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Title: Does cognitive behavioural therapy for insomnia improve cognitive performance? A systematic review and narrative synthesis

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Summary

Individuals with insomnia report difficulties pertaining to their cognitive functioning. Cognitive behavioural therapy for insomnia (CBT-I) is associated with robust, long-term improvements in sleep parameters, however less is known about the impact of CBT-I on the daytime correlates of the disorder. A systematic review and narrative synthesis was conducted in order to summarise and evaluate the evidence regarding the impact of CBT-I on cognitive functioning. Reference databases were searched and studies were included if they assessed cognitive performance as an outcome of CBT-I, using either self-report questionnaires or cognitive tests. Eighteen studies met inclusion criteria, comprising 923 individuals with insomnia symptoms. The standardised mean difference was calculated at post-intervention and follow-up. We found preliminary evidence for small to moderate effects of CBT-I on subjective measures of cognitive functioning. Few of the effects were statistically significant, likely due to small sample sizes and limited statistical power. There is a lack of evidence with regards to the impact of CBT-I on objective cognitive performance, primarily due to the small number of studies that administered an objective measure (n=4). We conclude that adequately powered randomised controlled trials (RCT), utilising both subjective and objective measures of cognitive functioning are required.

Keywords: Insomnia, cognitive behavioural therapy, CBT-I, cognitive functioning, narrative synthesis

Abbreviations

AFI	attentional function index
ANT-I	attentional network test – interactions task
AT	autogenic training
BBTI	brief behavioural treatment for insomnia
BPT	behavioural placebo treatment
CBT-I	cognitive behavioural therapy for insomnia
CBT-I AD	cognitive behavioural therapy for insomnia in recovering alcohol dependent patients
CBTI-Phone	telephone delivered cognitive behavioural therapy for insomnia
CT	cognitive therapy
DSM-IV	diagnostic and statistical manual of mental disorders, fourth edition
DSM-V	diagnostic and statistical manual of mental disorders, fifth edition
EEG	electroencephalogram
IC	information control
IPC	information pamphlet control
ISI	insomnia severity index
LM1	logical memory test immediate recall
LM2	logical memory test delayed recall
mCBT	minimal CBT-I
MFI-20	multidimensional fatigue inventory
MFSI-SF	multidimensional fatigue symptom inventory – short form
MMSE	mini-mental state examination
NR	not reported
NRT	non-randomised trial
PMR	progressive muscle relaxation
PSG	polysomnography
QR	quality rating
RCT	randomised controlled trial
RL	relaxation

RT	reaction time
PSQI	Pittsburgh sleep quality index
RCT	randomised controlled trial
SAT	switching Attention Test
SC	stimulus control
SH	sleep hygiene
SHUTi	sleep healthy using the internet
SMD	standardised mean difference
SR	sleep restriction
SRT	sleep restriction therapy
TONI	test of nonverbal intelligence
TST	total sleep time
USA	United States of America
UT	uncontrolled trial
WASO	wake time after sleep onset
WLC	wait list control
WMS-CR	Wechsler memory scale – Chinese revision

Introduction

Insomnia is characterised by persistent difficulties with sleep initiation and/or maintenance. Insomnia is recognised as a 24-hour disorder, with impairments in daytime functioning and distress attributed to poor sleep being one of the core diagnostic criteria (1, 2). Traditionally considered as a secondary symptom, there is now evidence that insomnia is involved in the aetiology and maintenance of psychopathology (3) and is an independent risk factor for the development of cardiovascular disease (4) and diabetes (5). This has led to an acknowledgement of the need for attention to and treatment of insomnia, regardless of the co-occurring presence of mental or physical health problems (6, 7).

Impairments in cognitive abilities are among the most commonly reported daytime symptoms of insomnia (8). Individuals with insomnia describe deficits in attention, concentration and memory which impact on decision making, social functioning and performance at work (9, 10) and leave individuals with insomnia feeling as though they are “struggling through the day” (11). Interestingly, subjective reports of cognitive deficits have not been consistently corroborated by objective measurements and a body of research assessing cognitive performance in people with insomnia compared to normal sleepers is marked by discrepant findings (12). A recent meta-analysis which combined the results of studies with small sample sizes concluded that insomnia is associated with mild to moderate impairments on tasks assessing working memory, episodic memory, problem solving, choice reaction time, information processing and selective attention (13). This review also highlighted the need for studies with greater statistical power and the assessment of a wider range of cognitive functions in order to improve our understanding of the nature and extent of cognitive impairment in insomnia. Uncertainty about the impact of insomnia on objective cognitive performance contrasts with research into the effects of experimental sleep loss, where findings have been more robust. Specifically, chronic sleep deprivation has been associated with deleterious effects across several cognitive domains, including memory and attention (14).

Evidence from prospective longitudinal studies indicates that chronic insomnia is an independent risk factor for cognitive decline (15, 16). It has also been suggested that changes in sleep architecture which tend to occur with advancing age (more sleep fragmentation, earlier awakenings and less slow wave sleep) contribute to normal, age-related cognitive decline (17, 18). Sleep is known to play a role in brain plasticity and memory formation and therefore chronically disturbed sleep is proposed to lead

to impairment in cognition through its impact on brain function and brain health (19, 20). The majority of evidence for this comes from animal models of chronic sleep deprivation, which have demonstrated reductions in hippocampal cell proliferation and generation of new neurons (for review see (19)). In humans, brain imaging studies have reported smaller hippocampi in those suffering from chronic insomnia (21, 22) and associations between hippocampi size and performance on a range of cognitive tests has also been demonstrated (21, 23), highlighting a potential pathway through which chronically disturbed sleep leads to cognitive deficits. Other studies report cortical atrophy in insomnia that might confer a risk for cognitive impairment (24).

CBT-I is a psychological treatment which aims to change the patterns of maladaptive thinking and behaviour which are proposed to maintain sleep difficulties (25, 26). Multiple reviews and meta-analyses support the efficacy of CBT-I in creating long lasting improvements in various indices of sleep, including sleep efficiency, sleep onset latency and wake-time after sleep onset (WASO) (27, 28). When asked to describe the experience of insomnia it is usually the problems encountered during wake and the pervasive impact that sleep difficulties have on quality of life and wellbeing that are emphasised, as opposed to specific difficulties with the sleep initiation/maintenance of sleep (10, 11). Indeed, there is evidence that the perceived impact of sleep disturbance on daytime functioning is what prompts individuals with insomnia to pursue treatment (29, 30). It seems that medical advice is sought once a certain level of daytime dysfunction is reached, in the hope that treatment will remedy perceived impairments (31). Accordingly, treatment options for insomnia should aim to improve not only the sleep deficits, but also the daytime symptoms that contribute to the burden of the disorder (32). However, relatively little is known about the effects of CBT-I on daytime symptoms. Recent reviews have concluded that psychological treatment for insomnia is associated with improvements in quality of life (11, 33). However, quality of life is a broad concept, encompassing aspects of physical and psychological wellbeing. Moreover, quality of life is usually assessed using instruments which were not developed specifically for use in insomnia populations. Therefore, the impact of treatment on those aspects of daytime functioning which are known to be of particular concern in insomnia is not clear.

