Sleep and Substance Use and Abuse in Adolescents

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Sleep problems and substance use disorders are common in children and adolescents. The prevalence of insomnia in adolescents is approximately 9.4%. Almost 1 in 10 (9.5%) youth aged 12 to 17 years reported use of at least 1 substance during the previous month in 2007. Sleep disorders and substance use disorders can have impact on development, physical and mental health and behavior, and social functioning of children and adolescents.

Long-term consequences of untreated insomnia are comparable to other psychiatric disorders and can have serious negative effects on the health and functioning of adolescents. In a 12-month prospective study, Roberts and colleagues demonstrated that among 4175 adolescents aged 11 to 17 years, 27% reported at least 1 symptom of insomnia, and 5% met the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV diagnostic criteria for insomnia at baseline. After 1 year, 3134 of the 4175 adolescents were available for follow-up, and 24% of those available met the DSM-IV criteria for chronic insomnia. Youth experiencing insomnia had an increased risk for health problems, received more mental health care, and had more interpersonal problems and difficulties with daily activities.

Untreated insomnia can significantly contribute to developmental stress and can cause a range of various behavioral and mental problems among children and adolescents. There is a higher rate of irritability, impulsivity, hyperactivity, anxiety, depression, substance use, and risk for suicide among children and adolescents with sleep disturbances. Ivanenko and colleagues pointed out that disruption in the sleep-wake cycle during maturation may predispose to the development of psychopathology and should be properly identified and treated. A study by Gau and colleagues confirmed a strong relationship between disrupted sleep-wake cycles, substance use,

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and behavioral problems in adolescents. The investigators studied correlations between different circadian rhythms and psychopathology, substance use, and suicidal thoughts and statements in seventh graders (682 boys and 650 girls) in Taiwan. Chronotypes were determined based on the $t$ score distribution of the Child Morningness/Eveningness Scale that reflected preferred individual timing of activity and sleep. Three groups of adolescents were defined as morning ($t$ score > 60), intermediate (40 < $t$ score < 60), and evening ($t$ score < 40). The evening group had more emotional problems, including inattention, aggressive and delinquent behaviors, suicidal thoughts, and increased habitual use of tobacco, alcohol, and betel nut (the most frequently abused substance by Taiwanese adolescents), in comparison to the morning and intermediate group. The association between evening circadian rhythm, substance use, and suicidality remained significant after controlling for internalizing (depression and anxiety) and externalizing (aggression and deviance) problems. The relationship between substance abuse and circadian rhythm in adolescents seems to be significant, and it is a subject of active ongoing research.

Sleep disturbances and substance use are highly correlated. Insomnia remains one of the most common clinical presentations and complications of substance use in adolescents. Short-term and long-term changes in sleep patterns and architecture are common during active substance use, withdrawal, and recent and prolonged abstinence. Sleep disorders, if unrecognized and untreated, may trigger substance use as a way of dealing with consequences of disordered sleep. Caffeine and other stimulants, for example, can be used to combat daytime sleepiness, and alcohol and hypnotics can be used to assist with sleep. Several studies have demonstrated significant bidirectional associations between sleep problems and substance use. Bootzin and Stevens identified sleep problems in adolescents as a pathway to substance use and as an obstacle to treatment of substance use disorders. Tynjala and colleagues described strong interrelationships between irregular sleep, substance use, and perceived tiredness among 15-year-old adolescents. Wong and colleagues examined the relationships between sleep problems in early childhood and subsequent alcohol and other drug use in adolescent boys from high-risk families. About 33.5% of 257 boys had sleep difficulty as early as age 3 to 5 years. Children with sleep difficulties, in comparison to those with no sleep difficulties, were 2.3 times more likely to have smoked, 2.3 times more likely to have used alcohol by age 12 to 14 years, and 2.6 times more likely to have used marijuana. Based on consistent correlation between childhood sleep problems and early onset of substance use in adolescent boys, the author proposed that childhood sleep problems should be considered an early identifier for substance use in adolescents.

Accumulated clinical and empiric data emphasize the need to consider a developmental approach to understand the chronic psychiatric and behavioral conditions. Several studies support a developmental view of correlations between sleep disorders, substance use, and other psychiatric conditions. Wong and colleagues examined the onset of substance use from childhood to adolescence (3–17 years) in 292 boys and 94 girls. Starting at age 3 to 8 years, participants and their parents were interviewed at 1- to 3- year intervals to gather information about sleep, substance use, and internalizing and externalizing problems. The investigators found that the effect of sleep problems on substance use was not influenced by internalizing or externalizing problems. However, gender differences with respect to sleep problems and subsequent substance use were observed. Sleep problems in childhood correlated with early use of alcohol in boys aged 8 to 14 years and in girls aged 15 to 17 years and early use of cigarettes (ages 7–11) and marijuana (7–15) in boys. The investigators concluded that sleep problems during childhood can serve as...
a marker for the risk for early use of alcohol and substances in adolescent boys and early use of only alcohol in adolescent girls.\textsuperscript{14}

