



Cognitive behavior therapy for chronic insomnia occurring within the context of medical and psychiatric disorders

Michael T. Smith^{a,*}, Mary I. Huang^b, Rachel Manber^b

^a*Department of Psychiatry and Behavioral Sciences, Johns Hopkins Medicine, Behavioral Medicine Research Laboratory and Clinic, 600 North Wolfe Street, Meyer 101, Baltimore, MD 21287-7101, United States*

^b*Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, United States*

Abstract

Insomnia is a pervasive problem for many patients suffering from medical and psychiatric conditions. Even when the comorbid disorders are successfully treated, insomnia often fails to remit. In addition to compromising quality of life, untreated insomnia may also aggravate and complicate recovery from the comorbid disease. Cognitive behavior therapy for insomnia (CBT-I) has an established efficacy for primary insomnia, but less is known about its efficacy for insomnia occurring in the context of medical and psychiatric conditions. The purpose of this article is to present a rationale for using CBT-I in medical and psychiatric disorders, review the extant outcome literature, highlight considerations for adapting CBT-I procedures in specific populations, and suggest directions for future research. Outcome studies were identified for CBT-I in mixed medical and psychiatric conditions, cancer, chronic pain, HIV, depression, posttraumatic stress disorder, and alcoholism. Other disorders discussed include: bipolar disorder, eating disorders, generalized anxiety, and obsessive compulsive disorder. The available data demonstrate moderate to large treatment effects (Cohen's d , range = 0.35–2.2) and indicate that CBT-I is a promising treatment for individuals with medical and psychiatric comorbidity. Although the literature reviewed here is limited by a paucity of randomized, controlled studies, the available data suggest that by improving sleep, CBT-I might also indirectly improve medical and psychological endpoints. This review underscores the need for future research to test the efficacy of adaptations of CBT-I to disease specific conditions and symptoms.

© 2005 Elsevier Ltd. All rights reserved.

Keywords: Cognitive behavior therapy; Comorbid insomnia; Cancer; Chronic pain; Human immunodeficiency virus; Depression; Posttraumatic stress disorder; Alcoholism

* Corresponding author. Tel.: +1 410 614 3396; fax: +1 410 614 3366.

E-mail address: msmith62@jhmi.edu (M.T. Smith).

Insomnia is a public health epidemic. Ten to fifteen percent of the adult population reports chronic difficulty initiating or maintaining sleep (Ancoli-Israel & Roth, 1999; Gallup Organization, 1995; Mellinger, Balter, & Uhlenhuth, 1985). The majority of these sleep complaints occur within the context of medical and psychiatric conditions, particularly in older adults (Lichstein, Wilson, & Johnson, 2000; Ohayon & Roth, 2001). Persistent insomnia in chronic medical disorders, such as back pain, heart disease, and diabetes, ranges from 16–82% (Katz & McHorney, 1998; Smith, Perlis, Smith, Giles, & Carmody, 2000; Sridhar & Madhu, 1994); and it is a ubiquitous symptom of most major mental disorders.

Both the American Psychiatric Association and International Classification of Sleep Disorder nosologies distinguish primary forms of insomnia from those considered secondary, i.e., caused by medical or psychiatric disease (American Psychiatric Association, 1994; American Sleep Disorders Association, 1997). Lichstein et al. (2001) further propose that for insomnia to be classified as secondary, fluctuation in its severity should parallel the course of the primary condition. In clinical practice, however, this distinction is often difficult, and sometimes impossible to make because the onset and severity of chronic insomnia are impacted by interrelated medical, psychiatric, behavioral, and psychosocial factors (Harvey, 2001). In this manuscript we, therefore, use the term co-morbid insomnia in reference to insomnia that co-occurs with another medical or psychiatric condition, unless causality was clearly established.

The neurobiology of insomnia is not fully understood. The extant literature suggests that sleep interfering states of somatic and/or central nervous system hyperarousal may represent a final common pathway of the disorder (e.g. Bonnet & Arand, 1998; Perlis, Merica, Smith, & Giles, 2001). Overactivation of stress response systems, notably the hypothalamic-pituitary-adrenal axis is associated with insomnia (Shaver, Johnston, Lentz, & Landis, 2002; Vgontzas & Chrousos, 2002). Some have argued that chronic activation of these physiologic systems may, in part, explain why insomnia is an independent risk factor for medical conditions such as coronary artery disease (Mallon, Broman, & Hetta, 2002). Another pathway by which insomnia might contribute to pathogenesis or enhanced morbidity is via chronic partial sleep deprivation. Experimental studies of healthy subjects demonstrate that partial sleep deprivation, a common consequence of insomnia, adversely impacts multiple neuroendocrine functions, including: the immune system, pain perception, metabolic functions, cognitive functions, and mood (Belenky et al., 2003; Dinges, Douglas, Hamarman, Zaugg, & Kapoor, 1995; Lentz, Landis, Rothermel, & Shaver, 1999; Onen, Alloui, Gross, Eschallier, & Dubray, 2001; Porcu, Ferrara, Urbani, Bellatreccia, & Casagrande, 1998; Spiegel, Leproult, & Van Cauter, 1999). These data suggest that insomnia may reciprocally feed back to exacerbate, hinder recovery, or predispose individuals to relapse and/or recurrences of the comorbid condition. This may occur regardless of whether the cause or causes of insomnia are believed to be explained by medical or psychiatric conditions. Aggressive treatment for insomnia, therefore, has the potential to improve comorbid disease states and might possibly have prophylactic value.

Another reason to target insomnia as a focus of direct intervention is its persistence in the majority (59–88%) of patients with chronic medical conditions receiving standard medical care (Katz & McHorney, 1998) and in almost half of individuals treated for depression (Nierenberg et al., 1999). This implies that treating the primary medical/psychiatric disorder is not likely to be sufficient for resolving chronic insomnia that occurs in chronic medical and psychiatric diseases.

Unfortunately, however, insomnia is vastly under recognized in medical settings and the majority of patients remain untreated (Simon & VonKorff, 1997). The reasons for this are multifaceted, but several of the most likely include: (1) the assumption that treatment for the primary medical or psychiatric

condition will resolve insomnia symptoms; (2) concerns by both physicians and patients regarding the potential for dependency and tolerance associated with long-term use of sedative hypnotics; (3) concerns regarding drug interactions or adverse events, especially in older adults, chronically ill, and those abusing drugs/alcohol (Allain, Bentue-Ferrer, Tarral, & Gandon, 2003; Asnis et al., 1999; Vermeeren, 2004); (4) a lack of awareness of the efficacy of nonpharmacologic treatment options for primary insomnia; and (5) absence of information on adaptation of nonpharmacologic treatment in the context of specific comorbid diseases.

There is ample evidence that psychological interventions for primary insomnia that are grounded in cognitive behavior theory and technique are efficacious. These include relaxation training (Nicassio, Boylan, & McCabe, 1982; Turner & Asher, 1979), stimulus control therapy (SCT, Bootzin, 1972), sleep restriction therapy (SRT, Spielman, Saskin, & Thorpy, 1987) and cognitive therapies (Buysse, Reynolds, & Hauri, 1994; Harvey, *in press*; Morin, Kowatch, Barry, & Walton, 1993). Many of these procedures are effectively combined as multicomponent approaches, collectively referred to as cognitive behavior therapy for insomnia (CBT-I) (Smith & Neubauer, 2003). Meta-analyses and randomized controlled trials of CBT-I for primary insomnia overwhelmingly demonstrate that CBT-I and some of its constituent components yield large effect sizes on a variety of sleep parameters with a global mean effect size of 0.96 and a range from 0.46 (for total sleep time) to 1.44 (for sleep quality) (Edinger, Wohlgemuth, Radtke, Marsh, & Quillian, 2001; Lichstein, Riedel, Wilson, Lester, & Aguillard, 2001; Morin, Culbert, & Schwartz, 1994; Morin, Colecchi, Stone, & Sood, 1999; Murtagh & Greenwood, 1995; Smith et al., 2002).¹ These effect sizes are comparable to those observed following 2–5 weeks of treatment with potent sedative hypnotic medications (benzodiazepine receptor agonists) (Smith et al., 2002). Moreover, the benefits of brief CBT-I are sustained at follow-up assessments conducted 6 months to 2 years after treatment completion (e.g., Jacobs, Benson, & Friedman, 1993; Morin et al., 1993) and often include a significant reduction in sedative hypnotic use when CBT-I is coadministered with sedative hypnotics or when patients taking sleep enhancing medications are not excluded from the clinical trial. (Lichstein et al., 1999; Morgan, Dixon, Mathers, Thompson, & Tomeny, 2004; Morin et al., 2004).

To date, the bulk of the psychologic treatment outcome literature for chronic insomnia has focused on primary insomnia and therefore, it remains unclear whether and in what manner this approach can be successfully applied to treat individuals with medical and psychiatric comorbidity. In recent years, clinical researchers have recognized the need to adapt and test the efficacy and effectiveness of CBT-I for insomnia occurring in medical and psychiatric disorders. While this work is in its early stages, this review identified a number of studies and evaluates their preliminary potential. For the purposes of this review, we use the term insomnia in a manner consistent with the DSM-IV definition, i.e., the complaint of trouble initiating or maintaining sleep or non-restorative sleep that is associated with significant distress or impairment in daytime functioning for at least 1 month (American Psychiatric Association, 1994). Studies were identified via literature searches using Medline and PsychInfo databases as well as bibliographies. Key search terms included: “cognitive behavior therapy,” “relaxation,” “stimulus control,” “sleep restriction,” “sleep hygiene,” “cognitive therapy,” and “insomnia.” These terms were then paired with an extensive list of major medical and psychiatric conditions. We included any study testing a cognitive-behavioral intervention for insomnia on a sample of subjects with an identified medical or psychiatric disorder. Because of the precocious state of this literature, we did not establish formal

¹ Throughout this manuscript, unless otherwise noted, effects sizes reflect Cohen’s *d* calculations for the difference between pretreatment values and posttreatment values.

severity or duration criteria for insomnia diagnosis. Subjects in all studies, however, reported insomnia complaints (trouble initiating or maintaining sleep or nonrestorative sleep with a minimum symptom duration of 1 month) for which they desired treatment. We excluded single case reports, but included uncontrolled case report series.

1. General rationale, indications, and contraindications for CBT-I in comorbid insomnia

It has been argued that cognitive-behavioral models of insomnia are particularly relevant to patients with medical and psychiatric diseases (e.g., [Morin, Kowatch, & Wade, 1989](#); [Smith et al., 2000](#)). Cognitive-behavioral conceptualizations of insomnia posit that as insomnia transitions from an initial acute symptom and/or stress reaction to a chronic problem, maladaptive compensatory strategies and behavioral contingencies begin to play a role in maintaining the sleep disturbance, independent from the primary medical or psychiatric disease processes ([Buysse et al., 1994](#); [Spielman, Caruso, & Glovinsky, 1987](#)). Common compensatory strategies adopted by patients to manage insomnia symptoms, such as napping, keeping irregular bed and wake times, use of alcohol as a sedative, excessive caffeine ingestion, may exacerbate and/or perpetuate insomnia. Behavioral theories further postulate that spending excessive time awake in the bedroom, which is a particularly prevalent behavior for many chronically ill patients, results in stimulus dyscontrol, whereby the bedroom environment becomes associated with a variety of behaviors other than sleep. Moreover, when excessive time awake is spent ruminating about trouble sleeping and/or the consequence of poor sleep, as is often the case, a classically conditioned association between the bedroom environment and autonomic nervous system hyperarousal might be established.

CBT-I single and multicomponent approaches, target the factors that perpetuate insomnia. The extent to which these factors play a role in maintaining chronic insomnia associated with medical and psychiatric comorbidity may determine, in part, the degree of effectiveness of interventions focused on these factors. Although data directly evaluating the role of maladaptive, compensatory behaviors in the etiology or maintenance of either primary or comorbid insomnia is sorely lacking, there is indirect evidence for the role of arousal producing cognition in the development of disturbed sleep ([Harvey Tang and Browning, this issue](#)). Thus, cognitive-behavioral theories of insomnia provide a rationale for treating chronic insomnia, particularly when patients report excessive pre-sleep arousal and/or maladaptive behaviors.

A major advantage of CBT-I approaches for the treatment of insomnia comorbid with other diseases, in comparison to pharmacological interventions, is its relatively low side-effect profile. CBT-I, is not without some risks, however. The most serious apply to the use of sleep restriction with bipolar and seizure disorder patients and for individuals with excessive daytime sleepiness. Sleep deprivation lowers seizure threshold and it may also trigger manic episodes in vulnerable individuals (e.g., [Colombo, Benedetti, Barbini, Campori, & Smeraldi, 1999](#); [Fountain, Kim, & Lee, 1998](#)). The application of sleep restriction in these two populations, therefore, needs to be administered conservatively, with careful monitoring, and ample safeguard. Another documented side effect of CBT-I is the paradoxical phenomenon of relaxation-induced anxiety ([Heide & Borkovec, 1983](#)), which is estimated to occur in about 15% of individuals attempting relaxation therapies. As discussed later in this manuscript, patients with nocturnal panic are particularly susceptible to this paradoxical phenomenon. In our experience, these adverse events can be managed clinically.

2. Cognitive behavior therapy for insomnia in mixed samples of medical and psychiatric disorders

Before reviewing the outcome literature for CBT-I in specific medical and psychiatric disorders, we will briefly review four studies that have evaluated the efficacy of CBT-I in patients with heterogeneous medical and/or medical/psychiatric conditions. Two of these studies were randomized clinical trials (Lichstein et al., 2000; Rybarczyk, Lopez, Benson, Alsten, & Stepanski, 2002) and the other two were case series (Morin, Stone, McDonald, & Jones, 1994; Perlis, Sharpe, Smith, Greenblatt, & Giles, 2001).

Lichstein et al. (2000) used a randomized, waitlist control design to test the efficacy of a four session CBT-I protocol, which consisted of relaxation training, stimulus control, and sleep hygiene therapies. Forty-four older adults were rigorously evaluated and required to meet criteria for insomnia secondary to either medical or psychiatric diagnosis, that is, the onset and fluctuations in severity of insomnia had to parallel the course of the primary condition. The most frequent medical diagnoses were pain conditions such as arthritis and neuropathy. Other medical diagnoses included prostate disease, neurologic diseases, and chronic respiratory illnesses. The most frequent psychiatric diagnoses were depression, followed by anxiety spectrum disorders. Diary measures of wake after sleep onset time, sleep efficiency (the ratio between time asleep and time in bed), and sleep quality ratings were significantly improved at the end of treatment. Further, these improvements were maintained at 3-month follow-up assessments. Post treatment effect sizes for the intervention ranged from 0.43 to 0.71. Fifty-seven percent of the treated individuals achieved sleep efficiency criteria for clinically significant improvement, compared to 19% for controls ($p < 0.05$). No differences in treatment response between the psychiatric and medical insomnia groups were observed. While there were too few subjects within specific disease categories to conduct subgroup analyses, this study is particularly noteworthy, because it suggests that cognitive-behavioral interventions can effectively improve sleep, even in cases where the primary factors judged to cause the sleep disturbance are thought to be medical and psychiatric diseases.

In a more recent randomized study of 38 older adults with mixed medical comorbidity, Rybarczyk et al. (2002) compared the effects of multicomponent group CBT-I with a self-help, audio recording program, based on relaxation, against a waitlist control group. Multicomponent CBT-I included: stimulus control, sleep restriction, relaxation therapy, sleep hygiene, and cognitive therapy. The most common illnesses were coronary artery disease, diabetes, and osteoarthritis. Sleep was assessed via diaries, the Pittsburgh Sleep Quality Index ([PSQI, Buysse, Reynolds, Monk, Berman, & Kupfer, 1989]), and actigraphy at baseline, the end of treatment (8 weeks), and at a 4-month follow up. At post-treatment, multicomponent CBT-I participants had significantly greater improvements compared to the waitlist in sleep efficiency, wake after sleep onset time, and global sleep quality (PSQI). In contrast, the self-help relaxation group demonstrated post-treatment improvement compared to waitlist for total sleep time and modest improvement in global sleep quality. Fifty-four percent of those receiving the multicomponent treatment met criteria for clinically significant gains at follow-up compared to 35% for the relaxation group and 6% for the waitlist. None of the three interventions were associated with improvement in actigraphic measures of sleep continuity or secondary measures of quality of life, however. Despite the limitations of this study (i.e., the lack of objective improvement and the waitlist control design), the results are encouraging because they demonstrate that patients with multiple chronic illnesses derive subjective benefit from CBT-I.

