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Review

Prescription Stimulants in College and Medical Students: A Narrative Review of Misuse, Cognitive Impact, and Adverse Effects

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Abstract: 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. The highest rates of nonmedical prescription drug misuse in the United States are seen most notably in young adults between 18 and 25 years, based on data from the Substance Abuse and Mental Health Services Administration in 2021. Aside from undergraduate students, nonmedical prescription stimulant use is prevalent among medical students worldwide. A recent literature 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%. Academic enhancement, reported in 50% to 89% of college students with stimulant misuse, is the most common reason for nonmedical stimulant use. With the increasing use of stimulants among adolescents and adults, it is unclear what long-term outcomes will be since little data are available that describe differences in how side effects are experienced for prescribed and non-prescribed users. The present narrative review focuses on these adverse effects in this population and the reasonings behind misuse and nonmedical use.

Keywords: stimulant misuse; college students; ADHD; nonmedical use; academic enhancement

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 [9–12]. 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 [15–17]. 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].

With the increasing use of stimulants among adolescents and adults, what will be the long-term outcome? Unfortunately, little data are available to assess this question. It is imperative to discourage the use of stimulants without physician supervision. This way, side effects may be monitored and doses adjusted. Without supervision, stimulant misusers may experience significant adverse effects and drug-related harms and could transition to tolerance (i.e., diminished response to a drug). This is especially pertinent in the college student demographic, managing greater demands than they may be accustomed to and turning to stimulants for assistance. The present narrative review, therefore, summarizes these adverse effects in this population.

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 non-medical stimulant misuse [20,21,23,24]. Aside from undergraduate students, nonmedical prescription stimulant use is prevalent among medical students worldwide. A recent literature 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 [11,14,19,26–32]. 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 [11,14,26,27,34–36]. 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]. It is important to note that this study only looked at osteopathic students and did not include allopathic students.

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 [50–52].

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 [53–58]. 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 [59–62]. 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, this study 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 recent 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, this study 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].

5. Studies in the Literature

5.1. Potential Reasons for Misuse

Studies amongst college students regarding ADHD and prescription stimulants aim to learn about the incidence of stimulant misuse among those with and without ADHD, including motivations for misuse, risk factors, and the cognitive impact and adverse effects of misusing prescription stimulants. It has been found that college students generally have a more liberal view towards misuse of prescription stimulant medications and feigning ADHD symptoms to gain access to prescription stimulants. According to a study of Dutch university students by Fuermaier et al., 68% of participants assumed there are benefits from taking stimulants without a prescription. Over half of the survey respondents indicated an assumption of benefit in feigning ADHD. In total, 16% of the students had already taken stimulants without a prescription, further contributing to the well-established notion of frequent stimulant misuse amongst college students [76].

Bossaer et al. performed a study amongst students without stimulant prescriptions at an academic health sciences center, and researchers found that approximately one in ten respondents, all of whom are future healthcare professionals, reported misuse of stimulant medications during their time in their respective programs (medical, pharmacy, and respiratory therapy) [77]. Respiratory therapy students reported higher rates of stimulant misuse, which was not significantly different than that of medical and pharmacy students [77]. Interestingly, 61.4% of respondents believed that their education may be negatively affected if faculty found out about their misuse of stimulant medications, leading investigators to believe that the true incidence in this group may be higher than reported in the survey [77].

Bossaer et al. suggests that more research should be done in the healthcare field specifically to gain more information about the incidence of stimulant misuse in these cohorts [77].

