

ADHD, SUBSTANCE USE DISORDERS AND TREATMENT

Andrej Kastelic
Global Addiction Association President
EUROPAD General Secretary
SEEA net President
Center for Treatment of Drug Addiction
University Psychiatric Clinic Ljubljana
Ljubljana, Slovenia

E-mail: andrej.kastelic@psih-klinika.si



Developmental Relationship Between ADHD & Substance Abuse

Adolescent

- ADHD treatment may protect against cigarette and SUD
- Exposure to parental SUD increases SUD in ADHD



Gestational

- Family-genetic factors link ADHD and SUD risk
- Alcohol and nicotine in utero exposure increase ADHD risk



Child

- Comorbid ADHD linked to early-onset cigarette smoking and SUD

Adult

- ADHD linked to more cigarette smoking and SUD
- ADHD linked to more severe and chronic SUD
- ADHD linked to less remission from cigarette smoking and SUD
- ADHD treatment does not increase SUD

- 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).

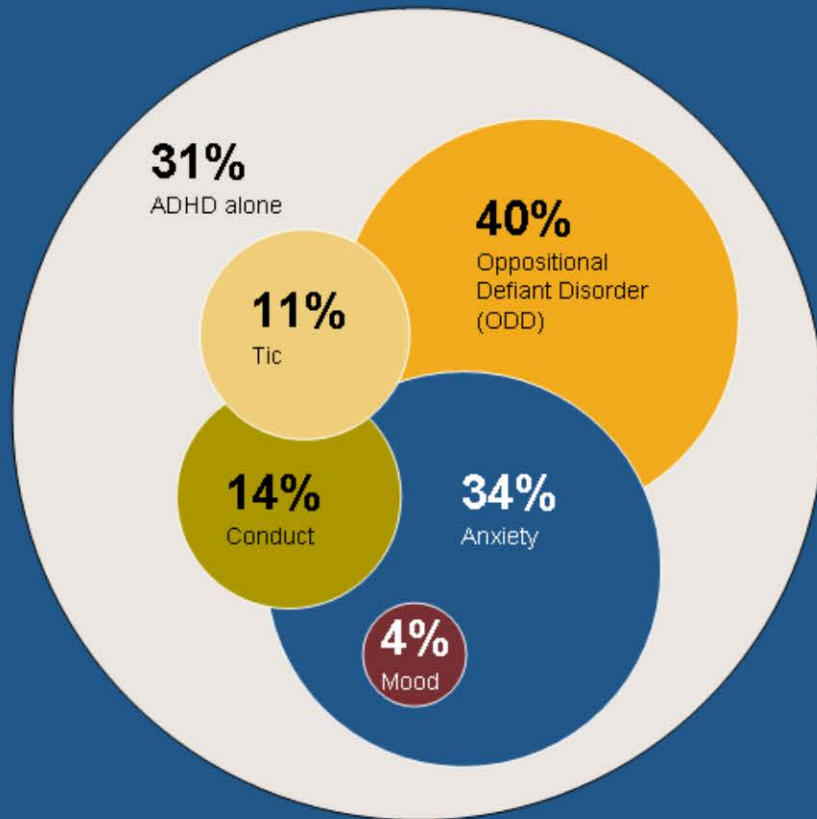
- SUD with ADHD patients start earlier, course of the disease is more serious and the prognosis is worse.

1. Philipsen A, Heslinger B, tebartz van Elst. Attention Deficit Hyperactivity Disorder in Adulthood; Diagnosis, Etiology and Therapy. Dtsch Arztebl Int 2008; 105(17): 311-7

