ADHD & Substance Use Disorders

Timothy E. Wilens, M.D.

Chief, Division of Child & Adolescent Psychiatry; (Co) Director, Center for Addiction Medicine

Massachusetts General Hospital
Harvard Medical School
Faculty Disclosure

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- Some of the medications discussed may not be FDA approved in the manner in which they are discussed including diagnosis(es), combinations, age groups, dosing, or in context to other disorders (eg, substance use disorders)
Overlap between ADHD and SUDs

Overall, 23% of adults with SUD have ADHD (N = 29 studies)*.

Likelihood (OR) to Develop SUD

**FIGURE 4** Meta-analysis of attention-deficit/hyperactivity disorder (ADHD) and psychoactive substance use disorder. Note: Results from a meta-analysis comparing ADHD versus control subjects for psychoactive substance use disorder. CI = confidence interval.

Likelihood (OR) to Develop Cigarette Smoking

**FIGURE 6** Meta-analysis of attention-deficit/hyperactivity disorder (ADHD) and nicotine use. Note: Results from a meta-analysis comparing ADHD versus control subjects for nicotine use. CI = confidence interval.
ADHD Symptoms are Directly Related to Higher Smoking Scores

$F_{\text{TQ}} = \text{Fagerström Tolerance Questionnaire.}$


$t = 5.00, P < .001$
A More Complicated Course of SUD is Associated with ADHD

- More severe SUD
- Higher rates of other psychiatric comorbidities (e.g., conduct/antisocial disorders)
- Lower retention in SUD treatment
- Less remission from SUD
- Longer course of SUD

FIGURE 1. Impulsivity-Related Theories of High-Risk ADHD: Exaggerated Imbalance of Brain Networks. (A) Compared to typically developing controls, (B) individuals with low-risk ADHD have impairments in both the inhibitory control and reward processing brain networks: weaker inhibitory control (reduced macro/microstructure, hypoactive at-rest and during associated tasks) and hyperprimed reward processing (greater macro/microstructure, hyperactive at-rest but hypoactive during associated tasks). High impulsivity is implicated as an important mechanism underlying increased SUD risk in ADHD and corresponds to greater disinhibition, delay discounting and sensation seeking. Impulsivity-related theories of high-risk ADHD suggest these impulsive behaviors stem from a greater degree of impairment (C) in both the inhibitory control and reward processing networks compared to low-risk ADHD, (D) in mainly the reward processing network or (E) in mainly the inhibitory control network.
Among Those Participants Treated with Stimulant ADHD Medication, There was a Significant Reduction in Rates of Substance Abuse

Percent Reduction

Individuals were born 1960–1998 and diagnosed with ADHD (26,249 men and 12,504 women; ~50% on stimulant medication in 2006). Authors examined the association between stimulant ADHD medication in 2006 and substance abuse during 2009 (e.g., substance-related crime, hospital visits or death; outcomes ~6% vs 0.5%, ADHD vs general population).

FU = follow-up; SES = socioeconomic status.

ADHD Medication and SUD; US Claims Data

Conclusions

- Largest US database examining ADHD medication treatment and later SUD (almost 3 million w ADHD)
- Medicated ADHD was associated with lower SUD risk when compared to unmedicated ADHD groups
  - >30% reduction in new onset SUD
  - 24% and 6% reductions in all SUD events in males/females
- Medication periods were generally associated with reduced risk of SUD events (30-35% reduction)
- SUD reductions associated with ADHD medication similar to Scandinavian and some US Studies
- No evidence of worsened SUD

(Patrick et al. Am J Psych 2017: 877-885)
Early ADHD Treatment Reduces Marijuana Use

Population risk

Stimulant use started prior to 9 years of age

Stimulant use started between 10–14 years

Stimulant use started after 15 years of age

Past Year Use

20%  30%  40%  50%  60%

10 Cohorts of high school seniors 2005 to 2014 (N = 40,358; ~10% with ADHD).
*P < .001 vs controls.
Diagnostic Dilemmas in ADHD and SUD

