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Interactions between Disordered Sleep, Post-Traumatic Stress Disorder, and Substance Use Disorders

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Abstract

Disordered sleep is associated with a number of adverse health consequences and is an integral component of many psychiatric disorders. Rates of substance use disorders (SUDs) are markedly higher among individuals with posttraumatic stress disorder (PTSD), and this relationship may be partly mediated by disturbed sleep. Sleep disturbances (e.g. insomnia, daytime sleepiness, vivid nightmares) are hallmark features of PTSD and there is evidence that individuals with PTSD engage in substance use as a means of coping with these symptoms. However, prolonged substance use can lead to more severe sleep disturbances due to the development of tolerance and withdrawal. Behavioral or pharmacological treatment of disordered sleep is associated with improved daytime symptoms and psychosocial functioning among individuals who have developed PTSD. Initial research also suggests that improving sleep could be similarly beneficial in reducing coping oriented substance use and preventing relapse among those seeking treatment for SUDs. Together, these findings suggest that ameliorating sleep disturbance among at-risk individuals would be a viable target for the prevention and treatment of PTSD and associated SUDs, but prospective research is needed to examine this hypothesis. Enhanced understanding of the interrelation between sleep, PTSD, and SUDs may yield novel prevention and intervention approaches for these costly, prevalent and frequently co-occurring disorders.

Introduction

Sleep is a dynamic and complex set of physiological states that is an essential component of life. Sleep is characterized by a constellation of CNS features, including a unique profile of

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brain-wave activity, eye movements, and muscle activity (Colrain, 2011). There are a number of ways in which sleep can be disrupted. In fact, there are now close to 90 distinct sleep disorders characterized in the International Classification of Sleep Disorders (ICSD, (AASM, 2001). Sleep disorders are classified under 2 sub-types: 1) dyssomnias, which are disorders that produce either insomnia (defined as the chronic inability to initiate or maintain sleep, or non-restorative sleep) or hypersomnia (defined as excessive sleepiness); and 2) parasomnias, which are disorders that directly impact or occur during sleep, but themselves do not cause insomnia or excessive sleepiness (e.g., sleep walking, bruxism, periodic limb movements).

Epidemiological research estimates that about 30-40% of the adolescent and adult population experience frequent and clinically important problems with sleep (CDC, 2011b). Insomnia is the most common sleep disorder, affecting approximately 6-10% of the adult population (Roth, 2007). Insufficient sleep (i.e. < 7 hours per episode, on average for adults), snoring/obstructed breathing, daytime sleepiness, and narcolepsy are also common types of disordered sleep reported in national surveys (CDC, 2011b; Hillman & Lack, 2013). Disordered sleep can negatively impact physical health (e.g. increased risk of cardiovascular disease, immune function, diabetes), psychological well-being (e.g. increased risk for and severity of anxiety, depression, posttraumatic stress disorder, substance use disorders), and cognitive function (e.g. decreased attention, memory, and decision-making skills, poor work/school performance, and increased incidence of occupational and motor vehicle accidents) (CDC, 2011b; Shekleton, Rogers, & Rajaratnam, 2010; Stores, 2007).

Posttraumatic stress disorder (PTSD) and substance use disorders (SUD) are prevalent and frequently co-occurring psychiatric illnesses that are both highly associated with disturbed sleep. PTSD affects an estimated 5 million people in the U.S. each year and is characterized by an inability to recover from a stress reaction following exposure to a traumatic event (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). The misuse of alcohol, tobacco, and illicit drugs is also a significant public health and economic burden with far reaching impact (CDC, 2011a; SAMHSA, 2011a; 2011b). Increasingly, research suggests bi-directional associations between disordered sleep, PTSD, and SUD, yet few have examined the inter-relation of all three disorders. The primary aim of this review is to summarize the extant evidence on the intersection of sleep disorders with PTSD and SUD respectively, including discussion of how sleep disturbances may uniquely contribute to the co-occurrence and severity of both PTSD and SUD. We conclude by reviewing the strength of the existing evidence suggesting that treatment of sleep disorders is a logical clinical target for efforts at the prevention and/or treatment of PTSD and SUDs. Literature searches were conducted using the PubMed database for articles relevant to the scope of the present review, but did not include a full systematic review of the literature.