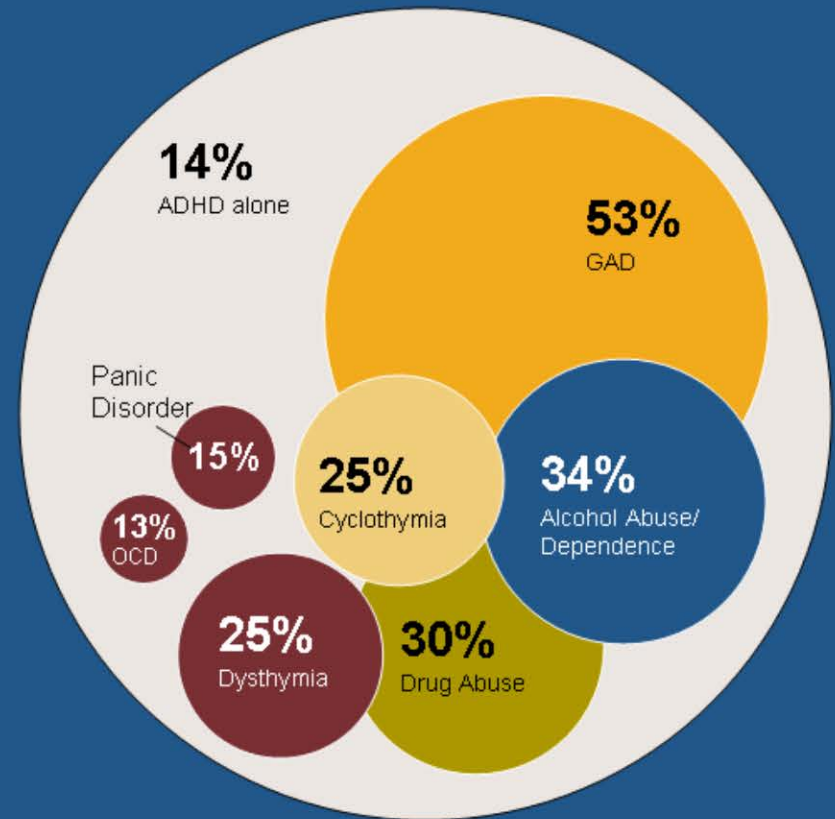
2. Huss M. Abschlussbericht and des Bundesministerium fur Gesundheit und Soziale Sicherung (BMGS). Bonn: 2004.

