ADHD & Substance Use Disorders

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Disclosures*

I have the following relevant financial relationship with a commercial interest to disclose:

Dr. Wilens has served as a consultant or has received grant support from the following:

- NIH (National Institute on Drug Abuse)
- Ironshore, Neurovance, Sunovion, Tris
- National Football League (ERM), Minor/Major League Baseball
- Bay Cove Human Services, Phoenix House (Clinical Services)
- (Co)Edited Straight Talk About Psychiatric Medications for Kids (Guilford Press); ADHD Across the Lifespan (Cambridge Univ Press); Comprehensive Clinical Psychiatry; Psychopharmacology & Neurotherapeutics (Elsevier)
- 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 (e.g. substance use disorders)

* Past 3 years
ADHD Overview

- Most common presenting neurobehavioral disorder in childhood
- Epidemiology: Worldwide 6-9% of children and adolescents; 4-5% of adults
- Chronic course characterized by inattention/distraction, impulsivity, and hyperactivity
- Associated with impairment in multiple domains
- Nonpharmacological and pharmacological agents effective for treatment

(Wilens and Spencer, ADHD Across the Lifespan, Postgraduate Medicine: 2010)
Lifetime Prevalence of DSM-IV Substance Use Disorders (SUD) in the National Comorbidity Survey-Adolescent

Overlap between ADHD and Substance Use Disorders (SUD)

Wilens T. Psychiatr Clin N Am. 2004;27:283-301
van Emmerick et al. Drug Alc Dep 2012 122: 11-10
Overall, 23% of adults with substance abuse have ADHD (N=29 studies)*

Childhood ADHD is Related to Future Cigarette and SUD

Likelihood (Odds Ratio; OR) to Develop SUD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biederman 2008¹⁸</td>
<td>0.1864</td>
<td>0.2759</td>
<td>39.0%</td>
<td>1.20 [0.70, 2.07]</td>
<td></td>
</tr>
<tr>
<td>Fischer 2002¹⁴</td>
<td>0.5166</td>
<td>0.3019</td>
<td>32.9%</td>
<td>1.68 [0.93, 3.03]</td>
<td></td>
</tr>
<tr>
<td>Gittelman 1985³</td>
<td>1.1367</td>
<td>0.4675</td>
<td>14.2%</td>
<td>3.12 [1.25, 7.79]</td>
<td></td>
</tr>
<tr>
<td>Mannuzza 1991⁵</td>
<td>0.4261</td>
<td>0.4725</td>
<td>13.9%</td>
<td>1.53 [0.61, 3.87]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>1.59 [1.12, 2.25]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.01; Chi² = 3.12, df = 3 (P = 0.37); I² = 4%
Test for overall effect: Z = 2.60 (P = 0.009)

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 (Odds Ratio; OR) to develop Cigarette Smoking

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barkley 1990¹</td>
<td>0.8995</td>
<td>0.3301</td>
<td>25.0%</td>
<td>2.46 [1.29, 4.69]</td>
<td></td>
</tr>
<tr>
<td>Biederman 2006¹⁷</td>
<td>1.4019</td>
<td>0.4791</td>
<td>11.9%</td>
<td>4.06 [1.59, 10.39]</td>
<td></td>
</tr>
<tr>
<td>Elkins 2007¹³</td>
<td>0.7514</td>
<td>0.2455</td>
<td>45.2%</td>
<td>2.12 [1.31, 3.43]</td>
<td></td>
</tr>
<tr>
<td>Milberger 1997²⁰</td>
<td>0.7207</td>
<td>0.3904</td>
<td>17.9%</td>
<td>2.06 [0.96, 4.42]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>100.0%</td>
<td>2.36 [1.71, 3.27]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 1.62, df = 3 (P = 0.66); I² = 0%
Test for overall effect: Z = 5.21 (P < 0.0001)

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.
Executive Function Deficits in Midadolescence Do Not Predict SUD 5 Years Later (N=412)

RED BAR = EFD
BLUE BAR = ADHD

(Hazards ratio for Executive Function Deficits in Midadolescence in relation to the risk of Substance Use Disorders (SUD) in adulthood, categorized by the presence or absence of ADHD.)


www.mghcme.org
However, Cigarette Smoking Increase the Likelihood of Subsequent Executive Functioning Deficits in Transitional Aged Youth

Pairwise Comparisons:

\[ a \ p < 0.05 \ vs. \ Controls; \ b \ p < 0.05 \ vs. \ ADHD; \ c \ p < 0.05 \ vs. \ both \ ADHD \ and \ Use \]