Morin and colleagues evaluated the effectiveness of an 8–10 session multicomponent CBT-I in 100 patients seeking treatment for chronic insomnia at a sleep disorders center (Morin, Stone, McDonald, & Jones, 1994). While the majority of the sample met criteria for primary insomnia, a significant

percentage of patients were diagnosed with comorbid psychiatric disorders (27%), medical disorders (13%), and insomnia related to drug dependency (21%). Treatment included stimulus control, sleep restriction, sleep hygiene and sedative hypnotic withdrawal. The overall sample demonstrated a 42–50% improvement on sleep diary measures of sleep latency, time awake after sleep onset, and early morning awakenings. Subgroup analysis found no differences in outcome between patients with primary insomnia, versus psychiatric and drug dependent insomnias. Post-treatment effect sizes for the psychiatric subgroup were large for total wake time (0.93) and sleep efficiency (0.94). Approximately half of the subjects treated in all groups achieved a 50% or greater reduction in symptoms and nearly 40% had post-treatment sleep continuity values in the normal range. Although this study lacked a control group, it was the first to show that the efficacy of CBT-I might translate to tertiary out-patient settings, where, more often than not, patients present with significant medical and psychiatric comorbidity.

A similar effectiveness study was conducted by [Perlis et al. \(2001\)](#). They compared data from 28 subjects with chronic insomnia who reported medical (53%) or psychiatric morbidity (50%) and who completed an adequate trial of CBT-I with data from 17 subjects treated for primary insomnia. The most common medical diagnoses were musculoskeletal pain, headache, and gastrointestinal disorders. The most common psychiatric diagnoses were mood and anxiety disorders, respectively. The eight treatment sessions included sleep restriction, stimulus control, cognitive therapy, and sleep hygiene. Subjects who completed at least four sessions reported improvement in a variety of diary-based measures of sleep continuity, with an average improvement of 33% (56% reduction in time awake after sleep onset, a 34% reduction in sleep latency, a 29% increase in total sleep time and a 13% decrease in the number of nightly awakenings). Effect sizes for the medical and psychiatric subgroup on the same sleep parameters ranged from 0.38 to 0.86. Treatment outcomes for these subgroups were not found to be different from those without medical or psychiatric comorbidity.

Despite methodologic limitations, these four studies are important because they suggest that the efficacy of CBT-I might extend to clinical settings and imply that efforts to study and adapt CBT-I methods to specific medical and psychiatric conditions may be fruitful. It should be noted, however, that conclusions about the efficacy of CBT-I for any particular medical or psychiatric disorder cannot be made from these mixed sample studies. Preliminary efforts to evaluate the efficacy of CBT-I for patients with specific medical and psychiatric comorbidities are reviewed below.

3. Cognitive behavior therapy for insomnia occurring in medical conditions

3.1. Cancer

Given the tremendous emotional and physical burden associated with cancer, it is not surprising that studies have found greater prevalence of self-reported and objectively documented difficulties initiating and maintaining sleep compared with healthy controls ([Kaye, Kaye, & Madow, 1983](#); [Silberfarb, Hauri, Oxman, & Schnurr, 1993](#)). Rates of self-reported sleep disturbance in mixed cancer populations range between 30% and 50%, with highest prevalence (37–38%) among breast and lung cancer patients ([Davidson, MacLean, Brundage, & Schulze, 2002](#); [Savard, Simard, Blanchet, Ivers, & Morin, 2001](#)). The majority of cancer patients report that sleep difficulties began at/or around the time of diagnosis; and for a significant percentage of individuals, these symptoms persist for several years after the end of treatment ([Couzi, Helzlsouer, & Fetting, 1995](#); [Lindley, Vasa, Sawyer, & Winer, 1998](#)).

Aside from the impact of insomnia on quality of life, this type of unmitigated sleep disturbance may have a particularly malignant effect on the cancer itself. Several experimental studies indicate that sleep loss may compromise the immune system, which provides a crucial defense against tumor cells (Dinges et al., 1994; Irwin et al., 1996). Savard et al. (1999) found that in women with abnormal pap smears, dissatisfaction with sleep was associated with reduced helper and suppressor T cells, even after controlling for depression and other confounders.

3.2. Outcomes for CBT-I in cancer

We identified four studies of CBT-I in cancer: three in mixed cancer populations and one in women with breast cancer. Cannici, Malcolm, and Peek (1983) randomly assigned 30 patients with chronic sleep onset insomnia associated with heterogeneous cancer diagnoses to either (1) usual care or (2) usual care plus three sessions of progressive muscle relaxation training. Compared to the control group, the relaxation group received instructions to practice relaxation twice per day for nine consecutive days. The relaxation group achieved a significant, 83-min differential reduction in latency to sleep onset (77% versus 6%), which was maintained at a 3-month follow-up. Ninety percent of subjects in the relaxation group were judged to have achieved “marked improvement” for sleep latency, although criteria for clinical significance were not reported. None of the other diary-based sleep parameters (e.g., total sleep time and sleep quality) or daytime ratings of pain changed after treatment.

Davidson, Waisberg, Brundage, and MacLean (2001) piloted a 6-session, multicomponent group treatment for insomnia in 12 patients with mixed cancer diagnoses. In this case series design, subjects learned stimulus control, relaxation techniques, sleep hygiene, and cognitive approaches to decrease worry and emotional arousal during pre-sleep intervals. Sleep diary measures of sleep quality, sleep latency, time awake after sleep onset, sleep efficiency, number of nightly awakenings, and total sleep time all showed significant improvements at 4-week and 8-week assessments. By the end of treatment, none of the subjects reported sleep latency (SL), wake after sleep onset times (WASO) and sleep efficiency (SE) values in the generally accepted clinical range (SL and WASO > 30 or SE < 85%). Post-treatment effect sizes ranged from 0.58 for total sleep time to 2.0 for sleep efficiency. Perhaps more interestingly, patients also showed a post-treatment reduction in fatigue, improvement in role functioning, and a trend toward improvement in depressive symptom severity. Because this study lacked a control group and had a small sample, its promising results remain preliminary.

More recently Simeit, Deck, and Conta-Marx (2004) conducted a large scale study of multicomponent CBT-I added to a standard 4-week medical and psychosocial rehabilitation program for mixed cancer patients. All patients had just undergone surgery, chemotherapy, or radiotherapy. Two CBT-I programs, differing only in the type of relaxation technique (progressive muscle relaxation ($n=80$) vs. autogenics training ($n=71$)) were compared against a non-randomly assigned control group ($n=78$) of patients who were monitored via sleep diaries. Control subjects participated in the standard rehabilitation and were recruited several months prior to the intervention groups. Both experimental groups were given stimulus control instructions, sleep hygiene, and cognitive therapy techniques, in addition to relaxation training. Three sessions were administered over a 3–4 week period. Compared to the control group, both CBT-I groups showed superior improvements in sleep latency, total sleep time, sleep efficiency, sleep quality, reduction in sleeping medications, and sleep-related daytime dysfunction (all assessed with the PSQI). Improvements in sleep for the treated patients were evident at the end of treatment and generally maintained at 10-week and 6-month follow-ups. There were no differences in efficacy between the two

CBT-I groups. All three groups improved on multiple dimensions of quality of life, but the two CBT-I groups had superior enhancement in a global index of quality of life. Although these results are quite promising with respect to the efficacy of CBT-I in cancer, they must be considered somewhat cautiously due to the possibility that nonrandom formation of the groups may have systematically biased the results.

Quesnel, Savard, Simard, Ivers, and Morin (2003) tested the efficacy of an 8 week, group CBT-I program in 10 post radiotherapy and chemotherapy patients. This multiple baseline study was unique in two ways: (1) the investigators combined sleep diary assessment with polysomnography and (2) traditional CBT-I was modified to take into account the special needs of cancer patients. To this end, the investigators added specific components related to coping with and reducing fatigue, a highly prevalent and disabling sequelae of cancer. The components of the intervention included sleep restriction, stimulus control, sleep hygiene, relaxation training and cognitive restructuring. Cognitive restructuring targeted the commonly held belief that insomnia is the sole cause of fatigue, a belief that might heighten sleep-related performance anxiety and therefore compromise sleep. Subjects were also instructed to increase activity levels, an effective strategy to counter fatigue in cancer patients (Mock, 2001). The authors reported significant post-treatment improvements for both diary and PSG measures of total awake time and sleep efficiency. Fifty percent of subjects had post-treatment sleep efficiency values in the normal range (>85%). Effect sizes were relatively large ranging from 0.73 to 1.7. Therapeutic gains were well maintained at both 3- and 6-month follow-ups. Between 71% and 86% of subjects were classified as showing clinically significant improvement in sleep at 6 months. Post-treatment improvements were also noted for depression severity, fatigue, and quality of life.

3.3. Special considerations for conducting CBT-I in cancer patients

The Quesnel et al. study demonstrates the utility of modifying CBT-I to meet the special needs of cancer patients by including a component of treatment that addressed fatigue. Other issues specific to cancer that may require special attention include: evaluating and treating psychological reactions to the disease, taking into account how radiotherapy or chemotherapy and other medical treatments may disturb sleep, and evaluating and ensuring adequate pain management. These four issues are discussed below.

With respect to fatigue, patients' strategies for coping with disease-related and iatrogenic fatigue, and the tendency to overly attribute fatigue to sleep loss may directly aggravate or maintain insomnia. Many reduce activity levels, take extended naps (Davidson et al., 2002), or spend a great deal of time resting awake in their bedrooms. All of these behaviors may weaken the homeostatic drive for sleep or contribute to stimulus dyscontrol. Setting activity/exercise goals, timing naps appropriately, and even managing fatigue pharmacologically may need to be considered (Mock, 2001). Cognitive restructuring can also be used to provide a realistic perspective regarding the relationship between sleep and fatigue, and to introduce the concept of sleepiness as distinct from fatigue. Sleepiness indexes the propensity to sleep onset, which, at its extreme, involves having to exert effort in order to stay awake. Fatigue, on the other hand indexes energy level (such as heaviness in limbs) and when extreme, prompts an individual to rest, not necessarily to sleep.

Patients' psychological reaction to their disease, particularly depression and anxiety, may also contribute to sleep disturbance in cancer patients. The most robust correlate of insomnia in cancer patients is depressed mood (Davidson et al., 2002). It is estimated that 49–53% of cancer patients experience anxiety and depression, which may require focused psychological and/or pharmacologic intervention (van't Spijker, Trijsburg, & Duivenvoorden, 1997).

Medical treatment of tumors may also disrupt sleep. Common sleep disrupting agents used in cancer treatment include radiotherapy, chemotherapy, antiemetics, etc. (Savard et al., 2001). Finally, many types of cancers cause persistent pain, particularly as the cancer progresses. It is, therefore, essential to determine the extent to which pain disrupts sleep and to ensure that pain is adequately managed with pharmacological and psychological methods. In this regard, relaxation therapies and distraction techniques could serve multiple roles by assisting in pain management, reducing anxiety associated with the disease, and improving sleep.

3.4. *Chronic pain*

It is estimated that 50 million Americans suffer from chronic pain conditions, such as back pain or headaches (Gatchel, 2001). Between 50% and 88% of chronic pain patients report significant sleep problems (Atkinson, Ancoli-Israel, Slater, Garfin, & Gillin, 1988; Mosko, Dickel, & Ashurst, 1988; Pilowsky, Crettenden, & Townley, 1985; Smith et al., 2000; Wilson, Watson, & Currie, 1998). Consistent with self-reports, studies using objective measures of sleep in chronic pain patients also documented longer latency to sleep onset, reduced total sleep time, and increased prolonged awakenings, compared to healthy controls (e.g., Schneider-Helmert, Whitehouse, Kumar, & Lijzenga, 2001; Wilson et al., 1998; Wittig, Zorick, Blumer, Heilbronn, & Roth, 1982). Some polysomnographic investigations have also found reduced slow wave sleep and/or increased intrusion of fast (alpha) EEG frequency during sleep of pain patients (e.g., Drewes et al., 1995; Moldofsky, 1993; Roizenblatt, Moldofsky, Benedito-Silva, & Tufik, 2001). The significance of these EEG abnormalities however, is unclear because they do not appear to be specific to pain (Hauri & Hawkins, 1973; Moldofsky, 1993).

Cross-sectional studies consistently show that sleep disturbance positively correlates with self-reported pain severity (Morin, Gibson, & Wade, 1998; Pilowsky et al., 1985; Smith et al., 2000; Wilson et al., 1998). Although complaints of poor sleep in chronic pain have been linked to cognitive-behavioral factors, including mood disturbance, inactivity, conditioned hyperarousal, and pre-sleep cognitive rumination (e.g., Haythornthwaite, Hegel, & Kerns, 1991; Morin et al., 1989; Pilowsky et al., 1985; Smith et al., 2000), it appears that sleep disturbance is associated with pain severity independent from these factors (Morin et al., 1998; Smith, Perlis, Smith, & Giles, 2001; Wilson, Eriksson, D'Eon, Mikail, & Emery, 2002). Longitudinal clinical studies indicate that the relationship between pain and sleep is likely reciprocal, such that pain interferes with sleep and disturbed sleep is associated with next day or longer-term increases in pain (Affleck, Urrows, Tennen, Higgins, & Abeles, 1996; Drewes et al., 2000; Raymond, Nielsen, Lavigne, Manzini, & Choiniere, 2001; Stone, Broderick, Porter, & Kaell, 1997). In the case of myalgic pain, it has been further hypothesized that sleep disturbance might play an etiologic role in the development and maintenance of intractable myalgias (Moldofsky & Scarisbrick, 1976). Support for this hypothesis comes from preliminary findings that total sleep deprivation and/or selective slow wave sleep deprivation (reduction in delta power) enhances pain sensitivity in healthy subjects (e.g., Lentz et al., 1999; Onen et al., 2001). This research suggests that in addition to improving sleep continuity, aggressively treating insomnia may contribute to the overall efficacy of chronic pain management.

3.5. *Outcomes for CBT-I in chronic pain*

We identified only two studies of CBT-I that have focused exclusively on chronic pain. Morin et al. demonstrated the feasibility of applying CBT-I to chronic pain patients using a multiple base-line case

report design (Morin, Kowatch, & O'Shanick, 1990; Morin et al., 1989). In these reports CBT-I consisted of sleep restriction and stimulus control therapies. Results indicated large effects on diary and polysomnographic measures of sleep latency and total wake time at the end of treatment, which were maintained at 2- and 6-month follow-up assessments (Morin et al., 1989). The authors noted that subjects also showed post-treatment enhancement in mood, particularly ratings of anxiety, but no change in pain ratings.

To date, there is only one randomized clinical trial of CBT-I in chronic pain patients (Currie, Wilson, Pontefract, & deLaplante, 2000). In this study 60 chronic pain patients of mixed etiologies received 7 weeks of CBT-I treatment delivered in a group format that consisted of stimulus control, sleep restriction, sleep hygiene, relaxation training, and cognitive therapy components. Subjects were randomized to immediately receive treatment or to a waitlist control condition. Significant post-treatment reductions were observed for sleep diary and objective (actigraphic) measures of sleep continuity as compared to the wait-list condition. Effect sizes were generally large (0.80) and treatment gains were enhanced or maintained on some, but not all, sleep parameters at a 3-month follow-up assessment. There were no between group differences in total sleep time after treatment. With respect to clinical significance, 56% of the CBT group achieved normal post-treatment sleep efficiency values (>85%) compared to 14% in the waitlist condition ($p < 0.05$). Only 22% met a Pittsburgh Sleep Quality Index cutoff (<5) indicating "good" sleeper status, compared to 0% for controls. Pain severity ratings improved over time for all subjects, but the CBT-I group showed a trend toward greater reductions in pain severity ($p = 0.12$, personal communication with author). The effect size for reduction in pain at 3 months for CBT-I group was 0.56 (moderate), compared to 0.15 for waitlist control. While this study, like most of the other CBT-I studies, did not include a placebo, attentional, or contact control condition, it never-the-less provides some support for the potential effectiveness of CBT-I in chronic pain.

