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Polysomnographic Sleep Disturbances in Nicotine, Caffeine, Alcohol, Cocaine, Opioid, and Cannabis Use: A Focused Review

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Background and Objectives: In the United States, approximately 60 million Americans suffer from sleep disorders and about 22 million Americans report substance dependence or use disorders annually. Sleep disturbances are common consequences of substance use disorders and are likely found in primary care as well as in specialty practices. The aim of this review was to evaluate the effects of the most frequently used substances—nicotine, alcohol, opioids, cocaine, caffeine, and cannabis—have on sleep parameters measured by polysomnography (PSG) and related clinical manifestations.
Methods: We used electronic databases such as PubMED and PsycINFO to search for relevant articles. We only included studies that assessed sleep disturbances using polysomnography and reviewed the effects of these substances on six clinically relevant sleep parameters: Total sleep time, sleep onset latency, rapid-eye movement, REM latency, wake after sleep onset, and slow wave sleep.
Results: Our review indicates that these substances have significant impact on sleep and that their effects differ during intoxication, withdrawal, and chronic use. Many of the substance-induced sleep disturbances overlap with those encountered in sleep disorders, medical, and psychiatric conditions. Sleep difficulties also increase the likelihood of substance use disorder relapse, further emphasizing the need for optimizing treatment interventions in these patients.
Conclusion and Scientific Significance: Our review highlights the importance of systematically screening for substance use in patients with sleep disturbances and highlights the need for further research to understand mechanisms underlying substances-induced sleep disturbances and on effective interventions addressing these conditions. (Am J Addict 2015;24:590–598)

INTRODUCTION

Humans spend about one-third of their lives asleep.[1] Although sleep is one of the core requirements of individual health and wellness, approximately 60 million Americans suffer from chronic sleep problems and disorders.[2] Lack of sleep is strongly associated with chronic diseases such as hypertension, obesity, diabetes, cardiovascular heart disease, and stroke.[2]

Lack of sleep is also associated with negative effects on mental health. Research shows that individuals with chronic sleep problems report mental distress, alcohol use, and symptoms of depression, and anxiety.[1,2] In addition, sleep problems have been shown to be associated with suicidal thoughts or behaviors.[3] A meta-analysis of 19 studies found that sleep deprivation affects mood to an even greater extent than it affects cognitive and motor function. The burden of sleep problems also reflects heavily financially; studies show that hundreds of billions of dollars are spent annually on direct medical costs associated with sleep issues.[1]

Sleep disturbances are prominent symptoms of substance-related disorders and could account for substantial proportion of sleep problems. An epidemiological survey conducted in 2012 reported that approximately 22.2 million Americans suffer from substance dependence or use disorders.[4] Approximately 4.2 million Americans are currently dependent or abusing marijuana, 1.7 million Americans are dependent or abusing cocaine, and 1.6 million Americans are using prescription-type pain relievers non-medically. In patients with alcohol use disorders, insomnia is common and persistent, and it is associated with increased relapse rates and suicidal thoughts.[5]

Both substance use and insomnia independently increase the risk of suicidal thoughts or behaviors, but it is important to recognize that evidence suggests that among individuals with alcohol problems, the presence of a sleep disorder substantially increases the risk of suicidality.[3] Additionally, the economic impact of sleep-disturbances attributed to these substances is substantial. For example, 10%—approximately 23.5 billion dollars a year—of all alcohol-related costs could be attributed to insomnia and other sleep disorders.[4,6,7] All substances highlighted in this review—alcohol, opiates, cannabis, cocaine, caffeine, and nicotine—have a major impact on sleep.