PTSD and Substance Use Directly Impact Sleep

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA, 2013) defines PTSD as the non-remittance of at least 6 of its symptoms (i.e., at least 1 intrusion symptom, 1 avoidance symptom, 2 negative cognition/mood symptoms and, 2 arousal symptoms) for 1 month or longer after exposure to a traumatic event. Sleep disturbance, including insomnia

and nightmares, is the primary presenting concern among individuals with PTSD and is considered the disorder's hallmark symptom (Germain, 2013; Ross, Ball, Sullivan, & Caroff, 1989). In fact, 70-87% of individuals with PTSD experience insomnia and up to 88% report the occurrence of frequent and distressing nightmares, rates that far exceed prevalence in the general population (Foa, Riggs, & Gershuny, 1995; Forbes, et al., 2003; Leskin, Woodward, Young, & Sheikh, 2002). Individuals with PTSD also have higher rates of sleep-disordered breathing (SDB) and parasomnias compared with the general population (Maher, Rego, & Asnis, 2006). The severity of sleep disturbance among those with PTSD does not appear to be mediated by gender, age, cooccurring psychiatric problems, or type of trauma that precipitated the development of PTSD (Germain, Buysse, Shear, Fayyad, & Austin, 2004). This suggests that disordered sleep is a core symptom of PTSD that develops directly from the disorder.

The acute use of psychoactive substances can also have significant effects on sleep, but the effect varies as a function of pharmacological mechanism and duration/frequency of use. One of the most basic methods of classifying psychoactive substances is by acute effects on physiological arousal (See Table 1). For example, alcohol, benzodiazepines, nonbenzodiazepine hypnotics, cannabis, and opioids are associated with increased subjective reports of sedation and reduced latency to sleep onset following acute drug administration (Cousens & DiMascio, 1973; Dimsdale, Norman, DeJardin, & Wallace, 2007; Gorelick, et al., 2013; Mitler, Dawson, Henriksen, Sobers, & Bloom, 1988; Meyer & Quenzer, 2005; Morin, Jarvis, & Lynch, 2007; Wang & Teichtahl, 2007). In contrast, amphetamines, caffeine, cocaine, MDMA, nicotine, and serotinergic hallucinogens (e.g. LSD, psilocybin-containing mushrooms) typically increase arousal following acute dosing, resulting in difficulty initiating sleep, less total sleep time, and daytime somnolence the following day in the absence of continued substance use (Davila, Hurt, Offord, Harris, & Shepard, 1994; Gillin, Lardon, Ruiz, Golshan, & Salin-Pascual, 1994; Johanson, Roehrs, Schuh, & Warbasse, 1999; Kirkpatrick, Gunderson, Levin, Foltin, & Hart, 2012; Kuypers, Wingen, Samyn, Limbert, & Ramaekers, 2007; Perez, et al., 2008; Vollenweider, Liechti, Gamma, Greer, & Geyer, 2002).

However, the effects of substance use on sleep are more complicated than this simple dichotomous categorization based on their acute effects on arousal. Psychoactive substances can impact sleep architecture and sleep continuity beyond initial effects on latency to sleep onset. Acute effects can also change with the development of tolerance, and withdrawal following cessation of chronic substance use is associated with sleep impairment across drug classes. For example, though acute alcohol administration has sedating qualities and reduces latency to sleep onset, acute use is also associated with an increase in the number of awakenings and respiratory disturbances during the night (Mitler et al., 1988). Thus, while alcohol may increase sedation and reduce sleep latency, the overall quantity and quality of sleep may be impaired. Moreover, chronic use of alcohol is associated with increased latency to sleep onset and decreased total sleep time (Clark, et al., 1998; Drummond, Gillin, Smith, & DeModena, 1998; Landolt & Gillin, 2001; Yules, Lippman, & Freedman, 1967), effects that persist for months, and possibly years, after cessation of heavy drinking (Brower, Krentzman, & Robinson, 2011). Comparable patterns of effects (tolerance to acute effects and significant sleep disturbance during withdrawal) have also been demonstrated