Patients With ADHD Frequently Have Coexisting Disorders

Children & Adolescents



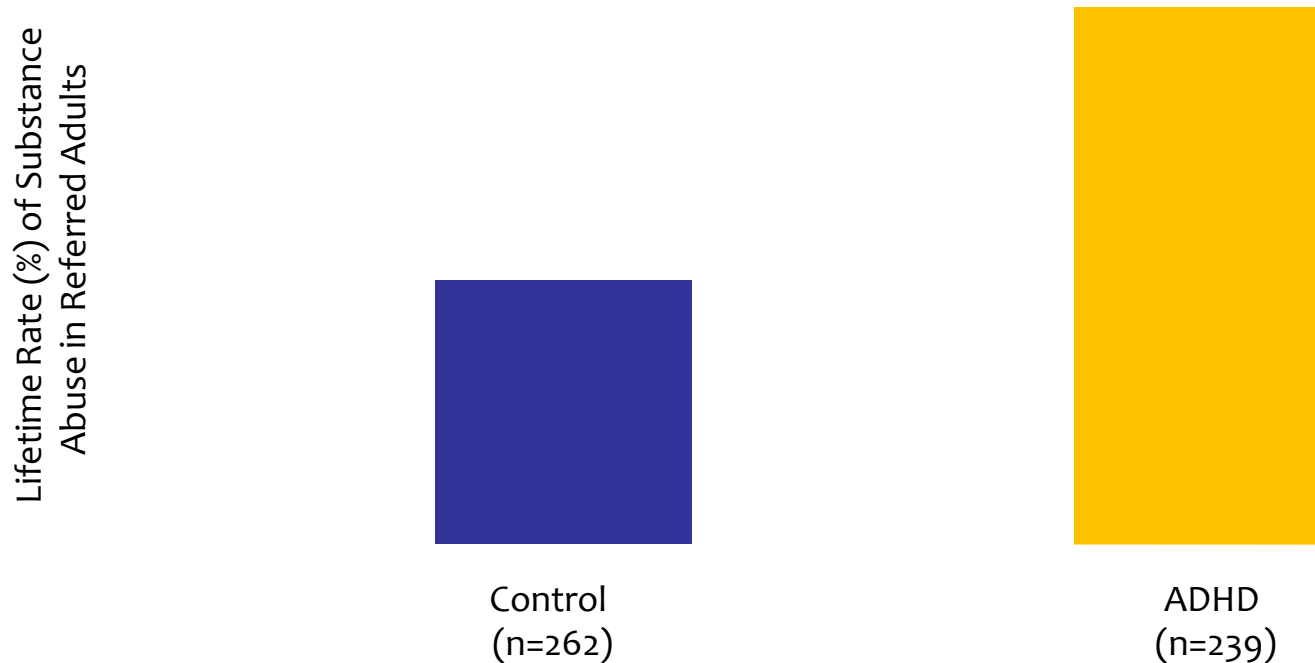
Adults





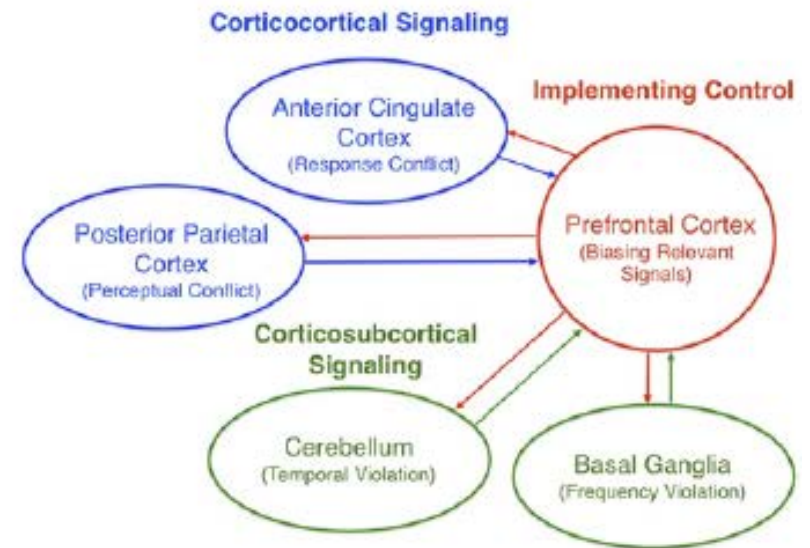
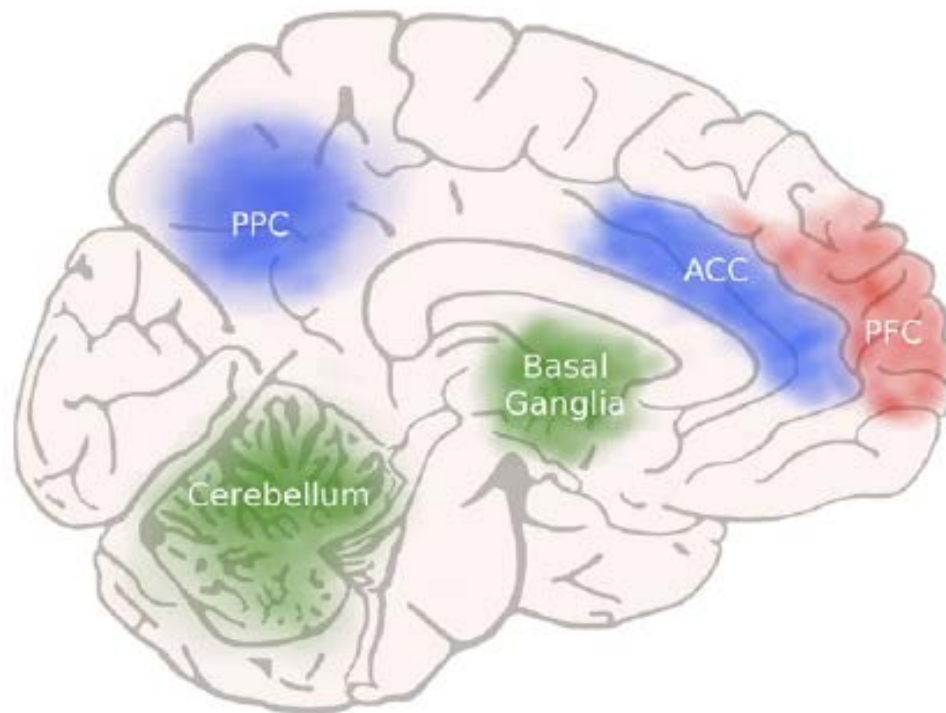
Increased Lifetime Substance Abuse

Lifetime history of psychoactive substance use disorder



- 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)

1. Arias et al. *Addictive Behaviors* 2008;33(9):1199–207.

2. Asherson. 1st European Network Adult ADHD Conference. London, 2011.

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).

1. Timothy E, Wilens M.D, R.Morrison N. The Intersection of Attention-deficit/Hyperactivity Disorder and Substance Abuse. *Curr Opin Psychiatry*. 2011 July; 24(4): 208-285
2. Kolar et.al. Treatment of adults with ADHD. *Neuropsychiatric Disease and Treatment* 2008; 4(2): 389-403
3. Wilens T, R Morrison N. Substance-use disorders in adolescents and adults with ADHD: focus on treatment. *Neuropsychiatry (London)*. August 2012; 2(4): 301-312

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

Wilson JJ, Levin FR. Attention deficit hyperactivity disorder (ADHD) and substance use disorders. *Curr Psychiatry Rep.* 2001 December; 3(6): 497-506.

