Prescription Stimulants in College and Medical Students

Subjects: Neurosciences

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Stimulants are effective in treating attention-deficit/hyperactivity disorder (ADHD). Psychiatrist Charles Bradley first made this discovery in 1937 when he found that children treated with amphetamines showed improvements in school performance and behavior. Between 1995 and 2008, stimulants to treat ADHD increased six-fold among American adults and adolescents at an annual rate of 6.5%. Stimulants without a prescription, known as nonmedical use or misuse, have also increased.

stimulant misuse college students ADHD

1. Introduction

Stimulants are effective in treating attention-deficit/hyperactivity disorder (ADHD). Psychiatrist Charles Bradley first made this discovery in 1937 when he found that children treated with amphetamines showed improvements in school performance and behavior [1]. However, an increase in the use of stimulants for the treatment of ADHD did not occur until almost 20 years later, when the American Psychiatric Association began focusing on hyperactivity symptoms in children [2]. Since then, the prevalence of stimulant use for ADHD has increased. Between 1995 and 2008, stimulants to treat ADHD increased six-fold among American adults and adolescents at an annual rate of 6.5% [3][4]. Stimulants without a prescription, known as nonmedical use, have also increased [5].

The primary motive for the nonmedical use of stimulants is enhancing concentration while studying, especially when preparing for multiple exams [6]. However, about a quarter of nonmedical users reported recreational reasons, such as “getting high” [7][8]. Many students without a prescription for stimulants obtained them from peers. Still, in one study, over one-third reported stealing it, and 20% exaggerated their symptoms to obtain a prescription from a physician [9][10][11][12]. Although most nonmedical users believed that stimulant use had an overall positive impact on their academic success, this is inconsistent with a documented link between nonmedical use and lower GPAs (grade point averages) [11][13][14].

Misuse of prescribed medication can be differentiated from nonmedical use. Misusers have a prescription for ADHD medication but may take the medication at a higher dose or more frequently than originally intended. Misuse has been reported by between 27% and 36% of students across numerous studies. The primary motivation behind this kind of use is similar to nonmedical users, improving academic performance [15][16][17]. Students may also

divert their medications to peers by giving them away or selling them, which has been reported by 62% of students in their lifetime [9].

2. Misuse in College and Medical Students

2.1. Prevalence

The highest rates of nonmedical prescription drug misuse in the United States are seen most notably in young adults between 18 and 25 years, according to the Substance Abuse and Mental Health Services Administration (SAMHSA) in 2020 [18]. Generally, stimulant misuse occurs more frequently in college students than young adults not attending college [18]. The estimated lifetime prevalence rate of prescription stimulant misuse in college students is 5.3% to 35% [19]. Using data collected from the National Survey on Drug Use and Health (NSDUH) to analyze the effects of educational status on stimulant misuse, outcomes demonstrated the highest past-year misuse rates in college students and highest lifetime misuse rates in college graduates [20]. A long-term study conducted by the University of Michigan in 2015 reported amphetamine, dextroamphetamine mixed salts (brand name Adderall®) misuse in 14.8% of U.S. college males compared to 7.4% in non-college males of the same age [21]. In 2017, 23% of students reported using stimulants without a prescription in a survey of 988 undergraduate students [22].

Furthermore, compared to opioid misuse, college students have higher rates of nonmedical stimulant misuse [20][21][23][24]. Aside from undergraduate students, nonmedical prescription stimulant use is prevalent among medical students worldwide. A review reported the utilization of stimulants without a prescription in 970 out of 11,029 medical students. The percentages of medical students across the country misusing stimulants varied from 5.2% to 47.4% [25].