following frequent use of benzodiazepines, cannabis, and opioids (Asaad, Ghanem, Abdel Samee, & El-Habiby, 2011; Bolla, et al., 2010; Chouinard, 2004; Freemon, 1974; Jones, Benowitz, & Herning, 1981; Paturi, Surani, & Ramar, 2011; Roehrs, Vogel, & Roth, 1990; Vandrey, Smith, McCann, Budney, & Curran, 2011; Wang & Teichtahl, 2007).

Not surprisingly, chronic use of substances that increase arousal is associated with significant sleep impairment, characterized by insomia during periods of use followed by hypersomia following abrupt cessation (i.e., a “crash”; Jaehne, Loessl, Barkai, Riemann, & Hornyak, 2009; Pace-Schott, et al., 2005; Wetter & Young, 1994; Zhang, Samet, Caffo, & Punjabi, 2006). Interestingly, the disordered sleep that occurs during stimulant withdrawal is often masked by subjective perceptions of improved sleep, a phenomenon referred to as “occult insomnia” (Morgan & Malison, 2007; Morgan, et al., 2006; Pace-Schott, et al., 2005). Long-term misuse of stimulant drugs is also associated with reduced sleep time, poor sleep continuity and daytime somnolence for weeks to months after abrupt cessation and initial “crash” hypersomnia (Allen, McCann, & Ricaurte, 1993; Colrain, Trinder, & Swan, 2004; Gossop, Bradley, & Brewis, 1982; Jaehne, et al., 2009; Matuskey, Pittman, Forselius, Malison, & Morgan, 2011; McCann & Ricaurte, 2007; McCann, Sgambati, Schwartz, & Ricaurte, 2009; McGregor, Srisurapanont, Mitchell, Wickes, & White, 2008; Morgan & Malison, 2007; Morgan, et al., 2006; Pace-Schott, et al., 2005).

Clinical Importance of Disturbed Sleep in PTSD and SUD

The sleep disturbances that result from PTSD and substance use can have significant clinical consequences. With respect to PTSD, recent research indicates that the presence and severity of sleep disturbance among those with PTSD is associated with increased substance misuse, greater daytime PTSD symptoms, poor physical health (e.g. increased pain, hypertension, obesity), increased suicidal ideation/behavior, reduced quality of life, and worse PTSD treatment outcomes (Clum, Nishith, & Resick, 2001; Germain, et al., 2004; Krakow, et al., 2000; Mustafa, Erokwu, Ebose, & Strohl, 2005; Nishith, Resick, & Mueser, 2001; Saladin, Brady, Dansky, & Kirkpatrick, 1995). In addition, disturbed sleep is a particularly treatment resistant symptom of PTSD, often not remitting in the context of PTSD interventions even when other symptoms of PTSD decrease (Neylan, et al., 1998; Zayfert & DeViva, 2004). Thus, sleep appears to have a substantial health impact among those with PTSD and is viewed as a critical clinical target for the treatment of PTSD.

While it has long been established that PTSD causes significant sleep disturbance (Buck & Walker, 1982; Ross, et al., 1989), recent research indicates that disordered sleep is also a risk factor for the development of PTSD (Babson & Feldner, 2010; Spoormaker & Montgomery, 2008). According to a large metropolitan survey, 61% of individuals with PTSD had disordered sleep prior to trauma exposure (Ohayon & Shapiro, 2000). In prospective research, pre-deployment insomnia was a significant predictor of post-deployment PTSD (Gehrman, et al., 2013) and sleep disturbances within the first month of trauma exposure predicted the likelihood of meeting diagnostic criteria for PTSD 6 weeks (Mellman, David, Kulick-Bell, Hebding, & Nolan, 1995), 2 months (Kobayashi & Mellman, 2012), 3 months (Bryant, Creamer, O'Donnell, Silove, & McFarlane, 2010), and 1 year after traumatic event exposure (Koren, Arnon, Lavie, & Klein, 2002). This finding reiterates the

overall importance of sleep on mental health, and suggests that sleep-focused interventions immediately after trauma exposure may be a target for possibly preventing or reducing the severity of PTSD.