The aim of the current review was to conduct a systematic appraisal of the literature and evaluate the evidence for the effects of CBT-I on cognitive functioning. We chose to focus on cognition because

impairments in this area are one of the most commonly endorsed daytime complaints (34, 35) and there is evidence from both subjective reports and objective measures that individuals with insomnia are characterised by cognitive deficits compared to good sleepers. To our knowledge, the impact of CBT-I on cognition has yet to be evaluated systematically. This is surprising because impaired cognition may underlie many of the adverse consequences of insomnia, such as lowered work productivity, increased frequency of accidents (36) and declining health (37).

METHOD

As part of the review, quantitative data regarding effect sizes are presented. The standardised mean difference (SMD) was used as a measure of effect size and was calculated for studies utilising an RCT design, providing the necessary post-treatment and follow-up data. A meta-analysis was not considered appropriate for the current review due to the small number of studies available and the considerable heterogeneity in the methodology and outcomes of included studies.

Search strategy and selection

Online databases EMBASE, PsycINFO, MEDLINE, MEDLINE In-Process, All EBM Reviews, CINAHL and the Cochrane Library were searched from inception to 19th March 2016.

The review used a title and abstract word strategy, which included the following terms: (sleeplessness OR insomnia* OR “sleep initiation” OR “sleep maintenance” OR “sleep disorder*” OR dysomnia* OR “poor sleep*” OR “sleep problem*” OR “sleep disturbance*”) AND (“cognitive behav* therap*” OR “behav* therap*” OR CBT OR CBT-I OR ICBT OR “self-help” OR “sleep hygiene” OR “stimulus control” OR “sleep restriction” OR relaxation OR “behav* modification” OR “cognitive therap*” OR imagery OR psychotherap*). Reference lists of published meta-analyses and systematic reviews of CBT-I trials were also searched to locate additional papers (27, 38).

Citations were exported to reference management software and duplicates were removed. Titles and abstracts were reviewed. If the abstract indicated that the study evaluated a psychological treatment for insomnia, the full text was acquired to identify if cognitive functioning was measured as a treatment outcome. Relevant articles were then assessed against the inclusion and exclusion criteria.

For each of the articles identified, the reference list was searched and the article was entered into the “similar articles” search tool in PUBMED, in order to find additional relevant articles. Reviews, opinions, editorials, grey literature and conference abstracts were not included.

Criteria for inclusion of research articles

Empirical studies were included if they recruited an adult sample (18 years and over) with insomnia at either the disorder or symptom level, as defined by the diagnostic and statistical manual for mental disorders (e.g. DSM-V) (7) , the international classification of sleep disorders (1), research criteria for

insomnia (2) or measures of insomnia severity, such as the insomnia severity index (ISI) (39) and the Pittsburgh sleep quality index (PSQI) (40). Studies using samples where insomnia was comorbid with, or secondary to, a health or psychiatric condition were eligible for inclusion.

The treatment for insomnia was required to incorporate at least two of the five most widely accepted components of CBT-I (41); a cognitive therapeutic component (e.g., cognitive restructuring), stimulus control, sleep restriction, sleep hygiene and relaxation. There was no requirement for the treatment to combine cognitive and behavioural components and we did not specify inclusion criteria on the basis of delivery modality or duration of treatment. Treatments which were modified for a particular population and/or comorbid condition were eligible. Studies in which the treatment comprised therapies from other treatment modalities (e.g. bright light therapy or hypnotic medication) were not included.

In order to be eligible the study was required to assess cognitive functioning as a treatment outcome. Studies were classified as having assessed cognitive functioning if they administered a measure which probed one of the following domains: attention, concentration, perception, memory, verbal functions, construction, concept formation, reasoning, executive functions or motor performance (42). Cognitive functioning could be assessed subjectively using standardised questionnaires or single items (e.g. visual analogue scales), or objectively using cognitive tests. Studies utilising subjective measures of cognitive functioning were jointly inspected by all three authors (VH, SDK and DP) to consider if the subjective measure adequately assessed an aspect of cognitive functioning. A consensus was required for the study to be deemed as eligible.

As the literature is limited, all types of treatment evaluation study designs were included. Studies were required to be written in English and published in peer-review journals.

Quality Assessment

The Downs and Black checklist (43) was used to assess the methodological quality of included studies. It includes 27 items assessing study reporting, external validity, internal validity and power in relation to randomised and non-randomised studies. It has adequate levels of internal consistency, good inter-rater reliability and high test-retest reliability (43). Item 27 relating to power was omitted due to the fact that cognitive functioning was a secondary outcome within the majority of the included

studies and therefore power calculations were not based on this variable. Quality assessment was performed by two researchers independently, for three of the included studies. There was strong levels of agreement between the researchers (Kappa = .90).

Data extraction

Each article was read in full in order to extract and record details of the included studies within a standardised extraction form. This form included the following information: authors and year of published report, methods (study design, assessment time points, blinding, procedure for randomisation), participant characteristics (study population, sample size, age, gender distribution), intervention details (components and mode of delivery), information about the control or comparator intervention and outcomes on a measure of cognitive functioning.

Data synthesis

Findings were combined and summarised in a narrative synthesis. Factors which may explain differences in the direction or size of effects across studies (e.g. study methodology) were considered and discussed, as per guidelines for conducting narrative synthesis (44) .

The SMD was used as a measure of effect size and was calculated for studies utilising a RCT design, providing the necessary post-treatment and follow-up data. Additional data was sought from authors where required. The SMD was derived by subtracting the mean for the control group from the mean for the treatment group and dividing the result by the pooled standard deviation. The direction of the values for the SMD was adjusted so that a positive value indicated better cognitive functioning in the treatment group compared to the control group at the post-treatment and follow-up time points.

RESULTS

Study selection

Searches of databases and bibliographies yielded 2336 potentially relevant citations, of which 436 were duplicates and 1377 were deemed ineligible on the basis of title and abstract. Full text was retrieved for 523 studies and these papers were assessed against the inclusion and exclusion criteria. A final sample of 18 studies was included in the review. A flow chart of the study selection process is presented in figure 1.

[Insert figure 1 here]

Description of studies included within the review

There were a range of study designs within the included studies; 11 RCTs (45-55), five uncontrolled trials (56-60), one non-randomised controlled trial (61) and one case series (62). Study characteristics are presented in table 1.

Study quality

The methodological quality of studies varied, with scores ranging between 10 and 20 out of a possible 26 (mean score = 15). The uncontrolled trials and the case series scored poorly due to the high risk of bias. There were only two studies that attempted to blind participants to the intervention. Few studies used intent-to-treat analysis to limit bias from attrition. In the studies that administered cognitive tests, there was no blinding of outcome assessment. When weighing up the evidence, more weight was given to data from RCTs and higher quality studies. Full quality ratings for each of the included studies are shown in table S1.