2.2. High-Risk Factors

The likelihood of prescription stimulant misuse correlates with certain student demographic criteria. Several studies observed a greater risk of stimulant misuse in male U.S. college students than female students [11][14][19][26][27][28][29][30][31][32]. Among 984 college students, 80.5% of stimulant misusers were Caucasian, another frequent finding [33]. Additionally, higher yearly family income has been noted in students misusing stimulants compared to non-users (USD76,000 vs. USD71,000, respectively) [33]. College students in sororities and fraternities report prescription stimulant misuse more often than non-Greek students [11][14][26][27][34][35][36]. Low-GPAs and other factors implicating poor academic performance correspond with a higher risk of stimulant misuse [11][33][37].

Risk factors for nonmedical stimulant use, including male gender and Caucasian race, also apply to medical students. The risk of stimulant misuse is elevated in medical students with a past medical history significant for psychiatric disorders [38]. Additionally, in a study, osteopathic medical students were more likely to engage in stimulant misuse when a close friend or roommate also used stimulants nonmedically [39].

2.3. Stimulant Sources

College students frequently disclose easy accessibility to prescription stimulants [27][36][40]. In this population, the use of peers as a source of obtaining prescription stimulants remains a common finding [27][36][37][40]. Moreover, misused stimulants are more likely to be obtained for free through peers or relatives in current full-time undergraduate students or recent college graduates compared to non-college individuals [20].

2.4. Motivation for Misuse

Academic enhancement, reported in 50% to 89% of college students with stimulant misuse, is the most common reason for nonmedical stimulant use [27]. Examples include receiving higher exam scores, increasing concentration, and achieving greater productivity [19][34][37]. Although less common, additional motivations regarding the misuse of stimulants in college students include recreational purposes (2% to 31% of misusers), self-treating undiagnosed ADHD (4% to 12% of misusers), and weight loss (3.5% to 11.7% of misusers) [27].

Similar to college students, improving school performance motivates stimulant misuse in medical students. The high-stress environment and pressure to score well on exams can motivate increased use of stimulants in medical students [41]. In one study, most French medical students using stimulants reported drug initiation during their first year to promote wakefulness while studying [42]. On the other hand, over half of the Saudi Arabian medical students who reported stimulant misuse were in their final two years of medical school. Researchers suggested that senior-level medical students showed a greater risk of stimulant use because of elevated stress of board exams, choosing a medical specialty, and competing for residency positions [41]. These studies suggest a worldwide phenomenon of stimulant misuse.

2.5. Placebo Effect and Perceived Cognitive Enhancement

Some studies question the contribution of the placebo effect on subjective outcomes of stimulant use in students without ADHD. One randomized trial revealed a subjective increase in arousal in students at high risk for stimulant misuse who believed they were receiving methylphenidate [43]. Another trial in college students without ADHD associated stimulant expectation with better cognitive performance, regardless of receiving the active stimulant or placebo. Cognitive performance declined when participants believed the placebo was given [44]. A small placebo-controlled trial, which consisted of 13 college students without ADHD, found significant results regarding perceived effects of Adderall 30 mg. Minor neurocognitive effects were found for healthy college students. Still, substantial outcomes were noted for perceived drug effects, self-reported stimulant experience, and mood positivity [45].

3. Adverse Effects of Stimulant Misuse by People with ADHD

Stimulant use has been increasing among college students, with rates as high as one-third of students who generally use them for enhanced academic performance and recreational use [6]. Unfortunately, little data exist that describe differences in how side effects are experienced for prescribed and non-prescribed users [46].

Studies show that prescribed users report side effects more frequently, which might be explained by some users feeling they have less control over their use of stimulants, leading them to perceive the effects as undesirable [46]. However, prescribed users may have more experience with the drug and its side effects than non-prescribed users, leading them to remember the most prominent effects over the time they have used stimulants [47].

3.1. General Adverse Effects among Nonmedical Use and Misuse

Other studies have shown that stimulant misusers appeared to experience more side effects than those that use stimulants under medical supervision. In one study, both those who misuse and those who have non-medical use were more likely to experience exaggerated well-being (euphoria) and restlessness than those who have it prescribed and use it as directed. They were also more likely to report changes in sex drive [48]. Specifically, in athletes with ADHD, stimulants may lead to an increased risk of cardiac injury, possibly due to stimulant-induced hyperthermia. This is exacerbated by long durations of exercise athletes regularly experience, so caution should be used when prescribing stimulants to athletes [49].