The clinical importance of sleep disturbance in SUDs is evident in the fact that disturbed sleep is a valid and reliable withdrawal symptom across substances of abuse, independent of drug class or acute effects of the substance on sleep/arousal. Moreover, research increasingly indicates that abstinence-induced sleep disturbances can contribute to relapse among those trying to quit substance use. Among treatment-seeking problem drinkers, especially those with cooccurring psychiatric illnesses, severity of sleep problems is a strong predictor of relapse (Brower, Aldrich, & Hall, 1998; Brower, et al., 2011; Chakravorty, et al., 2013; Kolla, Mansukhani, & Schneekloth, 2011). Similarly, clinical survey and prospective studies indicate that self-reported sleep disturbance predicts and/or contributes to relapse among those trying to quit using cannabis (Babson, Boden, & Bonn-Miller, 2013; Babson, Boden, Harris, Stickle, & Bonn-Miller, 2013; Budney, Vandrey, Hughes, Thostenson, & Bursac, 2008) and tobacco (Zhou, et al., 2009), though this relation was not observed in a second tobacco study (Okun, Levine, Houck, Perkins, & Marcus, 2011). Thus, disordered sleep is a common problem for people attempting to quit chronic substance use, and is considered by some a “universal” substance withdrawal symptom that is strongly associated with relapse (Brower et al., 2010).

In addition to sleep disturbance as a withdrawal symptom, chronic use of some substances has been associated with sleep disturbances that persist beyond the time window typically associated with other withdrawal symptoms. For example, among cannabis users, abrupt cessation of daily use is associated with experiencing unusually vivid/intense dreams. In one laboratory study, this effect persisted through the end of a study where participants were observed for 45 days of abstinence (Budney, Moore, Vandrey, & Hughes, 2003). Poor sleep continuity may persist after several months of sustained abstinence following chronic opioid use (Howe, Hegge, & Phillips, 1980; Wang & Teichtahl, 2007). Several laboratory studies have objectively demonstrated that abstinent MDMA users have impaired sleep relative to matched controls, including decreased total sleep time and non-REM sleep, and increased rates of sleep-related breathing disorders (Allen et al., 1993; McCann & Ricaurte, 2007; McCann et al., 2009). Interpretation of these findings is somewhat difficult though because MDMA users typically misuse several other substances, and the literature on long-term effects of MDMA on sleep is scant relative to other substances.

Is Sleep a Good Target for Prevention/Treatment of SUD Among Those With PTSD?

The prior sections have detailed how sleep disturbance is a key feature for both PTSD and SUDs individually, but it is important to note that PTSD and SUDs themselves are highly co-occurring and the increased rate of SUDs among individuals with PTSD may be partly mediated by disturbed sleep. Indeed, people with a lifetime diagnosis of PTSD are up to 3 times more likely to have a SUD than those without PTSD, and rates of PTSD are significantly greater among those with SUD compared with the general population (Jacobsen, Southwick, & Kosten, 2001; Mills, Teesson, Ross, & Peters, 2006). Individuals,

particularly females, with SUDs are more likely to experience trauma, which puts them at an increased risk for developing PTSD (Johnson, Striley, & Cottler, 2006). Importantly, longitudinal research has shown that PTSD, not just trauma exposure, predicts increased substance use (Chilcoat & Breslau, 1998). In addition, specific neurobiological responses to stress/trauma (e.g. reduced cortisol, endocannabinoids, and hippocampal brain volume, increased corticotrophin-releasing factor) may explain the increased vulnerability for substance misuse among those with PTSD (Gordon, 2002; Jacobsen, et al., 2001; Neumeister, et al., 2013; Norman, et al., 2012). Studies that evaluate substance use motives clearly indicate that people with PTSD engage in substance use behavior as a means for coping with or "self-medicating" symptoms of PTSD (Blanco, et al., 2013; Bonn-Miller, Babson, Vujanovic, & Feldner, 2010; Bonn-Miller, Boden, Bucossi, & Babson, 2014; Dixon, Leen-Feldner, Ham, Feldner, & Lewis, 2009; Nishith et al., 2001; Villagonzalo, et al., 2011). Additionally, among those who present for treatment with concurrent PTSD and SUD, remission of PTSD symptoms during treatment is associated with better SUD outcomes compared with patients whose PTSD symptoms do not remit (Read, Brown, & Kahler, 2004). However, little research has been conducted to specifically evaluate the role sleep-related symptoms of PTSD play in the development and maintenance of SUD.