Academic enhancement is the most endorsed reason for stimulant use regardless of prescription status for stimulant medications. These findings have been consistently replicated in studies across much of the United States and Europe [17]. In a study by Fuermaier et al., the most assumed benefit reported on the survey was in an academic context (50.1%), followed by access to stimulant medication (41.2%) and for use in a social context (39.4%) [76]. A study by Bossaer et al. found similar results regarding motives for stimulant misuse—enhancing alertness (65.9%), improving academic performance (56.7%), experimenting (18.2%), and using recreationally (4.5%) [77]. Gudmundsdottir et al. found that academic enhancement was the primary reason for stimulant misuse amongst a group of college students in Iceland regardless of prescription status [17]. Even when considering prescription status, academic enhancement remains the primary reason for stimulant misuse. In a study by Rabiner et al., zero participants with medical misuse (those with an ADHD diagnosis and stimulant prescription) endorsed stimulants solely for non-academic purposes [78]. However, a study by Francis et al. discovered no significant association between stimulant misuse, study skills, and GPA, which suggests that misuse does not significantly affect study skills, GPA, or cumulative academic success [79]. Francis et al. report that these findings coincide with previous reports from Arria et al. indicating that there is no significant advantage in students misusing stimulants when compared to their non-misusing peers [74,79]. Amongst nonusers, reasons for not taking stimulants included no perceived need, fear of health issues, and ethical issues [17].

A study by Ponnet et al. investigated whether using stimulants in college students is a rational or more spontaneous decision using the Prototype Willingness Model (PWM) [80]. The study found that misuse of stimulants in students to enhance academic performance is significantly associated with their intention to use stimulants; therefore, the misuse of stimulants, for this reason, is a result of rational decision-making rather than a spontaneous choice. Students' willingness to use stimulants was not significantly associated with their actual behavior, indicating that stimulant misuse is not a spontaneous decision [80]. Furthermore, Ponnet et al. discovered a link between students' intention to use stimulants for cognitive enhancement and the subjective norm of parents. This behavioral linkage is thought to be due to the parental pressure to succeed and approach perfection academically, combined with positive attitudes towards prescription stimulants, ultimately leading to the students' perception that taking stimulants is necessary [80]. A similar study by Hartung et al. corroborated these findings—those exhibiting misuse without prescriptions reported feeling higher perceived parental pressure than those with nonuse, further indicating a linkage between parental expectations for academic success and the inappropriate usage of stimulants [48].

5.2. Possible Sources for Medication Access

Many clinical studies regarding stimulant misuse seek information about where those without prescriptions obtain access to stimulant medications. Fuermaier et al. found that most university students taking stimulant medications without a prescription obtained the medication from peers, which is a consistent finding across all studies regarding prescription stimulant misuse among college students [76]. In a study by Rabiner et al., more than half of the students with an ADHD diagnosis were approached by other students within the last six months about diverting their prescription stimulants, and over 25% had done so [78]. Diversion of prescription stimulants is more likely in students who have misused medications themselves [78].

5.3. Risk Factors of Stimulant Misuse

Many clinical studies have investigated trends to determine which groups are more at risk of or have a higher incidence of stimulant misuse. A consistent finding has been more stimulant misuse amongst students with a prescription for stimulants and an ADHD

diagnosis [17,79]. A study by Francis et al. found that 50% of the students with an ADHD diagnosis reported stimulant misuse, whereas only 19.6% without a diagnosis reported misuse; therefore, an ADHD diagnosis is considered a risk factor for prescription stimulant misuse [79]. Rabiner et al. specifically studied a group of college students with ADHD diagnoses and stimulant prescriptions. Most participants use their prescription stimulants as prescribed; however, a significant minority (31%) misuse their ADHD medications [78]. In this study, misuse of one's prescription was defined as taking the medication more often than prescribed, at higher doses than prescribed, or using another individual's prescription medication since beginning college [78].

Male sex is also an identified risk factor for stimulant misuse; however, recent studies have recently decreased gender differences in misuse [17,79]. Of those reporting stimulant misuse, more females have ADHD diagnoses (73.7%) than males (59.3%) [81]. Interestingly, male gender significantly predicted misuse of stimulants specifically for the purpose of partying or "getting high" [17]. The study by Ponnet et al. reproduced the gender difference in stimulant misuse but further investigated the reason for such observed differences. The study revealed a significant relationship between gendered stimulant misuse for academic performance and the subjective norm of friends; therefore, male students likely misuse stimulants at higher rates because male students more often believe that their friends would consider taking stimulants for academic purposes an acceptable behavior as compared to female students [80]. Gender was also significantly related to willingness to use and actual use, indicating that males are more willing to and more frequently use stimulants for academic reasons than female students [80]. Regardless of gender, Ponnet et al. found that students are more likely to misuse stimulants when they consider themselves similar to another individual who uses stimulants, a phenomenon termed prototype similarity [80].