- 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).

1. Brook DW, Brook JS, Zhang C, Koppel J. Association between attention-deficit/hyperactivity disorder in adolescence and substance use disorder in adulthood. *Arch Pediatr Adolesc Med.* 2010 Oct; 164(10): 930-4.
2. Wilens TE. Attention-deficit/hyperactivity disorder and the substance use disorders: the nature of the relationship, subtypes at risk, and treatment issues. *Psychiatr Clin North Am.* 2004 Jun; 27(2): 283-301.
3. Lynskey MT, Hall W. Attention deficit hyperactivity disorder and substance use disorder: Is there a causal link? *Addiction.* 2001 Jun; 96(6): 815-22.

- 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).

1. Ohlmeier et.al. Alcohol and drug dependence in adults with attention-deficit/hyperactivity disorder: Data from Germany. Eur J Psychiat 2011. Vol 25. N3: 150-163.
2. Timoty E, Wilens M.D, R.Morrison N. The Intersection of Attention-deficit/Hyperactivity Disorder and Substance Abuse. Curr Opin Psychiatry. 2011 July; 24(4): 208-285

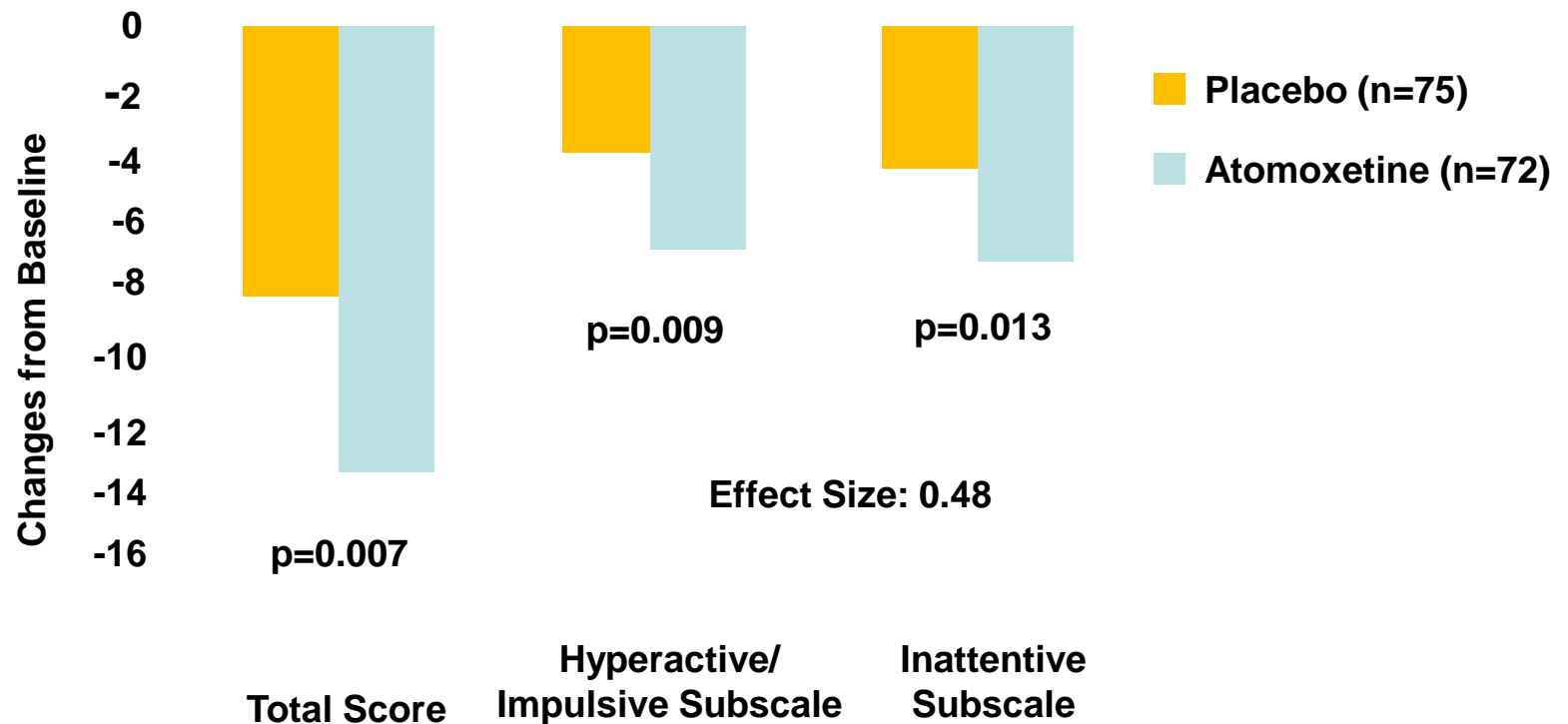
- As ADHD is recognized ahead of PAS abuse it can be successfully treated and so the possibility of the development of SUD and also ADHD in adulthood may be reduced (1).
- Persons who abuse drugs are more often hospitalized and have worse outcomes in ADHD in this population (2).
- Wilens et.al have demonstrated significant reduction in ADHD symptoms in adults with alcohol dependence but no effect on alcohol consumption (3).