Improved sleep has been documented as a motivation for illicit use of substances that decrease arousal (Barth, et al., 2013; Roehrs & Roth, 2001; Schofield, et al., 2006). This type of "self-medicating" behavior, and the tolerance that can result from chronic use of these substances puts these individuals at risk of becoming reliant on substances to sleep. This is particularly true for individuals with PTSD, who have high rates of insomnia, nightmares, and other sleep problems. Moreover, once a chronic pattern of substance use has been established, deleterious effects of withdrawal can exacerbate sleep problems related to PTSD, thus creating an interdependent cycle of substance use to manage sleep disturbances stemming from both PTSD and SUD.

Three empirical studies have examined coping-oriented substance use among individuals with PTSD. One study examined the influence of PTSD symptoms and sleep difficulties on alcohol use motives among female rape victims with severe PTSD (Nishith et al., 2001). Though no associations were observed between PTSD symptoms and alcohol use motives, disordered sleep was independently associated with coping-oriented alcohol use (i.e. patients reported using alcohol to reduce negative affect). In a similar study, Bonn-Miller and colleagues (2010) investigated the role of PTSD symptoms and sleep problems with respect to cannabis use motives in adults with PTSD who reported past-month cannabis use. Similar to the first study (Nishith et al., 2001), no association was observed between PTSD symptoms and use motives, but disturbed sleep was independently associated with coping-oriented cannabis use. In addition to replicating the findings of Nishith and colleagues (2001) among cannabis users, this study also documented a significant interaction between sleep problems and PTSD symptom severity with regard to coping-oriented cannabis use. Specifically, self-reported sleep predicted levels of coping-oriented cannabis use among those with both low and high PTSD symptom severity.

More recently, a study examined the sleep-specific role of cannabis use among individuals with PTSD by explicitly assessing sleep motives, rather than coping motives more broadly

(Bonn-Miller, Babson, & Vandrey, 2014). Assessments conducted among a sample of medical cannabis users indicated that individuals with high PTSD scores were more likely to use cannabis to improve sleep, as well as for coping reasons more broadly, compared with those who reported low PTSD scores. Further, a significant interaction between cannabis use and PTSD scores was observed indicating that those with high PTSD scores who used cannabis for sleep promoting purposes reported greater cannabis use frequency compared with individuals with low PTSD scores or those who did not use cannabis to improve sleep.

The research reviewed thus far suggests that sleep problems are common among individuals with PTSD, and that many of these individuals "self-medicate" with alcohol or other depressant drugs in attempt to ameliorate their sleep-related symptoms. This maladaptive coping behavior can lead to the development of SUDs, greater physical and psychological problems, and reduced quality of life. Also, as described earlier, the use of substances to improve sleep may lead to the development of tolerance to the sleep promoting effects of the substance being used, and a worsening of sleep problems during periods of abstinence. Thus, it would seem that interventions simultaneously targeting sleep quality improvement and prevention/treatment of SUDs have the potential to dramatically improve health outcomes among individuals with PTSD, particularly if implemented shortly after initial PTSD diagnosis or at the first signs of coping-oriented substance use.

Treatment of Sleep Disturbance Among Those With PTSD and SUD

Effective treatments exist for sleep disorders, SUDs, and PTSD, but programs that integrate these three interrelated clinical specialties are lacking. Indeed, to date, we are not aware of any studies that have evaluated the effect of treating insomnia as a means of reducing sleep-specific coping-oriented substance use among individuals with PTSD. That said, there is a growing science base, in which poor sleep has been specifically targeted in the course of treating PTSD or SUD, which suggest such a clinical approach is viable and would confer clinical benefit.