Additional risk factors for stimulant misuse in college students include belonging to a fraternity or sorority, having used other illicit substances, lower GPA, higher family income, higher levels of impulsivity, higher antisocial behavioral scores, environments of high competition and stress (ex. medical school), anxiety symptoms, and having a higher performance orientation [17,79,81,82]. A study by Francis et al. found that symptoms of depression, anxiety, and inattention all predicted stimulant misuse independently, but when controlling for symptoms of inattention, depression and anxiety no longer remained significant predictors of misuse. However, symptoms of inattention did remain a significant predictor when studied independently [79]. It is thought that the loss of predictive value for depression and anxiety symptoms, when explored individually, could be explained by symptoms of inattention that co-occur with depression and anxiety, thus contributing to the initially significant findings [79]. De Bruyn et al. found significant associations between competition, stress, and stimulant misuse in medical school specifically. They concluded that misuse is more likely in students with higher stress levels and a higher perception of medical school being a competitive environment [82]. Researchers believe that medical students may be particularly vulnerable to stimulant misuse due to the high stress levels created by the competitive climate of medical school [82].

The research in North American and European countries indicates widespread stimulant misuse on university campuses and a high risk of feigned ADHD among university students; therefore, adverse effects due to stimulant misuse are of increased concern [76]. Acute use of stimulants is associated with several undesirable side effects, including but not limited to restlessness, anxiety, psychological distress, insomnia/sleep difficulties, appetite reduction, irritability, and headaches [78,79]. In a study by Rabiner et al., four side effects were reported by more than half of the survey respondents who have misused stimulants, with appetite reduction being most frequently reported (74%), followed by sleep difficulties, irritability, and headaches [78]. Conversely, stimulant misusers were more likely to endorse more "desirable" side effects such as exaggerated well-being [48]. The presence of "desirable" side effects reported by misusers may encourage misuse by off-setting undesirable or negative side effects and reinforcing the expectation of euphoria [48]. Misusers also have

less awareness of stimulants' serious side effects and addictive character and lower risk perception, which may further perpetuate misuse [76].

5.4. Potential Adverse Effects of Stimulant Misuse

Beyond acute side effects, those misusing stimulants are at greater risk of neuropsychologic dysfunction and psychiatric illness and an increased likelihood of endorsing substance use disorders than those with non-misuse [75,76]. A study by Wilens et al. found an increased risk for neuropsychological dysfunction, specifically clinical executive dysfunction, among students who misuse stimulants compared to non-misusing peers [75]. Students buying or trading prescription stimulants more frequently reported more executive dysfunction on all but one scoring subscale. Clinical executive dysfunction can manifest as a myriad of dysfunctional processes, including impaired ability to monitor self and situation for socially acceptable behaviors, appropriately inhibit impulsive reactions, maintain and organize information in working memory, and plan and execute a response strategically [75]. Researchers speculate that the executive dysfunction in those with misuse is likely pre-existing functional deficits that are present, which the misuse is attempting to reconcile with the use of prescription stimulants; therefore, college students who misuse prescription stimulants may be self-medicating executive dysfunction, attention difficulties, and academic impairment [75]. Such findings are corroborated by Benson et al., who found a higher incidence of stimulant misuse in those meeting ADHD symptom criteria, noting that higher incidence rates are likely due to inadequate care for executive functioning impairments associated with ADHD [27].

