



CIP2015



**4TH GLOBAL CONGRESS FOR
CONSENSUS IN PEDIATRICS & CHILD HEALTH**

MARCH 19-22, 2015 | BUDAPEST, HUNGARY



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ADD-ADHD

A CHALLENGE FOR PRIMARY CARE PEDIATRICIANS

Manuel Katz MD, MPH

Head Physician. Maternal and Child Health , Ministry of Health, South Region, Israel

Ben Gurion University , Israel. Maimonides University , Argentina

President Israel Ambulatory Pediatric Association

President CIP –www.cippediatrics.org-

Former Secretary general UNEPSA-EPA

ISSOP and ECPCP Council member

WHO-PAHO technical advisor



ADD-ADHD: A CHALLENGE FOR PRIMARY CARE PEDIATRICIANS



1. Diagnosis
2. Natural History
3. Co- Morbidities
4. A little about medications
5. Main recommendations for Primary and Community Pediatricians
6. Conclusions
7. 5minutes for general discussion

DIAGNOSIS CRITERIA OF ADHD

DSM is the manual used by clinicians and researchers to diagnose and classify mental disorders. The American Psychiatric Association (APA) published DSM-5 months ago, culminating a 14-year revision process.

ADHD was slightly changed !!

DIAGNOSIS CRITERIA OF ADHD

- A. Either inattention or hyperactive features (at least 6 of each), persisting for more than 6 months . In older people more than 17 years old only 5 of each are necessary in order to meet the criteria
- B. Some symptoms that caused impairment are present before age 12 years (DSM 5)
- C. Some impairment from the symptoms is present in two or more settings (e.g., at school [or work] and at home ;
- D. There must be clear evidence of clinically significant impairment in social, academic, or in-job functioning;
- E .Would co-occur with a PDD disorder (DSM 5)
- F. ADHD symptoms must not occur exclusively during the course of schizophrenia or another psychotic disorder and must not be better explained by another mental disorder, such as a depressive or bipolar disorder, anxiety disorder, dissociative disorder, personality disorder, or substance intoxication or withdrawal. (DSM 5)

Attention-Deficit/Hyperactivity Disorder

The diagnostic criteria for attention-deficit/hyperactivity disorder (ADHD) in DSM-5 are similar to those in DSM-IV.

The same 18 symptoms are used as in DSM-IV, and continue to be divided into two symptom domains (inattention and hyperactivity/impulsivity), of which at least six symptoms in one domain are required for diagnosis. However, several changes have been made in DSM-5:

- 1) examples have been added to the criterion items to facilitate application across the life span;
- 2) the cross-situational requirement has been strengthened to “several” symptoms in each setting;
- 3) the onset criterion has been changed from “symptoms that caused impairment were present before age 7 years” to “several inattentive or hyperactive-impulsive symptoms were present prior to age 12”;

4) subtypes have been replaced with presentation specifiers that map directly to the prior subtypes;

5) a comorbid diagnosis with autism spectrum disorder is now allowed; and

6) a symptom threshold change has been made for adults, to reflect their substantial evidence of clinically significant ADHD impairment, with the cutoff for ADHD of five symptoms, instead of six required for younger persons, both for inattention and for hyperactivity and impulsivity.

Finally, ADHD was placed in the neurodevelopmental disorders chapter to reflect brain developmental correlates with ADHD and the DSM-5 decision to eliminate the DSM-IV chapter that includes all diagnoses usually first made in infancy, childhood, or adolescence.