Although significant strides have been made regarding the neurobiology of these substances, little research has been done

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to investigate the etiological and causative role these substances of abuse play in sleep disturbances.[6] Given the high frequency of substance use in the community, it is essential that clinicians are aware of how substances impact sleep and how each drug class affects the various sleep parameters and stages.[8]

We sought to review the substances of abuse and their effects on sleep parameters, related symptomatic presentation and subsequent impact on clinical care. Our review will present a brief outline on the physiology of sleep and sleep disturbances (see Tables 1 and 2), followed by a discussion of the specific drug's effects on sleep physiology and their clinical presentations during intoxication, withdrawal and chronic use.

METHODS

We used electronic databases such as PubMED and PsycINFO to search for relevant articles. The key words used included "alcohol," "caffeine," "cocaine," "opioid," "methadone," "heroin," "cannabis," "cannabidiol," "marijuana," "tetrahydrocannabinol," "THC," "tobacco," "and "nicotine." In addition we used key words such as "sleep," "sleep parameters," "polysomnography," and "PSG." Articles were also obtained by searching reference lists found in relevant articles. We supplemented data found in research articles with information gleaned from online textbooks obtained through the E-book collection at the Calder Medical Library at the University of Miami Miller School of Medicine.

We only included in this review articles published from 2001 to 2015 that used polysomnography (PSG), which measures sleep parameters utilizing electroencephalographic (EEG) recordings, as their objective measure of sleep.[9]

We limited our review to tobacco, alcohol, cannabis, cocaine, caffeine, and opioids, as those are the most frequently abused drugs by Americans and are more likely to be encountered by practitioners. We have not included pharmacotherapy studies as they are outside the focus of this review.

TABLE 1. Stages of sleep

Sleep stage	% total sleep time	EEG waveforms	Description
Wakefulness	<5[13]	Alpha waves 8–3 Hz/sec[9]	Relaxed state with closed eyes[9]
NREM1 (Stage 1)	2–5[1]	Theta waves 4–7 Hz/sec[9]	Light sleep, low arousal threshold[9]
NREM2 (Stage 2)	45–55[1]	Sleep spindles, K-complexes[1]	Higher arousal threshold than NREM[11]
NREM3			
(Stage 3)	3–8[1]	Delta waves 0.5–2 Hz/sec[9]	Deep sleep, "slow wave sleep" (SWS), associated with growth hormone release[9]
(Stage 4)	10–15[1]		
REM	20–25[1]	Low voltage, mixed frequency[1]	Muscle atonia,[1] Bursts of rapid eye movement,[1] Dreaming,[1] Memory consolidation[1]

REM, rapid eye movement; NREM, non-rapid eye movement; Sleep spindles, Sinusoidal waves with frequency of 12–14 Hz, lasting for 0.5–1.5 seconds; K-complex, high-amplitude, biphasic wave of 0.5 second duration.[1] New terminology for sleep staging scoring in adults has proposed three stages of Non-REM sleep (NREM 1, 2, and 3 corresponding to Stage 1, Stage 2, and Stages 3 and 4, respectively).[9]

TABLE 2. Sleep parameters: definitions and timing

Sleep parameter	Definition	Average time in healthy individual
Total sleep time (TST)	Length of nocturnal sleep, varies greatly with age[8]	7.5–8.5 h[8]
Sleep onset latency (SOL)	Amount of time it takes for the individual to initiate the first period of any stage of sleep[10,13]	< 5–10 min[13]
Sleep efficiency	Refers to the total sleep time divided by the time in bed multiplied by 100[10]	At least 85%[13]
REM sleep latency	Refers to the amount of time from sleep onset to the first epoch REM sleep[10,13]	60–120 min[13]
Arousal	Defines a sudden, brief change in electroencephalogram (EEG) from sleep to wakefulness, can describe abrupt change from deeper sleep (stages 3 and 4 sleep) to lighter sleep (stages 1 and 2 sleep)[13]	3–14 s[13]
Wake after sleep onset (WASO)	Defines time spent awake from sleep onset until the final awakening; used as an indicator of sleep continuity and disruption[13]	

The following six clinically relevant sleep parameters assessed by PSG were included in this review: (1) total sleep time (TST); (2) sleep onset latency (SOL); (3) slow wave sleep (SWS); (4) rapid eye-movement sleep (REM); (5) rapid eye-movement sleep latency (REM latency); and (6) wake after sleep onset (WASO).