5.5. Stimulant Misuse and Other Substance Use Disorders

The association between stimulant misuse and substance use disorders is of particular concern and has been investigated in several clinical studies. Hartung et al. found that those with stimulant misuse, regardless of prescription status, were more likely to endorse more harmful correlates than those not using stimulants or using stimulants according to their prescription [48]. Those with misuse more frequently equated stimulants with recreation or "getting high" and were more likely to endorse other substance use concurrently with stimulants, including but not limited to marijuana, hallucinogens, alcohol, pain medication, and cigarettes [48]. Hartung et al. did not find any incidence of concurrent stimulant and cocaine use; however, previous studies have found a significant link between stimulant misuse and cocaine use [48,79]. Additionally, those with misuse are more likely to use unsafe ingestion methods, with snorting being the most frequent unsafe route of administration. Rabiner et al. found in their study that 8% of those with misuse snorted prescription stimulants in the last six months [78]. Hartung et al. report nasal ingestion rates as high as 17.7–20% among those with misuse (versus 0% inappropriate use) [48].

Finally, researchers note particular concern for groups reporting high concurrent stimulant and alcohol use rates. In Hartung et al.'s study, college students reported a 30% rate of concurrent stimulant and alcohol use [48]. Prescription stimulants may blunt the effects of alcohol, which may lead to underestimating inebriation, increasing the possibility of poor decision making leading to potential motor vehicle accidents, sexually transmitted diseases, unplanned pregnancy, and other avenues for potential harm [48]. Table 1 is a summary of the studies discussed in this section.

Table 1. Studies in the literature.

Author (Year)	Groups Studied and Methods	Results and Findings	Conclusions
Fuermaier A. et al. (2021)	Students without an ADHD diagnosis ($n = 1071$) from the University of Groningen, the Netherlands, completed a survey with self-rated reports ranging from very bad (1) to very good (5) regarding ADHD and stimulant misuse.	Of the respondents, 68% endorsed benefits in taking prescription stimulants without an ADHD diagnosis 15.9% reported having taken stimulants without a prescription. 17% know someone who feigns ADHD for perceived benefits, including prescriptions for stimulant medications.	Approximately half of the university students assume benefits in feigning ADHD and expressed confidence in the ease of feigning ADHD.
Gudmundsdottir B. et al. (2016)	Students from four universities in Iceland ($n = 929$) completed an online survey to analyze predictors of stimulant misuse behavior and prevalence rates of stimulant misuse and its relation to ADHD symptoms, depression, anxiety, stress, student sex, and GPA.	The prevalence of lifetime prescription stimulant misuse in the overall sample was 13.2%. The prevalence of stimulant misuse was 11.2% in those without a current prescription for stimulant medication and 42.4% in those with a prescription.	Individuals with a current prescription for stimulant medication reported higher levels of stimulant misuse in all areas of the stimulant survey questionnaire.
Antshel K. et al. (2019)	College students without an ADHD diagnosis ($n = 309$) completed an online questionnaire regarding stimulant misuse and achievement goal orientations.	The prevalence of prescription stimulant misuse in the sample was 12%. Male students reported stimulant misuse (17.1%) than female students (9.4%).	Performance orientation independently predicted stimulant misuse; therefore, higher-performance orientation students are more likely to misuse stimulant medications. Those meeting ADHD symptom criteria were more likely to both misuse stimulant medications and reported academic motivation as a reason for misusing stimulants than those not meeting the criteria.
Benson K. et al. (2018)	College students ($n = 900$) completed an online survey measuring ADHD and ODD symptoms, stimulant medication misuse, and motivations for medication misuse.	Those meeting ADHD diagnostic criteria were 2.90 times more likely to misuse stimulants and 2.80 times more likely to report academic motives for misuse than those not meeting diagnostic criteria for ADHD.	Increased stimulant misuse in those with ADHD is likely due to inadequate care for executive functioning impairments associated with ADHD.
Francis A. et al. (2021)	Data were collected from college students ($n = 144$) about study strategies, psychological functioning, stimulant misuse, and GPA.	Students with ADHD more often misuse stimulants than those without ADHD.	Symptoms of inattention significantly predict stimulant misuse. Study skills, anxiety, and depression are not significant predictors.
Wilens T. et al. (2017)	Direct interviews and self-report questionnaires were used to compare the cognitive functioning of college students who misuse prescription stimulants to that of non-misuse peers.	Stimulant misusers scored significantly greater than non-misusers on self-reported levels of executive dysfunction on three major indices of the BRIEF-A and five of the nine subscales.	Students who misuse stimulant medications have more evidence of neuropsychological dysfunction than their non-using peers, specifically clinical executive dysfunction.
Ponnet K. et al. (2020)	A survey was used to study whether using stimulants in college students is a rational or more spontaneous decision using the Prototype Willingness Model (PWM).	The students' use of stimulants was most significantly associated with intention. The subjective norm of friends or willingness was not significantly associated with stimulant use.	The use of "stimulants for cognitive enhancement is a rational choice rather than an unplanned one."
Hartung C. et al. (2013)	College students ($n = 1153$) completed rating scales online regarding stimulant use and associated side effects, other substance use, ADHD symptoms, and personality characteristics.	Those with stimulant misuse were more likely to endorse other substance abuse concurrently with stimulants, such as marijuana, hallucinogens, alcohol, cigarettes, and more.	Regardless of prescription status, those with stimulant misuse reported a higher prevalence of "debilitating" side effects than non-misuse, and concerning patterns for other substance use.
Rabiner D. et al. (2009)	College students with an ADHD diagnosis and stimulant prescription ($n = 115$) completed a survey regarding stimulant medication misuse's motives, correlations, and perceived consequences.	31% with a current prescription misused their stimulant medication, with the most endorsed motive being enhancing academic performance.	Motives for misusing stimulant medications are similar between those prescribed and those not prescribed stimulants, primarily academic enhancement.