3.6. Special considerations for conducting CBT-I in chronic pain

The published CBT-I trials that included chronic pain populations did not report any major modifications in technique to tailor the approach to the specific needs of pain patients. Some of the types of considerations that were discussed in the context of treating insomnia in cancer patients however, may also have relevance for pain patients. These include correcting inaccurate beliefs about the interplay between pain and sleep, ensuring that pain is adequately managed, evaluating the effects of pain medications on sleep, and modifying some of the pain-related coping strategies that might interfere with sleep.

Pain is a complex experience involving sensory, affective, and cognitive elements. Several studies have indicated that maladaptive cognitive responses to pain, such as catastrophizing are positively associated with pain severity and disability (e.g., Keefe et al., 2001). A study by Smith et al. (2001) of pre-sleep cognitions found that pain patients who reported increased catastrophic thoughts pertaining to pain and/or thoughts about environmental stimuli (e.g., noises, temperature, etc.) prior to falling asleep reported increased sleep continuity disturbance. Interestingly, these thought processes were more robust predictors of poor sleep than nightly pain severity ratings. Cognitive therapy techniques designed to manage these catastrophic cognitions may be particularly helpful in treating insomnia associated with chronic pain. Harman et al. (2002) reported that back pain patients may have deficits in sleep spindling activity, a central mechanism associated with sensorimotor gating, which is permissive of sleep. This finding coupled with the finding that pain patients who focus on environmental stimuli have increased

wake after sleep onset time, suggest that devices such as white noise machines, designed to mask extraneous sounds, may help pain patients maintain sleep. This type of intervention, however, has yet to be tested.

Similar to cancer patients, patients with chronic pain are vulnerable to depression and anxiety associated with the physiologic effects of the disease as well as the impact of the disease on quality of life. Treating these comorbid conditions is therefore an important aspect of treatment, which may improve sleep quality.

Finally, given the experimental evidence that sleep loss enhances laboratory measures of pain sensitivity, sleep restriction procedures may need to be modified or implemented as a secondary intervention for some pain patients. None of the CBT-I studies using sleep restriction, however, reported a worsening in pain. It may be that well consolidated sleep, even if shorter in duration, is more restorative than a longer period of fragmented sleep (Bonnet & Arand, 2003). One possible approach to the issue of the association between sleep loss and pain sensitivity, would be to implement sleep compression therapy with chronic pain patients, instead of the more commonly used sleep restriction approach. Sleep compression, a technique developed by Lichstein et al., gradually shortens sleep opportunity over a 5-week period, instead of drastically curtailing the sleep opportunity window precipitously at the onset of therapy (Lichstein et al., 2001). This approach might minimize the degree of sleep loss experienced during the active phase of treatment, while still accomplishing the goals of consolidating sleep. This technique, however, has yet to be applied to insomnia associated with chronic pain. Adaptation of CBT-I can also be readily and synergistically integrated with psychological techniques used in the management of pain (Astin, 2004), such as relaxation therapy, self-hypnosis, and distraction.

3.7. *Human immunodeficiency virus infection (HIV)/acquired immunodeficiency syndrome (AIDS)*

Given the tightly coupled relationship between sleep and the immune system, it is not surprising that HIV infection is associated with changes in sleep and that many HIV patients complain of insomnia. Self report surveys indicate that rates of sleep continuity and sleep quality problems range from 33% to 100% of asymptomatic seropositive individuals (Funesti, Rothenberg, Zozula, & McAuliffe, 1991; Hand, Phillips, Sowell, Rojas, & Becker, 2003; Rothenberg, Zozula, Funesti, & McAuliffe, 1990). Polysomnographic studies of asymptomatic individuals generally corroborate self-reports of prolonged sleep latency and decreased sleep efficiency (e.g., Norman et al., 1992; Weigand, 1990; Weigand, Zwillich, & White, 1989). In the past decade numerous studies have also documented sleep architecture abnormalities associated with HIV infection that persist at 1-year follow-up (Norman, Chediak, Kiel, Gazeroglu, & Mendez, 1990). These abnormalities include the following: increased slow wave sleep, even distribution of slow wave sleep through the night (rather than predominance in the first half), an increased fast frequency (alpha) EEG during sleep, and diminished REM sleep (Norman et al., 1992; Weigand, 1990; Weigand et al., 1989).

The severity of sleep disturbance appears to worsen with the progression of the disease and some have found a significant relationship between deficits in CD4+ counts,² viral load, and sleep onset and maintenance problems (Darko, McCutchan, Kripke, Gillin, & Golshan, 1992; Darko, Mitler, & Miller,

² CD4+ T-lymphocytes are specialized immune cells that are attacked by the HIV virus. CD4+ counts are used to categorize the progression of the disease. As the number of CD4+ cell decreases, the chance of opportunistic illness increases.

1998; Epstein et al., 1995; Rothenberg et al., 1990). Cruess et al. (2003) recently reported that sleep disturbance may mediate the detrimental effects of psychological distress on immune status in HIV. Others, however, have failed to find such relationships between sleep and immune status (Breitbart, McDonald, Rosenfeld, Monkman, & Passik, 1998; Lee, Portillo, & Miramontes, 2001).

3.8. *Outcomes for CBT-I in HIV*

As medical advances and antiretroviral therapies continue to significantly extend the life of HIV patients, the management of sleep disturbance in HIV becomes increasingly important for maximizing the quality of life of infected individuals. Surprisingly, the efficacy of CBT-I has yet to be adequately examined in HIV patients. We are aware of only one investigation that tested the efficacy of a single CBT-I component consisting of caffeine reduction to treat insomnia in HIV. Dreher tested the effects of a self-managed caffeine reduction protocol in 88 HIV+, regular caffeine users with insomnia (Dreher, 2003). Subjects were stratified on caffeine intake and degree of sleep disturbance and randomly assigned to a self-help caffeine reduction program or a monitoring only control group. The control group was instructed to maintain their usual level of caffeine consumption. Subjects in the experimental condition were provided detailed instructions to taper off caffeine and maintain a 90% reduction for 30 days. Both groups monitored caffeine intake and sleep via self-report. Post-treatment reduction in a global measure of sleep disturbance (PSQI) was 35% in the experimental group versus 6% for the control group. The post-treatment mean PSQI score for the caffeine reduction group = 7.4, which still indicates a significant degree of sleep disturbance after the intervention. This suggests that reducing caffeine consumption might be an important target for intervention when a high level of caffeine consumption is present, and that additional interventions may be needed to fully normalize sleep. Although the average caffeine consumption in this sample was more than twice the national average (476 mg/day), it is not definitively known whether increased caffeine consumption is particularly common in HIV patients.

3.9. *Special considerations for conducting CBT-I in HIV*

As with other medical conditions, multiple factors, in addition to disease processes, are likely to impair sleep quality in HIV patients. Physical symptoms associated with the infection, such as night sweats, cough, dyspnea, and diarrhea, might interfere with sleep and, therefore, require adequate management. Pain, present in approximately 67% of adults with HIV could independently impair sleep in HIV (Dobalian, Tsao, & Duncan, 2004; Robbins, Phillips, Dudgeon, & Hand, 2004) and, therefore, pain management, including relaxation training and distraction, might need to be integrated with CBT-I in HIV. Enlarged tonsils, caused by HIV infection may increase the risk for sleep disordered breathing (Epstein et al., 1995) and, therefore, sleep apnea needs to be carefully evaluated and treated if indicated. Several of the antiretroviral medications are known to significantly impair sleep continuity and architecture (Gallego et al., 2004; Nunez et al., 2001; Portsmouth et al., 2004), which, in turn, may lead to poor medication compliance and even the possibility of medication withdrawal. This cycle, however awaits empirical investigation. Sleep disturbance associated with these medications often, but not always, remits within the first weeks of therapy. Early insomnia prevention measures could include preparing patients to the possibility that the symptom might be transient and educating patients that some of the compensatory strategies used to cope with acute insomnia may contribute to a self-perpetuating sleep problem and should, therefore, be avoided.

As with cancer, fatigue is a major problem affecting the quality of life of individuals with HIV. Fatigue has been linked to the immune response to HIV as well as to inadequate sleep (Darko et al., 1995; Lee et al., 2001). Two of the most common counter fatigue measures that HIV patients may adopt (Dreher, 2003; Lee et al., 2001), consuming caffeine and taking extended naps, could aggravate insomnia and should be avoided. Appropriate timing of caffeine consumption, caffeine reduction, scheduling brief naps (<30 min), and properly timed physical exercise are CBT-I elements that may help patients manage fatigue without disrupting sleep patterns.

As with other life threatening and debilitating illnesses, special attention needs to be focused on the patient's mental well being. Individuals living with HIV often cope with a staggering array of psychosocial stressors, such as suffering multiple losses of friends to the disease, financial strain, social stigma, all of which may aggravate insomnia (Crueess et al., 2003). Depression and anxiety have been found to be significant correlates of sleep quality in HIV (Nokes & Kendrew, 2001; Robbins et al., 2004). While increased risk of depression is a commonly recognized aspect of HIV, anxiety disorders, especially panic disorder, should also be specifically evaluated (Tsao, Dobalian, Moreau, & Dobalian, 2004), because 12% of HIV positive individuals meet criteria for panic disorder (Vitiello, Burnam, Bing, Beckman, & Shapiro, 2003). Clinical trials of adaptations of CBT-I for HIV positive patients are needed.

4. Cognitive behavior therapy for insomnia occurring in psychiatric conditions

Disturbed sleep is listed as a diagnostic symptom of mood and anxiety disorders and is an associated symptom of most other psychiatric disorders. A report on the patterns of symptomatic recovery in psychotherapy indicates that sleep complaints do not change as a result of general psychotherapy (Kopta, Howard, Lowry, & Beutler, 1994). This implies that the sleep complaints of psychiatric patients need to be specifically targeted if they are to be improved. In addition to difficulties initiating and/or maintaining sleep, sleep in psychiatric patients is often disturbed by additional disease specific symptoms, such as nocturnal eating in eating disordered patients (ED), nightmares in posttraumatic stress disorder (PTSD), and nocturnal panic (NP) in panic disorder (PD). These sleep-related symptoms often contribute to the severity of insomnia and to the severity and course of the psychiatric illness. Untreated sleep disturbance may, furthermore, hinder response to treatment of the specific psychiatric condition. In addition, as is the case for medical diseases, many medications used to treat psychiatric diseases disrupt sleep and alter sleep architecture.

Although there is evidence that CBT-I might be effective for patients with co-morbid psychiatric illnesses, there is little empirical data to guide clinicians on how or whether to alter CBT-I to best treat insomnia that co-occurs with psychiatric disorders. There is also very little empirical data to guide therapists on the selection of the best strategies to treat insomnia experienced by psychiatric patients. Because insomnia sometimes resolves with successful treatment of the psychiatric condition, some advocate treating insomnia only if it does not abate with the remission of the psychiatric disorder. This approach might be more feasible than offering concomitant treatments for insomnia and the co-morbid condition, both because of limited health care resources and because the number of clinicians trained in behavioral sleep medicine is currently insufficient. On the other hand, because insomnia might hinder response to treatment of the psychiatric disorder, such as depression, concomitant treatments might ultimately improve overall efficacy of the psychiatric disease itself. We review below what is known about insomnia in psychiatric disorders for which CBT-I holds particular promise. This includes

affective disorders, anxiety disorders, eating disorders, and alcohol dependence and abuse disorders. The application of CBT-I for other substance abuse disorders is covered elsewhere in this issue (Bootzin, in this issue).

4.1. Major depressive disorder, dysthymia, and seasonal affective disorder

Most individuals with a major depressive disorder (MDD) report that their sleep is of poor overall quality with specific symptoms of difficulties initiating sleep (initial insomnia), multiple or prolonged awakenings after sleep onset (middle insomnia), and/or awakening in the morning earlier than desired (late insomnia) (Ripu & Thase, 2004). Laboratory sleep studies document longer latencies to sleep onset, wake after sleep onset time and more evidence of early morning awakening in individuals with MDD compared with healthy controls (Saletu-Zyhlarz et al., 2002). Although patients with dysthymia sleep better than patients with MDD, with shorter latency to sleep onset and longer overall total sleep time (Arriaga, Cavaglia, Matos-Pires, Lara, & Paiva, 1995; Arriaga, Rosasdo, & Paiva, 1990), their sleep quality is worse than that of healthy controls, with more wake after sleep onset time and greater difficulty falling asleep (Saletu-Zyhlarz et al., 2001).

Laboratory studies also document alterations in sleep architecture of patients with MDD and dysthymia, which include a decrease in the latency to the first REM episode, an increase in the amount of REM sleep in the beginning of the night (e.g., Kupfer & Reynolds, 1992; Saletu-Zyhlarz et al., 2001) and for patients with MDD, a reduction in the amount of slow wave sleep. The latter is more pronounced in men than in women (Reynolds et al., 1990) and is less likely to normalize upon recovery (Buysse, Frank, Lowe, Cherry, & Kupfer, 1997). The alterations in the distribution of REM sleep, some of which normalize following successful psychotherapy for depression (Buysse, Kupfer, Frank, Monk, & Ritenour, 1992; Thase et al., 1994), appear to be more prevalent in patients with MDD than in any other psychiatric disorder (Benca, Obermeyer, Thisted, & Gillin, 1992). REM sleep alterations have been viewed as signs of dysregulations of circadian rhythms regulating core body temperature, sleep, and cortisol (Wehr & Wirz-Justice, 1982), and of the serotonergic and cholinergic systems (Adrien, 2002; Perlis et al., 2002). The amplitude of the temperature rhythm, which is a marker of the strength of a circadian oscillator (Wever, 1965), is smaller in MDD patients who experience shorter REM latency compared to those with longer REM latencies (Avery, Wildschiodtz, Smallwood, Martin, & Rafaelsen, 1986) and it often normalizes during recovery (Avery, Gildschiodtz, & Rafaelsen, 1982). It is therefore not surprising that early morning awakening and sleep quality are the two sleep parameters most likely to improve with the remission of depression (Lee et al., 1993).

Paradoxically, a large and consistent body of literature documents that one night of sleep deprivation produces significant improvement in mood in depressed individuals, with peak benefits in the afternoon following the night of sleep deprivation. The improvement in mood is observed in 60% of all patients with affective disorders (Riemann et al., 1999). Higher rates of improvement are observed among patients with melancholic unipolar depression (Benedetti, Zanardi, Colombo, & Smeraldi, 1999), among those with diurnal mood variability, particularly those whose mood is worse in the morning (Riemann et al., 1999), and among those with a single episode of depression (Barbini et al., 1998). The clinical utility of sleep deprivation, however, is limited because the improvement is transient and usually dissipates after a night of recovery sleep. Prolonged sleep deprivation is not only impractical, but it also leads to worsening of mood (Green et al., 1999). There are some indications, however, that even a single night of sleep deprivation may speed therapeutic response among those treated with antidepressant medications

(Neumeister et al., 1996), and that bright light exposure can prolong the therapeutic effects of sleep deprivation (Wiegand, Lauer, & Schreiber 2001).

Seasonal Affective Disorders (SAD) is a depressive disorder involving an annual fluctuation in mood, which is hypothesized to be linked to circadian phase abnormalities. However, whereas MDD is associated with an advanced circadian rhythm phase, SAD is associated with a delayed phase of the melatonin and cortisol rhythms (Avery et al., 1997). Unlike patients with MDD, symptomatic SAD patients do not have early REM onset (Anderson et al., 1994) or the associated symptom of early morning awakenings. Instead, SAD patients manifest hypersomnolence, difficulty waking up in the morning during winter depressive episodes, and reduced sleep quality (Anderson et al., 1994; Shapiro, Devins, Feldman, & Levitt, 1994), which is probably a result of extended time in bed. Bright light therapy effectively elevates mood, activates, and reduces sleep problems and hypersomnia (Avery, Bolte, & Millet, 1992).

4.2. *Significance of insomnia symptoms in depression*

Sleep continuity disturbances in MDD, including early morning awakening, are associated with increased global severity of depression and a greater likelihood of suicidal ideation (Reynolds & Kupfer, 1987; Thase, 1998). Depressed patients who experience insomnia may have higher overall depression scores not only because of elevated scores on the insomnia items of scales measuring depression severity, but also because poor sleep contributes to other depressive symptoms such as daytime malaise, negative mood, irritability, decreased motivation, and difficulty with attention and concentration (Spielman & Anderson, 1999). In addition, insomnia adversely affects the course of standard antidepressant therapy. Studies have repeatedly shown that poor subjective and objective (electroencephalographic) sleep is associated with slower and lower rates of remission from depression (Buysse et al., 1997a; Dew et al., 1997; Winokur & Reynolds, 1994) and that treatments that provide early improvement in sleep hasten antidepressant response (DiMascio et al., 1979; Manber et al., 2003; Thase et al., 2002). Patients with abnormal sleep profiles have significantly poorer clinical outcome with respect to symptom ratings, attrition rates, and remission rates than patients with a more normal sleep profile (Thase et al., 1997). Collectively, these findings indicate that the presence of insomnia hinders response to antidepressant treatment.