Pharmacotherapy is the most common approach for treating sleep disorders. Currently an estimated 80% of veterans with PTSD are prescribed a medication to manage specific PTSD symptoms, most notably sleep disturbance (Mohamed & Rosenheck, 2008). Unfortunately, with the exception of prazosin (an alpha1-adrenergic receptor antagonist) there are few controlled trials to inform prescription practices for addressing sleep disturbances among individuals with PTSD. The therapeutic effects of prazosin were first demonstrated in a small, uncontrolled study of combat veterans with PTSD (Raskind, et al., 2002), but have since been replicated in placebo-controlled trials (Raskind, et al., 2007; Raskind, et al., 2003; Raskind, et al., 2013; Taylor, et al., 2008). Compared with placebo, prazosin improves sleep quality and reduces nightmares and overall PTSD symptom severity among civilians with non-combat related PTSD (Taylor, et al., 2008) and among military veterans with PTSD secondary to combat (Raskind, et al., 2007; Raskind, et al., 2003; Raskind, et al., 2013).

Efforts to develop sleep-focused interventions to assist in the treatment of SUDs are surprisingly sparse and have yielded variable results. Several pharmacological treatments

(acamprosate, benzodiazapines, carbamazepine, gabapentin, magnesium, quetiapine, topiramate, or trazodone) have demonstrated the ability to improve sleep among alcohol dependent persons in withdrawal (Bjorkqvist, Isohanni, Makela, & Malinen, 1976; Brower, et al., 2008; Friedmann, et al., 2008; Karam-Hage & Brower, 2000; Le Bon, et al., 2003; Malcolm, Myrick, Roberts, Wang, & Anton, 2002; Malcolm, Myrick, Veatch, Boyle, & Randall, 2007; Staner, Boeijinga, et al., 2006). Many of these studies, however, were open label, relied on self-reported sleep outcomes, and failed to assess medication effects on rates of abstinence or relapse (see Kolla et al., 2011 for review). With regards to the latter, both gabapentin and topiramate have been shown to reduce heavy drinking in clinical studies, but it is unknown whether improved sleep mediated this effect (Brower, et al., 2008; Johnson, et al., 2008).

In laboratory studies of pharmacotherapy for cannabis withdrawal, dronabinol (oral THC), lofexidine, mirtazepine, nabilone, quetiapine, and zolpidem have been shown to reverse abstinence-induced insomnia (Budney, Vandrey, Hughes, Moore, & Bahrenburg, 2007; Cooper, et al., 2012; Haney, et al., 2013; Haney, et al., 2010; Haney, et al., 2008; Haney, et al., 2004; Vandrey, et al., 2011; Vandrey, et al., 2013). However, clinical studies measuring the effects of these medications on sleep and cannabis use outcomes among those trying to quit are lacking. Among tobacco users, Nicotine Replacement Therapy (NRT) is an evidence-based treatment that effectively reduces sleep disturbances resulting from nicotine withdrawal (Staner, Luthringer, Dupont, Aubin, & Lagrue, 2006; Wetter, Fiore, Baker, & Young, 1995). However, high doses of 24-hour NRT may have the opposite effect and exacerbate insomnia in some patients, demonstrating the importance of selecting a dose level appropriate for each patient relative to their level of nicotine dependence (Leischow, et al., 1997). Regarding stimulant dependence, recent studies suggest that sleep quality among abstinent cocaine users may be improved with GABAergic agents, such as tiagebine, before bedtime (Morgan & Malison, 2008) or by administration of the dopamine reuptake inhibitor Modafinil upon awakening (Morgan, Pace-Schott, Pittman, Stickgold, & Malison, 2010). Modafinil has also been shown to reduce daytime sleepiness among recently abstinent methamphetamine users (Mahoney, et al., 2012; McGregor, et al., 2008). Thus, sleep can be improved in abstinent stimulant users using two fundamentally different pharmacological approaches (i.e., administration of a hypnotic-type agent before bedtime or administration of a wakefulness-promoting agent shortly after awakening).