Table 1. Cont.

Author (Year)	Groups Studied and Methods	Results and Findings	Conclusions
De Bruyn S. et al. (2019)	Medical students ($n = 3159$) completed a questionnaire regarding stimulants.	The study found significant associations between competition, stress, and stimulant misuse.	Higher levels of competition and stress in medical school results in medical students being more likely/vulnerable to misuse of stimulant medications.
Bossaer J. et al. (2013)	Students at an academic health sciences center without stimulant prescriptions ($n = 372$) completed an electronic survey about reasons for, frequency of, and side effects of stimulant misuse.	Approximately one in 10 respondents (11.3%), all of which are future healthcare professionals (medical, pharmacy, respiratory therapy), reported misuse of stimulant medications. 61.4% of responders indicated their education might be negatively affected if faculty found out about their stimulant misuse.	The survey results indicating that most respondents believed their education would be negatively affected by faculty finding out about students' stimulant misuse suggests that the true incidence of stimulant misuse may be higher than reported in the survey due to fear.

6. Conclusions

Stimulant medications are frequently misused in young adults, including college, medical, osteopathic, pharmacy, and respiratory therapy students. Nonmedical use occurs in students both with and without prescriptions for ADHD medications. Obtaining stimulants in this age group is typically described as easy. Most students involved in the misuse of amphetamines desire to improve academic performance, but whether cognitive enhancement occurs in non-ADHD students is unknown. The role of the placebo effect has been questioned and provides a possible explanation of perceived stimulant benefits.

Common side effects such as decreased appetite, headache, difficulty sleeping, and stomach upset occur in medical and nonmedical stimulant users. As ED presentations related to amphetamine misuse have increased over the past several years, there is a concern for more severe side effects. Severe adverse outcomes include critical care or psychiatric facility admissions, suicide attempts, cardiovascular events, seizures, and overdoses. There is not enough data on long-term outcomes of stimulant use or misuse in adults. In young adults with stimulant misuse, a greater risk of psychiatric disorders, including substance use disorder, depression, and ADHD is one well-documented association. Additionally, stimulant-induced psychocutaneous disorders have been reported.

Regarding high self-confidence in feigning ADHD symptoms, healthcare providers must be cautious when diagnosing young adults and students with ADHD. Additionally, providers should watch for signs of stimulant misuse. Negative cognitive outcomes have been reported. Interestingly, the thought that the use of stimulants can help boost GPAs and test performance has not been found in the literature. That leads to the question of if there are additional motivations for misuse. Additional research is necessary to study the long-term consequences of stimulant misuse in adults, upgrade ADHD screening methods to detect those who are feigning symptoms, and reduce the prevalence of stimulant misuse among students.

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