RESULTS

Effects of Substances of Use on Sleep Parameters

Our review selected studies that only assessed sleep disturbances using polysomnography. For each substance, we will first outline the basic physiological action of the drug on the brain. We will then expand on the effects of these substances on sleep during different stages of use—intoxication, withdrawal, and chronic use (see Table 3).

Caffeine

Stimulants, such as caffeine and nicotine, have profound impact on sleep. Research shows that approximately 80% of world's population is estimated to have used caffeine.[11] Sleep alterations with caffeine use include increased sleep latency, decreased TST, and increased SWS.[11] In addition, dependence on caffeine is found to cause poor sleep quality, day-time dysfunction, and increased sleep disturbances.[11] These sleep disturbances caused by caffeine may be due to caffeine's ability to antagonize adenosine receptors, as adenosine acts as an antagonist of neuronal activity and promotes sleep.[11]

Nicotine

Studies examining the effect of acute nicotine intoxication on sleep using transdermal nicotine application in non-smokers reported a dose-dependent reduction of REM sleep, slow wave sleep, and total sleep time.[12,13] During acute intoxication, nicotine, similar to other stimulants, increases REM latency, sleep onset latency, and NREM 2 sleep.[13]

Chronic smokers were reported to have twice the risk of experiencing sleep disturbances, the most common including increased sleep latency and daytime sleepiness.[12] Nicotine consumption in chronic smokers was also linked to decreased total sleep time and increased REM latency. When compared to non-smokers, chronic smokers had a decreased slow wave sleep (SWS) and reduced sleep efficiency. [12]

Nicotine withdrawal, following cessation of nicotine administration in non-smokers, was associated with increased total sleep time and REM rebound (a phenomenon in which increased frequency and length of REM sleep occurs) on PSG studies.[12,13] The effects of withdrawal on sleep are dose dependent, but usually begin 6–12 hours after cessation of nicotine, reach a maximum within 1–3 days, and can continue for up to 3 weeks.[12] Effects include an increase in REM sleep and wake after sleep onset, and decrease in REM latency and sleep onset latency.[12,13] Subjective measurements depict a decrease in sleep quality and increased depressive symptoms.[13]

Alcohol

Alcohol effects on certain neurotransmitters may partially explain its impact on sleep. Alcohol alters synaptic functions of the dopamine receptor in the mesolimbic striatum, causing dopaminergic activity to increase.[14] It also increases sensitivity of 5-HT3 serotonin receptors and acts as an indirect γ-aminobutyric acid (GABA) agonist.[14] Alcohol also antagonizes the *N*-methyl-D-aspartic acid (NMDA) receptors of glutaminergic neurotransmission and inhibits δ-opiate receptors.[15]

The effects of acute alcohol intoxication on sleep are dose dependent. A recent review assessed the differences between low (1–2 standard drinks or .15 and .49 mg/kg), moderate (2–4 standard drinks or .5–.74 mg/kg), and high doses (above 4 standard drinks or >.74 mg/kg) of alcohol on sleep.[16] At all doses, acute alcohol intoxication reduced sleep onset latency.[16] Low doses of alcohol produced an increase in REM sleep, REM latency, and wake after sleep onset, and a reduction in Stage 3 NREM. Moderate to high doses of alcohol caused a decrease in REM sleep. During the first half of sleep, alcohol increased slow wave sleep at all doses; this effect was found for both genders and across all age groups.[16] Because alcohol is metabolized quickly, its effects on the second half of sleep differ, with a reported increase in arousals and sleep fragmentation, REM rebound, and reduction in slow wave sleep.[13]

Alcohol ingestion also reported to worsen snoring and exacerbate obstructive sleep apnea due weakening of pharyngeal dilator muscle tone and subsequent increase in upper airway resistance.[13] Acute alcohol ingestion may cause nightmares, arousal disorders, and increased restless legs syndrome symptoms.[13]

Brower (2001) conducted PSG studies in hospitalized patients with alcoholism who were given alcohol for 1 or more days before entering the withdrawal period.[17] The results showed prolonged sleep onset latency, decreased total sleep time and REM sleep, and increased SWS sleep and REM latency.