Of note, those with medical misuse were more likely than those with non-medical use to endorse the use of cigarettes, amphetamines, marijuana, and anxiety medication concurrently with stimulants. They have also reported alcohol use at a relatively high rate compared to those who have non-medical use. This is concerning due to the potential interaction between stimulants and alcohol. Stimulants may counteract the perceived effect of alcohol intoxication on an individual, leading them to consume more alcohol to have a greater perceived effect, leading to poor decision-making [48].

3.2. Potential Neuropsychiatric Effects

Since stimulants are psychoactive, there is always a theoretical risk of developing a neuropsychiatric disorder due to their use; the risk is augmented with prolonged exposure and increased doses. Studying these possible psychiatric effects is complicated by comorbidities and the overlap between ADHD symptoms and symptoms of other psychiatric disorders, such as anxiety, mood disorders, sleep disorders, and psychotic disorders [50][51][52].

There is widespread concern regarding the induction of depression, both suicidal behavior, and ideation, and substance use disorders as possible adverse effects of long-term methylphenidate (MPH) use [53][54][55][56][57][58]. However, the preponderance of data collected to date indicates that while these are potential adverse effects, MPH is relatively safe [59]. However, caution should be used in individuals with suicidal ideation who may potentially overdose on stimulants. Some studies have reported anxiety and irritability as a potential result of long-term MPH use. Still, many studies also indicate that MPH is also generally safe regarding these outcomes [59][60][61][62]. A consensus opinion on the long-term safety of prescription stimulant use, especially when initiated during adolescence, has not yet been achieved. Studies have also reported the induction of tics and repetitive muscle contractions resulting in sudden and difficult-to-control body jolts or sounds resulting from long-term effects of MPH use [61][63][64]. These studies suggest that MPH be used with caution in those with tic disorders or prone to develop a tic disorder [59]. Psychosis has also been cited in several studies as a possible effect of long-term MPH use.

However, these studies have also provided evidence that MPH reduces psychotic symptoms and psychosis-related hospitalization [53][65][66], and ADHD itself may also be a risk factor for psychosis [67]. Although more studies are needed to investigate this relationship, those with psychosis or prone to it should be more cautious with stimulants [59].

4. Adverse Effects of Stimulant Misuse by People without ADHD

4.1. Medical Adverse Effects

Commonly self-reported adverse effects of stimulant misuse include headache, dizziness, stomach upset, negative mood, diminished appetite, and difficulty sleeping [27]. Stimulants can increase autonomic activity, such as blood pressure and heart rate, which is especially dangerous in nonmedical use without appropriate medical observation [37]. Stimulant-related emergency department (ED) visits from 2005 to 2010 increased from 13,376 to 31,244. Specifically, ED presentations involving nonmedical stimulant use increased from 5212 to 15,585 [68]. Compared to prescribed stimulant users, cases of amphetamine exposures reported to poison control centers from 2012 to 2016 occurred more frequently in those with misuse. Non-prescription use of amphetamines is associated with a greater risk of intensive care unit or inpatient psychiatric facility admission [69]. Adverse effects of misused stimulants often vary by route of administration. Although oral intake of nonprescription stimulants is the most common route of administration, adverse effects among stimulant misusers are seen across all administration methods [27]. Intravenous (IV) stimulant misuse is associated with more side effects than nasal or oral intake, with critical care admission being the most frequent consequence [69]. Prevalence of hospital admission from 2012 to 2016 was elevated for all young adults with stimulant misuse (64.7% oral, 49% nasal, and 68% IV) compared to those who did not misuse amphetamines (22% control) [69].