Insomnia also affects the stability of response to treatment (Dew et al., 1997). It is the most common persistent residual symptom following depression treatment, present in approximately 44% of treatment completers (Nierenberg et al., 1999). Continued insomnia poses a significant risk factor for relapse of MDD. For example, two-thirds of patients with persistent insomnia at the end of treatment with the combination of nortriptyline and interpersonal psychotherapy relapsed within 1 year after switching to pill placebo. In contrast, 90% of patients with good sleep at the end of the acute treatment remained well during the first year after discontinuing antidepressant medications (Reynolds et al., 1997). In general, responders to treatment who have residual symptoms may experience a return of a major depressive episode sooner after remission (in the first 4 months) than those without residual symptoms (mostly after 12 months) (Van Londen, Molenaar, Goekoop, Zwiderman, & Rooijmans, 1998).

Two common pharmacological heuristics are used in the clinical management of insomnia in depressed patients. One heuristic is to select an antidepressant that is sedating and/or improves sleep continuity. Such antidepressants include those that block post-synaptic serotonin (5-HT₂) receptors and those that have pronounced antihistaminic effects (e.g., amitriptyline, trazodone, nefazodone,

mirtazapine, doxepin and trimipramine) (DiMascio et al., 1979; Thase, 1999). Another commonly used strategy is to co-administer, along with the antidepressant, a hypnotic such as a benzodiazepine (Buysse et al., 1997b; Dominguez, Jacobson, Goldstein, & Steinbook, 1984) or zolpidem (Asnis et al., 1999), or another sedating medication, such as H₁ antihistamines (Cook & Conner, 1995) or trazodone (Nierenberg, Alder, Peselow, Zornberg, & Rosenthal, 1994). Despite early concern (Birkenhager, Moleman, & Nolen, 1995), sedative hypnotics appear to improve the sleep of depressed patients without hindering short-term antidepressant response (Asnis et al., 1999; Buysse et al., 1997b; Fawcett, Edwards, Kravitz, & Jefferiss, 1987; Rickels, Feighner, & Smith, 1985). This augmentation strategy does not appear to improve depression outcome above and beyond what was produced by antidepressant medication alone, perhaps because the improvement in sleep may be offset by adverse side effects of the hypnotic medication (e.g., impaired concentration and memory, grogginess, lethargy, and psychomotor retardation). In addition, hypnotics with a short half life, such as zolpidem and zaleplon (Mendelson, 2000) may be of limited help ameliorating early morning awakening, which is a common manifestation of insomnia in depressed individuals.

4.3. Outcomes for CBT-I in depression

Although we were unable to identify any controlled studies of CBT-I in depression, two uncontrolled studies suggest that CBT-I might be effective for reducing insomnia and depression scores in insomniacs. One case series report evaluated the efficacy of a self-help intervention, “sleep better without drugs” in a sample of insomniacs with or without depression (a third without depression, a third with mild depression, and a third with moderate to severe depression). The intervention consisted of stimulus control, relaxation, and cognitive components delivered over 6 weeks. The study found a “substantial improvement” in sleep with no difference between those with or without depression (Morawetz, 2003). In addition, 70% of patients who responded to the insomnia treatment, and were also initially depressed, experienced clinically significant improvements in depression (Beck Depression Inventory) without any change in the treatment they already received for depression. A second preliminary study, published as an abstract, analyzed data gathered at the Insomnia Program at the Stanford Sleep Disorders Clinic. This study similarly found that patients with elevated depression scores had comparable outcomes to patients with low depression scores following seven sessions of CBT-I, consisting of stimulus control, sleep restriction, relaxation, sleep education, and cognitive restructuring. Further, the overall severity of depression was improved in a substantial proportion (58%) of patients who had elevated scores on a depression inventory at baseline (Kuo, Manber, & Loewy, 2001; Manber et al., 2001). Despite their methodological limitations, most notably absence of a control group, these preliminary data, along with the results from several studies of CBT-I in mixed samples (e.g., Dashevsky & Kramer, 1998; see Section 2) suggest that (a) CBT-I can be helpful for insomniacs with depressive symptoms, and (b) depression might be improved secondarily to improvements in sleep, even with no additional depression specific treatment.

4.4. Special considerations for conducting CBT-I in depression

There are several important factors to consider when deciding whether to initiate a trial of CBT-I in patients with unipolar forms of depression. One potential hindrance to the efficacy of CBT-I in depression is the possibility that depressed individuals will have difficulties complying with some of the

behavioral changes that are prescribed in the CBT-I protocol, such as sleep restriction, getting out of bed when unable to sleep, and setting up at a regular wake time. Low motivation and low energy, common in depression, and especially common in SAD, might compromise patients' ability to comply with these behavioral instructions, which are counter intuitive and difficult to adhere to even by non-depressed patients. Therefore, special attention needs to be paid to compliance issues. These include a clear and convincing explanation of each recommendation and early discussion of cognitions and beliefs that might interfere with compliance. Matter of fact discussion of compliance failures combined with flexible re-adjustment of the recommendations might be particularly relevant.

Conceptually, CBT-I can be easily integrated with directive forms of psychotherapy for depression, most notably CBT for depression. In fact, the *Cognitive Behavioral Therapy For Depression* manual (Beck, Rush, Shaw, & Emery, 1979) provides a brief discussion of strategies for addressing insomnia, including decatastrophizing the consequences of poor sleep, activation during the day, relaxation in the evening, stimulus control, and sleep hygiene education. Integrating CBT-I and psychotherapy for depression might be particularly helpful when sleep becomes an escape from the distress associated with the depression itself. This increased desire for sleep is, in turn, likely to increase the effort to sleep, which inevitably increases arousal in bed and interferes with sleep. Working simultaneously on both issues might enhance outcome of CBT-I in depression. Improved sleep might, in turn, improve depression outcome as well. In this way, integration or co-administration of CBT-I with psychotherapy for depression is likely to create a therapeutic synergy.

4.5. Bipolar disorder

In general, alterations in sleep during a depressive episode of a bipolar illness are similar to those found in patients with major depressive disorder. One difference is that patients with cyclothymia and bipolar depression are more likely to experience daytime sleepiness, and spend longer time asleep during the day than patients with major depressive disorder. Manic episodes are associated with extended periods of wakefulness, short total sleep times, long sleep latencies, deficits in slow wave sleep (American Sleep Disorders Association, 1997), shortened REM latencies, and more dense REM episodes (Jernajczyk, 1986). Mood stabilizers, such as lithium and lamotrigine (Lamictal), although acutely effective, can often disrupt a patient's sleep (Goldsmith, Wagstaff, Ibbotson, & Perry, 2004).

4.6. Special considerations for conducting CBT-I in bipolar disorder

To the best of these writers' knowledge, there are no published reports on the efficacy of CBT-I in bipolar depressive disorders. Nevertheless, a few important findings regarding sleep and rest in bipolar disorders might need to be considered when implementing CBT-I in this disorder. The first finding is that disruptions to sleep continuity and sleep deprivation are activating (Berger et al., 1997) and are considered "signal events" for a switch into a manic episode (Sachs, 2003). The rates of switch from depression to mania or hypomania following sleep deprivation (about 5%) appear to be comparable to rates of switch following treatment with antidepressant medication (Colombo et al., 1999). Even partial sleep deprivation, such as that induced by a newborn infant, are associated with high rates of relapse into a manic episode (Wehr, 1990). This finding suggests that severe sleep restriction might be contraindicated in bipolar depressive disorders. A second relevant finding is that temporal placement of the sleep episode might be another "signal event". This assertion is based on the finding that a switch

from depression to mania might be preceded by a delay in the phase of the circadian rhythm (Wher, Sack, & Duncan, 1983). The delay in the circadian phase is observable and is marked by a switch to a later bedtime and rise time. One possible intervention, particularly when rapid cycling is present, is to institute extended bed rest in darkness to stabilize the timing and duration of sleep (Wehr et al., 1998). Overall, this body of literature suggests that modifications to CBT-I might be necessary before it can be safely applied in bipolar disorders. Targets for modification, which will need to be empirically tested, include the modifications suggested for MDD, avoiding severe restriction of time in bed, and in the case of cyclothymia, introducing bed rest.

4.7. *Generalized anxiety disorder (GAD)*

The defining characteristic of GAD is excessive anxiety and worry that the patient finds difficult to control. Despite the high prevalence of insomnia associated with GAD, we were unable to identify any studies of CBT-I in GAD. Individuals with GAD often have difficulty initiating (47.7%) or maintaining sleep (63.6%). Although insomnia in GAD is typically associated with excessive worries, the correlation between the severity of insomnia and the severity of GAD is not statistically significant (Belanger, Morin, Langlois, & Ladouceur, 2004). Laboratory sleep studies are consistent with self reported sleep onset and maintenance difficulties in GAD (Fuller, Waters, Binks, & Anderson, 1997; Reynolds, Shaw, Newton, Coble, & Kupfer, 1983), but the evidence for alterations in sleep-stage parameters is less compelling (Monti & Monti, 2000). Because heightened arousal at night interferes with sleep and is commonly associated with reports of “a racing mind”, relaxation and cognitive restructuring might be particularly relevant components of CBT-I in GAD patients. Indeed a recent study using cognitive therapy targeting excessive worries of GAD patients resulted in a significant improvement in self reported insomnia severity, even though the intervention did not specifically target sleep (Belanger et al., 2004). Our clinical experience suggests that some very anxious patients find it particularly difficult to comply with sleep restriction. Sleep restriction consolidates sleep in part, because it increases sleep debt, which in turn “fuels” sleep. For very anxious individuals the idea that the time in bed is restricted increases anxiety so much that it counteracts the effects of sleep debt and results in a spiral of anxiety whereby, sleep restriction leads to heightened anxiety, which further restricts sleep. Stimulus control, another behavioral component of CBT-I, might be less anxiogenic than sleep restriction for severely anxious patients. Stimulus control instructions for insomnia shift the location where intrusive thoughts occur from the bed to another room and therefore might be helpful for patients with GAD, who tend to have difficulties in the timing and persistency of worrisome thoughts. However, another salient stimulus control instruction, adherence to a fixed rise time regardless of the amount of sleep obtained, might heighten sleep related anxiety. Scheduled worry is a stimulus control based procedure that can effectively reduce worries in GAD patients (Borkovec, Wilkinson, Folensbee, & Lerman, 1983) and, therefore, it might be useful for reducing pre-sleep intrusive thoughts and worries. This assertion, however, has not been empirically tested. The procedure involves dedicating a specific time each day for worries and postponing worries from all other times to the next scheduled worry time. The clinical issues discussed above, suggest that CBT-I might need to be altered for the optimal treatment of insomnia in patients with GAD so that the emphasis will be on techniques that reduce arousal and shift attention away from the demand to sleep. Relaxation, cognitive restructuring techniques (Harvey in this issue), and modified behavioral components are most likely to be relevant to this patient group. Yet, this assertion has not been empirically tested.

4.8. *Panic disorder (PD)*

Although we were unable to identify any studies of CBT-I in panic disorder, there are a number of sleep-related issues in PD, which may facilitate clinical work with these patients. Panic disorder patients have increased sleep latencies, decreased sleep efficiency, and increased duration and number of body movements (Mellman & Uhde, 1989; Mellman & Uhde, 1989). Unlike depression, which is associated with alterations in REM sleep, there is no consistent evidence of any abnormality of REM in PD. Similarly, unlike depressed patients, when PD patients are subjected to a night of total sleep deprivation they do not experience improvement in mood and anxiety and some actually displayed an increase in next-day panic attacks and anxiety ratings (Roy-Byrne, Uhde, & Post, 1986).

In addition to difficulties initiating and maintaining sleep, a sizable proportion of PD patients experience nocturnal panic attacks, which occur mostly during non-REM sleep (Mellman & Uhde, 1989). Panic attacks during sleep are sudden awakenings associated with intense fear. The spontaneous abrupt arousal with panic is distinguishable from arousal from a nightmare in that it is typically not associated with dream recall. Nocturnal panic is also distinguishable from night terrors in that it does not begin with a piercing scream and there is complete awakening with no amnesia to the event. In general the sleep architecture of PD patients with and without nocturnal panic is not distinguishable (Sloan et al., 1999). An important difference between PD patients with nocturnal panic and those without nocturnal panic is that the former appear to be more fearful of states that involve a diminution of conscious awareness or vigilance, and are therefore more likely to experience relaxation induced anxiety (Craske, Lang, Tsao, Mystkowski, & Rowe, 2001). It might, therefore, be important to manipulate attributions about physiological events during sleep in order to: (1) decrease the likelihood of the occurrence of nocturnal panic (Craske et al., 2001); (2) reduce the likelihood that relaxation will result in a paradoxical increase in arousal; and (3) ultimately reduce fears associated with the process of falling asleep. Nocturnal panic does not appear to hinder response to CBT for PD (Craske, Rowe, Lewin, & Noriega-Dimitri, 1997). Another consideration for the application of CBT-I in PD is the possibility that partial sleep deprivation commonly associated with a strict application of sleep restriction might increase next day panic attacks. This possibility has not yet been evaluated. Nevertheless, we recommend caution in the application of strict sleep restriction in this patient group. If, indeed, the procedure induces an increase in day time panic, it is also likely to increase fear of insufficient sleep in PD patients, which might lead to increased demand for sleep, and, in turn, increased pre-sleep arousal, further interfering with the sleep process.

4.9. *Obsessive compulsive disorder (OCD)*

Similar to GAD and PD, we were not able to identify any studies of CBT-I, specific to patients with obsessive-compulsive disorder (OCD). The majority of patients with OCD do not complain of sleep disruptions (Uhde, 2000). Laboratory sleep studies confirm sleep disruptions in those with subjective complaints (Insel et al., 1982) and normal sleep in those who do not complain (Robinson, Walsleben, Pollack, & Lerner, 1998). On the other hand, studies of sleep stage parameters in this patient population are few and their results are not consistent (Hohagen et al., 1994; Insel et al., 1982). There is no indication in the published literature or in our clinical experience that the treatment of insomnia in OCD

patients needs to be altered. When obsessive-compulsive themes, such as compulsive checking that the doors are locked, directly interfere with the process of falling asleep, they need to be addressed.

4.10. Post traumatic stress disorder (PTSD)

Sleep continuity disturbances, including nightmares, are a hallmark of PTSD and are conceptualized as a reflection of heightened arousal characteristics of this disorder (Mellman, Kulick-Bell, Ashlock, & Nolan, 1995). Although the frequency of nightmares in PTSD is high, particularly in war veterans (van der Kolk, Blitz, Burr, Sherry, & Hartmann, 1984), polysomnographic evaluations of REM sleep in PTSD patients have yielded inconsistent results on most sleep REM parameters. A recent large scale polysomnographic study of sleep in PTSD (Breslau et al., 2004) found that compared with controls, patients with PTSD had significantly more fragmented REM sleep but no significant differences on other measures of sleep continuity, sleep stage distribution, prevalence of sleep apnea index greater than 10, or prevalence of periodic limb movement index greater than 10. This report suggests that complaints of trouble initiating and maintaining sleep might represent magnified perceptions of brief arousals from REM sleep.

4.11. Outcomes of CBT-I in post traumatic stress disorder

To the best of our knowledge, only one study reports on the outcome of CBT-I in PTSD patients (Krakow et al., 2001). This study of 67 crime victims added to CBT-I a component called dream rehearsal. Dream rehearsal is a cognitive imagery approach that encourages the patient to recall the nightmare, “change the nightmare any way you wish,” then rehearse the “new dream” while awake. Several uncontrolled pilot studies have found the procedure to be effective for reducing nightmare frequency and intensity (Forbes et al., 2003; Krakow, Kellner, Pathak, & Lambert, 1995). This study found that sleep quality/insomnia severity, as measured by two well-validated questionnaires (the PSQI and the Sleep Impairment Index (Morin, 1993), improved substantially after treatment (effect sizes= 1.02 and 1.23). Mean scores on both indices were within the normal range at the 3-month follow-up. Nightmare frequency was also significantly reduced. Not only did subjects report improvement on sleep parameters, but they also demonstrated significant, moderate effects for measures of posttraumatic stress disorder severity, anxiety, and depression (effect sizes: 0.43–0.71).