Participants

The sample size of the included studies ranged from seven to 229. There were a total of 923 individuals with insomnia symptoms in the eighteen included studies. Across the studies, the mean age of participants was 50.0 years and 71.0% of participants were female. This is comparable to findings from another meta-analysis of outcomes following CBT-I (27) and is consistent with research showing that insomnia symptoms are more common in women and with advancing age (63).

The criteria used to verify insomnia varied across studies. Half of the studies used the DSM-IV (64), DSM-V (7) or research diagnostic criteria (2) (46, 50-52, 54, 55, 58, 61, 62). Six studies used scores on the ISI combined with self-report difficulties with sleep onset/maintenance (45, 47, 49, 56, 59, 60). One study used scores on the PSQI (53). Two studies developed their own criteria based on DSM-IV (48, 57).

The included studies sampled individuals from a range of populations. There were two studies of individuals with fibromyalgia (50, 58), six studies of cancer patients (47, 49, 52, 57, 61, 62), two studies of adults recovering from alcohol dependence (45, 56), one study of college students (54), three studies of older adults (51, 53, 55), one study of women with post-partum depression (59), one study of pregnant women (60) and two studies of adults without any psychiatric or physical health comorbidities (46, 48). In the majority of included studies (13/18), insomnia was considered “secondary” to, or comorbid with, a physical or mental health condition (45, 47, 49, 50, 52, 55-62). Of those studies which reported the duration of insomnia symptoms (10/18), mean values for the sample ranged from 3.9-174 months, with an average duration across studies of 75.83 months.

Interventions

The majority of studies (16/18) delivered an intervention which combined cognitive, behavioural and educational components. There were two exceptions; Wilckens et al. (55) incorporated only the educational and behavioural components of CBT-I (sleep hygiene, stimulus control and sleep restriction) and Sun et al. (53) combined sleep hygiene with relaxation techniques. Many of the included studies failed to provide sufficient details of the intervention components to enable replication, particularly for sleep restriction.

A range of methods were used to deliver the intervention. Eight studies delivered the intervention in a group setting (48, 50, 53, 57, 58, 60-62). In three studies, the intervention was delivered by a clinician through individual face-to-face sessions (51, 54, 59). Four studies combined individual face-to-face sessions with telephone consultations (45, 49, 55, 56). One study delivered the intervention via weekly telephone calls aided by written treatment modules (46). One study combined a self-help manual with three brief telephone consultations (47). One study utilised an online format (52). The length of treatment ranged from 3 to 9 weeks (mean length of treatment = 6 weeks). All of the studies indicated that a structured treatment protocol was used and eleven studies made explicit reference to

the treatment being manualised (45-48, 50, 52, 54, 58, 60-62). Eight studies described efforts to ensure treatment fidelity (e.g. use of checklists, meetings between researchers, evaluation of recordings of treatment delivery) (45, 46, 49, 54, 55, 58, 60, 62).

It was common for the studies included in this review to adapt the intervention to address the links between comorbid or secondary conditions and sleep. The two studies of adults recovering from alcohol dependence adapted the intervention to include psychoeducation about the effects of alcohol use and withdrawal on sleep (45, 56). One of these studies also included cognitive restructuring of unhelpful thoughts and beliefs about relapse (45). A study in cancer patients provided psychoeducation about how to cope with fatigue using physical activity (62). Both of the studies in fibromyalgia patients provided psychoeducation about the link between fibromyalgia, pain and sleep (50, 58).

Description of control and comparative conditions

Both passive and active control conditions were used. Two RCTs compared CBT-I to behavioural placebo treatment (BPT) (45, 49). One RCT compared CBT-I to Zopiclone (51). Four studies used self-help information as a comparator (46, 48, 53, 55). One study compared CBT-I delivered in a group format to sleep hygiene delivered in a group format (50). One non-randomised controlled trial compared “sleep management training” delivered within a standard cancer rehabilitation treatment to the rehabilitation treatment alone (61). Three RCTs compared CBT-I to no treatment (47, 52, 54).

Description of subjective cognitive outcome measures

Fourteen studies employed a subjective measure of cognitive functioning. Six studies used the mental fatigue subscale from the multidimensional fatigue inventory (MFI-20) (45, 46, 52, 54, 56, 58-60). This subscale contains four items which assess cognitive symptoms of fatigue, such as difficulties concentrating (“When I am doing something, I can keep my thoughts on it”, “I can concentrate well”, “My thoughts easily wander” and “It takes a lot of effort to concentrate on things”) (65). Two studies used the mental fatigue subscale of the multidimensional fatigue symptom inventory – short form (MFSI-SF) (52, 60). This subscale contains six items (“I have trouble remembering things”, “I am confused”, “I have trouble paying attention”, “I am unable to concentrate”, “I make more mistakes than usual” and “I am forgetful”). Four studies used the cognitive subscale from the European organisation for research and treatment of cancer QLQ-C30, which is an instrument that evaluates quality of life in

cancer patients (47, 57, 61, 62). This subscale contains two items probing concentration and memory (“Have you had difficulties concentrating on things, like reading a newspaper or watching television” and “Have you had difficulty remembering things?”) (66). One study used the attentional function index (AFI) (49), which is a measure of perceived effectiveness in common activities requiring attention and working memory. The total score on this instrument is thought to provide an overall index of attentional functioning (67). One study used a Likert scale measure of difficulties with concentration (48).

Description of objective cognitive outcome measures

Four studies employed an objective measure of cognitive functioning. The attentional network test - interactions task (ANT-I) was utilised by Miro et al (50). This is a computerised cognitive test which assesses three aspects of attentional functioning (orienting, alerting and executive functioning), as well as the interactions between these three networks (68). One study (51) used the vigil test which is a computerised test of sustained attention (69). Two of the included studies used neuropsychological tests to assess cognitive performance (53, 55). The study by Wilckens et al. (55) administered the logical memory test to assess episodic memory (70), the test of nonverbal intelligence III (TONI) to assess abstract reasoning and figural problem solving (71) and the letter-number sequencing test to assess working memory (72). The study by Sun et al. (53) administered the mini mental state examination (MMSE) (73) to assess global cognitive functioning and the Wechsler memory scale (WMS-CR) (74) to examine memory function.

Effect sizes for cognitive outcomes

The SMD could not be calculated for five studies due to lack of a control or comparator group (56-60). For one study, SMD at post-treatment and follow-up was not calculated due to non-random assignment to groups (61). Two studies reported follow-up data only (48, 53). SMD values at post-treatment and follow-up for subjective outcomes are presented in table S2 and for objective outcomes are presented in table S3.