Parental Smoking During Pregnancy and ADHD in Children: The Danish National Birth Cohort

### TABLE 1 Number and Percentage of Children With ADHD by Parental Smoking Status

<table>
<thead>
<tr>
<th>Mother</th>
<th>Father</th>
<th>Number of Children</th>
<th>With ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Smoker</td>
<td>Smoker</td>
<td>8771</td>
<td>368</td>
</tr>
<tr>
<td>Nicotine replacement user</td>
<td>Smoker</td>
<td>240</td>
<td>7</td>
</tr>
<tr>
<td>Smoking quitter</td>
<td>Smoker</td>
<td>3199</td>
<td>113</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>Smoker</td>
<td>14,004</td>
<td>360</td>
</tr>
<tr>
<td>Smoker</td>
<td>Nonsmoker</td>
<td>4776</td>
<td>164</td>
</tr>
<tr>
<td>Nicotine replacement user</td>
<td>Nonsmoker</td>
<td>574</td>
<td>22</td>
</tr>
<tr>
<td>Smoking quitter</td>
<td>Nonsmoker</td>
<td>4167</td>
<td>83</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>Nonsmoker</td>
<td>49,072</td>
<td>892</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>84,803</td>
<td>2,009</td>
</tr>
</tbody>
</table>
ADHD Symptoms are Directly Related to Higher Smoking Scores

FTQ denotes Fagerstrom Tolerance Questionnaire

\[ t = 5.00, \ p < 0.001 \]

Smoking Severity is Greater in ADHD

FTQ Score for Smokers

FTQ denotes Fagerstrom Tolerance Questionnaire

Age: Mean=19.6, Range 15-25

A More Complicated Course of SUD Is Associated with ADHD

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

What Links ADHD and SUD?
ADHD Adults Do Not Selectively Abuse Specific Drugs

Classes of Drugs Abused in Adults With a Drug Use Disorder

ADHD and Control Adolescents are Similar in that Most Report Continuing to Use Substances for Self Medication

\[ p = 0.90 \]

Adolescent impulsivity phenotypes characterized by distinct brain networks

Robert Whelan¹,², Patricia J Conrod³,⁴, Jean-Baptiste Poline⁵, Anbarasu Lourdusamy³, Tobias Banaschewski⁶, Gareth J Barker³, Mark A Bellgrove⁷, Christian Büchel⁸, Mark Byrne⁵, Tarrant D R Cummins⁷, Mira Fauth-Bühler⁹, Herta Flor¹⁰, Jürgen Gallinat¹¹, Andreas Heinz¹¹, Bernd Ittermann¹², Karl Mann⁹, Jean-Luc Martinot¹³,¹⁴, Edmund C Lalor², Mark Lathrop¹⁵, Eva Loth³,¹⁶, Frauke Nees¹⁰, Tomas Paus¹⁷–¹⁹, Marcella Rietschel¹⁰, Michael N Smolka¹¹,²², Rainer Spanagel²³, David N Stephens²⁴, Maren Struve¹⁰, Benjamin Thyreau⁵, Sabine Vollstaedt-Klein⁹, Trevor W Robbins²⁵, Gunter Schumann³,¹⁶, Hugh Garavan¹,² & the IMAGEN Consortium²⁶

The impulsive behavior that is often characteristic of adolescence may reflect underlying neurodevelopmental processes. Moreover, impulsivity is a multi-dimensional construct, and it is plausible that distinct brain networks contribute to its different cognitive, clinical and behavioral aspects. As these networks have not yet been described, we identified distinct cortical and subcortical networks underlying successful inhibitions and inhibition failures in a large sample (n = 1,896) of 14-year-old adolescents. Different networks were associated with drug use (n = 1,593) and attention-deficit hyperactivity disorder symptoms (n = 342). Hypofunctioning of a specific orbitofrontal cortical network was associated with likelihood of initiating drug use in early adolescence. Right inferior frontal activity was related to the speed of the inhibition process (n = 826) and use of illegal substances and associated with genetic variation in a norepinephrine transporter gene (n = 819). Our results indicate that both neural endophenotypes and genetic variation give rise to the various manifestations of impulsive behavior.
Prevention of SUD in ADHD Youths

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**Percent Reduction**

- Periods of medication vs. non-medication within the same individual
- In those ≤ age 15 at baseline
- Each year of taking stimulant before FU
- FU in 2009 (controlling for SES, psych disorder, and other confounders)
- FU in 2009 (controlling for age, sex and meds)