Roane and Taylor\textsuperscript{1} examined adolescent insomnia as a risk factor for mental health problems in a longitudinal study. A national sample of adolescents aged 12 to 18 years was interviewed at baseline and again 6 to 7 years later. Almost 1 in 10 (9.4\%) adolescents met the criteria for insomnia at baseline. Adolescents with insomnia (insomnia group) had a higher occurrence of use of alcohol, cannabis, and other drugs, and they were more likely to have depressive symptoms and suicidal ideation. At follow-up, the insomnia group was 1.34 to 3.58 times more likely to develop depression. Prospectively, there was a significant gender effect: males were more likely to endorse the use of alcohol, cannabis, and substances other than cannabis, whereas females were more likely to develop depressive symptoms. This study demonstrated a strong association between insomnia and psychiatric symptoms. The authors concluded that insomnia should be treated with specific interventions as an independent disorder.\textsuperscript{1}

The comorbidity of sleep disorders, substance use, and other psychiatric conditions in youth has been investigated by several researchers. Johnson and Breslau\textsuperscript{5} emphasized the complexity of associations between these disorders and proposed that sleep disorders, substances use disorders, and psychiatric conditions may “cluster within individuals.” Similarly, Haynes and colleagues\textsuperscript{15} observed that sleep problems in adolescence can contribute to affective and behavioral instability and subsequent substance abuse.

Insomnia is a prevalent chronic condition in children and adolescents. Various factors, such as diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD), inappropriate use of stimulant and other prescription and over-the-counter medications, caffeine consumption, use of alcohol, and use of other substances, can significantly interfere with sleep. The effects of substance use on sleep are examined in more detail throughout this article.

**ALCOHOL, TOBACCO SMOKING, AND CAFFEINE**

*Alcohol*

Alcohol use in adolescents remains a significant public health concern. Approximately 10.8 million young people aged 12 to 20 years drink alcohol. A 2002 to 2006 report of the National Survey on Drug Use and Health revealed that the lifetime prevalence of underage drinking is 53.9\%. Almost 1 in 10 (9.4\%) young people who used alcohol met DSM-IV criteria for alcohol abuse or dependence. Because alcohol use is widely accepted in society, it is not surprising that more than two-thirds of all underage drinkers are given alcohol by either an adult or another underage person.\textsuperscript{2} It has also been suggested that the expectation of social and physical pleasure from alcohol consumption might be a significant risk factor for transition from first drink to heavy drinking in adolescents.\textsuperscript{16} Alcohol use correlates with sleep problems in adolescents. Saarenpaa-Heikkila and colleagues\textsuperscript{17} evaluated reports of subjective daytime sleepiness in adolescents aged 12 to 19 years, 3 years after the initial interview. Frequent alcohol drinking was 1 of the predictors of chronic daytime sleepiness, in addition to sleep disorders, delayed sleep rhythm, and frequent medication intake.\textsuperscript{17} Underage drinking can significantly impede healthy development and potentially predispose to numerous negative health consequences later in life.

Alcohol abuse has significant comorbidity with other substance use and psychiatric disorders. Heavy drinkers (eg, those who drink 5 or more alcoholic beverages a day) are more likely to use marijuana and other drugs and also have higher rates of alcohol dependence, depression, and other mood disorders, in addition to suffering increased
social consequences from alcohol use. Adolescents who have their first alcoholic drink before age 13 years are significantly more likely to exhibit suicidal behaviors than peers who do not drink. Onset of drinking at age 15 carries a 5-time greater risk of developing alcohol-related problems later in life. For children with ADHD, problems with alcohol can begin at an early age and may moderate life stress pathways that appear to contribute to risk of alcoholism. Marshal and colleagues investigated the drinking behavior of 142 adolescents with a childhood ADHD diagnosis and 100 matched control adolescents without childhood ADHD. At least 1 parent of each child was interviewed. Study results showed a relationship between family or peer stress among adolescents with ADHD and a history of paternal alcoholism. In addition, there was a positive correlation between ADHD in adolescents and pathologic alcohol use. Based on these findings, the authors proposed a hypothesis that ADHD can moderate the life stress pathways and thus promote transition of paternal alcoholism to child’s pathologic involvement with alcohol.

Investigating the hypothesis that ADHD confers an increased risk of heavy drinking in later adolescence, Molina and colleagues compared 364 children diagnosed with ADHD with a control group of 240 age-matched non-ADHD adolescents and young adults at baseline and again after 8 years. The investigators found that rates of heavy drinking, drunkenness, symptoms of alcohol use, and alcohol use disorders were elevated in 15- to 17-year-old adolescents with ADHD but not in younger ADHD adolescents. In adolescents younger than 15 to 17 years, ADHD was associated with alcohol problems only if there was comorbid conduct disorder. In 92 adolescents with ADHD and coexisting conduct disorder, 20.7% were diagnosed with alcohol abuse, and 10.3% were diagnosed with alcohol dependence. In comparison, when 272 adolescents with ADHD without comorbid conduct disorder were studied, 4.8% were diagnosed with alcohol abuse, and 1.6% were diagnosed with alcohol dependence.