4.12. Special consideration in conducting CBT-I in PTSD

The above study combined with recent PSG findings suggesting that sleep complaints in PTSD may be largely driven by REM disturbances, suggest that cognitive-behavioral efforts to desensitize and diminish arousal associated with nightmares via imagery rehearsal may be a crucial component for successful CBT-I in PTSD. An additional factor that sometimes complicates the treatment of insomnia associated with PTSD is fear of going to sleep because it might involve re-experiencing traumatic nightmares. This fear, in turn, can prolong sleep latency and contribute to irregular bedtimes. This may be particularly problematic when the original trauma(s) occurred within a sleep-related context, as is the case in some sexual abuse related traumas. A recent study of subjects with PTSD who were treated to remission found that 48% continued to complain of insomnia and that experiencing trauma in a sleep-related context was associated with residual insomnia symptoms (Zayfert & DeViva, 2004).

4.13. Eating disorders

Eating disordered patients report more insomnia than controls. Severely underweight Anorexia Nervosa (AN) patients report poor sleep quality that improves during periods of weight restoration (Laurel & Krieg, 2004; Pieters, Theys, Vandereycken, Leroy, & Peuskens, 2004). Patients with Bulimia Nervosa (BN) also report more insomnia symptoms than controls, with greater difficulty initiating sleep, restless sleep, and early morning awakening (Latzer, Tzischinsky, WEpstein, Klein, & Lavie, 1999). During periods of change in weight, sleep appears to be altered, with insomnia and reduced slow wave sleep during times of rapid weight loss and hypersomnia during periods of significant weight gain (Evans, 1983). Slow wave sleep, which is typically an index of the homeostatic sleep drive and the primary period of growth hormone secretion, appears to be sensitive to weight change. For example, the amount of slow wave sleep at baseline is a positive predictor of the length of time to weight normalization (Pieters et al., 2004), and it increases during an initial weight gain (Lacey, Crisp, Kalucy, Hartmann, & Chien, 1975).

Sleep EEG and actigraphy-based sleep parameters on ED patients are, for the most part, not different from those observed in controls (for a review see Benca & Casper, 2000). In part, the inconsistency in the literature may be related to the heterogeneity of samples with respect to the gradient of weight change. One interesting finding is that sleep is more fragmented and of poorer quality in obese patients compared with normal weight controls. This might be because obesity is a significant risk factor for sleep disordered breathing (Tzischinsky, Latzer, Epstein, & Naveh, 2000), which causes sleep fragmentation and non-restorative sleep.

In the past decade, sleep-related eating and nocturnal eating syndromes have emerged as new sleep disorders. Both combine characteristics of sleep disorders and eating disorders. Sleep-related eating disorders are characterized by nocturnal arousal, followed by a rapid ingestion of food, and poor memory of the episode the following day. This behavior is most commonly observed in individuals with sleep walking and other sleep disorders of partial arousal from slow wave sleep, particularly when food intake is restricted during the day (Benca & Casper, 2000). The prevalence of sleep-related eating disorder in psychiatry is estimated at 5%, with higher prevalence among eating disordered patients (Winkelman, Herzog, & Fava, 1999).

Nocturnal eating disorder is a different diagnostic category characterized by recurrent awakening, followed by a need to eat, and inability to fall back asleep unless food is ingested. Its estimated prevalence among insomnia patients is 6% (Manni, Ratti, & Tartara, 1999). Nocturnal eating episodes have been reported in association with periodic limb movements and sleep apnea, two disorders that cause sleep fragmentation and might increase the likelihood of unusual behaviors associated with partial arousal in predisposed individuals.

4.14. Special considerations for the use of CBT-I in eating disorders

To the best of these writers' knowledge, there are no published systematic studies on the treatment of insomnia in eating disordered patients. Therefore the efficacy of CBT-I in this psychiatric disorder remains unclear. It is not known to what extent insomnia resolves with successful treatment of the eating disorder and we do not know if residual insomnia constitutes a risk for relapse in this difficult to treat population, as it is for MDD. Many eating disordered patients who come to sleep disorders clinics seek treatment because they are distressed about their nocturnal

eating episodes. The research agenda in this domain is to better understand the night and daytime manifestations of sleep related eating disorders. For example, is it exacerbated by sleep deprivation, as is sleep walking? If so, sleep deprivation can become a target for therapy. Does it occur in a predictable time after sleep onset? If so, scheduled awakening prior to the event might help prevent nocturnal eating episodes.

4.15. Alcohol abuse and dependence disorders

Insomnia is a common feature of alcoholism (American Sleep Disorders Association, 1997) with surveys indicating a prevalence ranging between 36% and 72% (Brower, 2003). Alcohol, like other depressants, is a REM suppressant, but it enhances slow wave sleep early in the night (Kobayashi et al., 1998). Consumption of alcohol for the purpose of inducing sleep is common even in the absence of alcohol-related disorders. The initial effect for alcohol ingested at bedtime is relaxation and sedation, which facilitates sleep onset, but it is followed by increased wakefulness, increased REM, and overall fitful sleep during the second half of the night (Gillin & Drummond, 2000). Continued use of alcohol at bedtime results in tolerance to the sleep-inducing effects of alcohol and increased prominence of sleep fragmentation. Withdrawal from heavy drinking produces a REM rebound effect that is accompanied by restless sleep, nightmares, and decreased slow wave sleep. The latter may persist even following 3–14 months of sobriety (Brower, 2003). Alcohol also exacerbates sleep apnea, since it affects ventilation during sleep. It is, therefore, important to rule out sleep disordered breathing, especially when alcoholics with insomnia report excessive daytime sleepiness (Issa & Sullivan, 1982; Taasan, Block, Boysen, & Wynne, 1981). Several studies have found that insomnia may be a risk factor for subsequent relapse, although it is unknown whether treating insomnia diminishes this risk (e.g., Brower, Aldrich, Robinson, Zucker, & Greden, 2001; Foster & Peters, 1999).

4.16. Outcomes for CBT-I in alcoholism

To our knowledge only one study has tested the effects of a psychological intervention for insomnia in chronic alcoholics (Greeff & Conradie, 1998). In this investigation, 22 male alcoholics undergoing inpatient treatment for alcoholism were randomized to receive ten sessions of progressive muscle relaxation training for insomnia or to a 2-week waitlist control condition. Diary ratings of sleep quality improved substantially at post-treatment (effect size=2.2), whereas the control group showed minimal improvement (effect size=0.22). Other measures of sleep and daytime functioning were not reported. While this reflects, an unusually large treatment effect, the limited measurement strategy (Likert scale rating) renders the clinical significance of this finding unclear. It should also be noted that the inpatient setting limits the generalizability of the findings.

4.17. Special considerations for use of CBT-I in alcoholism

Given the acute physiologic effects of alcohol on sleep, it is not reasonable to expect that CBT-I will reverse these effects. Nevertheless, as is the case with insomnia occurring in the context of medical or psychiatric conditions, CBT-I might help eliminate behaviors that might maintain and/or exacerbate insomnia beyond the direct effects of alcohol. In addition, CBT-I might play a role during and after detoxification. For example, educating alcoholics that cessation of drinking induces severe

transient sleep fragmentation (Gillin & Drummond, 2000) might help patients to cope more adaptively with the initial sleep loss. Similarly, informing patients that mild sleep fragmentation might persist for as long as 2 years after drinking cessation (Adamson & Burdick, 1973) can also help set realistic expectations that in turn are likely to moderate the severity of the problem. Finally, we speculate that sleep restriction might be particularly helpful for the treatment of insomnia in recovered alcoholics because it might help reduce sleep fragmentation.

5. Conclusions and future directions

In summarizing the existing outcomes literature for CBT-I, the preliminary data regarding the efficacy of CBT-I for chronic insomnia when it occurs in patients with various medical and psychiatric conditions are encouraging (see Table 1). Effect sizes across most of the studies are quite large and consistent with effect sizes reported in the outcomes literature for primary insomnia. The possibility that improvements in sleep might reciprocally feedback and impact the primary disease processes and/or quality of life, however, is not yet clear, given the limited number of studies. This possibility is most promising in the studies of cancer patients. More investigations that measure disease markers and daytime functioning, in addition to objective and subjective sleep parameters, are needed. As the literature matures, future studies will likely be aimed at testing disease-specific modifications to CBT-I, which may enhance outcomes.

Future research will also need to address several limitations that are evident in the existing research. It will be particularly important to adequately control for non-specific therapeutic elements and demand characteristics. This has not been the case in the 15 published studies we reviewed here. Only seven of these studies included control groups and when control groups were present, the control condition was a usual care wait list, which does not adequately control for non-specific therapeutic factors or demand characteristics. Although true double-blinded placebo controlled studies are quite difficult to implement with psychological interventions, Edinger and colleagues have demonstrated the credibility of a sham insomnia treatment that provides an adequate placebo control for CBT-I (Edinger et al., 2001).

Consistent with contemporary statistical recommendations for the design of treatment outcome research, future studies should be designed to allow for intention-to-treat analyses. Intention-to-treat analyses statistically adjust the data to account for subjects who drop out of treatment before the designated end of treatment measurement of outcome. To allow for a meaningful intent-to-treat analysis, efforts should be made to collect the main outcome data from individuals who drop out of the study.

Finally, in addition to large randomized controlled trials of CBT-I in the medical and psychiatric disorders that were discussed in this review, we wish to encourage investigation of CBT-I for patients suffering from diabetes and coronary artery disease, two disease conditions that have not been previously studied. We highlight these two conditions because longitudinal, epidemiologic studies have identified insomnia as an independent risk factor for both diseases (Kawakami, Takatsuka, & Shimizu, 2004; Mallon et al., 2002). With respect to the psychiatric literature, given the preponderance of studies showing that insomnia is an independent risk factor for new onset episodes and recurrence in depression, controlled clinical trials of CBT-I in depression are especially needed.

Table 1
Summary of studies evaluating effectiveness of cognitive-behavior therapy for insomnia occurring in medical and psychiatric disorders

Author	Population (<i>n</i> , subgroup)	<i>N</i>	Insomnia RX type(s) ^a	Design	Sleep measures	Sleep Parameters ^b improved (Effect Size Estimate ^c)	Daytime SX improved?
(Lichstein et al., 2000)	Mixed Med. and Psych.; Older Adults	44	SCT, RLX, SH: 4 Sess.	Randomized Waitlist Control	Self-Report, Diaries	SE (0.70); WASO (0.43); SQ (0.71)	N
(Morin et al., 1994)	Mixed Medical (13), Psych (27) , and Primary Insomnia (39), Drug dependent (21)	100	SCT, SRT, SH, CT, 8–10 Sess.	Case Series	Self-Report, Diaries	Psychiatric: TWT (0.93); SE (0.94) Medical: (data not reported)	N/A
(Perlis et al., 2001)	Mixed Med. (16) Psych (12) and Primary Insomnia;	28	SCT, SRT, SH, CT: 8 Sess.	Case Series	Self-Report, Diaries	Medical: SL (0.59); FNA (0.38); WASO (0.75) Psychiatric: SL (0.66); FNA (0.60); WASO (0.86)	N/A
(Rybarczyk et al., 2002)	Mixed Medical; Older adults	38	SCT, SRT, SH, CT, RLX: 8 Sess., group vs. Self-help RLX	Randomized Wait-list Control	Self-Report Diaries Actigraphy	Full CBT-I Diary: SE (1.7), WASO (1.1) PSQI: (1.1) Relaxation Diary: TST (0.99) PSQI (0.56) Actigraphy: N.S. ^d	N
Dashevsky & Kramer, 1998	Mixed Psychiatric and failed Meds for insomnia	48	SCT, SRT, SH, RLX: 6 Sess.	Case Series	Self-Report, Diaries	SL (0.92); FNA (1.1); WASO (0.85), TST (0.35), SE (1.3); SQ (1.1), Sleep Concern (0.91)	Y
Cannici et al., 1983	Mixed Cancer	30	RLX: 3 Sess.	Randomized Usual Care Control	Self-report Diary	SL (77% reduction RLX vs. 6% reduction Control)	N
(Davidson et al., 2001)	Mixed Cancer	12	Group: SCT, RLX, SH, CT: 6 Sess.	Case Series	Self-report, Diaries	FNA (1.0); WASO (1.8), TST (0.58); SE (2.0); SQ (1.5)	Y
(Quesnel et al., 2003)	Breast Cancer, Women; SI	10	Group: SCT, SRT, SH, CT: 8 Sess.	Multiple Baseline Case series	PSG and Diaries	PSG: TWT (0.98); SE (0.73) Diary: TWT (1.7); SE (1.6) [median]	Y

Simeit et al., 2004	Mixed Cancer	229	SCT, RLX, SH, CT, 3–4 weeks	Usual care controlled comparison	Self-report, Retrospect (PSQI ^e)	SL (0.65), TST (0.65), SE (0.98)	Y
Dreher, 2003	HIV, daily caffeine consumers (60% AIDS)	88	SH, Caffeine reduction, program, 30 days	Randomized Monitoring Only Control	Self-report, Retrospect (PSQI ^e)	Global SQ (1.1)	N
(Currie et al., 2000)	Mixed Chronic Pain without depression	60		Randomized Waitlist Control	Actigraphy Self report, Diaries	Activity counts during sleep period decreased. DSD: SL (1.3); WASO (0.85), SE (1.0), SQ (1.33)	N
(Morin et al., 1989)	Chronic Back Pain	3	SRT and SCT: 6 Sess.	Multiple Baseline Case series	PSG and Diaries	PSG: SL (0.94); WASO (2.2); TWT (1.2) Diary: SL (1.1); FNA (0.42); WASO (1.5); TWT (2.1)	Y
(Morawetz, 2003)	Chronic Insomnia, 2/3 suffering clinically sig. Depressive symptoms	86	SCT, CT, RLX, SH: 6–8 week self-help program	Case Series	Retrospective self-report	SL, TST, FNA 87% categorized as meeting investigator's criteria for substantially improved ^f Means and SDs not reported	Y
(Krakow et al., 2001)	Posttraumatic stress disorder	62	Group: SCT, SRT, SH, CT, Imagery rehearsal: 10 hours	Open label, Case Series:	Self-report, Retrospect PSQI, Insomnia Severity Index	SQ [PSQI (1.02)], Insomnia severity (1.23), Nightmare nights/week (0.76), nightmare/week (0.74)	Y
Greeff & Conradie, 1998	Alcohol dependency, Men	22	RLX: 2 weeks, daily sessions	Randomized usual care control, waitlist	Self-report-likert scale, sleep quality	SQ (2.2)	N/A

^a SCT=Stimulus Control Therapy; SRT=Sleep Restriction Therapy, RLX=Relaxation therapy; SH=Sleep Hygiene; CT=Cognitive Therapy.

^b SL=Sleep Latency; FNA=Frequency of Nightly Awakenings; WASO=Wake After Sleep Onset Time; TWT=Total Wake Time (SL+WASO+ early morning awakening time); TST=Total Sleep Time; SE=Sleep Efficiency (TST/Time in Bed).

^c Within subjects effect sizes estimated by Calculating Cohen's *d* (posttreatment mean – pretreatment mean/pooled standard deviation), follow-up data not calculated. When groups included patients with primary insomnia, only means for groups with medical and psychiatric morbidity were included in calculating effect sizes. When study included a control group, only variables showing a differential posttreatment improvement compared to controls are reported.

^d Pittsburgh Sleep Quality Index, global score.

^e N.S.=Not significant ($p > 0.05$).

^f Only patients meeting 1 or more of the following criteria were classified as substantially improved: (1) reduction in SL ≥ 120 min, (2) increase in TST ≥ 120 min, (3) reduction in FNA ≥ 8 , (4) elimination of sleeping medication without deterioration in sleep parameters. Approximately 50% of subjects improved on at least 2 of the 4 criteria.