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Individuals were born 1960-1998 and diagnosed with ADHD (26,249 men and 12,504 women; circa 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 ca 6% vs 0.5% ADHD vs gen pop)
Early and Longer Duration ADHD Treatment Reduces Past-Year Substance Use

(N=40,358: Monitoring the Future Survey, 10 Cohorts of senior years 2005 to 2014)


www.mghcme.org
Early ADHD Treatment Reduces Marijuana Use

15 year follow-up study
(N=40,358; 10% with ADHD)

Population risk

- Stimulant use started prior to 9 years of age
- Stimulant use started between 10-14 years of age
- Stimulant use started after 15 years of age

Past Year Use

20%  30%  40%  50%  60%

* p<0.001 vs controls

Treating Adolescents with OROS MPH Improves Smoking (and SUD) Outcomes (mean 10 mo [up to 24 mo]):

<table>
<thead>
<tr>
<th>Group</th>
<th>% Current Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-ADHD (n=188)</td>
<td>8</td>
</tr>
<tr>
<td>OROS MPH (n=154)</td>
<td>7.1</td>
</tr>
<tr>
<td>ADHD Current Meds (n=46)</td>
<td>10.9</td>
</tr>
<tr>
<td>ADHD Not Current Meds (n=57)</td>
<td>19.6</td>
</tr>
</tbody>
</table>

- **p=0.01**
- **p=0.009** *
- Not significant (all p>0.20)
- * Not significant when controlled for CD, ETOH, drug abuse

Screening Adolescents for Drugs and Alcohol (CRAFFT)

• During past 12 months did you
  A) Drink any alcohol
  B) Smoke any marijuana or hashish
  C) Use anything else to get high?

• If **NO**: Ask if you have ever ridden in a CAR driven by someone who was high or had been using drugs or alcohol

• If **YES**-complete **CRAFFT** (next page)
Screening Adolescents for Drugs and Alcohol

C  Have you ever ridden in a **CAR** driven by someone who was “high” or had been using alcohol or drugs?

R  Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?

A  Do you ever use alcohol or drugs while you are by yourself, **ALONE**?

F  Do you ever **FORGET** things you did while using alcohol or drugs?

F  Do your family or **FRIENDS** ever tell you that you should cut down on your drinking or drug use?

T  Have you ever gotten into **TROUBLE** while you were using alcohol or drugs?

• Two or more yes answers on the **CRAFFT** suggest a serious problem and a need for further assessment

(Knight et al., Arch Pediatr Adolesc Med 1999: 153: 591-6)
According to Group Health’s standards for substance use disorder documentation, clinical staff may and should document the following information related to substance use:

• Patient disclosures about substance use, abuse, or dependence.
• Patient disclosures about current or past chemical dependency treatment.
• Completed screening tools including:
  - Adolescent substance use screening tool (CRAFFT) and CRAFFT results.
  - Others (NIDA 9; NIDA-1)
  - A DSM diagnosis of SUD and the pertinent clinical information that supports the diagnosis.
  - Referrals for a chemical dependency evaluation (includes all levels of care, behavioral, medical, inpatient, partial, outpatient).

Protection of chemical dependency information begins at the start of a treatment program, not at the time of screening, identification, or referral (as outlined in confidentiality regulation 42 CFR Part 2).

Adapted from Group Health Guidelines
www.ghc.org/all-sites/guidelines/drug-adolescent.pdf
Locating Treatment Facilities

- Looking for drug treatment programs and alcohol abuse treatment programs?
- Find the right drug abuse treatment program or alcohol abuse treatment program with the Substance Abuse Treatment Facility Locator Sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA)

Toll Free Helpline: 1-800-662-4357
Or http://findtreatment.samhsa.gov/

For more information on treating adolescent Substance Use Disorders (NIDA):
For every complex problem, there is a simple solution

And it is wrong

George Bernard Shaw
Diagnostic Dilemmas in ADHD + 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)
  - Effected domains, inadequate number of symptoms
- Concerns of drug-seeking behavior/ rationalization
- Use of rating scales for ADHD helpful (e.g. ASRS)

SUD in ADHD Adults Presenting for Treatment

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

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 Add XR showing improvement

• Efficacy (vs placebo)
  - No overall improvement in SUD (trend to improvement in one)
  - Two studies suggest benefit in reducing ADHD symptoms on some measures but not others
  - One study showing improvement in ADHD and SUD (high dose AddXR)

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

NIDA Clinical Trial Network: Study of OROS MPH in Adolescents with ADHD and Mixed SUD

Methods

16 week RCT of placebo vs OROS MPH (72 mg/day)
Mixed SUD (no opioid or methamphetamine abuse/dep)
N=150 subjects/arm (11 sites); mean age 16.5 years
Weekly individual CBT

Findings:

Both groups improved in ADHD & SUD

OROS MPH vs Placebo

No significant improvement in ADHD (investigator/parent)
No significant improvement in SUD (adol self report); trends to fewer (+) urines
Predictable adverse effects and low abuse liability

Higher Dose Mixed Amphetamine Salts XR in Helpful in ADHD & Cocaine Use Disorder (N=126)

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

N= 70 adolescents with ADHD. All subjects had at least one active non-nicotine SUD.