Other studies reported that chronic, habitual, alcohol use before bedtime can lead to insomnia and frequent awakenings.[13] As the blood ethanol levels declines throughout the sleep period, the sedative effects are no longer active.[13]

PSG sleep patterns in alcohol dependence after 2–3 weeks of abstinence (ie, during the withdrawal period) compared to healthy controls, showed an overall decreased sleep efficiency, total sleep time, and slow wave sleep, and increased sleep onset latency and awakenings, in addition to increased REM sleep and decreased REM latency due to REM rebound.[13,18] Four out of 5 studies correlated alcohol relapse with increased sleep onset latency, decreased sleep efficiency, and decreased total sleep time—effects all found in the withdrawal period, increasing the difficulty of prolonged abstinence.[19] Changes in REM sleep, particularly increased REM and decreased REM latency may also be used as a marker of relapse.[5]

Opioid

Opioid receptors are located in the ventrolateral preoptic nucleus, the same nucleus that is involved in sleep regulation.[7]

TABLE 3. Substance intoxication, withdrawal, chronic use and effects on sleep

Drug class	Intoxication	Withdrawal	Chronic use
Cocaine	↑SOL[21]	Acute	↓REM[22]
	↓TST[21]	↑TST[22]	↑REM latency[22]
	↓REM[21]	↑REM (rebound)[21,22]	↑SOL[22]
	↑REM latency[21,22]	↓SOL[22]	↓TST[22]
		↓REM latency (rebound)[21]	
		Subacute	
		↑SOL[22]	
		↓Sleep efficiency[22]	
		↓TST[22]	
		↓REM[22]	
		↑SWS[22]	
Alcohol	Low dose	↑SOL[18]	↑SOL[17]
	↑REM[16]	↓TST[18]	↓TST[17]
	↓SOL[16]	↑REM (rebound)[18]	↑SWS[17]
	Moderate dose	↓Sleep efficiency[18]	↓REM[17]
	↓SOL[16]	↓REM latency (rebound)[18]	↑REM latency[17]
	↓REM[16]	↑WASO[13]	
	High dose	↓SWS[13]	
	↓SOL[16]		
	↓REM[16]		
	↑SWS[17]		
	↓WASO[17]		
	↑REM latency[14]		
Cannabis	Low THC	↑SOL[13,21,23,24]	Suppression of SWS[21]
	↓SOL[13,21]	↓SWS[21,23,24]	
	↓REM[13,21]	↑REM[14,21,24]	
	↑SWS[13,21]	↓REM latency[23,24]	
	↑TST[13,21]	↓TST[13,23,24]	
	High THC	↓Sleep efficiency[23,24]	
	↓REM[13,21]		
	↓SWS[13,21]		
	↑SOL[13,21]		
Opioid	↓REM[7]	↓REM[7]	Normalization of ↓SWS ↓REM[7]
	↓SWS[7]	↑WASO[7]	Normalization of ↑WASO, ↑REM sleep latency[7]
	↓TST[7]		
	↑REM latency[7]		
	↑WASO[7]		
	↓Sleep efficiency[13]		
Nicotine and caffeine	↓REM[12]	↑WASO[13]	↑SOL[12]
	↑REM latency[13]	↑REM (rebound)[2,23]	↓TST[12]
	↓SWS[13]	↓SOL[12]	↑REM latency[12]
	↓TST[13]	↑TST[13]	↓SWS[12]
	↑SOL[13]	↓REM latency[13]	↓Sleep efficiency[12]