Alcohol has profound effects on sleep. Sleep changes are common and can occur as a result of acute intoxication, chronic alcohol consumption, and withdrawal from alcohol. Electroencephalographic parameters of alcohol-induced sleep changes include suppressed REM sleep, increased time spent in stages 3 and 4 of NREM sleep, increased sleep latency, and decreased total sleep time. Upon recent abstinence from alcohol, total sleep and sleep efficiency are decreased, and REM sleep remains disrupted. Difficulty falling and staying asleep and lack of restorative sleep are common in prolonged abstinence and persist for months after alcohol cessation. Sleep problems in recovering drinkers can contribute to relapse if not addressed and treated. Higher prevalence of alcohol use was found in adults with insomnia, suggesting the role of self-medication of insomnia in the development of alcohol dependence. Finally, sleep-related breathing disorders and periodic leg movements occur more frequently among chronic alcohol users.

**Tobacco Smoking**

Tobacco use results in more preventable death than any other drug and represents a significant public health problem. Nevertheless, tobacco smoking continues to be prevalent, and it is the preferred drug of choice among young people. In 2008, 20.4% of 12th graders reported cigarette smoking during the previous month. The association between daily smoking and health was evaluated in a study of 8040 adolescents aged 13 to 18 years. Daily smokers were more frequently absent from school and had more hospitalizations. They also had more somatic and psychological complaints than nonsmokers and used more medications. Use of analgesics was more frequent among daily smokers because of increased incidence of pain, and
use of tranquilizers and sleeping pills was more frequent because of increased feelings of nervousness, restlessness, and sleep problems. Sleep problems, such as difficulty falling asleep or early awakening, were 2.6 to 3.0 times more common in daily smokers versus nonsmokers.27

The long-term consequences of tobacco smoking among adolescents who initiated use before age 18 years were examined by Mathers and colleagues28 in a review of 16 published longitudinal trials. The results suggest that experimental and frequent smoking at age 13 years predict a range of social and behavioral problems by early adulthood. Those who did not start smoking by the end of high school rarely acquired a subsequent smoking habit. Tobacco use at age 15 to 17 years was related to alcohol abuse and dependence at age 24 to 27 years. Frequent smokers at baseline (age 17 years) had a threefold increase in the probability of developing binge drinking by age 22 years. A positive association was also shown between early daily smoking (by age 13–17 years) and subsequent cannabis use at age 18 to 25 years. Teens’ tobacco smoking predicted academic and social problems, and it may predict mental health problems, such as antisocial personality disorder, depression, anxiety, and sleep problems. The study confirmed several links between tobacco use in adolescents and subsequent developmental problems in early adulthood. The investigators suggested that tobacco use during active brain development may modify reward pathways and thus elevate the risk of alcohol use. Other possible mechanisms of the observed associations might include genetics and early environmental factors, such as parents’ supervision and peer influences.28

The effect of cigarette smoking on sleep has been investigated by several researchers. Because nicotine is a stimulant, it increases sleep latency and decreases total sleep time and REM sleep. Patten and colleagues29 found that frequent smokers at age 15 years without baseline sleep problems had subsequent occasional and frequent sleep problems by age 18.5 years. Phillips and Danner30 examined sleep disturbances as a result of smoking in 99 high school students in grades 9 to 12 (38% smokers) and 385 adults (20% smokers). Smokers reported significantly more daytime sleepiness, difficulty going to sleep and staying asleep, depression, higher caffeine intake, and minor accidents during the preceding year than nonsmokers. The investigators concluded that because unhealthy behaviors tend to cluster, sleep problems in smoking adolescents may reflect the tendency to engage in unhealthy behaviors in general. They recommended that clinicians inquire about smoking habits in individuals complaining of sleep problems.30

Obstructive sleep apnea and its common manifestation, habitual snoring, are common in children and adolescents and can lead to physical and social problems if unrecognized and untreated. Researchers have demonstrated the relationship between these conditions and smoking cigarettes. Shin and colleagues31 investigated habitual snoring in 3871 11th graders in Korea and found that in addition to elevated body mass index (BMI > 23) and witnessed apneic episodes, cigarette smoking was 1 of the independent risk factors for habitual snoring.31 Smoking can contribute to snoring by causing mucosal inflammation and narrowing of the airway, but it can also stimulate breathing and combat somnolence and weight gain as a result of sleep apnea. Smoking, therefore, might appeal to some youth by virtue of decreasing the symptoms of sleep apnea. Schrand32 explored these associations and strongly suggested that recognition and treatment of sleep apnea are essential in adolescent smoking cessations programs. In addition to adversely affecting physical and mental health, tobacco smoking can contribute to changes in sleep patterns and the development of sleep-related disorders in children and adolescents.
Caffeine