Design: 12 weeks of atomoxetine or placebo in addition to motivational interviewing/cognitive behavioral therapy.

Results: There were no differences between ADHD scores or in use of substances between treatment groups that emerged during the study.

Note: The authors speculated that the therapy may have contributed to a larger than expected placebo response.
An event ratio of 0.737 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.
# Treatment-emergent Adverse Events in Atomoxetine Heavy Drinkers, Nonheavy Drinkers and Non Alcohol Use Disorder

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>ATOMOXETINE</th>
<th>PLACEBO</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Heavy drinker N = 23</td>
<td>Nonheavy drinker N = 42</td>
<td>Non-alcohol use disorder N = 69</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (48)</td>
<td>16 (38.1)</td>
<td>7 (10.1)</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>8 (34.8)</td>
<td>9 (21.4)</td>
<td>8 (11.6)</td>
</tr>
<tr>
<td>Decrease Appetite</td>
<td>7 (30.4)</td>
<td>4 (9.5)</td>
<td>5 (7.2)</td>
</tr>
<tr>
<td>Headache</td>
<td>7 (30.4)</td>
<td>6 (14.3)</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>5 (21.7)</td>
<td>6 (14.3)</td>
<td>4 (5.8)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5 (21.7)</td>
<td>4 (9.5)</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>Nasophary..is</td>
<td>1 (4.3)</td>
<td>6 (14.3)</td>
<td>2 (2.9)</td>
</tr>
</tbody>
</table>

* At least 1 treatment group ≥10% and statistically significant among the 3 alcohol drinking subgroups.

** Signifies that no alcohol treatment group had that TEAE at a rate ≥5%.

Current Heavy Alcohol Use Worsens ADHD Symptoms (AISRS Item Scores vs. Presence or Absence of Alcohol Abuse* in Placebo Group)


*AISRS Item Scores vs. Presence or Absence of Alcohol Abuse* in Placebo Group


*Correlation Coefficient

<table>
<thead>
<tr>
<th>AISRS Item</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Careless errors</td>
<td>*</td>
</tr>
<tr>
<td>Difficulty w/attention</td>
<td>*</td>
</tr>
<tr>
<td>Conc. issues when listen</td>
<td>***</td>
</tr>
<tr>
<td>Feels restless/fidgety</td>
<td>**</td>
</tr>
<tr>
<td>Trouble complete proj.</td>
<td>***</td>
</tr>
<tr>
<td>Trouble relax/free time</td>
<td>*</td>
</tr>
<tr>
<td>Trouble organizing</td>
<td>**</td>
</tr>
<tr>
<td>Delays starting task</td>
<td>NS</td>
</tr>
<tr>
<td>Compelled to do things</td>
<td>**</td>
</tr>
<tr>
<td>Finishes others' sentences</td>
<td>**</td>
</tr>
<tr>
<td>Difficulty waiting turn</td>
<td>***</td>
</tr>
<tr>
<td>Problems w/appts</td>
<td>**</td>
</tr>
<tr>
<td>Interrupts others/busy</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Consumed ≥ 4 alcoholic drinks per day for women, or ≥5 drinks per 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 (i.e. ≥7 consecutive days), during the double-blind treatment period (visit 3–14 [BL to week 12]). P values were adjusted for multiple comparisons. AISRS = Adult ADHD Investigator Symptom Rating Scale; Appts = appointments; Conc. = concentration; NS = not statistically significant.
Sample: 54 incarcerated males (Mean age 42 years)

Dose: Start dose 18 mg MPH/placebo titrated over a period of 19 days to max dose of 108 mg/day

CBT: individual CBT once weekly for 12 weeks

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

Findings: MPH treated group showed reduced ADHD symptoms ($P=0.011$), significantly higher proportion negative urine screens ($P=0.047$) and better retention ($P=0.032$)

Figure 2. Change in self-rated ADHD symptoms (95% CI: -13.78 to -1.91, $P=0.011$).
Methylphenidate for ADHD and Drug Relapse in Criminal Offenders with Substance Dependence: A 24-week Randomized Placebo-controlled Trial

Figure 3. Proportion negative urine-toxicology after release from prison (week 3 to week 24) for the two treatment groups; methylphenidate (MPH) and placebo over 24 weeks of treatment: 2a. any drugs amphetamine + other drugs mean difference 95% CI: 0.05 – 0.32, 2b. amphetamines only, mean difference 95% CI: 0.07 - 0.36 and 2c. other drugs, mean difference 95% CI: 0.02 – 0.25.