- Overlap symptoms of SUD in ADHD
  - Intoxication or withdrawal
  - Neuropsychological deficits (transient/permanent)
  - SUD “traits” misinterpreted as ADHD (e.g., impulsive traits/risk-taking, harm avoidance)
- Other comorbidity (e.g., anxiety, disruptive disorders)
- Reliability of retrospective report
- Subthreshold ADHD vs full ADHD
  - Age-of-onset criteria (NOS)
  - Affected domains, inadequate number of symptoms
- Concerns of drug-seeking behavior/rationalization
- Use of rating scales for ADHD helpful (e.g., ASRS)

ASRS = Adult ADHD Self-Report Scale; NOS = not otherwise specified.
Current Heavy Alcohol Use Worsens ADHD Symptoms
(AISRS Item Scores vs Presence or Absence of Alcohol Abuse* in Placebo Group)

*Consumed ≥ 4 alcoholic drinks/day for women, or ≥ 5 drinks/day for men, within 24 hours (cumulative; drink = 1.5 oz liquor, 5 oz wine, 12 oz beer), or ≥ 3 drinks/day for ≥ 1 week (ie, ≥ 7 consecutive days), during the double-blind treatment period (visit 3−14 [baseline to week 12]). P values were adjusted for multiple comparisons.

SUD in ADHD Adults Presenting for Treatment

- SUD Current (10%)
- SUD History (40%)
- No SUD Hx (50%)

Adhd Adults

Double-Blind Studies of Stimulants to Treat Current Substance Abusers with ADHD

• **6 Studies**
  - 1 study in adolescent substance abusers administered pemoline
  - 2 studies in adult cocaine abusers administered IR or SR MPH
  - 1 study in adult methadone maintenance patients administered SR MPH or SR-bupropion
  - 1 study in adults with briefly abstinent amphetamine abusers given OROS MPH
  - 1 RCT with high-dose MAS XR showing improvement

• **Efficacy (vs placebo)**
  - No overall improvement in SUD (trend to improvement in 1 study)
  - 2 studies suggest benefit in reducing ADHD symptoms on some measures but not others
  - 1 study showing improvement in ADHD and SUD (high-dose MAS XR)

• **Safety**
  - No serious adverse events
  - No worsening of SUD
  - No evidence of diversion

IR = immediate release; MAS XR = mixed amphetamine salts; RCT = randomized controlled trial; SR = sustained release.
Higher Dose MAS XR is Helpful in ADHD and Cocaine Use Disorder

13-week RCT
Diagnosis: Cocaine Use Disorder and ADHD
Treatment: CBT +/- MAS XR

N = 126. *P < .05.
**Sample**: 54 incarcerated males (mean age = 42 years)

**Dose**: Start dose 18 mg MPH/placebo titrated over a period of 19 days; mean dose of 108 mg/day

**CBT**: Individual CBT once weekly for 12 weeks

**Measurements**: Change in self-reported ADHD symptoms, urine toxicology, retention to treatment

**Findings**: MPH treated group showed reduced ADHD symptoms \(P = .011\), significantly higher proportion negative urine screens \(P = .047\), and better retention \(P = .032\)

Figure 2. Change in self-rated ADHD symptoms (95% CI: -13.78 to -1.91, \(P=0.011\)).
An event ratio of .737 indicates that, relative to patients treated with placebo, atomoxetine-treated patients experienced an approximately 26.3% greater reduction in the rate of heavy drinking. Separation between groups first occurred at day 55.

The Complicated Relationship Between Attention Deficit/Hyperactivity Disorder and Substance Use Disorders

Courtney A. Zulauf¹, Susan E. Sprich², Steven A. Safren³ and Timothy E. Wilens¹, 4, 5

Abstract

Adolescents and young adults with substance use disorders (SUD) and attention deficit/hyperactivity disorder (ADHD) are increasingly presenting in clinical practice. The overlap and role of treatment for these co-occurring conditions are not well understood. The authors conducted a systematic review of the recent literature on the treatment of high-risk for comorbid ADHD and SUD. They found that structured therapies may be effective in treating adolescents and young adults with ADHD and SUD. Further controlled trials evaluating the sequence and effect of structured psychotherapies and/or ADHD pharmacotherapy on SUD relapse in these groups are warranted.