[Insert table 1 here]

Narrative synthesis

Current evidence for the effect of CBT-I on subjective measures of cognitive functioning

Seven RCTs administered a subjective measure of cognitive functioning. A significant improvement following the intervention compared to control was reported in three RCTs (47, 48, 52). The SMD at the post-intervention time-point was calculated for two of these studies (47, 52) (see figure 2). The study by Casault et al. (47) in cancer patients, demonstrated an improvement in scores on the cognitive functioning subscale of the QLQ-C30 at post-intervention, in the group that received minimal CBT-I compared to a no treatment control group. This difference was not maintained at the 12 or 24-week follow-up, due to improvement in scores in the control group (see figure 4). The study by Ritterband et al. (52) reported a greater improvement in mental fatigue in the group that received internet delivered CBT-I (SHUTi) compared to control. Our calculations of SMD revealed no significant difference between the groups in mental fatigue at the post-intervention time-point. This discrepancy is likely due to the fact that post-intervention SMD does not take baseline scores into account. In this RCT, in spite of random allocation, there were significant differences between the groups at baseline in the variables sex and type of cancer, which were not adjusted for in the analysis. Moreover, participants in the SHUTi group displayed higher levels of mental fatigue than participants in the control group at baseline and therefore the significant improvement in the intervention group could be explained by regression towards the mean. Thus, the results from this study should be interpreted with caution.

[Insert figure 2 here]

The study by Jansson and Linton (48) evaluated the impact of CBT-I on difficulties with concentration, one-year post intervention. They reported significantly greater improvements in concentration between baseline and follow-up in the CBT-I group compared to control, however our calculations of SMD revealed that the groups were not significantly different at follow-up (SMD = 0.19). Similar to the study by Ritterband et al. (52), this discrepancy is likely due to the fact that post-intervention SMD does not take baseline scores into account. In this study there was attrition between randomisation and follow-up (17.6%), which may have introduced bias. The researchers reported that individuals who dropped out were not significantly different from those who completed the study in terms of demographic or clinical data (including concentration difficulties) and there was no differential loss of participants across the groups. However, an intention-to-treat analysis of the data was not performed

and therefore potential bias from attrition is possible. The lack of statistically significant differences between the groups at follow-up may be explained by low sensitivity of the measure utilised and the long period of time between intervention and follow-up, during which the impact of the intervention may have diminished (see figure 4).

Four RCTs reported a non-significant difference between groups in change in subjective cognitive outcomes between baseline and post-intervention (45, 46, 49, 54). The study by Matthews et al. (49) demonstrated a trend towards a significant group x time interaction for scores on the AFI. The reported effect size was moderate (Cohens $d = 0.56$) and therefore the lack of statistical significance is likely due to insufficient power. Our calculations of SMD showed a significant difference between the group that received CBT-I and the group that received BPT in scores on the AFI at the post-intervention time point, which was maintained at the 12 week follow-up but not the 24 week follow-up. Two studies using active controls (BPT and a CBT-I self-help information pamphlet) showed significant improvements in mental fatigue between baseline and post-intervention, for both the intervention groups and the control groups (45, 46). For both of these studies, improvements were larger in the intervention groups, however differences were not statistically significant. Finally, the study by Taylor et al (54) showed no effect of CBT-I on mental fatigue in college students. The authors suggest that this may be due to possible floor effects.

There were five uncontrolled trials that administered a subjective measure of cognitive functioning (56-60). Three of these studies reported significant improvements between baseline and post-intervention (58-60) and one study reported a trend for improved cognitive functioning (57). The studies that did not find a statistically significant improvement had small samples ($N = 14$ and $N = 7$). The case series conducted by Quesnel et al. (62) reported a significant improvement in score on the QLQ-C30 between baseline and post-intervention, which was maintained at follow-up. The non-randomised controlled trial reported by Simeit et al. (61) reported that all groups showed significant improvements in self-report cognitive functioning between baseline and follow-up. There were no significant group x time interactions.

The weight of evidence from the non-randomised control trial, case series and uncontrolled trials point to positive effects of CBT-I on subjective measures of cognitive functioning. However the risk of bias in these studies is high. Evidence from the RCTs included in this review is mixed and only two RCTs

(47) demonstrated a significant difference between groups at the post-intervention time point. There is a great deal of heterogeneity within the included studies and factors which differentiate between those RCTs that report significant improvements in cognitive functioning following the intervention, and those RCTs that report non-significant findings, are not clearly discernible. Our SMD calculations suggest that on the whole, CBT-I is associated with larger improvements in subjective measures of cognitive functioning compared to control, however confidence intervals are large, reflecting the small sample size and low statistical power (eight out of the eleven RCTs had $N \leq 60$ which means that studies would only have the ability to detect an effect size f of 0.37), limiting the conclusions that can be drawn.

Current evidence for the effect of CBT-I on objective measures of cognitive functioning

Four RCTs evaluated the impact of CBT-I on objective measures of cognitive functioning (50, 51, 53, 55). Two of these studies reported positive findings (50, 53) and two studies reported null findings (51, 55). SMD for objective measures at post-intervention are presented in figure 3. The study by Miro et al. (50) in individuals with fibromyalgia found greater improvements in two aspects of attention (alerting and executive control) in the intervention group compared to the control group. Our calculation of SMD revealed no significant difference between the groups on any aspect of performance on the ANT-I task at the post-intervention time-point. This discrepancy may be due to baseline differences between the groups in age, which were adjusted for in the statistical analysis performed by Miro et al. The study by Sun et al. (53) reported improvements in scores on the MMSE and the WMS-CR following the intervention, which became larger at subsequent follow-ups. These findings were corroborated by our calculations of SMD, which showed statistically significant differences between groups on scores on the MMSE and WMS-CR at each of the follow-up time-points (12, 24 and 52 weeks) (see figure 4). In this study, participants were provided with sleep hygiene information and were taught relaxation skills which they were encouraged to practice both individually and within groups, for a period of one year. Performance on cognitive tests was compared to a group that received sleep hygiene information only. The large effects observed in this study may be explained by non-specific effects of the intervention such as participant expectations of improvement and the increased social contact provided by group relaxation practice. In addition, researchers administering the neuropsychological tests were not blind to group assignment, which may have led to an exaggeration of treatment effects through ascertainment bias.

[Insert figure 3 here]

[Insert figure 4 here]

The study by Wilckens et al. (55) examined the impact of brief behavioural treatment for insomnia (BBTI) on cognitive functioning in older adults. BBTI focuses on the behavioural aspects of CBT-I and utilises stimulus control and sleep restriction. In this study they found no significant difference between the groups on change in performance on the cognitive tests. One possible reason for null findings is the short duration between baseline and post-intervention (4 weeks). A greater decrease in TST at the post-intervention time point was reported in the intervention group, which is likely a result of sleep restriction therapy (SRT). SRT has been associated with increases in daytime sleepiness and impairments in vigilance during the acute phase (75). Therefore, the side-effects of sleep restriction may have impacted on performance on cognitive tests, contributing to null findings. In addition the time of day at which the cognitive tests were administered was not controlled for, and this may have introduced additional variance, possibly obscuring the effects of the intervention (76).