Caffeine is the most widely consumed psychostimulant. It is socially acceptable and readily available for children, adolescents, and adults. About 98% of children and adolescents aged 5 to 18 years consume caffeine at least once weekly. The most common source of caffeine consumed by children and adolescents is soft drinks. Caffeine is also 1 of the most frequently abused substances, although many young people are not aware of its potentially addictive properties. Tolerance and physical dependence to caffeine have been demonstrated in adults after regular use. Nearly one-fourth (23.4%) of young people who abuse a substance also abuse caffeine. In children, as in adults, caffeine can cause elevated blood pressure, headaches, either irritable or overly excitable mood, and disrupted sleep. Caffeine, a central nervous system (CNS) stimulant, causes arousal by competing with adenosine receptors. Caffeine affects temporal organization of REM and NREM sleep and increases sleep latency and the frequency of nighttime awakenings in a dose-related fashion.

Pollack and Bright surveyed 191 students in seventh to ninth grades to examine the effect of their caffeine consumption on sleep. They found correlations between higher caffeine intake and shorter and interrupted nocturnal sleep and increased daytime sleepiness. Sleep was more interrupted on the day after the high caffeine intake, especially on weekends. Using caffeine along with other substances can also negatively impact sleep. Concomitant use of caffeine and alcohol, for example, can cause profound insomnia because of the different half-lives and opposing pharmacologic actions of these substances.

In a longitudinal study of 30 girls aged 7 to 17 years, Whalen and colleagues investigated the possible role of caffeine as an affect regulator in depressed youth with major depressive disorder (MDD) and in 23 healthy control subjects. Caffeine use, sleep, and affective status were measured at baseline and after 8 weeks. At baseline, there was more caffeine consumption per day and a higher frequency of sleep problems in the group with MDD. The depressed subjects also reported more anxiety symptoms during the days they used caffeine. As the MDD was treated during the course of the study, caffeine consumption decreased fourfold. The findings suggest that adolescents with MDD may use caffeine as a means of regulating mood to help alleviate symptoms of depression. Caffeine consumption, therefore, may play a role in the clinical manifestation of depression. The researchers also proposed that sleep problems could be early markers of depression that persist after remission of acute depressive symptoms. Treatment of sleep problems should be considered to enhance the benefits of treatment for depression. Because caffeine is widely available, its use should be evaluated more routinely with regard to its effects on sleep, concomitant substance use, other psychiatric disorders, and general functioning in children and adolescents.

PRESCRIPTION MEDICATIONS

Nonmedical use of prescription medications by adolescents has shown steady growth in recent years. In an analysis by the National Survey on Drug Use and Health of a large sample of adolescents aged 12 to 17 years, 1 in 12 adolescents (8.3%) reported misuse of prescription medications. Misuse of prescription medications, such as opioids, stimulants, tranquilizers, and sedatives, in youth was significantly associated with other risk-taking behaviors, major depressive episodes and a history of treatment for mental health problems in the past year, poor academic performance, and use of alcohol, cigarettes, marijuana, cocaine, and inhalants during the previous year. More than one-third (36%) of adolescents who misused prescription medications had
a concurrent substance use disorder. Adolescent girls more frequently misused opioids, stimulants, and tranquilizers than boys. Opioids were the most commonly misused prescription medications followed by stimulants, tranquilizers, and sedatives.40

Prescription Opioid Analgesics

Nonmedical use of prescription pain relievers in youth remains at a high level. Nearly 1 in 10 (9.1%) 12th graders reported use of pain relievers in 2008. Oxycodeone (OxyContin) and hydrocodone (Vicodin), the most common opioids, were reported to be used by 4.7% and 9.7% of the 12th graders, respectively.25 In 2006, nonmedical use of methadone and single-ingredient and combination forms of hydrocodone and oxycodone resulted in 33% of the emergency room (ER) visits in patients under age 21.41 Significant prevalence of the use of pain relievers in adolescents reflects the development of a new pattern of drug use in this population. Wu and colleagues42 observed that a significant proportion of adolescents gain experience with pain relievers before they try other drugs, such as marijuana and inhalants. Exposure to opioids during intensive brain development may have unknown and potentially serious consequences for youth.43

The effects of opioids on sleep have been examined by several researchers. Dimsdale and colleagues44 investigated the effect of single-dose administration of sustained-release morphine and methadone on sleep in 42 healthy adults. Oral administration of both opioids decreased the percentage of deep sleep and increased the percentage of stage 2 sleep. The investigators suggested that the observed increase in stage 2 sleep might contribute to the fatigue related to chronic opioid use.44 Withdrawal from opioids causes insomnia and long-lasting rebound in REM sleep.45 Chronic opioid use, methadone in particular, has been associated with increased frequency of sleep-disordered breathing and incidence of central sleep apnea.46 Use of prescription pain analgesics is a growing problem in adolescents. Their widespread use, easy access, and high addiction potential require vigilance and ongoing education of youth, who are vulnerable to the risk of abuse.