Recent research has demonstrated that use of behavioral sleep interventions can also be effective as a means to reduce symptom severity and improve functional outcomes among individuals with PTSD and SUD. Cognitive Behavioral Therapy for Insomnia (CBT-I) is an effective behavioral intervention for the treatment of insomnia that incorporates components of sleep education, stimulus control and relaxation training, sleep restriction, and cognitive restructuring with regard to handling arousal and sleep interfering cognitions (Germain, et al., 2012; Manber, et al., 2012; Morin, et al., 2009). Imagery Rehearsal Therapy (IRT) is an effective behavioral intervention for specifically treating nightmares among individuals with PTSD. Patients choose a recurring distressing nightmare, are instructed to alter details of the nightmare to make it less distressing, and then rehearse the new “tamed” version of the nightmare scenario on a frequent basis (Gehrman & Harb, 2010; Krakow & Zadra, 2006; Lu, Wagner, Van Male, Whitehead, & Boehnlein, 2009).

In one study, delivery of CBT-I improved sleep in recently abstinent alcoholics compared with matched controls who received sham therapy (Arnedt, Conroy, Armitage, & Brower, 2011). In this study, relapse rates were low for all participants, thus no group differences were observed in terms of alcohol use outcomes. Unfortunately, this is currently the only published evaluation of a behavioral sleep intervention used in the context of SUD treatment. With respect to the behavioral treatment of sleep among those with PTSD, interventions that combine CBT-I and IRT have yielded results that indicate great promise for alleviating sleep disturbances (e.g. reduced sleep latency, nightmares; improved sleep continuity) and daytime symptoms such as anxiety or depression (Davis & Wright, 2007; Germain, et al., 2012; Ulmer, Edinger, & Calhoun, 2011). However, it should be noted that results of combined CBT-I and IRT interventions have not always been consistently positive. One study found that combined CBT-I and IRT did not result in significant improvements in sleep, but did reduce PTSD symptom severity related to re-experiencing and hyper-arousal symptoms (Germain, Shear, Hall, & Buysse, 2007), and another study demonstrated a significant reduction in sleep disturbances, but no change in PTSD symptom severity (Swanson, Favorite, Horin, & Arnedt, 2009). However, small sample sizes (7 and 8, respectively) may have limited the ability of these studies to detect a treatment effect.

Regarding long-term efficacy, research suggests that evidence-based behavioral and pharmacologic treatments of insomnia have comparable efficacy pre- to post-treatment, but that sleep improvements tend to be sustained for longer periods post-treatment following behavioral interventions (Morin, et al., 2009). However, only one comparative efficacy trial has been conducted among patients with PTSD. In this three-arm trial, Germain and colleagues (2012) randomized veterans with PTSD to receive a behavioral sleep intervention (BSI), pharmacological treatment (prazosin), or placebo. The BSI and prazosin treatment arms were equally effective at reducing self-reported and clinician-rated sleep disturbance and PTSD symptom severity. In fact, 62% of those receiving either active treatment experienced improved sleep compared with 25% of those receiving placebo. Consistent with the general literature on behavioral treatment of insomnia, patients in the BSI arm sustained larger reductions in insomnia severity at 4 months post-treatment compared with patients in the prazosin and placebo arms. There were no differences between groups on measures of overall sleep quality, disruptive nocturnal behaviors, or PTSD severity at the post-treatment follow-up, though this may be a result of improvements in these study measures, relative to pre-treatment baseline, for all 3 study arms. Additional research is needed to optimize treatment strategies for maximizing long-term gains in sleep among patients with PTSD.