The study by Omvik et al. (51) compared the effects of CBT-I and Zopiclone on sustained attention. They found the number of correct responses on the vigilance task significantly worsened in the CBT-I group between baseline and post-intervention. Again, this may be related to the short-term effects of SRT (75). However, there were no significant group x time interactions for any index of performance on the vigilance task, either at post-intervention or follow-up. This study had a very small sample size ($N=45$) and an active control. Therefore, the lack of group x time interactions may reflect insufficient statistical power to detect small effects. The authors did not account for participants who dropped out of the study and therefore attrition bias may also be a factor.

We identified few studies that evaluated the impact of CBT-I on objective measures of cognitive functioning. The evidence from the studies included in this review is mixed. Heterogeneity in the nature of the tasks used to probe cognitive functioning may contribute to the disparate findings. Confidence intervals for SMD at post-intervention and follow-up tend to be smaller for objective

measures of cognitive functioning compared to the subjective measures of cognitive functioning, reflecting more precise measurement of constructs.

Relationship between sleep and cognitive functioning

Three studies examined the relationship between changes in sleep and changes in cognitive functioning, from pre to post-intervention (50, 51, 55). The study by Omvik et al. (51) reported no significant associations between change in sleep efficiency or slow wave sleep and change in performance on the vigilance task. The study by Wilckens et al. (55) calculated correlations between change in performance on cognitive tests and change in WASO, delta power (absolute and relative) and sigma power (absolute and relative). They found a significant positive association between increased absolute delta power and improved abstract reasoning. In addition, decreased relative sigma power was significantly associated with improvements in abstract reasoning. Neither of these associations was moderated by treatment group. There were no significant associations between change in sleep and change in performance on delayed recall or working memory tasks. Enhanced delta power, and a corresponding decrease in sigma power, may benefit brain regions that sub-serve executive functions in older adults, however BBTI does not appear to drive these relationships.

Miro et al. (50) calculated the association between change in sleep quality and change in performance on the ANT-I. They found a significant positive association between sleep quality and performance on the attention control index from the ANT-I, which is proposed to be a measure of executive functioning. There were no significant associations between change in sleep quality and any other index of the ANT-I. On the basis of these results, Miro et al. concluded that improvements in sleep quality are associated with better executive functioning in individuals with fibromyalgia.

Associations between changes in sleep and changes in cognitive functioning were exploratory outcomes in these trials and there was, therefore, limited correction for multiple testing, which increases the chances that some of the significant associations uncovered are due to type-one error. There were no studies that conducted mediation analyses to assess whether CBT may influence cognitive outcomes via temporally-separated mediators (e.g., insomnia severity, sleep continuity). The associations reported do not provide evidence with regards to the direction of the effect and experimental manipulations are required in order to determine whether there are specific aspects of sleep architecture that are causally related to cognitive performance. In spite of these limitations,

these findings do highlight possible variables to target in future treatments seeking to deliver sleep-related cognitive improvement.

Discussion

Summary of evidence

The aim of this review was to summarise the literature and evaluate evidence for the effects of CBT-I on cognitive functioning. Using broad inclusion criteria, we identified 18 relevant studies. For the majority of these studies, cognition was a secondary outcome and assessed within a general measure of self-reported daytime functioning. Only four of the included studies administered an objective measure of cognitive functioning and across these studies, the range of cognitive domains examined was limited. The lack of research into the impact of CBT-I on cognitive functioning is surprising, given that impairments in concentration and memory are among the most commonly reported and most troubling daytime symptoms of insomnia (35).

On the basis of post-intervention and follow-up SMDs, the majority of studies showed small to moderate effects of CBT-I on cognition. Three of the included studies reported statistically significant improvements, which our calculation of SMD at post-intervention/follow-up did not corroborate. Baseline imbalances resulting from small sample sizes or failure in randomisation may have contributed to the reported significant improvements in the intervention group compared to the control group. The included studies generally had small samples with limited statistical power to detect less than large effects. There was one high quality RCT, which incorporated an active control condition, participant blinding and utilised intention-to-treat analysis to minimise bias from attrition (49). This study found a trend for a significant effect of CBT-I on self-report attentional function, with a moderate effect size. SMD at post-intervention and 12-week follow-up demonstrated a significant difference between the intervention and active control groups. On the basis of this study and other lower quality RCTs and uncontrolled trials (47, 48, 52, 58-60), there appears to be preliminary evidence for a small to moderate size effect of CBT-I on subjective measures of cognitive functioning. The impact of CBT-I on objective measures of cognitive functioning is more equivocal, predominantly due to lack of research. It is clear that further adequately powered RCTs, utilising both subjective and objective measures of cognitive performance are required, before firm conclusions can be drawn.

In terms of maintenance of the effects, there were nine studies that conducted a follow-up assessment of cognitive functioning, three to six months following the intervention. The majority of these studies found no significant difference between post-intervention and follow-up scores,

indicating that where there were initial gains, these tended to be maintained. In one study, performance on the vigilance test worsened between baseline and post-intervention but returned to baseline levels between post-intervention and follow-up (51). This may be related to the sleep restriction component of the intervention, which has been associated with increased daytime sleepiness and impairments in vigilance during the acute phase of implementation (75, 77). There is evidence that improvements in sleep parameters following CBT-I evolve over time (78) and therefore it is possible that improvements in cognitive performance also take time to be manifest. Thus the timing of assessments is an important consideration for future studies, especially where sleep restriction is part of the treatment.

Study quality and sources of bias

The risk of bias from inadequate control and lack of blinding in the included studies is high. Although double-blinded placebo controlled studies are difficult to implement when evaluating psychological interventions, a sham insomnia treatment (known as BPT) has been developed (79). Indeed, BPT was utilised as a control in two of the included studies (45, 49). However, the majority of studies in this review used inactive control conditions and participants were not blind to group assignment. Therefore, the specific effects of CBT-I cannot be separated from non-specific effects, such as therapist attention and participant expectation of benefit. The issue of expectancy may be particularly relevant when assessing cognitive functioning, since expectancy effects have been shown to exert a strong influence on objective measures (80) and subjective perceptions of cognitive performance (81).

There were five uncontrolled trials and one case-series included within this review. Three of these studies reported effect sizes, all of which were large effects. Meta-analyses of outcomes following psychological interventions commonly observe that uncontrolled studies report larger effects than RCTs (82, 83). This is likely due to biases that result from issues such as regression to the mean. Due to the high risk of bias, we gave less weight to results from the uncontrolled trials and case-series, when considering the evidence in this review. Nevertheless, the evidence from uncontrolled trials largely supports data from the RCTs, indicating positive effects of CBT-I on self-report measures of cognitive functioning.

Putative Mechanisms

If CBT-I does lead to improvements in cognition, it will be important to discover the mechanism through which this occurs. There is some evidence that individuals with insomnia show impairments on complex rather than simple tasks and this is thought to result from greater dependence of complex tasks on functioning of the prefrontal cortex (13), which may be compromised in insomnia (84). Hypo-activation of the prefrontal cortex during performance of a category fluency task in individuals with primary insomnia compared to controls has been reported and this hypo-activation was attenuated following sleep therapy (which comprised CBT-I, bright light therapy and body temperature manipulations), with concomitant improvements in phonemic fluency (85).