SOL, sleep onset latency; SWS, slow wave sleep; TST, total sleep time; REM, rapid eye movement; WASO, wake after sleep onset

There are four types of endogenous opioid receptors in the Central Nervous System (CNS): μ, δ, κ, and nociceptin/orphanin FQ receptor. Clinically, most opioids, such as morphine and methadone, are selective for the μ receptors.[7]

Studies assessed morphine-like opioid effects on sleep architecture. Acute intoxication caused reduction in REM sleep and slow wave sleep and increased REM latency and wake after sleep onset. Chronic opioid use normalizes the PSG findings caused by acute intoxication, and individuals often experience central and obstructive sleep-disordered breathing (SDB), which goes largely unnoticed, increasing the likelihood of morbidity and mortality.[7,20] Literature reveals that

the prevalence of SDB in patients being treated with chronic opioids is staggeringly high, at approximately 42–85%.[20] This increased risk for SDB includes chronic use of partial μ agonists such as methadone and buprenorphine, used in the maintenance treatment of opioid use disorder.[20]

Respiratory drive in the ventrolateral medulla is reduced independently by both sleep and opioids as evidenced by decreased ventilation in hypoxia and hypercapnia.[20]

Following withdrawal from chronic opioid use, sleep disturbances include frequent arousals and decreased REM sleep.[7] During prolonged abstinence there is a significant increase in total sleep time and rebound in slow wave sleep and REM sleep. This occurs usually between 13 and 22 weeks following opioid cessation.[7]

Cocaine

Cocaine impacts on sleep largely by its effects on dopamine. Cocaine use leads to competitive inhibition of presynaptic dopamine transporters in the nucleus accumbens and prefrontal cortex of the brain, leading to increased dopamine availability in the synapse.[21]

PSG studies showed longer sleep latency, decreased total sleep time, and suppression of REM sleep. These effects on sleep are similar to the ones produced by other stimulants such as amphetamines.[21]

According to Morgan, only 6 studies investigated the effects of chronic cocaine use on sleep.[22] These effects include increased slow wave sleep, sleep onset latency, and REM latency, along with decreased total sleep time, REM sleep, and sleep efficiency.

Studies show that cocaine withdrawal behaves differently in the acute and subacute phases.[22] After 2.5 days of abstinence, individuals experience the REM rebound effect, where there is decreased REM latency and increased REM sleep. After 2.5 weeks of abstinence, there is an increased sleep latency and slow wave sleep and decreased sleep efficiency and total sleep time. In addition, compared to healthy controls, a decrease in REM latency was found, but the absolute amount of REM sleep is very short.[22]

Sleep after approximately 2.5 weeks of abstinence is very similar to insomnia-like sleep—chronic users complain of difficulty falling asleep both at night and during the day after subacute abstinence.[22] Despite these findings, abstinent cocaine users did not report having any subjective report of trouble with *sleep quality* and had similar sleep satisfaction to healthy controls.[22]

Cannabis

Although the cannabis plant contains over 60 cannabinoids, tetrahydrocannabinol (THC) is the component of the plant that is responsible for most of the psychotropic effects of marijuana, including effect on sleep. The cannabinoid CB1-receptors, which are linked to REM sleep, are found in high concentrations in the frontal cortex, cerebellum, and basal ganglia, are the main receptors involved in producing these psychotropic effects.[21]

Differences with respect to time and route of administration, amount of THC, and previous drug consumption make it difficult to assess cannabis acute intoxication effects on sleep.[21] Studies indicate that intoxications with low-dose THC is found to have a mild sedative effect manifested as a decrease in sleep onset latency and REM sleep and increase in total sleep time and slow wave sleep. In high doses, THC was found to have hallucinatory action in addition to decreased REM and slow wave sleep and increased sleep onset latency.[13,21] With chronic use, tolerance to the effects of sleep latency were found, whereas tolerance to REM sleep effects were less pronounced.[21] In addition, chronic ingestion of THC was found to produce long-term suppression of slow wave sleep.[23]

