ADHD, SUBSTANCE USE DISORDERS AND TREATMENT

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The intersection of attention-deficit/hyperactivity disorder and substance abuse.

Wilens TE, Morrison NR.
• Substance abuse disorders (SUD) are the most common co-morbidity disorder.
• Nicotine dependence in Germany is 27 %, about 40 % in the USA (1).
• Second most common disorder is the harmful use of alcohol.

In general, patients with ADHD are twice as much at risk of development of drug dependence (2). Co-morbidity of drug dependence is between 45 and 70 % (22-24) and one third of those addicted to alcohol has ADHD. (3,4). 15-25 % of adults with SUD fulfill criteria for ADHD. The most common illicit drug is cannabis – 21 %. Cocaine - 11-35 % (5,6).
• SUD with ADHD patients start earlier, course of the disease is more serious and the prognosis is worse.

Patients With ADHD Frequently Have Coexisting Disorders

Children & Adolescents

- 31% ADHD alone
- 11% Tic
- 14% Conduct
- 34% Anxiety
- 4% Mood
- 40% Oppositional Defiant Disorder (ODD)

Adults

- 14% ADHD alone
- 53% GAD
- 25% Cyclothymia
- 13% OCD
- 25% Dysthymia
- 34% Alcohol Abuse/Dependence
- 30% Drug Abuse
- 15% Panic Disorder

MTA cooperative: N=579.
Increased Lifetime Substance Abuse

**Lifetime history of psychoactive substance use disorder**

<table>
<thead>
<tr>
<th>Lifetime Rate (%) of Substance Abuse in Referred Adults</th>
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<tr>
<td>Control (n=262)</td>
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<tr>
<td>ADHD (n=239)</td>
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• ADHD and SUD share common neurobiological mechanisms and treatment of ADHD decreases craving and relapse rate.

Brain Networks Implicated in ADHD

ADHD and Substance Misuse

• Reason for the relationship:

  High stimulus seeking behaviour:
  Inherent component of ADHD (e.g. novelty seeking)
  Shared genetic risk

  Impaired social/academic/work function:
  Secondary consequence of psychosocial impairments

  Relief from symptoms:
  Self-treatment of symptoms (e.g. cannabis, alcohol, cocaine)

75% patients with ADHD in childhood have ADHD in adolescence and 50% in adulthood (1).

66% children with ADHD have in adulthood at least clinical significant symptom of mental health disorders (2).

25-50% adolescents with SUD have ADHD. 40-50% those smoking marihuana have ADHD.

Adults with ADHD and SUD have more serious symptoms of those disorders and have started using PAS when they were younger (3).

Understanding reasons for using PAS is important for treating these patients.

• Children with ADHD and comorbid conduct or bipolar disorder have the worst prognosis for SUD (1).

• Those without these disorders have a moderate risk (2).

• There is not much research about the role of ADHD and comorbid SUD in women (3).


• In many patients with SUD ADHD was not recognized or diagnosed. In the group of patients with SUD 54 % had symptoms of ADHD in childhood and it was related to the earlier use of alcohol and other PAS (1). Because ADHD symptoms express earlier as SUD there is a small possibility that the SUD cause ADHD (2).
ADHD is a significant risk factor for starting smoking before 15 years and when associated behavioral disorders or mood disorders are particularly risky. Early exposure to nicotine may make the brain more susceptible to subsequent behavioral and emotional disorders and PAS abuse.
• Hypothesis of selfmedication is of course linked to the fact that ADHD often associated with a loss of motivation, failure as are important factors for the abuse of drugs (2).

As ADHD is recognized ahead of PAS abuse it can be successfully treated and so the possibility of the development of SUD and also ADHD in adulthood may be reduced (1).

Persons who abuse drugs are more often hospitalized and have worse outcomes in ADHD in this population (2).

Wilens et.al have demonstrated significant reduction in ADHD symptoms in adults with alcohol dependence but no effect on alcohol consumption (3).

Atomoxetine in adult patients with ADHD and co-morbid alcohol abuse treated for 12 weeks: LYBY

Effect Size: 0.48

Atomoxetine efficacy in adult ADHD and co-morbid alcohol use disorders: alcohol use

- No worsening of alcohol abuse in patients treated with atomoxetine

**Recurrent Heavy Drinking**

- This post-hoc analysis demonstrated robust effects of atomoxetine for reducing ADHD symptoms in adult ADHD patients with comorbid alcohol-use disorder and suggests a positive effect on reducing cumulative heavy drinking events over time

• Because of high incidence of ADHD in SUD population we should always have in mind the possibility of ADHD.

• Correlates with worse quality of life(1).

• All patients with SUD should be screened for ADHD as soon as their PAS use is stabilised (2).

• Stabilisation of PAS use is priority though the treatment should be integrative and complex including pharmacotherapy starting with less addictive medications like atomoxetine or bupropion and if these are not affective start using stimulants.

Methylphenidate Increase Dopamine Levels in Rat Nucleus Accumbens and Striatum

*Bp<.05, overall concentration during 4-hour time period vs. baseline

Atomoxetine Does Not Increase Dopamine Levels in Rat Nucleus Accumbens and Striatum


Atomoxetine
3 mg/kg i.p for PFC and nA; 10 mg/kg i.p for striatum

*
Proposed Effects of Atomoxetine in Brain Regional Catecholamine Neurotransmission


Regions potentially affected by atomoxetine’s action on the NE transporter:
- Prefrontal cortex
- Striatum
- Nucleus accumbens
- Amygdala
- Hippocampus
- Post parietal
Early beginning of treatment of ADHD delays the start of drug abuse. But the treatment should not be interrupted prematurely in adolescence (1). An extensive meta-analysis has clearly shown that if treatment with stimulants begun in childhood is less possibility of 27% of stimulant abuse in adulthood (Wilens et al 2003).

If the treatment is started only in adolescence, the possibility of SUD is increased to 44% (Collins et al. 2008).

It was also shown that abuse of stimulants in connection with the development of antisocial personality disorder.

• There is a constant concern about the abuse and misuse of the stimulant prescribed to treat ADHD. The vast majority of patients use medicament for the treatment of ADHD properly.

• But a significant proportion reports pressures to approve or sold medicines that have been prescribed to them (1,2).


• Around 5% of students abuse stimulants for help with the study. More for improve cognitive functions than to achieve euphoria (1).

The effect of 20 mg MPH on long-term memory and understanding of the information did not differ from placebo effect. Amphetamine does not affect short-term memory, long term memory improves, but only when new knowledge already is there. The reason that some students abuse them is to increase in the concentration (58 %), attention (43 %) and feel euphoria (43 %).

The link between the core ADHD symptoms and the prefrontal cortex

- dorsal ACC
- select attention
- hyperactive symptoms
- supplementary motor cortex
- prefrontal motor cortex
- DLPFC
- sustained attention problem solving
- impulsive symptoms
- orbital frontal cortex