The study by Wilckens et al. (55) found that changes in electroencephalogram (EEG) spectral power (increased delta and reduce sigma activity) were associated with better executive functioning in older adults, although this was not moderated by the BBTI intervention. One proposal is that delta power during non-rapid eye movement sleep reflects enhanced connectivity within cortical networks and preferentially benefits brain regions such as the prefrontal cortex.

On the basis of these findings, one hypothesis which deserves further investigation is that improvements in sleep continuity and normalisation of sleep architecture, leads to enhanced functioning of the prefrontal cortex and, by extension, performance on tasks that recruit this brain region (86). Of note, a more recent, uncontrolled study by Wilckens and colleagues (87) observed improvements in task-switching performance, pre-to-post CBT-I, in older adults with insomnia. These improvements were associated with reductions in WASO, however there was no association with whole night delta power. Controlled studies, employing both standard polysomnography and high-density EEG protocols (88) will help to define a) how CBT-I modifies sleep macro and micro-structure (including the temporospatial dynamics of delta power); and b) whether such changes mediate improvement in cognitive performance.

Anxiety and low mood, which are often present in insomnia (particularly comorbid insomnia), have also been associated with cognitive impairment (42). There is evidence that CBT-I leads to improvements in these variables (89-92) and therefore, in addition to investigating the potential

mediating role of various sleep parameters, future studies should also examine the contribution of changes in secondary psychological variables.

Measures of cognitive functioning

Discordance between self-report measures of cognitive functioning and performance on neuropsychological and cognitive tests has been demonstrated in individuals with primary insomnia (93). Specifically, self-report measures tend to show higher levels of impairment than is found using objective assessment. This discordance is thought to be driven by selective attention to the daytime consequences of insomnia, a phenomenon which is proposed to contribute to the maintenance of the disorder (94). It is possible that CBT-I impacts on subjective and objective measures differentially, for example it may alter perceptions of impairment without impacting on objective performance. In addition, it is possible that there are different mechanisms through which CBT-I impacts on subjective and objective cognition. We were not able to examine this in the current review because there were no studies that investigated cognitive functioning using both subjective and objective measures. Moreover, it was not possible to compare the effects of CBT-I on subjective and objective measures across studies, due to heterogeneity. Future studies should consider the inclusion of both subjective and objective assessments of cognitive function to enable such a comparison.

In spite of guidelines espousing the importance of investigating the daytime correlates of insomnia, there are no specific cognitive performance measures or self-report questionnaires that are recommended for routine use in insomnia samples (95). A meta-analysis (13) concluded that insomnia is associated with impairments on tasks assessing episodic memory, problem-solving and working memory. A caveat to these findings is that for some of the cognitive domains examined, there were few studies available and therefore low statistical power may explain lack of group differences. Accordingly, assessment of a broad range of cognitive domains is encouraged.

In this review, we did not uncover any patterns across studies in terms of cognitive domains that appear to be more sensitive to the effects of CBT-I (see table S4). We recommend that where it is not feasible to assess a broad range of cognitive domains, researchers should focus on the assessment of those cognitive domains where impairments in insomnia samples has been demonstrated most robustly in cross-sectional studies (episodic memory, problem solving and working memory). On the

basis of the findings from the highest methodological quality studies included in this review, future studies should also consider including the AFI (a self-report measure probing perceived effectiveness in activities requiring attention and working memory) and ANT-I (a computerised cognitive task probing attentional functioning). In addition, future studies should consider the impact of time of day on cognitive performance and seek to standardise this variable across participants and test sessions (76).

There are a number of factors which require consideration with regards to the selection of tools for assessing change in cognitive performance, in individuals with insomnia. Possible explanations for null findings in the studies in this review which utilised objective assessment of cognitive performance, include that the cognitive tasks were not sensitive to sleep or were confounded by ceiling effects. Clearly the test needs to demonstrate sufficient sensitivity to enable the detection of potentially subtle changes over time. There appears to have been little consideration of this issue by the studies included within this review. Individuals with insomnia may compensate for deficits through increased cognitive effort and the recruitment of additional cerebral resources (93). Such compensation may obscure both objective deficits and improvements over time. Accordingly, it seems important to include cognitive tests which are sufficiently difficult to overwhelm compensatory processes (96). Edinger and colleagues (97) recommend the use of the Switching Attention Test (SAT). The SAT is a computerised cognitive test that presents a series of increasingly challenging psychomotor tasks that assess the participants ability to maintain concentration, switch attention, inhibit responses and make decisions rapidly. Alternatively, future studies could combine manipulations of task difficulty with neuroimaging, so that the role of compensatory mechanisms can be elucidated (98).

The subjective outcome measures utilised in the included studies were developed for use in clinical samples, predominantly cancer patients. The validity of using these measures to assess cognitive functioning following an insomnia intervention is questionable. The experience of cognitive impairment related to insomnia may be qualitatively different to that associated with a physical health problem such as cancer. To the best of our knowledge, there are no subjective measures of cognitive functioning that have been specifically-developed for individuals with insomnia. This should be addressed in future research.

Heterogeneity

Meta-analyses have highlighted various factors which moderate sleep outcomes following CBT-I. These include rate of attrition, length of treatment, level of personal support, method of treatment delivery and duration of insomnia symptoms (99, 100). Due to the preliminary nature of the literature and the large number of ways in which the included studies varied, it was not possible to identify specific moderators of improvements in cognitive performance. However, future reviews should consider whether there are any variables which enhance the impact of CBT-I on cognitive functioning. It is possible that particular characteristics of an individual with insomnia promote greater improvements in cognitive functioning following treatment. One characteristic that should be examined is cognitive reserve. There is evidence that older adults with less cognitive reserve (as indicated by lower levels of education) are more vulnerable to the negative effects of poor sleep on some aspects of cognitive functioning (101). This is thought to result from less capacity for compensation. Improvements in cognitive functioning may therefore be more easily identified in this group. The nature of the insomnia complaint may also moderate outcomes. Specifically, there is evidence that those with objective short sleep duration show greater deficits in cognitive performance (102, 103) and therefore we might expect to see greater improvements in cognitive functioning in this group, following an intervention.

The majority of studies investigated the impact of CBT-I on cognitive functioning in comorbid samples. This contrasts with the literature on sleep outcomes following CBT-I, which has tended to focus on primary insomnia. It is possible that improvements in cognitive performance following CBT-I, are more likely to be observed in comorbid populations, particularly where cognitive dysfunction is a symptom of the comorbid condition.

