The ABCs of CNS Stimulant Misuse

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There has been increasing evidence that CNS stimulants are being used "off label" by those not formally diagnosed with attention-deficit/hyperactivity disorder (ADHD), primarily for cognitive enhancement. Most of the attention has been paid to college students, with a recent meta-analysis reporting that 17% have misused CNS stimulants. Prior work has examined the prevalence of this practice and predictors of diversion and misuse. Multiple studies have found that substance use and academic stress combine to predict misuse, with one study even finding confirmatory evidence in the wastewater of an American college campus. Interestingly, ADHD symptoms have also been associated with misuse even among those not formally diagnosed with the disorder. Surveys have routinely found that adolescents and young adults view CNS stimulants as innocuous, socially acceptable, and effective for improving academic performance. Even the medical field has debated the value of using CNS stimulants as cognitive enhancers for the general population.

The increasing awareness of this trend has pushed the medical field to more closely examine the cognitive benefits of CNS stimulants in those without ADHD. The data are at best mixed, with recent reviews finding limited effects. The most robust effects are for episodic memory and reaction time, especially for simple, unfamiliar tasks versus complex and familiar ones. Moreover, baseline functioning appears to moderate response, with those with the greatest deficits experiencing the largest gains, suggesting that college students may be a subset least likely to reap appreciable benefits. A recent placebo-controlled examination of the cognitive effects of a standard clinical dose of mixed amphetamine salts tablets (MAS) in college students with no prior psychiatric history found little evidence of cognitive enhancement except for those with greatest impairment. Even then, measurable gains were detectable in only a minority of the 13 tasks. Most interestingly, participants reported improved performance with blinded MAS over placebo, with no association between the degree of reported improvement and observed performance. It may be that the physical sensation of MAS and other CNS stimulants leads people to assume that these medications are enhancing their cognitive performance. Alternatively, CNS stimulants may impact academic performance through other processes such as motivation. However, longitudinal studies of school-aged youth have failed to find that medication produces large, meaningful improvements in academic performance, despite acute reductions in ADHD symptom severity. Given these combined results, it appears that the practice of using CNS stimulants for cognitive enhancement may be driven more by perception than reality.

The current literature has predominantly focused on subsets of the population (primarily college students) and on the actual behavior itself. There has been less exploration of what is driving the practice (Antecedents) or of its consequences. In this issue, Chen and colleagues are to be applauded for their efforts to holistically examine the "ABCs" of CNS stimulant misuse. To do this, the authors mined the National Disease and Therapeutic Index (NDTI) for information on prescribing trends, the National Survey on Drug Use and Health for trends on the misuse of CNS stimulants, and the Drug Abuse Warning Network to examine emergency department visits related to CNS stimulant exposure, assessing from 2006 to 2011 for each. Prior work has examined these databases in isolation to assess trends regarding misuse of CNS stimulants, but this is one of the first studies attempting to integrate information regarding stimulant availability, misuse, and medical consequences.

The authors' medication selection criteria for the NDTI database led to an unusual finding that complicates interpretation of their results, which they recognized. Namely, not all CNS stimulants were included in their primary analysis, leading to the observation that medication prescription rates (as measured by the proxy of outpatient office visits) declined over time, which is inconsistent with multiple other reports on this topic. This incongruous finding appears to largely stem from the omission of lisdexamfetamine from the amphetamine family. Likewise, dexamphetamine was not included in the methylphenidate family. Other limitations include the variable definition of misuse employed across the databases as well as the inability to link cases across the 3 datasets.

Several noteworthy findings arose. Consistent with past reports, the majority of cases for nonmedical use and emergency department visits were with amphetamine-based versus methylphenidate-based products, for both adolescents and adults. In a secondary analysis examining misuse, inclusion of lisdexamfetamine did not impact rates of nonmedical use even though lisdexamfetamine comprises a sizable share of the current market for amphetamine products. Despite the decrease in non-lisdexamfetamine amphetamine preparations, rates of misuse and visits to the emergency department either held steady or increased for this class of medication. It appears that specific CNS stimulant formulations may be preferentially associated...
with misuse despite their declining market share. While this analysis did not separate out short-acting from extended-release stimulants, greater concern exists for the misuse of short-acting products. Colleges have implemented stricter policies regarding access to CNS stimulants on campus. These results suggest that restrictions on certain formulations may prove effective at curbing misuse while not completely eliminating an effective treatment option for those suffering from rigorously diagnosed ADHD.

Chen et al found also that the majority of emergency department visits involved other substances, and only a little more than a third of emergency department visits for amphetamine or methylphenidate use were classified as an adverse reaction. It appears that intentional misuse in combination with other substances is most likely to lead to adverse medical consequences.

Consistent with prior work, friends and family were the primary source of the misused CNS stimulants. However, the authors went one step further and found the secondary source to be a prescribing physician, accounting for up to 83% of all misused stimulants. Those misusing both classes of CNS stimulants were most likely to go directly to a physician. Policies impacting the prescription, refilling, and storage of CNS stimulants, especially in high-risk sites such as college campuses, may be efficacious targets for curbing rates of misuse.

We are now beginning to understand the risk factors, pathways, and motivations driving misuse of CNS stimulants, especially for cognitive enhancement. Armed with the results from this study and others, the educational and medical systems are now positioned to move forward in an informed and coordinated effort to begin to address this problem.

REFERENCES


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