Prescription Stimulants

Stimulants used to treat ADHD include methylphenidate, dextroamphetamine, and mixed-amphetamine salts. They remain a well-established first-line treatment of ADHD. Psychostimulants are frequently prescribed for children and adolescents in the United States. Prevalence of the prescription of stimulants for children and adolescents in the United States in 2000 was significantly higher than in the Netherlands and Germany. Prescription rates were 4.3% in the United States as compared with 1.2% and 0.7% in the 2 European countries.47

The relationship among the diagnosis of ADHD, use of stimulants for treatment of ADHD, and development of substance use disorders has spurred significant clinical interest. Several studies have demonstrated that childhood ADHD is a risk factor for cigarette smoking, is related to substance use disorders in adolescents and adults, and causes greater severity of addiction when it occurs.48,49 It has also been shown that incidence of ADHD is higher in substance users.50–52 The self-medication hypothesis is 1 of the possible explanations for why youth and adults with ADHD use cigarettes and substances. Wilens,53 for example, demonstrated that young adults with ADHD used nicotine and drugs more frequently than non-ADHD control subjects to control their mood and to improve their sleep. Several studies have examined the relationship between treatment of ADHD with stimulants and the development of substance use disorders. Faraone and Wilens54 have shown that psychostimulants
for the treatment of ADHD are protective against substance use disorder by a factor of 1.9. Treatment of ADHD adolescents with psychostimulants significantly decreases the risk for substance use disorders to approximately the same level as in adolescents without ADHD. In a study of adults with ADHD previously treated with psychostimulants, the authors found no elevation in prevalence of cigarette smoking and substance use and dependence. Increased risk for substance use has been demonstrated in children with ADHD and concurrent conduct disorder. The brain areas involving circuitry of rewards (orbitofrontal cortex) and punishments (amygdala) may be significantly disturbed in these children, who are especially prone to have disruptive behavioral abnormalities, including high-risk behaviors and substance use.

Studies have demonstrated that early initiation of stimulant treatment of ADHD might have protective long-term benefits. In the first prospective, longitudinal study of 176 boys aged 6 to 12 years with and without concurrent conduct disorder, Mannuzza and colleagues assessed whether age of initiation of treatment with methylphenidate influenced the development of a substance use disorder later in life. Results demonstrated that children treated with methylphenidate at an early age (as early as age 6 years) did not have increased risk of developing substance use disorders. However, children treated at a later age (as late as age 12 years) showed increased risk of developing a nonalcohol substance use disorder. The investigators proposed that early-initiated ADHD treatment with stimulants might decrease the risk for developing substance use disorders in adulthood by normalizing brain functioning during its maturation. Shaw and colleagues hypothesized that stimulant treatment of ADHD in children might contribute to normal cortical development and prevent long-term structural brain abnormalities. They demonstrated that stimulants do not cause structural changes in the brain but appear to prevent changes, such as decrease in cortical thickness associated with ADHD when left untreated. Willens and colleagues also demonstrated a protective effect for stimulant therapy in their longitudinal case-control study of 262 females aged 6 to 18 years with and without ADHD. About 94 girls with ADHD treated with stimulants had a 73% reduction in risk for developing a later substance use disorder and a 72% reduction in risk for starting smoking, as compared with girls with ADHD who were never treated with stimulants. Treatment with stimulants was not shown to be associated with increased risk of substance and alcohol dependence.

Appropriate stimulant pharmacotherapy has clear clinical benefits. Nevertheless, it is known that stimulants are being diverted and abused. Although the misuse of stimulants by high school students decreased during 2007, it remained high according to 2008 epidemiologic data. About 6.8% of 12th graders abused amphetamine and 3.4% of 12th graders abused methylphenidate during 2007. There were 7219 amphetamine-, dextroamphetamine-, and methylphenidate-related ER visits in 2006. Williams and colleagues found that 23% of a sample of adolescents treated for addictions reported nonmedical use of stimulants at some point in their lives. In a study by McCabe and colleagues, 7% of college students reported use of nonprescribed stimulants. Enhancement of academic achievement was commonly cited as a reason for nonmedical stimulant use by college students.