“...Structured therapies may be effective in treating adolescents and young adults with ADHD and SUD...”

Keywords Adolescence – Substance use disorders – Attention deficit/hyperactivity disorder – Stimulants comorbidity – Cognitive-behavioral therapy

This article is part of the Topical Collection on Child and Adolescent Disorders

Stimulant Misuse and Diversion

- N = 22 studies (N > 113,000 participants); mostly survey studies in college students (80%)
- 10% to 20% prevalence of nonmedical use of stimulants
- 65% to 85% of stimulants diverted from “friends”
  - Majority not “scamming” local doctors
  - Not seen as potentially dangerous
- Motivation typically for concentration/ alertness > getting “high”
- Appears to be occurring in substance (ab)users during academic decline
- High rates of full or subthreshold stimulant use disorder in misusers
- High rates of ADHD and neuropsychological dysfunction in stimulant misusers
- More misuse of immediate- vs extended-release stimulant preparations
College Stimulant Misusers Have High Rates of SUD

HR: 2.7; 95% CI: 1.7, 4.2; \( P < .001 \)
N = 100 stimulant misuser; 198 controls

More Executive Dysfunction in Stimulant Misusers

Subscales of the Self-Report Behavior Rating Inventory of Executive Functioning (BRIEF)

N = 299. *P < .05
Stimulant Preparation Linked to Dopamine Transporter Binding and Likeability

40 mg IR-MPH vs 90 mg OROS MPH

Misuse by Alternative Routes is Common: Snorting is Frequently Reported

Method of Stimulant Misuse by College Students (n = 1025)

- Swallow: 55%
- Snort: 40%
- Other: 4%

Random sample: Anonymous surveys at the University of New Hampshire administered via e-mail and paper, 1025 received out of 5000 distributed, 6.6% diagnosed with ADHD, over 16% of students abuse stimulants. White BP, et al. J Am Coll Health. 2006;54(5):261-268.
Intranasal Misuse of Stimulants is Linked to SUD in College Students (N=100)

(Wilens et al. AACAP, 2018)
SUD Symptoms at Age 35 Years as a Function of Medical and Nonmedical Use of Prescription Stimulants at Age 18 Years

All analyses control for race/ethnicity, sex, truancy, average grade during high school, parental education, geographical region, metropolitan statistical area, cohort year at baseline, annual alcohol use at baseline, annual cannabis use at baseline, and annual other drug use at baseline.

N = 8362.
Educational Attainment at Age 35 Years as a Function of Medical and Nonmedical Use of Prescription Stimulants at Age 18 Years

Obtained Associate’s Degree or Higher

- No medical or nonmedical use
- Medical use only: $\text{AOR}^a = .874$
- Medical and nonmedical use: $\text{AOR}^a = .672$
- Non-medical use only: $\text{AOR}^a = .749$, $P < .01$

All analyses control for race/ethnicity, sex, truancy, average grade during high school, parental education, geographical region, metropolitan statistical area, cohort year at baseline, annual alcohol use at baseline, annual cannabis use at baseline, and annual other drug use at baseline.
Strategies for ADHD and SUD

In context to SUD, ADHD treatment should be considered

If misuse or less severe SUD, treat ADHD concomitantly

More severe SUD --> address SUD first

If unable to address or recalcitrant SUD -> use CBT, nonstimulants, extended-release stimulants

Wilens and Morrison, ADHD & SUD In ADHD in Children and Adults, Cambridge Press, 2015
Kaminski and Wilens, Overlap of ADHD and SUD, in Textbook of SUD, 2019 in press
Impact on Practice

• Since ADHD is a risk factor for cigarette smoking and SUD, teenagers and young adults with ADHD should be queried for both potential problems
• ADHD should be considered in adolescents and adults who smoke cigarettes and/or have SUD
• Treating ADHD helps protect against the onset of cigarette smoking, SUD, and SUD-related criminality
• Strategies exist for management of substance use and use disorder in ADHD
• Since stimulants can be misused, consider extended-release preparations in high risk groups
Questions?