Diagnostic criteria for Attention-Deficit/Hyperactivity Disorder

(1) Inattention

- often fails to give close attention to details or **makes careless mistakes** in activities
- often has difficulty **sustaining** attention
- often does **not seem to listen** when spoken to directly
- often does **not follow through on instructions** and fails to finish work
- often has **difficulty organizing** tasks and activities
- often **loses things**
- often **avoids tasks**
- often easily **distracted** to stimuli
- often **forgetful**

(2) hyperactivity/impulsivity:

Hyperactivity

- often fidgets with hands or feet or **squirms in seat**
- often **leaves seat** in classroom or in other situations in which remaining seated is expected
- often **runs about or climbs** excessively in situations in which it is inappropriate
- often has **difficulty playing** or engaging in leisure activities quietly
- is often “on the go” or often acts as if “**driven by a motor**”
- often **talks excessively**

Impulsivity

- often blurts out **answers before questions** have been completed
- often has **difficulty awaiting turn**
- often **interrupts or intrudes on others** (e.g., butts into conversations or games)

Adulthood

Childhood



Adolescence

ADHD: Overview

- Estimated prevalence: 6%-8% of children; 6% of adolescents; 4% of adults
- *DSM-IV-TR*[®] ADHD types
 - Combined (50%-75%)
 - Predominantly inattentive (20%-30%), increasing with age
 - Predominantly hyperactive-impulsive (<15%)
- 2.5:1 male to female ratio in children and adolescents

DSM-IV-TR; *Diagnosis and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision.*

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed, text revision.*

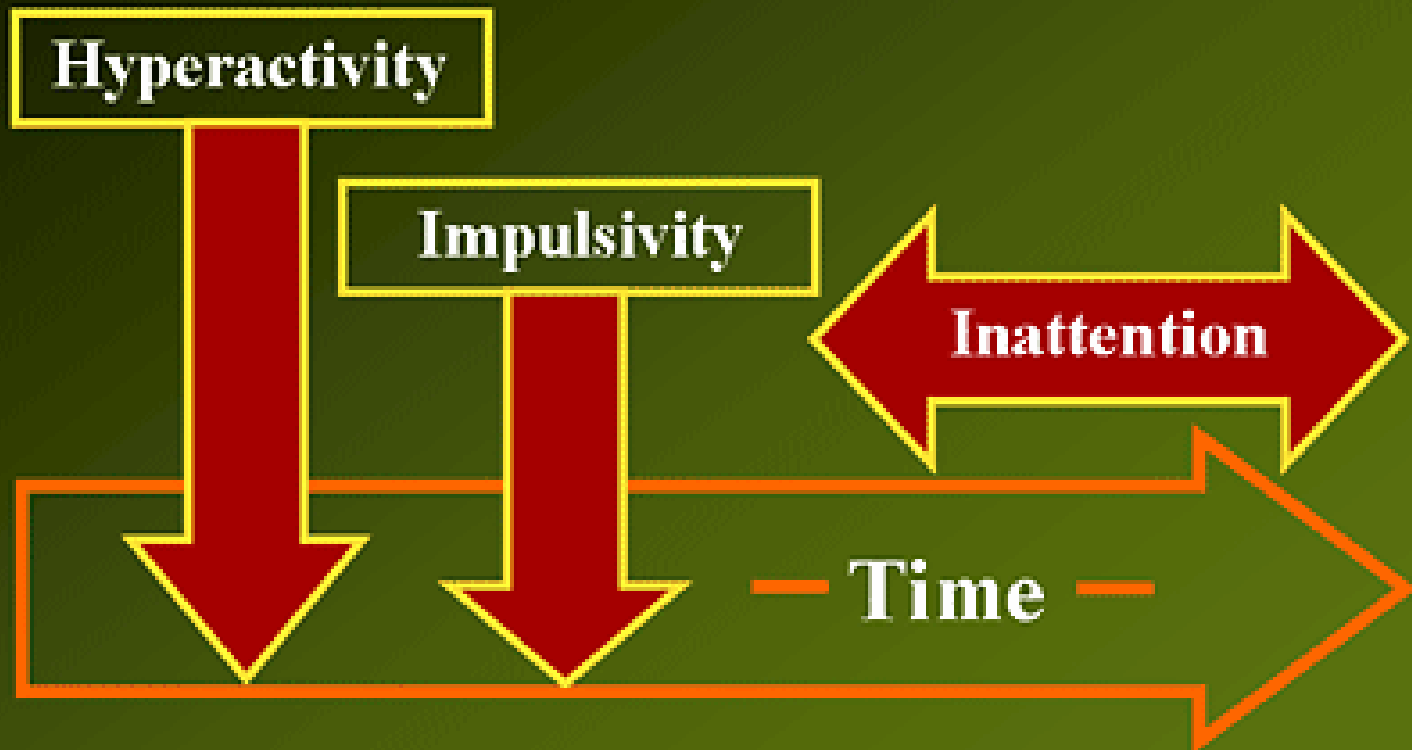
Washington, DC: American Psychiatric Association; 2000:85-93; Biederman J. *J Clin Psychiatry.* 2004;65:3-7;