1. Wilson JJ, Levin FR. Attention deficit hyperactivity disorder (ADHD) and substance use disorders. *Curr Psychiatry Rep.* 2001 December; 3(6): 497-506.

2. Thurstone C et.al. *J Am Acad Child Adolesc Psychiatry* 2010, 49:573-582

3. Wilens et.al. *Drug Alcohol Depend* 2008, 96: 145-154

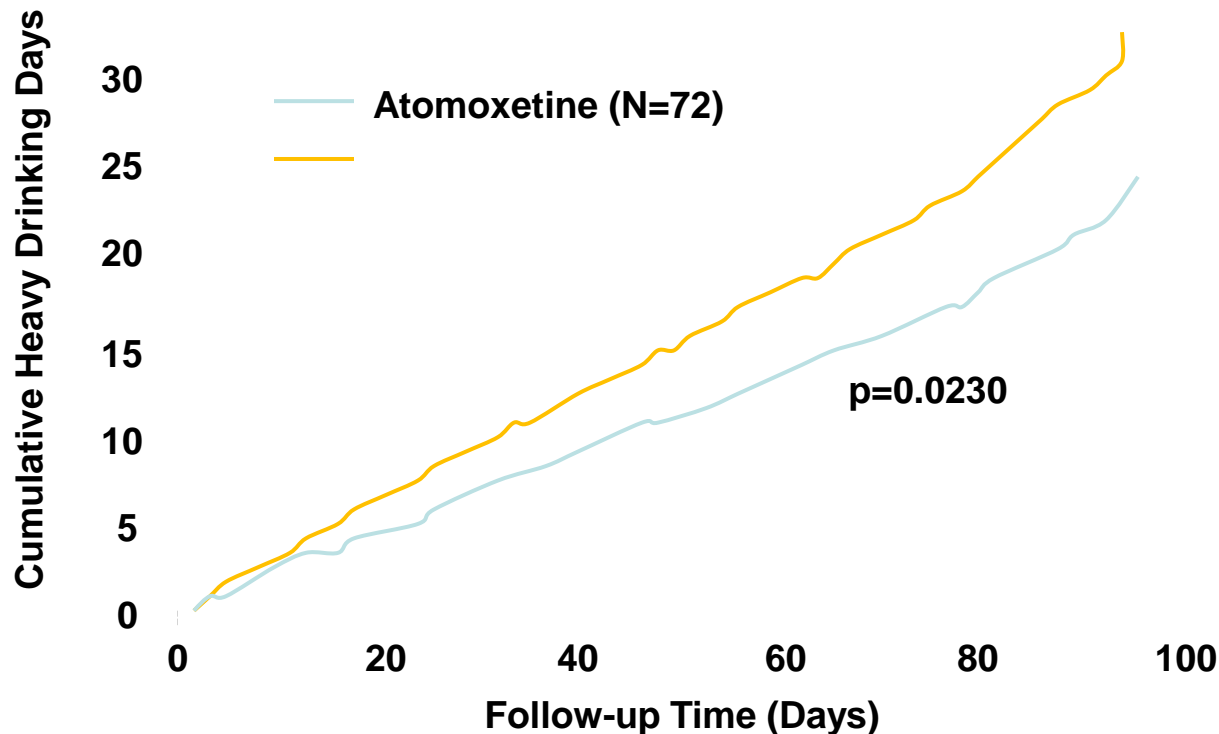
Atomoxetine in adult patients with ADHD and co-morbid alcohol abuse treated for 12 weeks: LYBY