Despite their widespread use for the treatment of ADHD, stimulants may not have negative effects on sleep. ADHD itself often has detrimental effects on sleep, because insomnia, restless leg syndrome, and sleep-related breathing disorders are common in children and adults with ADHD. Subjective sleep complaints in children and adolescents with ADHD include difficulty falling asleep, restless sleep, nocturnal awakenings, and daytime sleepiness. Electroencephalographic changes of sleep
architecture in children with ADHD include reduced REM sleep, increased periodic limb movements (PLMS), and PLMS-associated arousal. The impact of stimulant medications on sleep was investigated by O’Brien and colleagues. They measured subjective and objective sleep characteristics in children with ADHD treated and not treated with stimulant medications. Both groups reported more sleep disturbances and had decreased REM sleep in comparison with controls. Nevertheless, treatment with stimulants was not shown to significantly affect objective sleep measures in treated patients compared with the untreated group. In a study by Schedyl and colleagues, the use of stimulants for ADHD in adults also did not appear to significantly affect sleep parameters. Sobanski and colleagues reported results of their study of stimulants on sleep in adults with ADHD. Thirty-four adults with ADHD treated with methylphenidate were compared with 34 matched controls. Untreated patients had decreased REM sleep, diminished sleep efficiency, and more nocturnal awakenings than those adults who received stimulants. Patients treated with methylphenidate showed significant reductions in sleep latency and improved sleep efficiency. The investigators concluded that sleep abnormalities related to ADHD continue through the patient’s lifespan. They also suggested a potential benefit of stimulant treatment of ADHD on sleep.

Because of the high rate of stimulant prescriptions to young children and adolescents and the significant effects of these medications on sleep, general well being, and potential for abuse, it is imperative that more research be conducted in this area with emphasis on long-term consequences of stimulant use.

Tranquilizers and Sedatives

In 2008, 6.2% of 12th graders used tranquilizers (including benzodiazepines [BDZ]) during the previous year, and 2.8% used sedatives (including barbiturates) during the previous month. Almost one-third (32%) of ER visits associated with nonmedical use of pharmaceuticals in 2006 was attributed to this class of medications. ER visits involving BDZ increased by 36% from 2004 to 2006 and outnumbered other types of psychopharmacologic agents.

Use of sedatives and BDZ, in particular, is common in combination with other drugs. Concomitant use of BDZ with alcohol is particularly dangerous in overdose because of the additive effects of the substances. There is a positive correlation between use of BDZ in opioid and cocaine abusers, severity of addiction, and degree of psychosocial dysfunction. BDZ are CNS depressants with strong anxiolytic and sedative properties. Their effect on sleep is well known and consists of decreased REM sleep and slow wave sleep (SWS). Treatment with BDZ might be of particular benefit in night terrors and sleepwalking states in children, when suppression of the sleep stages mentioned is beneficial. Use of BDZ as therapeutic agents in youth should be appropriately monitored to minimize the risk of misuse or abuse.

Over-the-Counter Medications

There are a growing number of young people who abuse cough and cold remedies for recreational purposes. In 2008, 5.5% of youth reported abusing over-the-counter cough medicines. The main component of cough remedies is dextromethorphan, a cough suppressant. When abused, dextromethorphan can cause hallucinations and dissociative states. There are limited data on the health consequences of dextromethorphan abuse in young people. Educational programs targeting adolescents and their parents should be implemented in an effort to raise awareness and prevent this growing problem in adolescents.
In summary, prescription and over-the-counter medications are legal and therefore erroneously perceived to be safe and less problematic than illicit drugs. Teenagers might not fully understand the potential dangers of prescription medication misuse. It is important to educate the adolescents and parents about proper use and monitoring of prescription medications.

ILLICIT DRUGS AND OTHER SUBSTANCES OF ABUSE

Marijuana

Marijuana is an illegal drug most widely used by adolescents. Almost one-third (32.4%) of 12th graders have used marijuana during 2007. An even higher percentage (42.6%) of 12th graders have tried the drug at least once. Contrary to the misconception that marijuana is harmless, marijuana use may have significant adverse consequences. Onset of marijuana use before age 17 years can result in changes in the structure of the brain and in cognitive function. Marijuana can trigger psychotic episodes in predisposed individuals. In patients with schizophrenia, it can cause an increase in positive symptoms of the disorder, earlier onset, increased number of psychotic episodes, and more pronounced brain volume reduction with time.

Endogenous cannabinoids increase adenosine and thus promote sleep. In a study of the effects of cannabis extract on sleep in young adults, Nicholson and colleagues found that administration of 15 mg of δ-9-tetrahydrocannabinol (THC) caused decreased sleep latency, increased sleepiness, and impaired memory, and it also resulted in mood changes the next day. THC also has been shown to decrease REM sleep. Additionally, marijuana has been found to cause more frequent nocturnal arousals and a reduction in sleep efficiency in 3-year-olds who were exposed to marijuana prenatally.