Faraone SV et al. *Biol Psychiatry.* 2000;48:9-20; Kessler RC, et al. *Am J Psychiatry.* 2006;163:716-723; Michelson

D et al. *Biol Psychiatry.* 2003;53:112-120; *MMWR. Morb Mortal Wkly Rep.* 2005;54:842-847; Wender PH et al. *Ann*

N Y Acad Sci. 2001;931:1-16; Wilens TE et al. *Annu Rev Med.* 2002;53:113-131.

Course of ADHD



Biederman J. et al. *Am J Psychiatry*. 2000 May;157(5):816-8.

Symptoms in early childhood

Preschool age

Delay in language development

Delay in motor development

Rapid changes of mood, inattention and/or hyperactivity, impulsivity, poor ability to attend specific tasks, lack of fear

Sleep disorders

At Preschool age: Inattentive 15%; hyperactive-impulsive 50%; combined .35-40%

At school age: inattentive 50% and hyperactive-impulsive 20%

ADHD is a heterogeneous behavioral disorder with multiple possible etiologies



CNS: central nervous system.

Biederman J, Faraone SV. *Lancet*. 2005;366:237-248;
Pearl PL et al. *Ann N Y Acad Sci*. 2001;931:97-112.

Neurotransmitter function: ADHD is thought to be caused by an imbalance of 2 neurotransmitters, dopamine (DA) and norepinephrine (NE), which are believed to play an important role in the ability to focus and pay attention to tasks .

Genetics: Research strongly suggests that ADHD tends to run in families

Environment : Certain external factors such as smoking or poor maternal health during pregnancy may contribute to ADHD

Brain Injuries: May contribute to develop ADHD

Neural Networks of Attention

- Prefrontal cortex
- Parietal cortex
- Cingulate gyrus
- Limbic structures (amygdala-hippocampus)
- Basal ganglia
- Thalamus
- Brainstem (reticular formation)
- Cerebellum

Seidman LJ et al. *Biol Psychiatry*. 2005;57:1263-1272.

ADHD Imaging Studies Summary

- Neuroimaging studies confirm that brain abnormalities in frontosubcortical networks are associated with ADHD
- But neuroimaging techniques are **not** valid tools for ADHD diagnosis; imaging measures are not sensitive or specific enough to be used for diagnostic purposes

Castellanos FX, et al. *JAMA*. 2002;288:1740-1748;
Seidman LJ, et al. *Biol Psychiatry*. 2005;57:1263-1272.

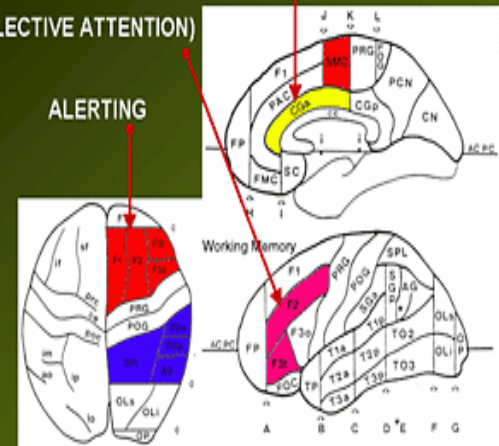
ADHD: Neurobiologic Basis

Attention Networks

EXECUTIVE CONTROL

ORIENTING (SELECTIVE ATTENTION)

ALERTING



Posner and Raichle. *Images of the Mind*. Scientific American Books; 1996.