Discussion

Posttraumatic stress disorder and SUDs are substantial public health concerns with high rates of co-occurrence. Disturbed sleep is not only a core feature of PTSD and a common substance withdrawal symptom, it is also a clear risk factor for the onset of PTSD and SUD. Following the onset of PTSD, disturbed sleep is particularly treatment resistant, and is associated with poor treatment outcomes (e.g. increased rates of suicide, daytime PTSD symptoms, and substance misuse). Behavioral interventions including CBT-I and IRT, as well as pharmacological interventions (e.g. prazosin), can improve overall sleep quality, and reduce nightmares and PTSD symptom severity. Based on these findings, future research

should further examine the use of sleep interventions for trauma-exposed individuals to determine the impact of sleep therapy on the development of PTSD. Additional research aimed at optimizing the delivery of sleep-focused interventions within the context of PTSD treatment as a means of reducing substance misuse is also needed.

Though the effects of substance use on sleep have been fairly well characterized, currently, the clinical significance of the relation between sleep disturbance and substance use remains poorly understood. While the supposition that disturbed sleep motivates substance use, which can then precipitate substance dependence, makes intuitive sense, prospective validation via empirical data is lacking. Further, clinical studies evaluating the effect of sleep improvement as a therapeutic tool in the treatment of SUD are few in number and suffer from methodological limitations including uncontrolled study designs, small sample sizes, and lack of appropriate substance use outcomes.

In summary, there is increasing evidence that disordered sleep, PTSD, and SUD are substantially and bi-directionally linked, but research to date has rarely integrated all domains. Controlled studies are needed to examine: 1) the role of sleep in the development of substance use disorders, particularly among individuals with psychiatric disorders such as PTSD, 2) the time course and severity of sleep disturbance following abrupt abstinence from substances of abuse, 3) relation between abstinence-induced sleep disturbance and relapse to substance use during a quit attempt, 4) if treatment of sleep disturbance, as it develops following trauma exposure can prevent or reduce the incidence of subsequent PTSD and/or SUD, and 5) whether behavioral, pharmacological, or combined treatments targeting improved sleep confer the most benefit for reducing substance use, particularly among those with PTSD. Enhanced understanding of the interrelation between sleep, PTSD, and SUDs may be critical for steering prevention and intervention efforts aimed at improving public health with respect to these prevalent disorders.

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The Effects of Substance Use on Sleep.

Class/Drug	Acute Exposure	Withdrawal
Drugs that Decrease Arousal		
Alcohol	Increased nocturnal awakenings, respiratory disturbances, Stage 3 sleep. Decreased sleep latency, REM sleep and sleep efficiency.	Increased sleep latency. Decreased total sleep time, sleep efficiency and Stage 3 sleep.
Benzodiazapines	Decreased sleep latency and number of nocturnal awakenings. Increased total sleep time.	Increased sleep latency and number of nocturnal awakenings. Decreased total sleep time.
Cannabis	Increased Stage 3 sleep. Decreased sleep latency and REM sleep.	Increased sleep latency, vivid dreams, REM sleep. Decreased total sleep time.
Non-Benzodiazapine Hypnotics	Decreased sleep latency and number of nocturnal awakenings. Increased total sleep time.	Mixed evidence. Rebound insomnia is either absent or mild relative to benzodiazapines.
Opioids	Increased sedation, stage 2 sleep, nocturnal awakenings, disordered breathing, and daytime somnolence. Decreased sleep latency, REM sleep, and Stage 3 sleep.	Increased nocturnal awakenings. Decreased Stage 3 sleep and REM sleep.
Drugs that Increase Arousal		
Amphetamines/Cocaine	Increased sleep latency. Decreased total sleep time and REM sleep.	Subjective hypersomnia, decreased total sleep time, sleep efficiency, REM sleep and Stage 1 and 2 sleep. Increased sleep latency and Stage 3 sleep.
Caffeine	Increased sleep latency and daytime somnolence. Decreased total sleep time, sleep efficiency, and Stage 3 sleep.	Daytime somnolence.
MDMA	Increased sleep latency and disordered breathing. Decreased total sleep time and REM sleep.	Insufficient evidence.
Nicotine/Tobacco	Increased sleep latency and Stage 2 sleep. Decreased sleep efficiency, REM sleep, and total sleep time.	Increased nocturnal awakenings and daytime somnolence, Decreased sleep latency and poor subjective sleep quality.