A study of sleep parameters during withdrawal from chronic marijuana use (defined as daily use for 5 ± 3 years and smoking a mean of 104 ± 51 joints/week), as compared to a drug free control group, indicated an increase in sleep onset latency and REM sleep, a decrease in slow wave sleep, total sleep time, REM latency, and sleep efficiency.[23] Vandrey et al. (2011)[24] who conducted a within subject crossover placebo-controlled study using PSG in daily cannabis users reported similar findings in those participants in the placebo-abstinence period (withdrawal test).

DISCUSSION

Our review indicates that the most commonly used substances—alcohol, cannabis, cocaine, opioids, caffeine, and nicotine—can have significant effects on sleep and that these effects differ during intoxication, withdrawal, and chronic use. These sleep disturbances have underlying etiologies attributed to neurobiological alterations caused by substances of use and are usually manifested objectively as polysomnographic changes.

The most common sleep disturbance seen in all substances of use is insomnia. For example, PSG findings seen with nicotine intoxication and chronic use are consistent with smoker's complaints of insomnia, increased sleep fragmentation and daytime sleepiness—symptoms that decrease with smoking cessation.[12] Similarly, approximately 36–72% of individuals with alcoholism admitted for treatment suffer from insomnia—this may be directly attributed to the decrease in TST found on PSG studies of chronic alcohol users.[19] Studies show that at 6 months after complete abstinence from alcohol 25% continued to have insomnia (compared to the baseline 46% of alcohol users with insomnia).[5] Thus, despite several months of treatment for alcohol use disorders, individuals continue to struggle with insomnia, increasing their risk for relapse.[5]

In addition, symptoms of fatigue and excessive daytime sleepiness experienced by chronic opioid users may be manifestations of the decrease in TST and increased WASO seen in PSG.[7] Excessive daytime sleepiness experienced may also be attributed to sleep disordered breathing that is experienced by chronic opioid use, decreasing the quality of sleep achieved during each sleep period.[20]

TABLE 4. Patterns of sleep disturbance caused by substance use

	Increase	Decrease
Sleep onset latency (SOL)	Intoxication: Cocaine intoxication[21] High THC cannabis intoxication[13,21] Abuse: Chronic alcohol use[17] Nicotine and caffeine and caffeine intoxication[13] Chronic nicotine and caffeine use[12] Chronic cocaine use[22] Withdrawal: Subacute cocaine withdrawal[22] Cannabis withdrawal[21,23,24] Alcohol withdrawal[22]	Intoxication: Alcohol intoxication[19] Low THC cannabis intoxication[16,19] Withdrawal: Acute cocaine withdrawal[22] Nicotine and caffeine withdrawal[12]
Total sleep time (TST)	Intoxication: Low THC cannabis intoxication[13,21] Withdrawal: Acute cocaine withdrawal[22] Nicotine and caffeine withdrawal[13]	Intoxication: Cocaine intoxication[21] Opioid intoxication[7] Nicotine and caffeine intoxication[13] Abuse: Chronic nicotine and caffeine use[12] Chronic alcohol use[17] Chronic cocaine use[22] Withdrawal: Alcohol withdrawal[18] Subacute cocaine withdrawal[22] Cannabis withdrawal[13,23,24]
Rapid-eye movement (REM)	Withdrawal: Alcohol withdrawal (REM rebound)[18] Cannabis withdrawal[21,24] Nicotine and caffeine withdrawal[12] Acute cocaine withdrawal[22]	Intoxication: Cocaine intoxication[21] High-dose alcohol intoxication (high dose)[16] Low/high THC cannabis intoxication[13,21] Opioid intoxication[7] Abuse: Chronic cocaine use[22] Chronic alcohol use[17] Withdrawal: Subacute cocaine withdrawal[22] Opioid withdrawal[7] Nicotine and caffeine intoxication[12]
REM latency	Intoxication: Alcohol intoxication (high doses)[13] Cocaine intoxication[13] Nicotine and caffeine intoxication[13] Opioid intoxication[7] Abuse: Chronic alcohol use[17] Chronic cocaine use[22] Chronic nicotine and caffeine use[12]	Withdrawal: Acute cocaine withdrawal[22] Alcohol withdrawal[18] Cannabis withdrawal[23,24] Nicotine and caffeine withdrawal[13]
Slow wave sleep (SWS)	Intoxication: Acute high dose alcohol intoxication[16] Low THC Cannabis intoxication[13,21]	Intoxication: Nicotine and caffeine intoxication[13] High THC Cannabis intoxication[13,21] Opioid intoxication[7]