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

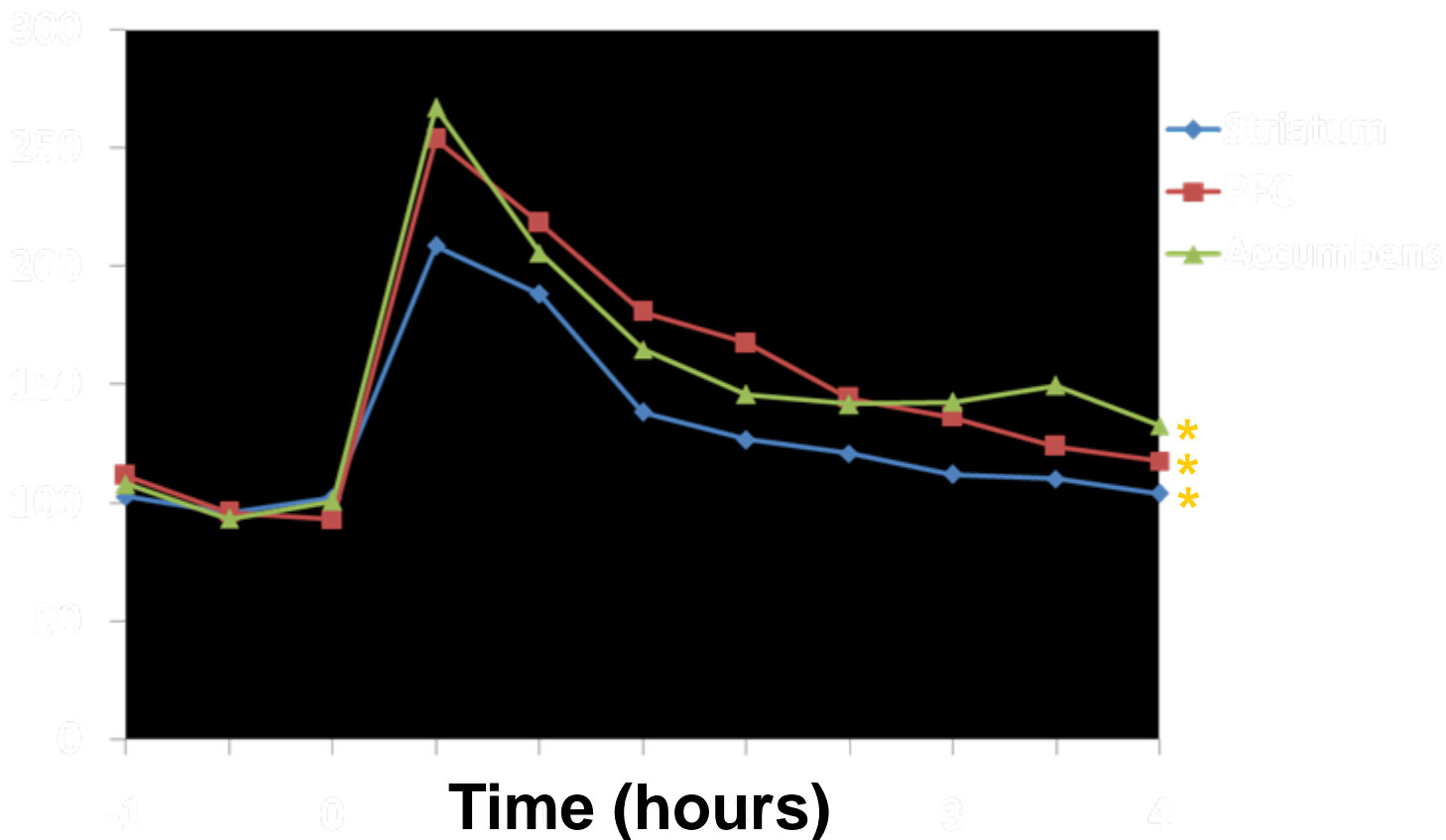
- Because of high incidence of ADHD in SUD population we should always have in mind the possibility of ADHD.
- Correlates with worse quality of life(1).
- All patients with SUD should be screened for ADHD as soon as their PAS use is stabilised (2).

1. Fatseas M, Debrabant R, Auriacombe M. The diagnostic accuracy of attention-deficit/hyperactivity disorder in adults with substance use disorders. *Curr Opin Psychiatry*. 2012 May; 25(3): 219-25.