References

- Adamson, J., & Burdick, J. A. (1973). Sleep of dry alcoholics. *Archives of General Psychiatry*, 28, 146–149.
- Adrien, J. (2002). Neurobiological bases for the relation between sleep and depression. *Sleep Medicine Review*, 6, 341–351.
- Affleck, G., Urrows, S., Tennen, H., Higgins, P., & Abeles, M. (1996). Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. *Pain*, 68, 363–368.
- Allain, H., Bentue-Ferrer, D., Tarral, A., & Gandon, J. M. (2003). Effects on postural oscillation and memory functions of a single dose of zolpidem 5 mg, zopiclone 3.75 mg and lormetazepam 1 mg in elderly healthy subjects. A randomized, cross-over, double-blind study versus placebo. *European Journal of Clinical Pharmacology*, 59, 179–188.
- American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* (4 ed.). Washington, DC: American Psychiatric Association.
- American Sleep Disorders Association (1997). *The International Classification of Sleep Disorders: Diagnostic and Coding Manual—Revised*. Rochester, MN: American Sleep Disorders Association.
- Ancoli-Israel, S., & Roth, T. (1999). Characteristics of insomnia in the United States: Results of the 1991 National Sleep Foundation Survey, I. *Sleep*, 22(Suppl. 2), S347–S353.
- Anderson, J. L., Rosen, L. N., Mendelson, W. B., Jacobsen, F. M., Skwerer, R. G., Joseph-Vanderpool, J. R., et al. (1994). Sleep in fall/winter seasonal affective disorder: Effects of light and changing seasons. *Journal of Psychosomatic Research*, 38, 323–337.
- Arriaga, F., Cavaglia, F., Matos-Pires, A., Lara, E., & Paiva, T. (1995). EEG sleep characteristics in dysthymia and major depressive disorder. *Neuropsychobiology*, 32, 128–131.
- Arriaga, F., Rosasdo, P., & Paiva, T. (1990). The sleep of dysthymic patients: A comparison with normal controls. *Biological Psychiatry*, 27, 649–656.
- Asnis, G. M., Chakraborty, A., DuBoff, E. A., Krystal, A., Longborg, P. D., Rosenberg, R., et al. (1999). Zolpidem for persistent insomnia in SSRI-treated depressed patients. *Journal of Clinical Psychiatry*, 60, 668–676.
- Astin, J. A. (2004). Mind–body therapies for the management of pain. *Clinical Journal of Pain*, 20, 27–32.
- Atkinson, J. H., Ancoli-Israel, S., Slater, M. A., Garfin, S. R., & Gillin, J. C. (1988). Subjective sleep disturbance in chronic back pain. *The Clinical Journal of Pain*, 65, 225–232.
- Avery, D., Bolte, M. A., & Millet, M. (1992). Bright dawn simulation compared with bright morning light in the treatment of winter depression. *Acta Psychiatrica Scandinavica*, 85, 430–434.
- Avery, D., Gildschiodt, G., & Rafaelsen, O. J. (1982). REM latency and temperature in affective disorder before and after treatment. *Biological Psychiatry*, 17, 463–470.
- Avery, D. H., Dahl, K., Savage, M. V., Brengelmann, G. L., Larson, L. H., Kenny, M. A., et al. (1997). Circadian temperature and cortisol rhythms during a constant routine are phase delayed in hypersomnic winter depression. *Biological Psychiatry*, 41, 1109–1123.
- Avery, D. H., Wildschjodtz, G., Smallwood, R. G., Martin, D., & Rafaelsen, O. J. (1986). REM latency and core temperature relationships in primary depression. *Acta Psychiatrica Scandinavica*, 74, 269–280.
- Barbini, B., Colombo, Benedetti, F., Campori, E., Bellodi, L., & Smeraldi, E. (1998). The unipolar–bipolar dichotomy and the response to sleep deprivation. *Psychiatry Research*, 79, 43–50.
- Beck, A. T., Rush, A. J., Shaw, B. F., & Emery, G. (1979). *Cognitive Therapy for Depression*. New York: Guilford Press.
- Belanger, L., Morin, C., Langlois, F., & Ladouceur, R. (2004). Insomnia and generalized anxiety disorder: Effects of cognitive behavior therapy for gad on insomnia symptoms. *Journal of Anxiety Disorders*, 18(4), 561–571.
- Belenky, G., Wesensten, N. J., Thorne, D. R., Thomas, M. L., Sing, H. C., Redmond, D. P., et al. (2003). Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: A sleep dose–response study. *Journal Sleep Research*, 12, 1–12.
- Benca, R. M., & Casper, R. C. (2000). Eating disorders. In M. H. Kryger, T. Roth, & W. C. Dement (Eds.), *Principles and practice of sleep medicine* (pp. 1169–1175). New York: WB Saunders.
- Benca, R. M., Obermeyer, W. H., Thisted, R. A., & Gillin, J. C. (1992). Sleep and psychiatric disorders: A meta analysis. *Archives of General Psychiatry*, 178, 405–414.
- Benedetti, F., Zanardi, R., Colombo, C., & Smeraldi, E. (1999). Worsening of delusional depression after sleep deprivation: Case reports. *Journal of Psychiatric Research*, 33(1), 69–72.

- Berger, M., Vollmann, J., Hohagen, F., König, A., Lohner, H., Voderholzer, U., et al. (1997). Sleep deprivation combined with consecutive sleep phase advance as a fast-acting therapy in depression: An open pilot trial in medicated and unmedicated patients. *American Journal of Psychiatry*, *154*(6), 870–872.
- Birkenhager, T. K., Moleman, P., & Nolen, W. (1995). Benzodiazepines for depression? A review of the literature. *International Clinical Psychopharmacology*, *10*, 181–195.
- Bonnet, M. H., & Arand, D. L. (1998). Heart rate variability in insomniacs and matched normal sleepers. *Psychosomatic Medicine*, *60*, 610–615.
- Bonnet, M. H., & Arand, D. L. (2003). Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Reviews*, *7*, 297–310.
- Bootzin, R. R. (1972). *Stimulus Control Treatment*. Paper presented at the American Psychological Association Annual Meeting.
- Borkovec, T. D., Wilkinson, L., Folsensbee, R., & Lerman, C. (1983). Stimulus control applications to the treatment of worry. *Behaviour Research and Therapy*, *21*(3), 247–251.
- Breitbart, W., McDonald, M., Rosenfeld, B., Monkman, N., & Passik, S. (1998). Fatigue in ambulatory AIDS patients. *Journal of Pain and Symptom Management*, *15*, 159–167.
- Breslau, N., Roth, T., Burduvali, E., Kapke, A., Schultz, L., & Roehrs, T. (2004). Sleep in lifetime posttraumatic stress disorder: A community-based polysomnographic study. *Archives of General Psychiatry*, *61*(5), 508–516.
- Brower, K. J. (2003). Insomnia, alcoholism and relapse. *Sleep Medicine Reviews*, *7*(6), 523–539.
- Brower, K. J., Aldrich, M. S., Robinson, E. A., Zucker, R. A., & Greden, J. F. (2001). Insomnia, self-medication, and relapse to alcoholism. *American Journal of Psychiatry*, *158*, 399–404.
- Buysse, D. J., Frank, E., Lowe, K. K., Cherry, C. R., & Kupfer, D. J. (1997). Electroencephalographic sleep correlates of episode and vulnerability to recurrence in depression. *Biological Psychiatry*, *41*(4), 406–418.
- Buysse, D. J., Kupfer, D. J., Frank, E., Monk, T. H., & Ritenour, A. (1992). Electroencephalographic sleep studies in depressed outpatients treated with interpersonal psychotherapy: II. Longitudinal studies at baseline and recovery. *Psychiatry Research*, *42*(1), 27–40.
- Buysse, D. J., Reynolds, C. F., & Hauri, P. J. (1994). Diagnostic concordance for DSM-IV sleep disorders: A report from the APA/NIMH DSM-IV field trial. *American Journal of Psychiatry*, *151*, 1351–1360.
- Buysse, D. J., Reynolds, C. F. d., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213.
- Buysse, D. J., Reynolds, C. F. r., Houck, P. R., Perel, J. M., Frank, E., Begley, A. E., et al. (1997a). Does lorazepam impair the antidepressant response to nortriptyline and psychotherapy? *Journal of Clinical Psychiatry*, *58*(10), 426–432.
- Buysse, D. J., Reynolds, C. F. r., Houck, P. R., Perel, J. M., Frank, E., Begley, A. E., et al. (1997b). Does lorazepam impair the antidepressant response to nortriptyline and psychotherapy? *Journal of Clinical Psychiatry*, *58*(10), 426–432.
- Cannici, J., Malcolm, R., & Peek, L. A. (1983). Treatment of insomnia in cancer patients using muscle relaxation training. *Journal of Behavior Therapy and Experimental Psychiatry*, *14*, 251–256.
- Colombo, C., Benedetti, F., Barbini, B., Campori, E., & Smeraldi, E. (1999). Rate of switch from depression into mania after therapeutic sleep deprivation in bipolar depression. *Psychiatry Research*, *86*(3), 267–270.
- Cook, M. D., & Conner, J. (1995). Retrospective review of hypnotic use in combination with fluoxetine and sertraline. *Clinical Drug Investigation*, *9*, 212–216.
- Couzi, R. J., Helzlsouer, K. J., & Fetting, J. H. (1995). Prevalence of menopausal symptoms among women with a history of breast cancer and attitudes toward estrogen replacement therapy. *Journal of Clinical Oncology*, *13*, 2737–2744.
- Craske, M. G., Lang, A. J., Tsao, J. C. I., Mystkowski, J. L., & Rowe, M. K. (2001). Reactivity to interoceptive cues in nocturnal panic. *Journal of Behavior Therapy and Experimental Psychiatry*, *32*, 173–190.
- Craske, M. G., Rowe, M., Lewin, M., & Noriega-Dimitri, R. (1997). Interoceptive exposure versus breathing retraining within cognitive-behavioural therapy for panic disorder with agoraphobia. *British Journal of Clinical Psychology*, *36*(1), 85–99.
- Cruess, D. G., Antoni, M. H., Gonzalez, J., Fletcher, M. A., Klimas, N., Duran, R., et al. (2003). Sleep disturbance mediates the association between psychological distress and immune status among HIV-positive men and women on combination antiretroviral therapy. *Journal of Psychosomatic Research*, *54*, 185–189.
- Currie, S. R., Wilson, K. G., Pontefract, A. J., & deLaplante, L. (2000). Cognitive-behavioral treatment of insomnia secondary to chronic pain. *Journal of Consulting and Clinical Psychology*, *68*, 407–416.
- Darko, D. F., McCutchan, J. A., Kripke, D. F., Gillin, J. C., & Golshan, S. (1992). Fatigue, sleep disturbance, disability, and indices of progression of HIV infection. *American Journal of Psychiatry*, *149*, 514–520.

- Darko, D. F., Miller, J. C., Gallen, C., White, J., Koziol, J., Brown, S. J., et al. (1995). Sleep electroencephalogram delta-frequency amplitude, night plasma levels of tumor necrosis factor alpha, and human immunodeficiency virus infection. *Proceedings of the National Academy of Sciences of the United States of America*, *92*, 12080–12084.
- Darko, D. F., Mitler, M. M., & Miller, J. C. (1998). Growth hormone, fatigue, poor sleep, and disability in HIV infection. *Neuroendocrinology*, *67*, 317–324.
- Dashevsky, B. A., & Kramer, M. (1998). Behavioral treatment of chronic insomnia in psychiatrically ill patients. *Journal of Clinical Psychiatry*, *59*(12), 693–699.
- Davidson, J. R., MacLean, A. W., Brundage, M. D., & Schulze, K. (2002). Sleep disturbance in cancer patients. *Social Science & Medicine*, *54*, 1309–1321.
- Davidson, J. R., Waisberg, J. L., Brundage, M. D., & MacLean, A. W. (2001). Nonpharmacologic group treatment of insomnia: A preliminary study with cancer survivors. *Psychooncology*, *10*, 389–397.
- Dew, M. A., Reynolds, C. F., Houck, P. R., Hall, M., Buysse, D. J., Frank, E., et al. (1997). Temporal profiles of the course of depression during treatment. Predictors of pathways toward recovery in the elderly. *Archives of General Psychiatry*, *54*(11), 1016–1024.
- DiMascio, A., Weissman, M. M., Prusoff, B. A., Neu, C., Zwilling, M., & Klerman, G. I. (1979). Differential symptom reduction by drugs and psychotherapy in acute depression. *Archives of General Psychiatry*, *36*, 1450–1456.
- Dinges, D. F., Douglas, S. D., Hamarman, S., Zaugg, L., & Kapoor, S. (1995). Sleep deprivation and human immune function. *Advances in Neuroimmunology*, *5*, 97–110.
- Dinges, D. F., Douglas, S. D., Zaugg, L., Campbell, D. E., McMann, J. M., Whitehouse, W. G., et al. (1994). Leukocytosis and natural killer cell function parallel neurobehavioral fatigue induced by 64 hours of sleep deprivation. *Journal of Clinical Investigation*, *93*, 1930–1939.
- Dobalian, A., Tsao, J. C., & Duncan, R. P. (2004). Pain and the use of outpatient services among persons with HIV: Results from a nationally representative survey. *Medical Care*, *42*, 129–138.
- Dominguez, R. A., Jacobson, A. F., Goldstein, B. J., & Steinbook, R. M. (1984). Comparison of triazolam and placebo in the treatment of depressed patients. *Current Therapeutic Research*, *36*, 856–865.
- Dreher, H. M. (2003). The effect of caffeine reduction on sleep quality and well being in persons with HIV. *Journal of Psychosomatic Research*, *54*(3), 191–198.
- Drewes, A. M., Gade, K., Nielsen, K. D., Bjerregard, K., Taagholt, S. J., & Svendsen, L. (1995). Clustering of sleep electroencephalographic patterns in patients with the fibromyalgia syndrome. *British Journal of Rheumatology*, *34*(12), 1151–1156.
- Drewes, A. M., Nielsen, K. D., Hansen, B., Taagholt, S. J., Bjerregard, K., & Svendsen, L. (2000). A longitudinal study of clinical symptoms and sleep parameters in rheumatoid arthritis. *Rheumatology*, *39*, 1287–1289.
- Edinger, J. D., Wohlgenuth, W. K., Radtke, R. A., Marsh, G. R., & Quillian, R. E. (2001). Cognitive behavioral therapy for treatment of chronic primary insomnia: A randomized controlled trial. *JAMA*, *285*, 1856–1864.
- Epstein, L. J., Strollo, P. J. J., Donegan, R. B., Delmar, J., Hendrix, C., & Westbrook, P. R. (1995). Obstructive sleep apnea in patients with human immunodeficiency virus (HIV) disease. *Sleep*, *18*, 368–376.
- Evans, F. J. (1983). Sleep, eating, and weight disorders. In K. Richard (Ed.), *Eating and Weight Disorders* (pp. 147–178). New York: Springer.
- Fawcett, J., Edwards, J. H., Kravitz, H. M., & Jefferiss, H. (1987). Alprazolam: An antidepressant? Alprazolam, desipramine, and an alprazolam-desipramine combination in the treatment of adult depressed outpatients. *Journal of Clinical psychopharmacology*, *7*, 295–310.
- Forbes, D., Phelps, A. J., McHugh, A. F., Debenham, P., Hopwood, M., & Creamer, M. (2003). Imagery rehearsal in the treatment of posttraumatic nightmares in Australian veterans with chronic combat-related PTSD: 12-month follow-up data. *Journal of Traumatic Stress*, *16*(5), 509–513.
- Foster, J. H., & Peters, T. J. (1999). Impaired sleep in alcohol misusers and dependent alcoholics and the impact upon outcome. *Alcoholism, Clinical and Experimental Research*, *23*, 1044–1051.
- Fountain, N. B., Kim, J. S., & Lee, S. I. (1998). Sleep deprivation activates epileptiform discharges independent of the activating effects of sleep. *Journal of Clinical Neurophysiology*, *15*, 69–75.
- Fuller, K. H., Waters, W. F., Binks, P. G., & Anderson, T. (1997). Generalized anxiety and sleep architecture: A polysomnographic investigation. *Sleep*, *20*(5), 370–376.
- Funesti, J., Rothenberg, S., Zozula, R., & McAuliffe, V. (1991). *Patterns of sleep in asymptomatic HIV seropositive individuals. International Conference AIDS, vol. 7.*

