet treatment compared to face-to-face treatment are also relevant, as there is less room in the former to repair misunderstandings in the communication. Additionally, self-administered treatments seem to be most effective for motivated clients.[90] In relation to internet-delivered CBT treatments, Andersson[89] argues that there are clear indications that the presence of an online therapist to provide feedback and guide patients is important for adherence and the outcome.

Distress, intensity and frequency reflected the three primary categories of outcome measures in the meta-analysis, in which all measures proved significant. There was no significant difference between the three categories of outcomes measures, even though a slight discrepancy in favour of intensity was observed.

IRT is the recommended treatment for idiopathic nightmares.[20] Although IRT overall yielded somewhat larger effect size (0.58) than multi-component interventions (0.28) and other psychological interventions collapsed (0.48) the difference in overall effect size between these interventions did not reach statistical significance.

In terms of a passive vs. active control group, there was no significant difference in effect sizes. Still, passive control groups tended to yield a larger total effect size (0.57) compared to active control groups (0.36). The active control groups consisted of a sleep and nightmare management group,[50] a nightmare recording group[58] and a nightmare discussion treatment group,[49] in addition to the placebo groups in the pharmacological interventions.[52,53,59,60,63]

We also compared the overall effect size of minimal interventions (relaxation and nightmare recordings) with the overall effect size from studies based on more extensive psychological treatments, finding that the former effect size (0.22) was significantly smaller than the latter (0.53). This finding is in line with other studies investigating the effects of other psychological interventions.[91–93]

In relation to PTSD, the overall effect size showed no significant difference between the PTSD-studies, the non-PTSD studies and the studies that did not report PTSD status. This result should be handled with caution as the contrast effects may overlap with other contrasts.

Outcome may for example be related to comorbidity that varies significantly, both in terms of degree and type across studies. A relevant question to ask is whether the underlying pathophysiology in PTSD-related nightmares is different from the underlying pathophysiology in idiopathic nightmares.[20] PTSD-related nightmares are typically characterized by realistic reenactments of traumatic events and excessive body movements and occur both in non-REM as well as in REM-sleep, whereas idiopathic nightmares normally comprise bizarre and illogical events involving large muscle paralysis and occur mainly during REM-sleep.[94–99] Thus, future studies should draw a firm distinction between types of nightmares when investigating treatment effects. Military trauma PTSD may be more resistant to treatment in general than civilian trauma PTSD.[100] In this respect it should be noted that two[52,64] of three psychological trials in military veterans yielded significant treatment effects, and all three prazosin trials in military veterans were associated with significant improvement.[52,59,60] Whether treatment resistance for military veterans with PTSD-related nightmares is higher than for civilian trauma PTSD-nightmares is so far not clear, however this issue should be a topic for future research.

Limitations and strengths

The present meta-analysis provides the first systematic comparison of randomized controlled trials on the treatment of nightmares. Our use of effect sizes (together with *p*-values) to compare psychological and pharmacological studies possesses strengths in terms of determining and recommending one treatment intervention over another. Publication bias seems to have influenced the results to a limited extent, thereby strengthening the representativeness of the results. The fact that the number of single studies included was relatively small (particularly the number of pharmacological studies) urges one to take caution in evaluating the conclusions. Although it could be argued that we should have coded the included studies according to study quality, it should be mentioned that all were RCTs; one may therefore assume that the variance with concern to study quality was rather limited. In addition, studies have shown that different study quality measures may yield very divergent results; hence, the use of quality indicators is associated with a risk of drawing doubtful conclusions.[101]

Conclusion

Our results show that the treatment of nightmares overall has moderate effect. No significant difference was found between the group of psychological studies and the group of pharmacological studies. Contrast analyses indicated that significant differences favour the individual format towards self-help. The results from the present meta-analysis provide no strong evidence for preferring specific psychological treatments over others. However, prazosin stands out as the pharmacological treatment of choice for PTSD-related nightmares. All categories of outcome measures (intensity, distress, and frequency) were associated with significant improvements and exhibited no significant differences when compared to each other in terms of overall effect size. The passive control group seemed to yield somewhat though not significantly more favourable results compared to the active control. No significant difference was detected between studies related to the PTSD status of the included patients. Only three studies provided follow-up data.

Implications

Treatments for nightmares are shown to be effective, both concerning psychological treatments and prazosin. This conclusion is in accordance with other available reviews. Nevertheless, the overall effect sizes obtained in this meta-analysis are of a moderate magnitude. The connection between treatment interventions in relation to nightmare disorder and nightmares in PTSD patients should be further examined in future research.

Guidelines for future research

Areas for future research should include a better and more systematic overview of the various interventions' effects on secondary measures such as anxiety, depression and PTSD-related symptoms. There is also a need to conduct more studies in which CBT and pharmacological treatments are directly compared. More studies should investigate the effects of psychological interventions for PTSD-related nightmares. More RCT's with long-term follow-up are warranted from a strictly empirical point of view, although keeping patients on a waiting-list for a long period of time may be ethically problematic. As trials combining effective psychotherapy with effective pharmacotherapy might produce larger effect sizes than either treatment modality alone, future studies should consequently investigate the effects of multimodal treatments for nightmares. The field would also benefit from developing a consensus on which outcome measures are used. In addition, more research is needed on alternative treatment methods for nightmare disorder. For example, promising results have been reported from uncontrolled studies of eye movement desensitization and reprocessing therapy,[102–104] although so far this has not been investigated in an RCT.

Practice points

- The treatments for nightmares have a moderate effect, in which both intensity, distress and frequency are associated with a significant improvement as outcome measures.
- Psychological interventions and prazosin are associated with significant improvements post-treatment.
- There is a significant difference favouring the individual format compared to self-help intervention.
- Minimal interventions yield poorer outcome than more extensive therapies.

Research agenda

- There is a need to conduct more controlled studies in which CBT and pharmacological studies are directly compared.
- Developing a consensus in regard to outcome measures should be strived for.
- Development of and research on alternative treatments methods are considered necessary due to the moderate effects of current treatment approaches.
- More studies should be conducted investigating whether different interventions yield different outcomes for PTSD-related and idiopathic nightmares, respectively.

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Appendix A

ICSD-2 Diagnostic criteria: nightmare disorder

A. Recurrent episodes of awakenings from sleep with recall of intensely disturbing dream mentation, usually involving fear or anxiety, but also anger, sadness, disgust, and other dysphoric emotions
B. Full alertness on awakening, with little confusion or disorientation, recall of sleep mentation is immediate and clear.
C. At least one of the following associated features is present:
   1. Delayed return to sleep after the episode.
   2. Occurrence of episodes in the latter half of the habitual sleep period

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