Limitations of the current review

This review has a number of limitations. First, a high proportion of the included studies were from cancer patients, which limits the generalisability of our synthesis. Second, the inclusion criteria used were broad, which resulted in studies that differed on a range of factors, including methodology, population studied, aspects of the intervention and outcomes measures. Such high levels of clinical and methodological diversity precluded the use of meta-analysis and also meant that we were not able to clearly identify factors that contributed to the heterogeneity in outcomes. Third, we included uncontrolled trials and studies with low methodological quality, but resisted drawing conclusions on

the basis of their findings, due to high risk of bias. It could be argued that there was little benefit to including these studies however we reasoned that it was necessary to summarise all of the available evidence, given that this is an area of very limited research. Fourth, we combined studies that were very different in terms of content of intervention and method of delivery. For example, we included studies where the intervention combined just two components of CBT-I (relaxation and sleep hygiene), with studies that delivered all of the components. The validity of this is questionable. We did not conduct a meta-analysis and therefore the results from heterogeneous studies were not statistically combined. We suggest that high levels of variability in terms of the interventions delivered is reflective of the current state of the field, whereby there is a lack of clarity concerning the necessary and sufficient components of a CBT-I intervention.

Conclusions

There is preliminary evidence for small-to-moderate effects of CBT-I on self-report cognitive functioning. Included studies tended to have small sample sizes and many failed to find statistically significant results, therefore adequately powered RCTs are required before firm conclusions can be drawn. There is a distinct lack of research with regards to the effects of CBT-I on objective cognitive performance, which is surprising given the importance of cognition for everyday functioning. A consensus with regards to specific cognitive domains that should be assessed in insomnia samples should be a priority for researchers. There was substantial heterogeneity in the included studies, reflecting the broad inclusion criteria used and the preliminary nature of this research area.

Practice Points

- Impairments in cognitive functioning are among the most commonly reported and troubling daytime symptoms of insomnia, however little is known about whether insomnia treatments lead to improvements in cognitive performance.
- There is preliminary evidence for small to moderate positive effects of CBT-I on self-report cognitive functioning however adequately powered RCTs are required before firm conclusions can be drawn.
- There is a lack of evidence with regards to the impact of CBT-I on objective cognitive performance.

Research Agenda

Further research should aim to:

- Establish a battery of cognitive tests to be used in insomnia samples.
- Evaluate the effects of CBT-I on cognitive functioning, using a well powered and high quality study design which incorporates an active control condition, so that the specificity of the effects of CBT-I on cognitive performance can be established.
- Include both subjective and objective measures of cognitive performance and seek to compare the effects of CBT-I on subjective and objective measures.
- Investigate the mechanisms through which CBT-I leads to improvements in cognitive functioning and establish whether this is different for subjective and objective outcomes.
- Identify the critical ingredients of CBT-I that enhance improvements in cognitive functioning.

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Table 1: Characteristics of studies

Author (year)	Design	Population	Intervention: components of CBT-I (No. of participants) Mode of delivery No of sessions Duration	Comparator (No. of participants) Mode of delivery No of sessions Duration	Mean age % female	Length of follow up	Cognitive outcome	Summary of cognitive outcomes at follow up	QR score out of 26
Arnedt et al. (2007) (56)	UT	Insomnia comorbid with alcohol dependence	CBTI-A: SR, SC, SH, CT, RP (6) ^a Individual 4 face-to-face and 4 telephone 8 weeks	None	38.6 ^c 42.9% ^c	8 weeks after baseline	MFI-20 Mental Fatigue	No significant improvement between baseline and mid-intervention or post intervention	12
Arnedt et al. (2011) (45)	RCT	Insomnia comorbid with alcohol dependence	CBTI-AD: SR, SC, SH, CT (9) ^a Individual 4 face-to-face and 4 telephone 8 weeks	BPT (8) ^a Individualised 4 face-to-face 4 telephone 8 weeks	CBTI-AD: 46.2 ^a 33.3% ^a BPT: 46.1 ^a 37.5% ^a	8 weeks after baseline	MFI-20 Mental Fatigue	Scores were reduced at post-intervention for both groups. At post-intervention the BPT group reported greater levels of mental fatigue than the CBTI-AD group, however differences	19

								were non-significant.	
Arnedt et al. (2013) (46)	RCT	Chronic insomnia	CBTI-Phone: SR, SC, SH, CT, RP (18) ^a Individual 4-8 telephone 4- 8 weeks	IPC (15) ^a Participants instructed to read and follow recommendations in a CBT-I pamphlet 1 telephone session with a study therapist to ensure material was reviewed.	CBTI-Phone: 38.1 ^b 100% ^b IPC: 40.0 ^b 80% ^b	4-8 and 12 weeks after baseline	MFI-20 Mental Fatigue	Scores were reduced at post-intervention for both groups and this remained at the 12-week follow-up. No significant difference between the groups at post-intervention or follow-up.	17
Casault et al. (2015) (47)	RCT	Insomnia comorbid with cancer	mCBT-I: SC, SR, SH, CT, RP (17) ^a Individual Self-help + 3 telephone consultations 6 weeks	No treatment control (18) ^a	mCBT-I: 56.9 ^c 95% ^c Control: 57.0 ^c 88.9% ^c	6, 12 and 24 weeks after baseline	QLQ-C30 Cognitive Functioning	Significantly greater improvement in the mCBT-I group from pre-to post-intervention compared to the control group.	20
Davidson et al. (2001) (57)	UT	Insomnia comorbid with cancer	Sleep therapy: SC, SH, CT, RL, RP (12) ^a Group 6 sessions 9 weeks	None	54.7 ^a 91.7% ^a	4 and 8 weeks after baseline	QLQ-C30 Cognitive Functioning	Trend for an improvement in cognitive functioning.	11
Jansson & Linton (2005) (48)	RCT	Chronic insomnia	CBT: SC, SR, SH, CT, RP (64) ^a Group 6 sessions + 1	Self-help information containing modules on SC,	CBT: 50.0 ^{a,d} 84% ^{a,d}	158 weeks after baseline	Concentration Difficulties (0-5)	Significantly greater reduction in concentration	17

			booster session 6 weeks + booster session 2 months after the 6 th session	SR and RL (72) ^a . Participants instructed to read and apply the material	Control: 49.0 ^{a,d} 71% ^{a,d}			difficulties in the CBT group compared to the control group.	
Lami et al. (2016) (58)	UT	Insomnia comorbid with fibromyalgi a	CBT-I: SC, SR, SH, CT, RL, RP (27 at posttreatment and 24 at follow-up) ^a Group 9 sessions 9 weeks	None	46.29 ^b 53.6% ^b	9 and 21 weeks after baseline	MFI-20 Mental Fatigue	Significant improvement in mental fatigue across the three time points.	11
Matthews et al. (2014) (49)	RCT	Insomnia in women following treatment for breast cancer	CBTI: SR, SC, SH, CT, RP (32) Individual 4 face-to-face and 2 telephone 6 weeks	BPT (28) Individual 4 face-to-face and 2 telephone 6 weeks	CBTI: 52.1 ^b 100% ^b BPT: 52.9 ^b 100% ^b	6, 12 and 24 weeks after baseline	Attentional Function Index	Trend for a significantly greater improvement from baseline to post- intervention and follow-up in the CBTI group relative to the BPT group.	18
Miró et al. (2011) (50)	RCT	Insomnia comorbid with fibromyalgi a	CBT: SC, SR, SH, CT, RL, RP (16) ^a Group 6 sessions 6 weeks	SH (15) ^a Group 6 sessions 6 weeks	CBT: 43.9 ^{a,d} 100% ^{a,d} SH: 50.2 ^{a,d} 100% ^{a,d}	7-8 weeks after baseline	ANT-I task	Significantly greater improvement in attention- alerting and attention- control in the CBT group compared to the SH group. No significant difference	17