- Gallego, L., Barreiro, P., del Rio, R., Gonzalez, d. R., Rodriguez-Albarino, A., Gonzalez-Lahoz, J., et al. (2004). Analyzing sleep abnormalities in HIV-infected patients treated with Efavirenz. *Clinical Infectious Diseases*, 38, 430–432.
- Gallup Organization (1995). *Sleep in America*. Princeton, NJ: Author.
- Gatchel, R. J. (2001). A biopsychosocial overview of pretreatment screening of patients with pain. *Clinical Journal of Pain*, 17, 192–199.
- Gillin, J. C., & Drummond, S. P. A. (2000). Medication and substance abuse. In M. Kryger, T. Roth, & W. Dement (Eds.), *Principles and Practices of Sleep Medicine* (2nd ed.). Philadelphia: W.B. Saunders Company.
- Goldsmith, D. R., Wagstaff, A. J., Ibbotson, T., & Perry, C. M. (2004). Spotlight on lamotrigine in bipolar disorder. *CNS Drugs*, 18(1), 63–67.
- Greeff, A. P., & Conradie, W. S. (1998). Use of progressive relaxation training for chronic alcoholics with insomnia. *Psychological Reports*, 82(2), 407–412.
- Green, T. D., Reynolds, C. F., Mulsant, B. H., Pollock, B. G., Miller, M. D., Houck, P. R., et al. (1999). Accelerating antidepressant response in geriatric depression: A post hoc comparison of combined sleep deprivation and paroxetine versus monotherapy with paroxetine, nortpyline, or placebo. *Journal of Geriatric Psychiatry and Neurology*, 12(2), 67–71.
- Hand, G. A., Phillips, K. D., Sowell, R. L., Rojas, M., & Becker, J. (2003). Prevalence of poor sleep quality in HIV+ populations of Americans. *Journal of the South Carolina Medical Association*, 99, 183–187.
- Harman, K., Pivik, R. T., D'Eon, J. L., Wilson, K. G., Swenson, J. R., & Matsunaga, L. (2002). Sleep in depressed and nondepressed participants with chronic low back pain: Electroencephalographic and behaviour findings. *Sleep*, 25, 775–783.
- Harvey, A. G. (2001). Insomnia symptom or diagnosis. *Clinical Psychology Review*, 21(7), 1037–1059.
- Harvey, A. G. (In press). Toward a cognitive theory and therapy for chronic insomnia. *Journal of Cognitive Psychotherapy: An International Quarterly*.
- Hauri, P., & Hawkins, D. R. (1973). Alpha-delta sleep. *Electroencephalography and Clinical Neurophysiology*, 34(3), 233–237.
- Haythornthwaite, J. A., Hegel, M. T., & Kerns, R. D. (1991). Development of a sleep diary for chronic pain patients. *Journal of Pain and Symptom Management*, 6, 65–72.
- Heide, F. J., & Borkovec, T. D. (1983). Relaxation-induced anxiety: Paradoxical anxiety enhancement due to relaxation training. *Journal of Consulting and Clinical Psychology*, 51(2), 171–182.
- Hohagen, F., Lis, S., Krieger, S., Winkelmann, G., Riemann, D., Fritsch-Montero, R., et al. (1994). Sleep EEG of patients with obsessive-compulsive disorder. *European Archives of Psychiatry and Clinical Neuroscience*, 243(5), 273–278.
- Insel, T., Gillin, C., Moore, A., Mendelson, W., Loewenstein, R., & Murphy, D. (1982). The sleep of patients with obsessive-compulsive disorder. *Archives of General Psychiatry*, 39, 1372–1377.
- Irwin, M., McClintick, J., Costlow, C., Fortner, M., White, J., & Gillin, J. C. (1996). Partial night sleep deprivation reduces natural killer and cellular immune responses in humans. *FASEB Journal*, 10, 643–653.
- Issa, F. G., & Sullivan, C. E. (1982). Alcohol, snoring and sleep apnea. *Journal of Neurology, Neurosurgery and Psychiatry*, 45(4), 353–359.
- Jacobs, G. D., Benson, H., & Friedman, R. (1993). Home-based central nervous system assessment of a multifactor behavioral intervention for chronic sleep-onset insomnia. *Behavior Therapy*, 24, 159–174.
- Jernajczyk, W. (1986). Latency of eye movement and other REM sleep parameters in bipolar depression. *Biological Psychiatry*, 21(5–6), 465–472.
- Katz, D. A., & McHorney, C. A. (1998). Clinical correlates of insomnia in patients with chronic illness. *Archives of Internal Medicine*, 158, 1099–1107.
- Kawakami, N., Takatsuka, N., & Shimizu, H. (2004). Sleep disturbance and onset of type 2 diabetes. *Diabetes Care*, 27, 282–283.
- Kaye, J., Kaye, K., & Madow, L. (1983). Sleep patterns in patients with cancer and patients with cardiac disease. *Journal of Psychology*, 114, 107–113.
- Keefe, F. J., Lumley, M., Anderson, T., Lynch, T., Studts, J. L., & Carson, K. L. (2001). Pain and emotion: New research directions. *Journal of Clinical Psychology*, 57, 587–607.
- Kobayashi, T., Misaki, K., Nakagawa, H., Okuda, K., Ota, T., Kanda, I., et al. (1998). Alcohol effect on sleep electroencephalography by fast Fourier transformation. *Psychiatry and Clinical Neurosciences*, 52(2), 154–155.
- Kopta, S., Howard, K., Lowry, J., & Beutler, L. (1994). Patterns of symptomatic recovery in psychotherapy. *Journal of Consulting and Clinical Psychology*, 62, 1009–1016.

- Krakov, B., Johnston, L., Melendrez, D., Hollifield, M., Warner, T. D., Chavez-Kennedy, D., et al. (2001). An open-label trial of evidence-based cognitive behavior therapy for nightmares and insomnia in crime victims with PTSD. *American Journal of Psychiatry*, *158*(12), 2043–2047.
- Krakov, B., Kellner, R., Pathak, D., & Lambert, L. (1995). Imagery rehearsal treatment for chronic nightmares. *Behavior Research and Therapy*, *33*, 837–843.
- Kuo, T., Manber, R., & Loewy, D. (2001). Insomniacs with comorbid conditions achieved comparable improvement in a cognitive behavioral group treatment program as insomniacs without comorbid depression. *Sleep*, *14*, A62.
- Kupfer, D., & Reynolds, C. I. (1992). Sleep and affective disorders. In E. Paykel (Ed.), *Handbook of Affective Disorders* (2nd ed.). Edinburgh: Churchill Livingstone.
- Lacey, J. H., Crisp, A. H., Kalucy, R. S., Hartmann, M. K., & Chien, C. N. (1975). Weight gain and the sleeping electroencephalogram: Study of 10 patients with anorexia nervosa. *British Medical Journal*, *4*, 556–568.
- Latzer, Y., Tzischinsky, O., Wepstein, R., Klein, E., & Lavie, P. (1999). Naturalistic sleep monitoring in women suffering from bulimia nervosa. *International Journal of Eating Disorders*, *26*, 315–321.
- Laurel, C. J., & Krieg, J. C. (2004). Sleep in eating disorders. *Sleep Medicine Reviews*, *8*(2), 109–118.
- Lee, J. H., Reynolds, C. F. r., Hoch, C. C., Buysse, D. J., Mazumdar, S., George, C. J., et al. (1993). Electroencephalographic sleep in recently remitted, elderly depressed patients in double-blind placebo-maintenance therapy. *Neuropsychopharmacology*, *8*(2), 143–150.
- Lee, K. A., Portillo, C. J., & Miramontes, H. (2001). The influence of sleep and activity patterns on fatigue in women with HIV/AIDS. *Journal of the Association of Nurses in AIDS Care*, *12*, 19–27.
- Lentz, M. J., Landis, C. A., Rothermel, J., & Shaver, J. L. (1999). Effects of selective slow wave sleep disruption on musculoskeletal pain and fatigue in middle aged women. *Journal of Rheumatology*, *26*, 1586–1592.
- Lichstein, K. L., Peterson, B. A., Riedel, B. W., Means, M. K., Epperson, M. T., & Aguillard, R. N. (1999). Relaxation to assist sleep medication withdrawal. *Behavior Modification*, *23*(3), 379–402.
- Lichstein, K. L., Riedel, B. W., Wilson, N. M., Lester, K. W., & Aguillard, R. N. (2001). Relaxation and sleep compression for late-life insomnia: A placebo-controlled trial. *Journal of Consulting and Clinical Psychology*, *69*, 227–239.
- Lichstein, K. L., Wilson, N. M., & Johnson, C. T. (2000). Psychological treatment of secondary insomnia. *Psychology and Aging*, *15*(2), 232–240.
- Lindley, C., Vasa, S., Sawyer, W. T., & Winer, E. P. (1998). Quality of life and preferences for treatment following systemic adjuvant therapy for early-stage breast cancer. *Journal of Clinical Oncology*, *16*, 1380–1387.
- Mallon, L., Broman, J. E., & Hetta, J. (2002). Sleep complaints predict coronary artery disease mortality in males: A 12-year follow-up study of a middle-aged Swedish population. *Journal of Internal Medicine*, *251*, 207–216.
- Manber, R., Loewy, D., Kuo, T., Black, J., Palombini, L., & Koester, U. (2001). The efficacy of cognitive behavioral group intervention in a tertiary setting. *Sleep*, *24*, A63.
- Manber, R., Rush, A. J., Thase, M. E., Amow, B., Klein, D., Trivedi, M. H., et al. (2003). The effects of psychotherapy, nefazodone, and their combination on subjective assessment of disturbed sleep in chronic depression. *Sleep*, *26*(2), 130–136.
- Manni, R., Ratti, M. T., & Tartara, A. (1999). Nocturnal eating: Prevalence and features in 120 insomniac referrals. *Sleep*, *20*(9), 734–738.
- Mellinger, G., Balter, M., & Uhlenhuth, E. (1985). Insomnia and its treatment: Prevalence and correlates. *Archives of General Psychiatry*, *42*, 225–232.
- Mellman, T., Kulick-Bell, R., Ashlock, L., & Nolan, B. (1995). Sleep events among veterans with combat-related posttraumatic stress disorder. *American Journal of Psychiatry*, *152*(1), 110–115.
- Mellman, T., & Uhde, T. (1989). Sleep panic attacks: New clinical findings and theoretical implications. *American Journal of Psychiatry*, *146*(9), 1204–1207.
- Mellman, T. A., & Uhde, T. W. (1989). Electroencephalographic sleep in panic disorder. *Archives of General Psychiatry*, *46*, 178–184.
- Mendelson, W. B. (2000). Hypnotics: Basic mechanism and pharmacology. In M. H. Kryger, T. Roth, & W. C. Dement (Eds.), *Principles and Practice of Sleep Medicine* (3rd ed.). Philadelphia: W B Saunders.
- Mock, V. (2001). Fatigue management: Evidence and guidelines for practice. *Cancer*, *92*, 1699–1707.
- Moldofsky, H. (1993). Fibromyalgia, sleep disorder and chronic fatigue syndrome. *Ciba Foundation Symposium*, *173*, 262–271.
- Moldofsky, H., & Scarisbrick, P. (1976). Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. *Psychosomatic Medicine*, *38*, 35–44.

- Monti, J. M., & Monti, D. (2000). Sleep disturbance in generalized anxiety disorder and its treatment. *Sleep Medicine Reviews*, 4(3), 263–276.
- Morawetz, D. (2003). Insomnia and depression: Which comes first? *Sleep Research Online*, 5(2), 77–81.
- Morgan, K., Dixon, S., Mathers, N., Thompson, J., & Tomeny, M. (2004). Psychological treatment for insomnia in the regulation of long-term hypnotic drug use. *Health Technology Assessment*, 8, iii-68.
- Morin, C. (1993). *Insomnia*. New York: Guilford Press.
- Morin, C., Culbert, J., & Schwartz, S. (1994). Nonpharmacological interventions for insomnia: A meta-analysis of treatment efficacy. *American Journal of Psychiatry*, 151, 1172–1180.
- Morin, C., Stone, J., McDonald, K., & Jones, S. (1994). Psychological management of insomnia: A clinical replication series with 100 patients. *Behavior Therapy*, 25(2), 291–309.
- Morin, C. M., Bastien, C., Guay, B., Radouco-Thomas, M., Leblanc, J., & Vallieres, A. (2004). Randomized clinical trial of supervised tapering and cognitive behavior therapy to facilitate benzodiazepine discontinuation in older adults with chronic insomnia. *American Journal of Psychiatry*, 161, 332–342.
- Morin, C. M., Colecchi, C., Stone, J., & Sood, R. M. (1999). Behavioral and pharmacological therapies for late-life insomnia: A randomized controlled trial. *JAMA*, 281, 991–999.
- Morin, C. M., Gibson, D., & Wade, J. (1998). Self-reported sleep and mood disturbance in chronic pain patients. *The Clinical Journal of Pain*, 14, 311–314.
- Morin, C. M., Kowatch, R. A., Barry, T., & Walton, E. (1993). Cognitive-behavior therapy for late-life insomnia. *Journal of Consulting and Clinical Psychology*, 61(1), 137–146.
- Morin, C. M., Kowatch, R. A., & O'Shanick, G. (1990). Sleep restriction for the inpatient treatment of insomnia. *Sleep*, 13, 183–186.
- Morin, C. M., Kowatch, R. A., & Wade, J. B. (1989). Behavioral management of sleep disturbances secondary to chronic pain. *Journal of Behavior Therapy and Experimental Psychiatry*, 20, 295–302.
- Mosko, S. S., Dickel, M. J., & Ashurst, J. (1988). Night-to-night variability in sleep apnea and sleep-related periodic limb movements in the elderly. *Sleep*, 11, 340–348.
- Murtagh, D., & Greenwood, K. (1995). Identifying effective psychological treatments for insomnia: A meta-analysis. *Journal of Consulting and Clinical Psychology*, 63, 79–89.
- Neumeister, A., Goessler, R., Lucht, M., Kapitany, T., Bamas, C., & Kasper, S. (1996). Bright light therapy stabilizes the antidepressant effect of partial sleep deprivation. *Biological Psychiatry*, 39(1), 16–21.
- Nicassio, P. M., Boylan, M. B., & McCabe, T. G. (1982). Progressive relaxation, EMG biofeedback and biofeedback placebo in the treatment of sleep-onset insomnia. *British Journal of Medical Psychology*, 55, 159–166.
- Nierenberg, A. A., Alder, L. A., Peselow, E., Zornberg, G., & Rosenthal, M. (1994). Trazodone for antidepressant-associated insomnia. *American Journal of Psychiatry*, 151(7), 1069–1072.
- Nierenberg, A. A., Keefe, B. R., Leslie, V. C., Alpert, J. E., Pava, J. A., Worthington, J. J., et al. (1999). Residual symptoms in depressed patients who respond acutely to fluoxetine. *Journal of Clinical Psychiatry*, 60(4), 221–225.
- Nokes, K. M., & Kendrew, J. (2001). Correlates of sleep quality in persons with HIV disease. *Journal of the Association of Nurses in AIDS Care*, 12, 17–22.
- Norman, S. E., Chediak, A. D., Freeman, C., Kiel, M., Mendez, A., Duncan, R., et al. (1992). Sleep disturbances in men with asymptomatic human immunodeficiency (HIV) infection. *Sleep*, 15, 150–155.
- Norman, S. E., Chediak, M., Kiel, H., Gazeroglu, H., & Mendez, A. (1990). HIV infection and sleep: Follow-up studies. *Sleep Research*, 19, 339.
- Nunez, M., Gonzalez, d. R., Gallego, L., Jimenez-Nacher, I., Gonzalez-Lahoz, J., & Soriano, V. (2001). Higher efavirenz plasma levels correlate with development of insomnia. *Journal of Acquired Immune Deficiency Syndromes*, 28, 399–400.
- Ohayon, M., & Roth, T. (2001). What are the contributing factors for insomnia in the general population? *Journal of Psychosomatic Research*, 51, 745–755.
- Onen, S. H., Alloui, A., Gross, A., Eschallier, A., & Dubray, C. (2001). The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. *Journal of Sleep Research*, 10, 35–42.
- Perlis, M. L., Merica, H., Smith, M. T., & Giles, D. E. (2001). Beta EEG in insomnia. *Sleep Medicine Reviews*, 5, 363–374.
- Perlis, M. L., Sharpe, M. C., Smith, M. T., Greenblatt, D. W., & Giles, D. E. (2001). Behavioral treatment of insomnia: Treatment outcome and the relevance of medical and psychiatric morbidity. *Journal of Behavioral Medicine*, 24(3), 281–296.