2. Matthys F, Joostens P, Van den Brink W, Sabbe B. Summary of the practice guideline for the diagnosis and treatment of ADHD in adolescents and adults with addictions. *Ned Tijdschr Geneeskd*. 2013; 157(24): A 6025.

- 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



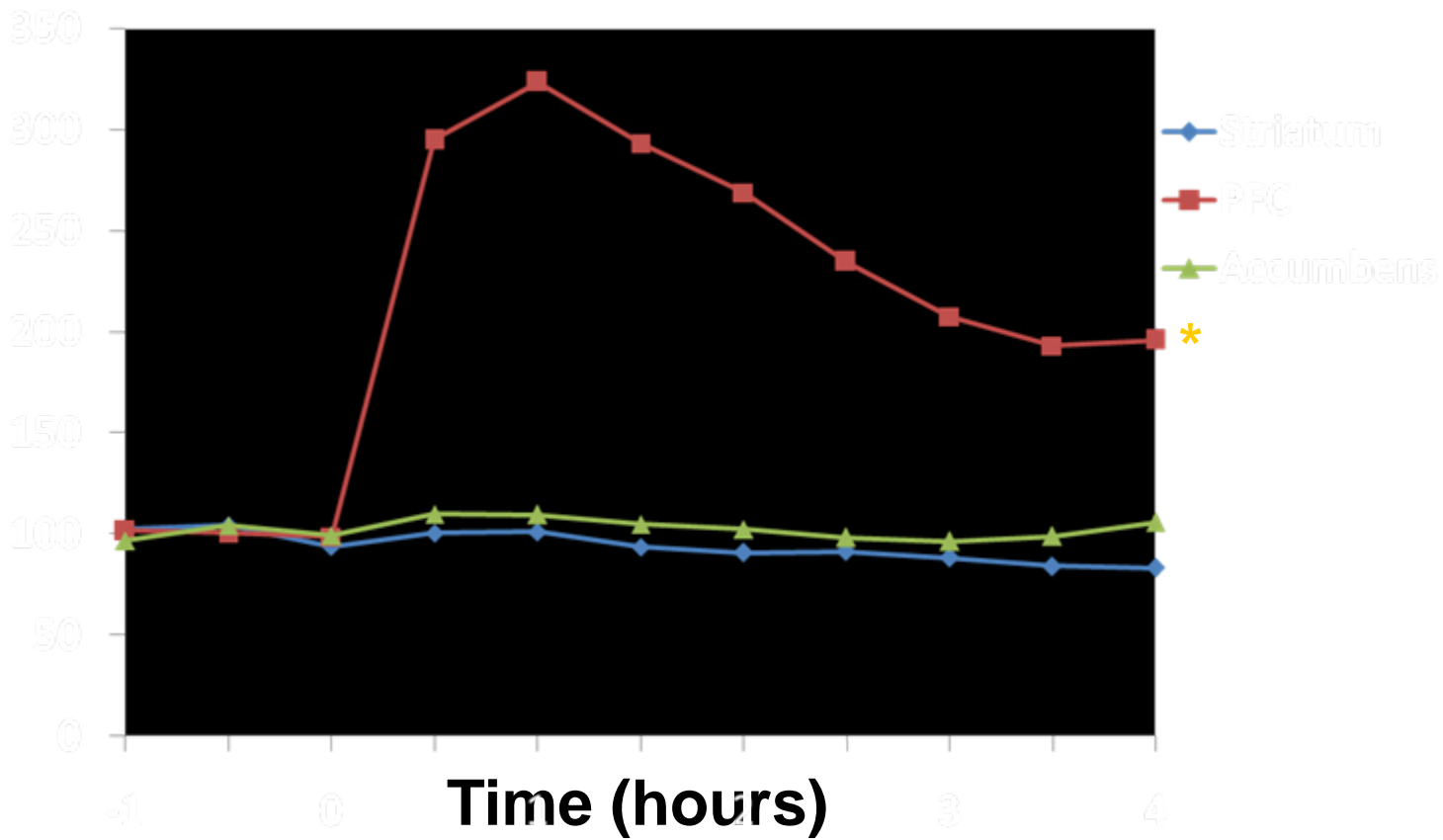
Methylphenidate 3 mg/kg i.p

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

Bymaster et al. *Neuropsychopharmacology* 2002;27(5):699-711.