Figure 4. Kaplan-Meier curve for retention in treatment through to last visit at the clinic (MPH: Md=51, placebo: Md=18; hazard ratio 0.38, 95% CI: 0.174 to 0.647)

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

Courtney A. Zulauf, Susan E. Sprich, Steven A. Safren and Timothy E. Wilens

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 current review is an update recent guidelines for the treatment of SUD. The high risk for comorbidity between ADHD and SUD is well established. Treatment alone does not appear to be particularly effective in treating SUD in currently active substance abusing individuals with ADHD. 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..."
Stimulant Misuse and Diversion

- N=22 Studies (N>113,000 participants); mostly survey studies in college students (80%)
- 10-20% prevalence of non medical use of stimulants
- 65-85% of stimulants diverted from “friends”
  - Majority not “scamming” local docs
  - 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

Any Substance Use Disorder

Hazard Ratio (HR): 2.7; 95% Confidence Interval (CI): 1.7, 4.2; p<0.001
N=100 stimulant misuser; 198 controls

College Stimulant Misusers Have High Rates of Polysubstance Abuse

Hazard Ratio (HR): 4.7; 95% Confidence Interval (CI): 1.9, 11.3; p=0.001

Rates of ADHD are Higher in College Students Who Misuse Stimulants Compared to Controls (N=300)

Subthreshold + full diagnosis of ADHD

More Executive Dysfunction in Stimulant Misusers

Subscales of the Self-Report Behavior Rating Inventory of Executive Functioning (BRIEF; N=299)

T-Score from 0-100
Axis formatted to start at a T-score of 40

Immediate-release Stimulants are Misused by College Students with a Stimulant Use Disorder (N=39; *BTW-about 40% have a stimulant use disorder*)

Stimulant Preparation Linked to Dopamine Transporter Binding and Likeability

40 mg IR-MPH versus 90 mg OROS MPH

Likeability

- IR-MPH
- OROS-MPH

Dopamine Transporter Binding (%)

* p < 0.05

(Spencer et al. AJP:163: 2006) www.mghcme.org
Illicit Use Survey From ADHD Clinic

- Of 335 survey responses – 73 (14%) reported stimulant abuse

**Type of Stimulant Abused**

- Short-acting: 80%
- Long-acting: 17%
- Both: 3%

- Most common method of abuse was crushing and inhaling (N=75%)

ADHD + SUD: Clinical Recommendations

- Non-pharmacologic approaches
  - For ADHD/SUD: Cognitive-behavioral therapy
  - Family Tx for adolescents and young adults
- Consider non-stimulants for current/recent substance abusers
- Atomoxetine
  - Lacks abuse liability
  - Maybe useful in comorbid cases (e.g. anxiety)
  - Efficacy data in abstinent alcohol + ADHD (for both ADHD and SUD)
  - No AEs with alcohol or THC
- Bupropion
  - No known interactions with alcohol or THC
  - Efficacy in cigarette cessation & mood disorders
- Guanfacine, clonidine, modafinil, tricyclics-untested

SUD in ADHD:
Clinical Recommendations Prior to Treatment

- **Stimulants:**
  - Use in substance-abusing patients is complex and controversial
  - Use extended-release formulations of stimulants (e.g. lisdexamfetamine, OROS MPH, d-MPH XR, MPH-LA, MAS XR or MPH SR, MTS/patch)
  - Monitor carefully, pre-discussed “renewal” guidelines

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.

- Stimulants do not worsen the later risk for SUD in treated ADHD kids.

- In fact, treating ADHD helps protect against the onset of cigarette smoking, SUD, and SUD-related criminality in adolescence & young adulthood.
• Individuals with SUD and ADHD require treatment of both the SUD and the ADHD. If possible, it is best to sequence treatment to address the SUD initially and then the ADHD.

• Because stimulants can be misused, it is parsimonious initially to use extended-release stimulants in high risk individuals such as those with SUD histories, or those at highest risk to misuse or divert their medication (e.g. 16-25 year olds)