- Perlis, M. L., Smith, M. T., Orff, H. J., Andrews, P. J., Gillin, J. C., & Giles, D. E. (2002). The effects of an orally administered cholinergic agonist on REM sleep in major depression. *Biological Psychiatry*, *51*, 457–462.
- Pieters, G., Theys, P., Vandereycken, W., Leroy, B., & Peuskens, J. (2004). Sleep variables in anorexia nervosa: Evolution with weight restoration. *International Journal of Eating Disorders*, *35*(3), 342–347.
- Pilowsky, I., Crettenden, I., & Townley, M. (1985). Sleep disturbance in pain clinic patients. *Pain*, *23*, 27–33.
- Porcu, S., Ferrara, M., Urbani, L., Bellatreccia, A., & Casagrande, M. (1998). Smooth pursuit and saccadic eye movements as possible indicators of nighttime sleepiness. *Physiology and Behavior*, *65*, 437–443.
- Portsmouth, S., Imami, N., Pires, A., Stebbing, J., Hand, J., Nelson, M., et al. (2004). Treatment of primary HIV-1 infection with nonnucleoside reverse transcriptase inhibitor-based therapy is effective and well tolerated. *HIV Medicine*, *5*, 26–29.
- Quesnel, C., Savard, J., Simard, S., Ivers, H., & Morin, C. M. (2003). Efficacy of cognitive-behavioral therapy for insomnia in women treated for nonmetastatic breast cancer. *Journal of Consulting and Clinical Psychology*, *71*, 189–200.
- Raymond, I., Nielsen, T. A., Lavigne, G., Manzini, C., & Choiniere, M. (2001). Quality of sleep and its daily relationship to pain intensity in hospitalized adult burn patients. *Pain*, *92*, 381–388.
- Reynolds III, C., Kupfer, D., Thase, M., Frank, E., Jarret, D., Coble, P., et al. (1990). Sleep, gender, and depression: An analysis of gender effects on the electroencephalographic sleep of 302 depressed outpatients. *Biological Psychiatry*, *28*, 673–684.
- Reynolds, C. F., Frank, E., Houck, P. R., Mazumdar, S., Dew, M. A., Cornes, C., et al. (1997). Which elderly patients with remitted depression remain well with continued interpersonal psychotherapy after discontinuation of antidepressant medication? *American Journal of Psychiatry*, *154*(7), 958–962.
- Reynolds, C. F., & Kupfer, D. J. (1987). Sleep research in affective illness: State of the art circa 1987 (state-of-the-art review). *Sleep*, *10*, 199–215.
- Reynolds, C. F., Shaw, D., Newton, T., Coble, P., & Kupfer, D. (1983). EEG sleep in outpatients with generalized anxiety. *Psychiatry Research*, *8*, 81–89.
- Rickels, K., Feighner, J. P., & Smith, W. T. (1985). Alprazolam, amitriptyline, doxepin, and placebo in the treatment of depression. *Archives of General Psychiatry*, *42*, 134–141.
- Riemann, D., Konig, A., Hohgen, F., Kiemen, A., Voderholzer, U., Backhaus, J., et al. (1999). How to preserve the antidepressive effects of sleep deprivation: A comparison of sleep phase advance and sleep phase delay. *European Archives of Psychiatry and Clinical Neuroscience*, *249*(5), 231–237.
- Ripu, D. J., & Thase, M. E. (2004). Treatment of insomnia associated with clinical depression. *Sleep Medicine Review*, *8*, 19–30.
- Robbins, J. L., Phillips, K. D., Dudgeon, W. D., & Hand, G. A. (2004). Physiological and psychological correlates of sleep in HIV infection. *Clinical Nursing Research*, *13*, 33–52.
- Robinson, D., Walsleben, J., Pollack, S., & Lerner, G. (1998). Nocturnal polysomnography in obsessive-compulsive disorder. *Psychiatry Research*, *80*(3), 257–263.
- Roizenblatt, S., Moldofsky, H., Benedito-Silva, A. A., & Tufik, S. (2001). Alpha sleep characteristics in fibromyalgia. *Arthritis and Rheumatism*, *44*(1), 222–230.
- Rothenberg, S., Zozula, R., Funesti, J., & McAuliffe, V. (1990). Sleep habits in asymptomatic HIV-seropositive individuals. *Sleep Research*, *19*, 342.
- Roy-Byrne, P. P., Uhde, T. W., & Post, R. M. (1986). Effects of one night's sleep deprivation on mood and behavior in panic disorder. Patients with panic disorder compared with depressed patients and normal controls. *Archives of General Psychiatry*, *43*(9), 895–899.
- Rybarczyk, B., Lopez, M., Benson, R., Alsten, C., & Stepanski, E. (2002). Efficacy of two behavioral treatment programs for comorbid geriatric insomnia. *Psychology and Aging*, *17*(2), 288–298.
- Sachs, G. S. (2003). Unmet clinical needs in bipolar disorder. *Journal of Clinical Psychopharmacology*, *23*(3 Suppl. 1), S2–S8.
- Saletu-Zyhlarz, G. M., Abu-Bakr, M. H., Anderer, P., Gruber, G., Mandl, M., Strobl, R., et al. (2002). Insomnia in depression: Differences in objective and subjective sleep and awakening quality to normal controls and acute effects of trazodone. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *26*(2), 249–260.
- Saletu-Zyhlarz, G. M., Abu-Bakr, M. H., Anderer, P., Semler, B., Decker, K., Parapatics, S., et al. (2001). Insomnia related to dysthymia: Polysomnographic and psychometric comparison with normal controls and acute therapeutic trials with trazodone. *Neuropsychobiology*, *44*(3), 139–149.

- Savard, J., Miller, S. M., Mills, M., O'Leary, A., Harding, H., & Douglas, S. D. (1999). Association between subjective sleep quality and depression on immunocompetence in low-income women at risk for cervical cancer. *Psychosomatic Medicine*, *61*, 496–507.
- Savard, J., Simard, S., Blanchet, J. B., Ivers, H., & Morin, C. M. (2001). Prevalence, clinical characteristics, and risk factors for insomnia in the context of breast cancer. *Sleep*, *24*(5), 583–590.
- Schneider-Helmert, D., Whitehouse, I., Kumar, A., & Lijzenga, C. (2001). Insomnia and alpha sleep in chronic non-organic pain as compared to primary insomnia. *Neuropsychobiology*, *43*, 54–58.
- Shapiro, C. M., Devins, G. M., Feldman, B., & Levitt, A. J. (1994). Is hypersomnolence a feature of seasonal affective disorder? *Journal of Psychosomatic Medicine*, *38*(1), 49–54.
- Shaver, J. L., Johnston, S. K., Lentz, M. J., & Landis, C. A. (2002). Stress exposure, psychological distress, and physiological stress activation in midlife women with insomnia. *Psychosomatic Medicine*, *64*, 793–802.
- Silberfarb, P. M., Hauri, P. J., Oxman, T. E., & Schnurr, P. (1993). Assessment of sleep in patients with lung cancer and breast cancer. *Journal of Clinical Oncology*, *11*, 997–1004.
- Simeit, R., Deck, R., & Conta-Marx, B. (2004). Sleep management training for cancer patients with insomnia. *Support Care Cancer*, *12*, 176–183.
- Simon, G., & VonKorff, M. (1997). Prevalence, burden, and treatment of insomnia in primary care. *American Journal of Psychiatry*, *154*, 1417–1423.
- Sloan, E. P., Natarajan, M., Baker, B., Dorian, P., Mironov, D., Barr, A., et al. (1999). Nocturnal and daytime panic attacks—comparison of sleep architecture, heart rate variability, and response to sodium lactate challenge. *Biological Psychiatry*, *45*(10), 1313–1320.
- Smith, M. T., & Neubauer, D. N. (2003). Cognitive behavior therapy for chronic insomnia. *Clinical Cornerstone*, *5*, 28–40.
- Smith, M. T., Perlis, M. L., Park, A., Smith, M. S., Pennington, J., Giles, D. E., et al. (2002). Comparative meta-analysis of pharmacotherapy and behavior therapy for persistent insomnia. *American Journal of Psychiatry*, *159*(1), 5–11.
- Smith, M. T., Perlis, M. L., Smith, M. S., & Giles, D. E. (2001). Pre-sleep cognitions in patients with insomnia secondary to chronic pain. *Journal of Behavioral Medicine*, *24*, 93–114.
- Smith, M. T., Perlis, M. L., Smith, M. S., Giles, D. E., & Carmody, T. P. (2000). Sleep quality and presleep arousal in chronic pain. *Journal of Behavioral Medicine*, *23*, 1–13.
- Spiegel, K., Leproult, R., & Van Cauter, E. (1999). Impact of sleep debt on metabolic and endocrine function. *Lancet*, *354*(9188), 1435–1439.
- Spielman, A., Caruso, L., & Glovinsky, P. (1987). A behavioral perspective on insomnia treatment. *Psychiatric Clinics of North America*, *10*, 541–553.
- Spielman, A., Saskin, P., & Thorpy, M. (1987). Treatment of chronic insomnia by restriction of time in bed. *Sleep*, *10*, 45–56.
- Spielman, A. J., & Anderson, M. E. (1999). The clinical interview and treatment planning as a guide to understanding the nature of insomnia: The CCNY insomnia interview. In S. Chokroverty (Ed.), *Sleep Disorders Medicine: Basic Science, Technical Considerations, and Clinical Aspects* (2nd ed.). Boston: Butterworth Heinemann.
- Sridhar, G. R., & Madhu, K. (1994). Prevalence of sleep disturbances in diabetes mellitus. *Diabetes Research and Clinical Practice*, *23*, 183–186.
- Stone, A. A., Broderick, J. E., Porter, L. S., & Kaell, A. T. (1997). The experience of rheumatoid arthritis pain and fatigue: Examining momentary reports and correlates over one week. *Arthritis Care and Research*, *10*, 185–193.
- Taasan, V. C., Block, A. J., Boysen, P. G., & Wynne, J. W. (1981). Alcohol increases sleep apnea and oxygen desaturation in asymptomatic men. *American Journal of Medicine*, *71*(2), 240–245.
- Thase, M. E. (1998). Depression, sleep, and antidepressants. *Journal of Clinical Psychiatry*, *59*, 55–65.
- Thase, M. E. (1999). Antidepressant treatment of the depressed patient with insomnia. *Journal of Clinical Psychiatry*, *60*, 28–31.
- Thase, M. E., Buysse, D. J., Frank, E., Cherry, C. R., Cornes, C. L., Mallinger, A. G., et al. (1997). Which depressed patients will respond to interpersonal psychotherapy? The role of abnormal EEG sleep profiles. *American Journal of Psychiatry*, *154*(4), 502–509.
- Thase, M. E., Reynolds, C. F. r., Frank, E., Jennings, J. R., Nofzinger, E., Fasiczka, A. L., et al. (1994). Polysomnographic studies of unmedicated depressed men before and after cognitive behavioral therapy. *American Journal of Psychiatry*, *151*(11), 1615–1622.

- Thase, M. E., Rush, A. J., Manber, R., Kornstein, S. G., Klein, D., Markowitz, J. C., et al. (2002). Effects of nefazodone and cognitive behavioral analysis system of psychotherapy, singly and in combination, on insomnia associated with chronic depression. *Journal of Clinical Psychiatry*, 63(6), 493–500.
- Tsao, J. C., Dobalian, A., Moreau, C., & Dobalian, K. (2004). Stability of anxiety and depression in a national sample of adults with human immunodeficiency virus. *Journal of Nervous and Mental Disease*, 192, 111–118.
- Turner, R. M., & Asher, L. M. (1979). Controlled comparison of progressive relaxation, stimulus control, and paradoxical intention therapies for insomnia. *Journal of Consulting and Clinical Psychology*, 47(3), 500–508.
- Tzischinsky, O., Latzer, Y., Epstein, R., & Naveh, T. (2000). Sleep–wake cycles in women with binge eating disorder. *International Journal of Eating Disorders*, 27, 43–48.
- Uhde, T. W. (2000). Anxiety disorders. In M. H. Kryger, T. Roth, & W. C. Dement (Eds.), *Principles and Practice of Sleep Medicine* (3rd ed.). New York: WB Saunders.
- van der Kolk, B., Blitz, R., Burr, W., Sherry, S., & Hartmann, E. (1984). Nightmares and trauma: A comparison of nightmares after combat with lifelong nightmares in veterans. *American Journal of Psychiatry*, 141(12), 187–190.
- Van Londen, L., Molenaar, R. P., Goekoop, J. G., Zwinderman, A. H., & Rooijmans, H. G. (1998). Three- to 5-year prospective follow-up of outcome in major depression. *Psychological Medicine*, 28(3), 731–735.
- van't Spijker, A., Trijsburg, R. W., & Duivendoorn, H. J. (1997). Psychological sequelae of cancer diagnosis: A meta-analytical review of 58 studies after 1980. *Psychosomatic Medicine*, 59, 280–293.
- Vermeeren, A. (2004). Residual effects of hypnotics: Epidemiology and clinical implications. *CNS Drugs*, 18, 297–328.
- Vgontzas, A. N., & Chrousos, G. P. (2002). Sleep, the hypothalamic-pituitary-adrenal axis, and cytokines: Multiple interactions and disturbances in sleep disorders. *Endocrinology and Metabolism Clinics of North America*, 31, 15–36.
- Vitiello, B., Burnam, M. A., Bing, E. G., Beckman, R., & Shapiro, M. F. (2003). Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry*, 160, 547–554.
- Wehr, T. (1990). Effects of wakefulness and sleep on depression and mania. In J. Montplaisir, & R. Godbout (Eds.), *Sleep and Biopsychological Rhythms: Basic Mechanisms and Application to Psychiatry* (pp. 42–86). New York: Oxford University Press.
- Wehr, T. A., Turner, E. H., Shimada, J. M., Lowe, C. H., Barker, C., & Leibenluft, E. (1998). Treatment of rapidly cycling bipolar patient by using extended bed rest and darkness to stabilize the timing and duration of sleep. *Biological Psychiatry*, 43(11), 822–828.
- Wehr, T. A., & Wirz-Justice, A. (1982). Circadian rhythm mechanism in affective illness and in antidepressant drug action. *Pharmacopsychiatry*, 15, 31–39.
- Weigand, L. (1990). Sleep and resistive loading influences on human upper airway collapsibility. *Progress in Clinical and Biological Research*, 345, 157–166.
- Weigand, L., Zwillich, C. W., & White, D. P. (1989). Collapsibility of the human upper airway during normal sleep. *Journal of Applied Physiology*, 66(4), 1800–1808.
- Wever, R. A. (1965). Mathematical model for circadian rhythms. In J. Aschoff (Ed.), *Circadian Clocks* (pp. 47–63). Amsterdam: North-Holland Publishing Co.
- Wher, T. A., Sack, D. A., & Duncan, W. C. (1983). Biological rhythms in manic depressive illness. In T. A. Wher, & F. K. Goodwin (Eds.), *Circadian Rhythms In Psychiatry* (pp. 129, 184). Pacific Grove, CA: The Boxwood Press.
- Wiegand, M. H., Lauer, C. J., & Schreiber, W. (2001). Patterns of response to repeated total sleep deprivations in depression. *Journal of Affective Disorders*, 64(2–3), 257–260.
- Wilson, K. G., Eriksson, M. Y., D'Eon, J. L., Mikail, S. F., & Emery, P. C. (2002). Major depression and insomnia in chronic pain. *Clinical Journal of Pain*, 18, 77–83.
- Wilson, K. G., Watson, S. T., & Currie, S. R. (1998). Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. *Pain*, 75, 75–84.
- Winkelman, J. W., Herzog, D. B., & Fava, M. (1999). The prevalence of sleep-related eating disorder in psychiatric and non-psychiatric populations. *Psychological Medicine*, 29(6), 1461–1466.
- Winokur, A., & Reynolds, C. F. I. (1994). The effects of antidepressants and anxiolytics on sleep physiology. *Primary Psychiatry*, 1, 22–27.
- Wittig, R. M., Zorick, F. J., Blumer, D., Heilbronn, M., & Roth, T. (1982). Disturbed sleep in patients complaining of chronic pain. *Journal of Nervous and Mental Disease*, 170, 429–431.
- Zayfert, C., & DeViva, J. C. (2004). Residual insomnia following cognitive behavioral therapy for PTSD. *Journal of Traumatic Stress*, 17, 69–73.