(*Continued*)

TABLE 4. Continued

	Increase	Decrease
	Abuse: Chronic alcohol use[17] Withdrawal: Subacute cocaine withdrawal[23]	Abuse: Chronic nicotine and caffeine use[12] Withdrawal: Alcohol withdrawal[13] Cannabis withdrawal[21,23,24]
Wake time after sleep onset (WASO)	Intoxication: Cannabis intoxication[21] Opioid intoxication[7] Withdrawal: Alcohol withdrawal[18] Opioid withdrawal[7] Nicotine and caffeine withdrawal[13]	Intoxication: Alcohol intoxication (high doses)[21]

Decreased TST is also seen in both subacute cocaine withdrawal and chronic cocaine use. Interestingly, researchers found an inconsistency between alterations in sleep parameters and chronic cocaine user's subjective report on sleep.[22] Although PSG findings in these patients suggest significantly dysfunctional sleep patterns, chronic cocaine users do not report trouble with their sleep. Chronic cocaine users reported overall sleep quality and satisfaction with sleep similar to control subjects. Chronic cocaine use is hypothesized to impair the brain mechanisms controlling sleep homeostasis, thus distorting cocaine users' ability to recognize the need for sleep. These findings suggest that chronic cocaine users experience "occult" insomnia and may explain the sleep-related cognitive, attention, and learning deficits observed in these individuals.[22]

Low-dose THC cannabis intoxication appears to decrease SOL, in addition to causing a decrease in REM sleep and increase SWS.[23] Reduced SOL was also recorded in acute alcohol intoxication. These PSG findings may explain why many patients report using small amounts of alcohol or marijuana before bed as sleep aids. In addition, the hypnotic qualities of low doses of THC support the findings of improved subjective sleep quality seen when cannabis-based medicines are given to patients with chronic pain syndromes.[23]

Slow wave sleep, or "deep sleep," is the period of sleep where an individual's brain recovers from daily activities—it is crucial for learning, memory consolidation, and memory retrieval.[10] This stage of sleep is also found to be the stage with the highest arousal threshold; an individual in this stage of sleep requires much higher stimulus for awakening to occur.[10] Thus, individuals intoxicated by using substances such cannabis with *high* THC content and opioids claim "restless" sleep with increased feelings of fatigue following the sleep period.[17] These subjective findings correlates with polysomnographic findings of decreased SWS and increased wake after sleep onset (WASO).[5,10,17] Conversely, an increase in SWS is seen in *low* THC intoxication and corroborates user's claiming sleep after marijuana is significantly more "restful."[13] Opposite effects were found during cannabis withdrawal.[21,23] Insomnia, strange dreams, and poor sleep quality are reported in up to 76% of cannabis users who abruptly stop using cannabis.[23] The increase in REM sleep that occurs in cannabis withdrawal may explain the reported symptom of increasing strange dreams.[12,18,21] It is worth noting that these disturbances in sleep lead to increased difficulty in achieving abstinence.[21] Similarly, inadequate sleep in cocaine withdrawal is also thought to have an unfavorable effect on substance use treatment outcomes.[21] Sleep disturbances reported in the withdrawal period are useful prognostic indicators for identifying high relapse risk requiring more tailored management strategies.[21]