Additionally, a higher odds of death is associated with IV and intranasal administration among stimulant misusers (nasal: 0.5%; IV: 1.2%; non-users: 0.3%) [69]. Intranasal stimulant misuse has increased the risk of cardiovascular events compared to oral use [37]. Prevalence of admission to a psychiatric inpatient facility and risk of suicide attempts are greater with oral misuse than IV or intranasal misuse [69].

4.2. Psychiatric Disorders

Recent data suggest a link between stimulant misuse and psychiatric disorders such as depression, conduct disorder, and substance use disorder [37]. Misuse of ADHD medications in students without a prescription is associated with a higher risk of ADHD symptoms. For instance, among 184 college students in Northern Virginia, 71% of those misusing stimulants received positive results when screened for ADHD symptoms [32]. Similar findings were reported in another study highlighting greater features of ADHD in college students with chronic stimulant misuse relative to non-users and chronic cannabis users. Whether untreated ADHD or illicit stimulant use contributed to worsening impulsivity and hyperactivity remains unclear [29].

Associations between stimulant misuse and psychocutaneous disorders are another topic of interest. A retrospective study of 317 patients presenting with psychocutaneous diseases revealed that 60.2% of patients reported stimulant use before dermatologic presentation, with over half of them utilizing nonprescription stimulants [70]. The association between stimulant use and the development of trichotillomania, delusional infestation, or tactile hallucinations was questioned in another recent study. Although most findings were related to authorized prescription stimulant use, adult patients presenting with delusional infestation, belief that parasites inhabit one's skin or body, were more likely to be misusing stimulants [71].

4.3. Substance Use Disorders

Associations have been made between stimulant misuse and illicit use of other drugs. Among 31,244 stimulant-related ED presentations in 2010, 26% were associated with anxiolytics and sleep aids, 16% were associated with narcotics, 14% with cannabis, and 19% with alcohol [68]. One longitudinal study of 948 college students from 2013 suggested a link between marijuana or alcohol use in students with prescription stimulant misuse. During their freshman year of college, 40% of those with stimulant misuse met the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV criteria for alcohol use disorder (vs. 18.5% in those with nonuse), and 25% met DSM-IV criteria for cannabis use disorder (vs. 7% in those with nonuse) [33]. Additionally, researchers reported that 89–92% of those with prescription stimulant misuse also used cannabis [33]. This association was further indicated in a study of 1016 college students in 2014, with 25% reporting prescription stimulant misuse and 11% reporting simultaneous alcohol and stimulant use. A greater number of standard alcoholic beverages and engagement in past-month binge drinking was associated with a higher likelihood of co-ingesting nonmedical prescription stimulants with alcohol [72].

Similarly, another study using data from the NSDUH from 2009 to 2014 indicated that a substance use disorder within the past year was more commonly reported in young adults with past-month prescription stimulant, opioid, or sedative/sedative/tranquilizer misuse history. Interestingly, compared to young adult misusers who obtained prescriptions for free from peers, researchers found the highest prevalence of substance dependence in misusers who purchased prescriptions, utilized fake prescriptions, or acquired prescriptions from multiple sources [20]. College students with a history of 14-day prescription stimulant and/or opioid misuse in 2016–2017 experienced a greater likelihood of 14-day alcohol use, increased alcohol intake, and alcohol-related adverse events than non-using students. Alcohol-related adverse events included a hangover, blackout, vehicle operation after a binge, car ride with an impaired driver, sexual assault, and injury to another person [73].

4.4. Academic Adverse Effects

The academic benefit of stimulants in students without an ADHD diagnosis is a topic of interest, as cognitive enhancement is a commonly reported motivation of students. Although a low GPA is associated with a greater risk of nonmedical stimulant use, one study of 898 undergraduate students in 2017 suggested that GPA improvement was significantly greater in students who did not utilize stimulants. There was no associated GPA change in college students who misused stimulants [74]. When observing changes in cognitive effects, college students with stimulant

misuse displayed greater deficits in executive function than students without misuse. Additionally, increased frequency of buying or trading stimulants was associated with greater executive dysfunction [75].

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