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

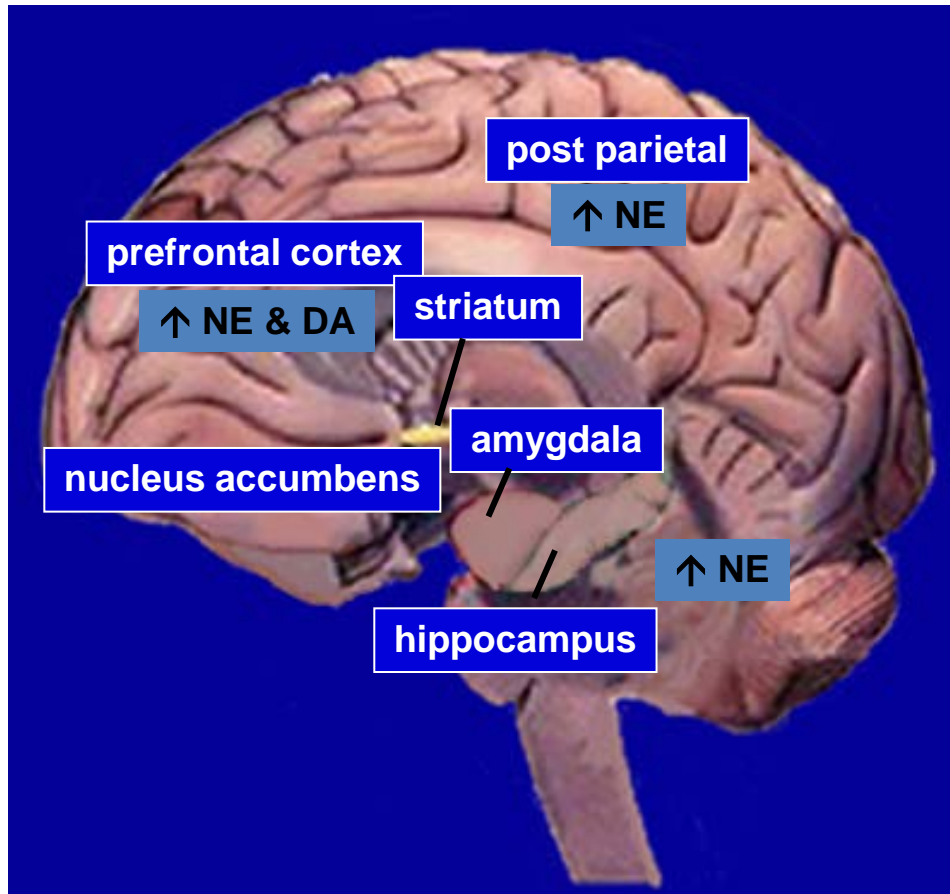


Atomoxetine
3 mg/kg i.p for PFC and nA; 10 mg/kg i.p for striatum

*

Bymaster et al. *Neuropsychopharmacology* 2002;27(5):699-711.

Proposed Effects of Atomoxetine in Brain Regional Catecholamine Neurotransmission^a



Regions potentially affected by atomoxetine's action on the NE transporter

^aBased on rat studies

Bymaster et al. *Neuropsychopharmacology* 2002;27(5):699-711.

- Early beginning of treatment of ADHD delays the start of drug abuse. But the treatment should not be was 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.

1. Bejerot S, Ryden EM, Arlinde CM. Two-year outcome of treatment with central stimulant medication in adult attention-deficit/hyperactivity disorder: a prospective study. *J Clin Psychiatry*. 2010 Dec; 71(12): 1590-7.

- There is a constant concern about the abuse and misuse of the stimulant prescribed to treat ADHD. The vast majority of patients use medication 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).

1. McCabe SE, Knight JR, Teter CJ, Wechsler H. Non-medical use of prescription stimulants among US college students: prevalence and correlates from a national survey. *Addiction*. 2005; 99(1): 96-106.
2. Teter CJ, McCabe SE, LaGrange K, Cranford JA, Boyd CJ. Illicit use of specific prescription stimulants among college students: prevalence, motives, and routes of administration. *Pharmacotherapy*. 2006; 26(10): 1501-1510.

- 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 %).

1. Wilens TE, Adler LA, Adamson J, et. al. Misuse and diversion of stimulants perscribed for ADHD: a systematic review of the literature. J Am Acad Child Adolesc Psychiatry. 2008 Jan; 47(1):21-31.

The link between the core ADHD symptoms and the prefrontal cortex