Marijuana discontinuation is associated with significant sleep abnormalities. Difficulties with sleeping and strange dreams have been reported as consistent symptoms of marijuana withdrawal. Bolla and colleagues examined polysomnographic (PSG) measures in recently abstinent heavy marijuana users. PSG studies were performed on 17 adult chronic marijuana users aged 18 to 30 years during 2 nights after marijuana cessation. Marijuana users had shorter total sleep time and lesser SWS. They had worse sleep efficiency, longer sleep latency, and shorter REM latency than controls, on night 2. Overall sleep was more disturbed on night 2. Withdrawal symptoms, craving, and depression did not seem to significantly affect these findings. The investigators emphasized that the data did not determine casual relationships between marijuana use and sleep patterns because there is a possibility that sleep problems during childhood and adolescence could predispose to drug use later in life. The findings nevertheless have important implications for the treatment of patients with cannabis abuse or dependence. Knowledge of significant sleep disturbance during early abstinence from marijuana may prompt the use of specific treatments and therefore improve outcomes in drug rehabilitation. Effects of marijuana withdrawal in adolescents have been investigated by several researchers. In a study, cravings for marijuana, irritability, depressed mood, sleep difficulty, and nervousness/anxiety were among the most frequently reported symptoms of withdrawal and were of moderate or greater severity in 30% of the adolescents. Irritability, trouble concentrating, tiredness, and trouble sleeping during withdrawal were reported by Dawes and colleagues. These symptoms were found to interfere with completing schoolwork. Marijuana use in adolescents thus may lead to significant cognitive impairments, sleep disruptions, and serious long-term consequences.
Cocaine

Use of cocaine among adolescents remains a significant problem. The annual prevalence of cocaine use among high school students was 4.4% in 2008. Young people who abuse cocaine tend to exhibit more delinquent behaviors and show rapid progression from initial use to the development of dependency on the drug. The acute effects of cocaine, a psychostimulant, include euphoria, motor restlessness, and mental alertness. Psychiatric sequelae of continuous cocaine use in adolescents include suspiciousness and overt paranoia, aggressiveness, dysphoria, and suicidal thoughts. Use of cannabis and sedatives for their calming effect is common in adolescents who regularly use cocaine. Cocaine administration adversely affects sleep; it increases wakefulness and sleep latency, and reduces total sleep time. During cocaine withdrawal, agitation, depression, changes in appetite, and fatigue are very common. Cognitive functioning, such as memory and vigilance, is impaired and may contribute to relapse on the drug. Sleep disturbances during cocaine withdrawal include increased sleep latency, decreased sleep efficiency, reduced REM latency, and an increased percentage of REM sleep. Cocaine is a highly addictive drug with multiple adverse consequences on adolescent physical and social development and health.

Methamphetamine

Methamphetamine (meth, speed, ice) is a stimulant that can easily be manufactured and distributed in clandestine laboratories in small communities. It possesses a high potential for dependency. Data show a decline in popularity and use of methamphetamine among young people. In 2008, 1.5% of 10th graders used methamphetamine. Effects of withdrawal from methamphetamine on sleep have been reported in adults. Acute withdrawal (“crash”) is characterized by an increase in total sleep followed by increased sleep latency, frequent awakenings, and decreased quality of sleep as withdrawal continues.

3,4-Methylenedioxymethamphetamine

3,4-Methylenedioxymethamphetamine (MDMA, ecstasy), which has hallucinogenic properties, is 1 of the preferred drugs used in rave parties and in dance clubs. A small, but not insignificant, percentage (4.3%) of 12th graders used ecstasy in 2008. Through the rapid release of serotonin and dopamine, MDMA causes feelings of closeness to others, empathy, and cognitive and perceptual changes. Frequent MDMA users report restlessness, impaired memory and learning, and disturbed sleep. Adolescents might be especially vulnerable to neuropsychiatric sequelae from MDMA use. There is evidence that even limited exposure to ecstasy can be harmful to the brain. de Win and colleagues found prolonged vasoconstriction in the frontal cortex and associated increased impulsivity scores in users of a small amount of ecstasy when compared with nonusers. Sleep changes also were reported in MDMA users. Sleeplessness and bruxism (grinding of teeth) have been reported in recreational users. PSG sleep changes in those abstaining from MDMA include reduction in total sleep and stage 2 sleep, increase in stage 1 sleep, and tendency toward reduced REM latency. There are only few research data describing the cognitive and physical consequences of ecstasy use in adolescents, and further research is needed. Generational forgetting, or the perception of ecstasy by young people not previously exposed to the drug as relatively harmless, highlights the urgent need for continuous education programs for adolescents in schools and communities.
Inhalants

Use of inhalants continues to be a common problem in youth. According to epidemiologic data, lifetime prevalence of inhalant use in 8th graders was 15.7% in 2008. Approximately 4 in 100 (4.1%) 8th graders reported using inhalants during the previous month. Inhalants are readily available. A report on inhalant use among adolescents indicated that 12- and 13-year-olds prefer to use inhalants to get high than to use marijuana. As these adolescents grow older, they move away from inhalants toward the use of other illicit drugs.