								between the groups in change in overall RT or attention-orienting.	
Omvik et al. (2008) (51)	RCT	Older adults with chronic insomnia	CBT: SC, SR, SH, CT, RL (17 post-treatment; 7 follow-up) Individual 6-8 sessions 6-8 weeks	Zopiclone 7.5 mg (14 post-treatment; 10 follow-up) 6 weeks 1 meeting with a psychologist to check adherence to the treatment	CBT: 59.7 ^c NR Zopiclone: 62.0 ^c NR	8-10 and 32-34 weeks after baseline	Vigilance Test	Change in performance on this test was not significantly different between the groups.	15
Quesnel et al. (2003) (62)	Case series	Insomnia secondary to metastatic breast cancer	CBT: SC, SR, SH, CT, RP (8 at post-treatment; 7 at follow-up) ^a Group 8 sessions 8 weeks	None	54.3 ^c 100% ^c	8-10, 20-22, and 32-34 weeks after baseline	QLQ-C30 Cognitive Functioning	Significant improvement from pre to post intervention and no significant change from post-treatment to follow-up.	10
Ritterband et al. (2012) (52)	RCT	Insomnia secondary to cancer	CBT-I: SC, SR, SH, CT, RP (14) ^a Internet 6 modules 6-9 weeks	Wait list control (14) ^a	CBT-I: 53.7 ^{a,c} 100% ^{a,c} WLC: 59.6 ^{a,c} 71.4% ^{a,c}	9-11 weeks after baseline	MFSI-SF Mental Fatigue	Greater reduction in mental fatigue in the SHUTi group compared to WLC.	17
Simeit et al. (2004) (61)	NRT	Cancer patients with insomnia undergoing rehabilitation	Sleep management programme: SH, SC, CT, RL, RP. RL: PMR (80) ^a or AT (71) ^a Group	Standard rehabilitation (78) ^a Group 3-4 weeks	PMR: 60.2 ^a 70% ^a AT: 57.6 ^a 80.3 ^a	3/4, 9/10 and 27/28 weeks after baseline	QLQ-C30 Cognitive Functioning	Significant improvement between baseline and follow-up for all the groups. Change in	12

			3 sessions 3-4 weeks		Control: 57.6 ^a 75.6% ^a			scores was not significantly different between the groups.	
Sun et al. (2013) (53)	RCT	Older adult poor sleepers	SH, RL (37) ^a Group 4 sessions 4 week intervention with assisted follow up for 1 year	SH (38) ^a Brochure	Experim ental: 68.6 ^{a,b} 70.3% ^{a,b} Control: 70.8 ^{a,b} 73.3% ^{a,b}	12, 24 and 52 weeks after baseline	MMSE, WMS-CR	Scores on the MMSE and four subtests from the WMS-CR significantly increased in the experimental group whereas they decreased in the control group.	14
Swanson et al. (2013) (59)	UT	Insomnia comorbid with post- partum depression.	CBTI: SC, SR, SH, RL, CT, RP (12) ^a Individual 5 sessions 5 weeks	None	30.0 ^a 100% ^a	5 weeks after baseline	MFI-20 Mental Fatigue	Significant improvement	10
Taylor et al. (2014) (54)	RCT	Chronic insomnia in college students	CBT-I: SC, SR, SH, RL, CT (16) ^a Individual 6 sessions 6 weeks	Wait list control (13) ^a	CBT-I: 19.5 ^c 23.5% ^c WLC: 19.9 ^c 58.8% ^c	6 and 18 weeks after baseline	MFI-20 Mental Fatigue	No significant difference between the groups in change in mental fatigue.	19
Tomfohr- Madsen et al. (2016) (60)	UT	Insomnia in pregnancy	CBT-I: SC, SR, CT, RP (13) ^a Group 5 sessions 5 weeks	None	31.0 ^{a,b} 100% ^{a,b}	7 weeks after baseline	MFSI-SF Mental Fatigue	Significant improvement	12

Wilckens et al. (2016) (55)	RCT	Chronic comorbid insomnia in older adults	BBTI: SR, SC (NR) ^a Individual 2 face-to face sessions and 2 telephone 3 weeks	Information-only Control (NR) ^a Participants were instructed to read 3 publications containing information about behavioural treatment for insomnia and received a telephone call after two weeks.	BBTI: 72.6 65.8% IC: 70.5 71.8%	4 weeks after baseline	Logical Memory Test, TONI, Letter-number sequencing	No significant difference between treatment groups in change in cognitive performance between baseline and follow-up.	12
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Note. ANT-I task = attentional networks test – interactions task, AT = autogenic training, BBTI = brief behavioural treatment of insomnia, BPT = behavioural placebo treatment, CBT-I = cognitive behavioural therapy for insomnia, CBT-I AD = cognitive behavioural therapy for insomnia in recovering alcohol dependent patients, CBTI-Phone = telephone delivered cognitive behavioural therapy for insomnia, CT = cognitive therapy, IC = information control, IPC = information pamphlet control, mCBT-I = minimal CBT-I, MFI-20 = multidimensional fatigue inventory, MFSI-SF = multidimensional fatigue symptom inventory short form, MMSE = mini mental state exam, NR = not reported, NRT = non-randomised trial, PMR = progressive muscle relaxation, QR = quality rating, RCT = randomised controlled trial, RL = relaxation, RP = relapse prevention, RT = reaction time, SC = stimulus control, SH = sleep hygiene, SR = sleep restriction, TONI = test of nonverbal intelligence, UT = uncontrolled trial, WLC = wait list control, WMS-CR = Wechsler memory scale -Chinese revision

^a = data are for participants included in the analysis.

^b = data are for participants who completed the intervention.

^c = data are for participants who were recruited/ randomised.

^d = data are for participants who completed the follow-up.

Figure 1: Search results

Figure 2: Post-intervention standardised mean differences and 95% confidence intervals for subjective measures of cognitive functioning

Figure 3: Post-intervention standardised mean differences and 95% confidence intervals for objective measures of cognitive functioning

Figure 4: Follow-up SMD and 95% confidence intervals for cognitive outcomes. Diamonds represent 12 week follow-up, circles represent 24-32 week follow-up and squares represent 52-58 week follow-up. Subjective cognitive outcomes are displayed above the horizontal line and objective cognitive outcomes are displayed below the horizontal line.