Another common symptom reported by individuals undergoing alcohol, cannabis, and subacute cocaine withdrawal is the subjective reporting of difficulty falling asleep. The increase in SOL reported in the withdrawal of these substances provides explanation for their clinical manifestations. In addition, both intoxication and chronic use of stimulants, such as cocaine and nicotine, cause an increase in SOL.[12,13,17,21,22] This polysomnographic finding coincides with the subjective complaint of troubles with sleep initiation commonly experienced by cocaine users.[12,13,17,21,22]

Conversely, reduced SOL is also reported in acute withdrawal from stimulants such as nicotine and cocaine. These findings explain cocaine-dependent individual's reported fatigue and psychomotor retardation experienced in the withdrawal period[12,16,21,22] (see Table 4).

Although our review did not encompass other medical conditions and medications effect on sleep, it is important to recognize that substance-induced sleep disturbances are similar to those encountered in sleep disorders, medical conditions, and side effects from medications. Many of the common sleep disorders and sleep disturbances due to psychiatric and chronic medical conditions manifest similarly to different stages of drug intoxication, chronic use, and withdrawal.

There were a variety of limitations to this review including the limited number of studies found addressing effects of substance use on sleep. The studies reviewed contained small sample sizes and recruited only male subjects limiting generalizability of the findings. It is unclear whether these findings apply to females as men and women respond to drugs differently and express different sleep physiology.[8] Furthermore, although all of the studies reviewed used PSG to assess sleep parameters, there is incongruity in drug dosage, time, and route of administration, prior drug use, and comorbid conditions, including multiple drug use. Differences in age, work schedules, and other factors such as caffeine use may also introduce bias and present difficulties when assessing sleep parameters. Our review was not comprehensive but focused on the most salient issues involving the most widely used substances.

CONCLUSION

Substance use induced sleep disturbances are highly prevalent in today's society. With 60 million Americans,[2] almost 40% of the adult population of the USA, suffering from chronic sleep problems, it is important to recognize and address substance-induced sleep disturbances given their ubiquitous presence in primary care and specialties practices. Research shows that physicians' diagnosis of alcohol or drug use in primary care patients was significantly associated with the presence of sleep disturbances, such as severe insomnia.[19]

In addition to aiding in diagnosis of substance-induced sleep disturbances, physician awareness can aid substance use treatment, and decrease relapse rates. Persistent sleep difficulties increase the likelihood of substance use relapse, indicating the importance of recognizing, addressing, and preventing these potentially detrimental disturbances from hindering abstinence. For example, increase in REM sleep and a decrease in REM latency and SWS, findings associated with alcohol withdrawal, are identified as predictors of alcohol relapse in alcoholism.[13]

Furthermore, our findings highlights the importance of systematically screening for substance use in patients with sleep disturbances and points to the importance of conducting research on the pathophysiological mechanisms underlying these symptoms.

Our findings also highlight potentially significant adverse effects on sleep of treatment with opioid substitution therapy, such as methadone or buprenorphine as such agents can induce sleep disordered breathing.[20]

Brief behavioral therapies appear to be the treatment of choice for substance-related insomnia and relapse prevention.[5] There is still a need for increased understanding of the etiology of substance-induced dyssomnias. This is highlighted by the lack of safe, effective and non-addictive medications.[25] Limited evidence shows that certain medications such as acamprosate and the anticonvulsants gabapentin and topiramate are helpful in treatment of insomnia and relapse prevention, particularly in patients with alcohol use disorders.[5] These agents should be taken in consideration and are superior and safer than benzodiazepines which were commonly used to address insomnia in the past. Benzodiazepine receptor agonists should be avoided due to their high abuse potential, cross-dependence and risk for negative consequences when used with other depressants including alcohol.[5]

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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