Use of inhalants is associated with several serious medical and psychiatric conditions. Inhalants can damage multiple organs and lead to death. Inhalant users are more likely to have been victims of neglect and abuse and to have a higher incidence of affective, conduct, and personality disorders, and suicide attempts. Inhalant use is associated with alcohol and illicit drug use and might therefore be a marker for severity of drug involvement. Withdrawal from inhaled gasoline in children has been described by Shah and colleagues. Symptoms included sleep disturbances, irritability, psychomotor retardation, and cravings. Because of the dangers of inhalant use in youth, it is important to raise awareness of this problem and to improve education among children, adolescents, and adults.

Anabolic Steroids

Use of anabolic steroids in adolescents remains a significant clinical concern. Data from 2008 indicate that 2.2% of 12th graders used steroids at least once in their lifetime and 1.5% used them during the previous year. Adolescents often use steroids to enhance athletic performance, and to improve physical appearance and body image. Steroid use is associated with multiple medical and psychiatric problems. Aggression, violence, rage, and suicidal thoughts are common in adolescents abusing steroids. In addition to sleep disorders, depression, and hypomania, testicular atrophy in boys and menstrual abnormalities in girls are common after repeated exposure to steroids. Signs of behavioral activation, such as increased energy, increased sexual feelings, and diminished sleep, have been observed in healthy adults after administration of methyltestosterone. These symptoms were associated with increased levels of 5-hydroxyindoleacetic acid, the major metabolite of serotonin, in the cerebrospinal fluid. Thus, the influence of steroids on serotonergic function might be 1 of the possible explanations for its effects on mood and sleep. Steroid use remains an attractive option for many adolescents. Proper prevention, identification, and treatment are required to minimize serious long-term consequences of steroid use in adolescents.

SUMMARY AND RECOMMENDATIONS

Sleep problems and substance use disorders in children and adolescents remain major public health concerns. Comprehensive clinical management should include awareness of the prevalence and co-occurrence of these disorders. This approach requires interdisciplinary, multispecialty team involvement in the prevention, screening, diagnosis, and treatment of sleep disorders and substance use disorders in youth. Continuity of care along the continuum from acute states into the maintenance phase and then total remission is important. Close interaction with teachers and cooperation from family members contribute to continuity of care and ensure reduced risk of relapse and reoccurrence of the disorders.

Research and clinical data have provided considerable evidence that childhood insomnia and other sleep disorders can increase the probability of developing...
substance use and other psychiatric disorders later in life. On the other hand, substance use can lead to sleep difficulties. In light of this finding, it is strongly recommended that the treatment of childhood insomnia not be delayed. Parents should be encouraged to seek information and to explore recommendations for the treatment for sleep problems from their primary care providers and health care professionals. Untreated substance use disorders in adolescents can lead to significant health, social, and economic problems. Substance use disorders should be diagnosed and treated appropriately. Because it is impossible to predict which treatment modality or combination of treatments for substance use disorders will be most effective, all available standard treatment options that have been shown effective should be considered. Treatment options include medication and psychosocial and self-help programs (eg, Alcoholic Anonymous). New treatment modalities are also being developed. Among them, motivational enhancement therapy, group and individual therapies based on cognitive behavioral therapy, and multidimensional family therapy for youth with drinking problems have been shown effective.

ADHD is viewed as a developmental disorder prevalent in many individuals from childhood to adulthood. The significant impact of ADHD on cognitive development in children and adolescents and its association with sleep disturbances, substance use, and other psychiatric disorders require proper assessment and treatment of ADHD and all comorbid conditions. The relatively high rate of stimulant abuse requires that adolescents treated for ADHD with stimulants be educated and closely monitored for appropriate use of stimulant medications to prevent misuse and diversion. The potentially addictive properties of stimulants warrant the development of longer-acting stimulant medications. These formulations for the pharmacologic treatment of ADHD minimize the risk of reinforcement and potential abuse. Longer-acting stimulant and nonstimulant medications are recommended to treat ADHD in the high-risk group of adolescents with co-occurring substance use disorder and conduct disorder.

Gender differences in correlations between early sleep problems and substance use have also been shown. These differences may be related to developmental physiologic changes in girls. There is also evidence that teenage girls tend to misuse prescription medications more frequently than teenage boys. More longitudinal studies are needed to investigate gender effects in the relationships between early sleep problems, substance use, and other co-occurring disorders and to understand possible risk pathways and developmental links between the disorders.

Difficulty differentiating chronic insomnia from sleep disturbances related to ADHD, alcohol and substance use disorders, depression, and other psychiatric disorders dictates the need to develop a validated algorithm for clinicians to properly diagnose and appropriately treat these conditions.

The relationship between sleep and substance use disorders is an underdeveloped and yet extremely important area for researchers to dedicate their efforts. The high prevalence of sleep and substance use disorders and the wide interplay between these and other comorbid psychiatric and behavioral conditions require clinicians to be more proactive in educating students, parents, and the community about the potential dangers of substance use and the serious consequences if sleep and substance use disorders go unrecognized and untreated.

REFERENCES