Frontosubcortical Networks and Catecholamines

- Dysregulation of inhibitory influences of frontocortical activity (predominantly noradrenergic) on lower striatal structures (predominantly dopaminergic)
- Striatal structures driven by dopaminergic agonists controlled or modulated by higher inhibitory structures sensitive to adrenergic agents

Zametkin AJ, et al. *J Am Acad Child Adol Psychiatry*. 1997;26:676-686.

Developmental Trajectories of Brain Volume Abnormalities in Children and Adolescents With ADHD

Main Findings:

- Smaller brain volumes in all regions independently of medication status
- Smaller total cerebral (−3.2%) and cerebellar (−3.5%) volumes
- Volumetric abnormalities (except caudate) persisted with age
- No gender differences
- Volumetric findings correlated with severity of ADHD

Castellanos FX et al. *JAMA*. 2002;288:1740-1748.

A pathophysiologic approach to growth problems in children with attention-deficit/hyperactivity disorder.

Authors Tenore A, Tenore A.

Endocrinol Metab Clin North Am. 2012 Dec;41(4):761-84

**Patient with ADHD
(Untreated)**

**Erratic
eating patterns**

**Increased
activity**

**More time to
eat properly**

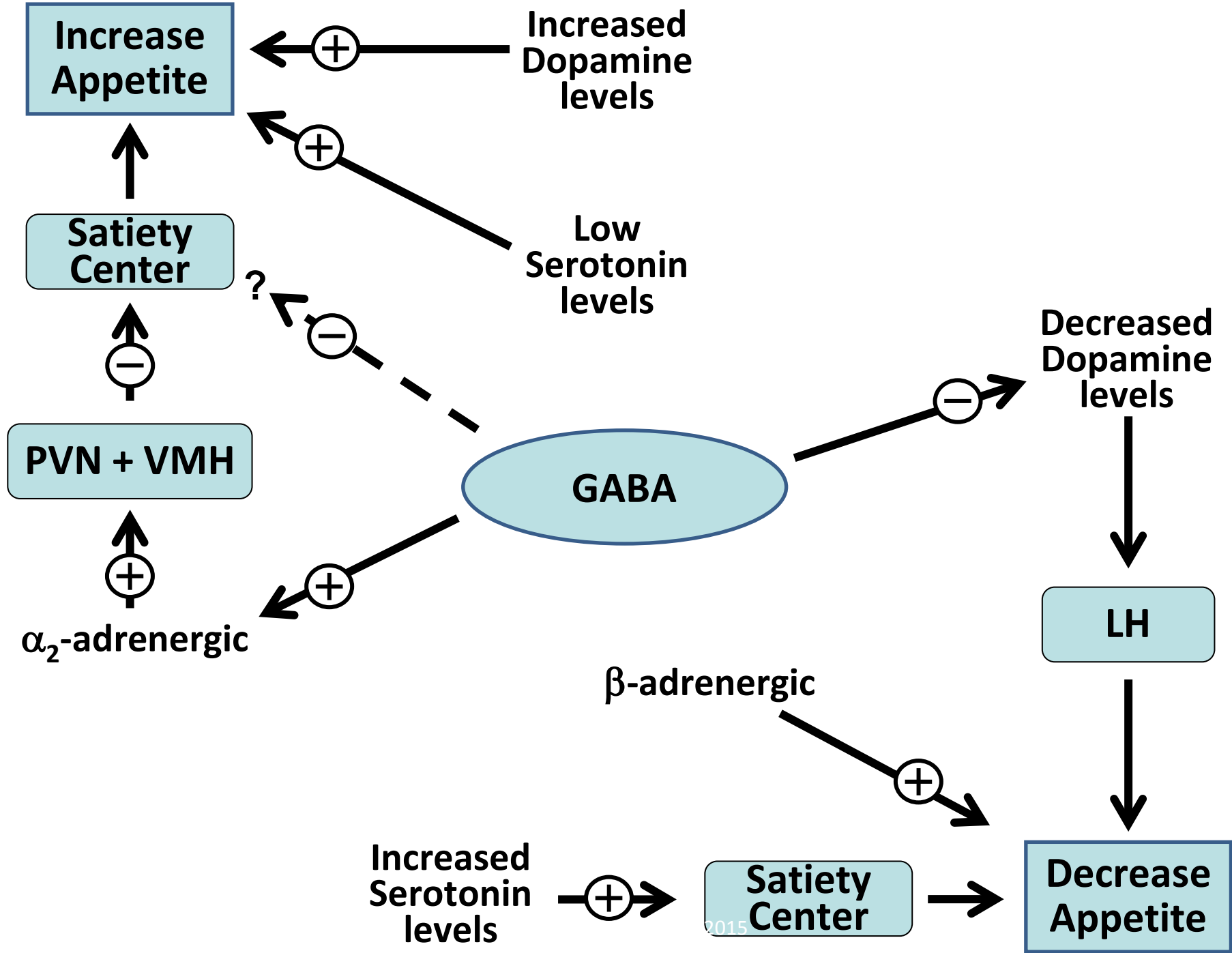
⊕ Weight ⊖

**Unable to
sit and eat**

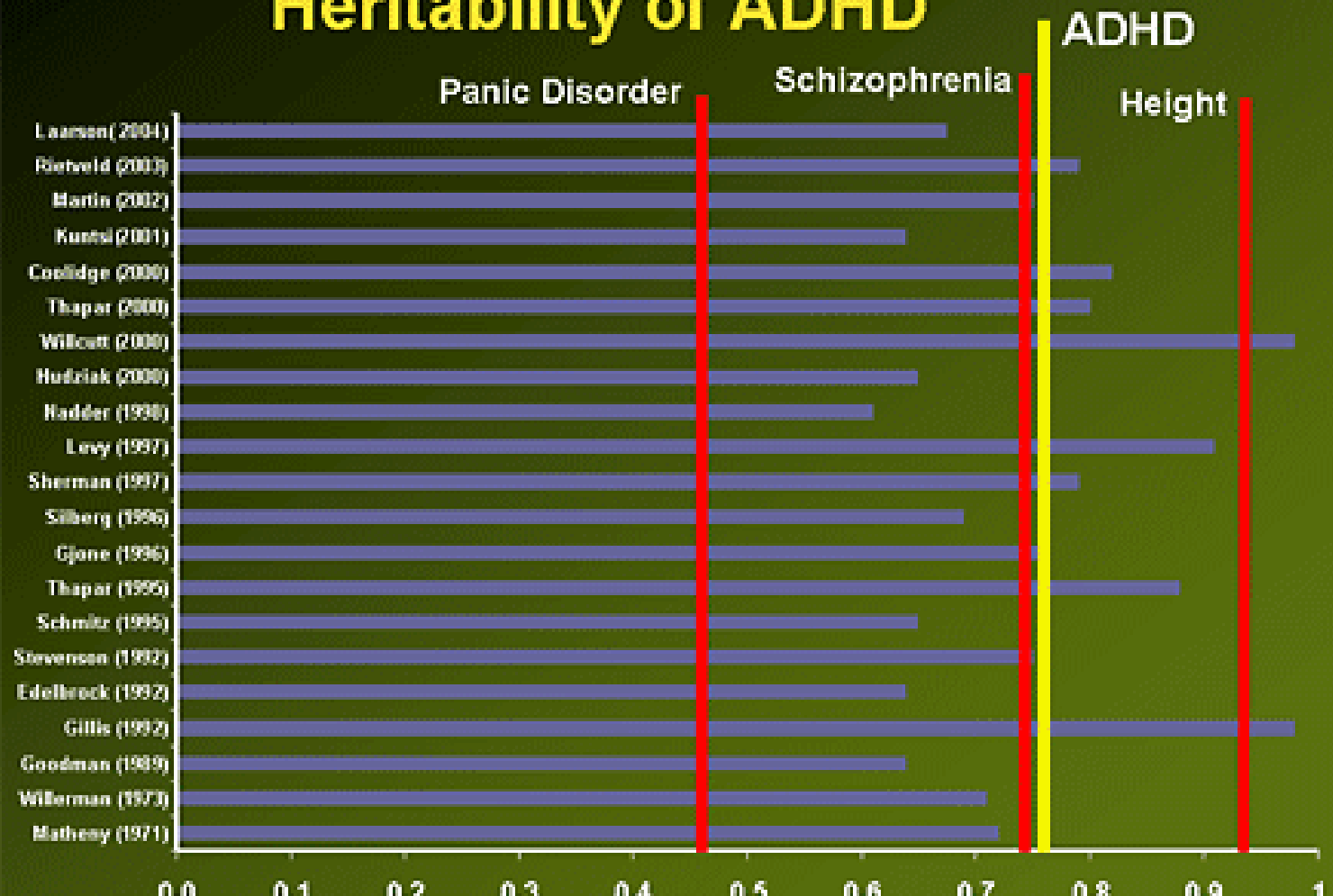
**Decreased
activity**

**Anorexic
effects**

**Patient with ADHD
(Treated)**



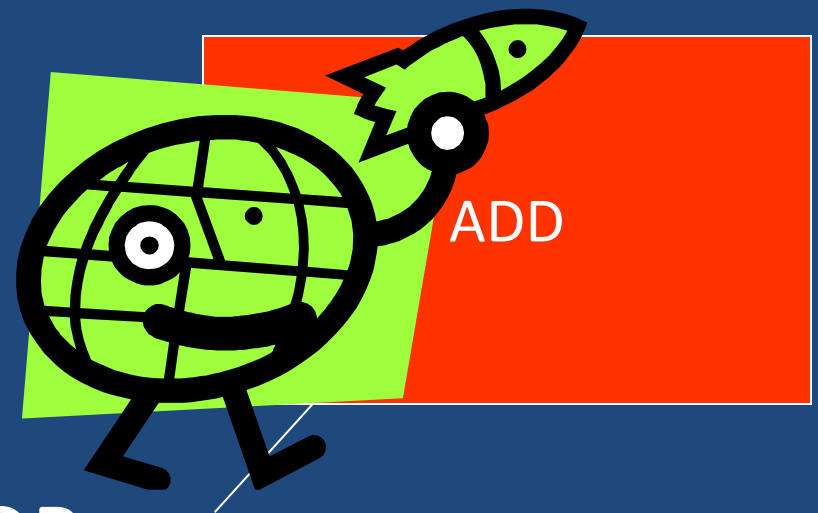
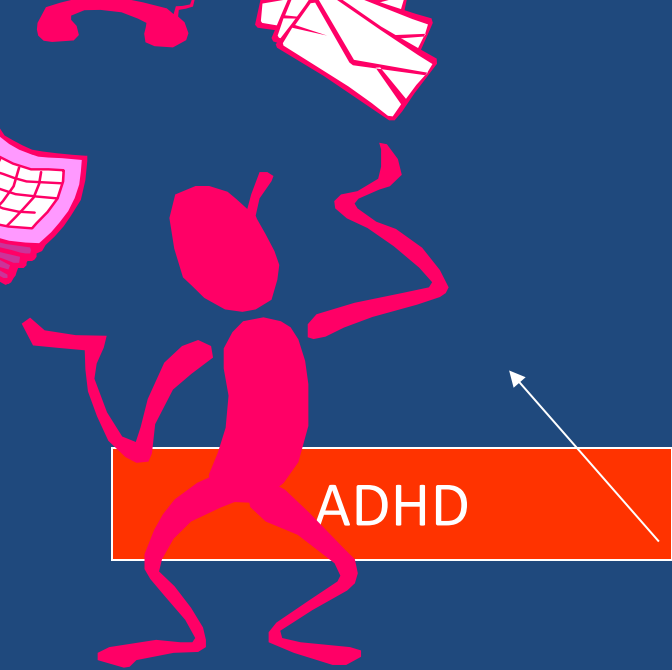
Heritability of ADHD



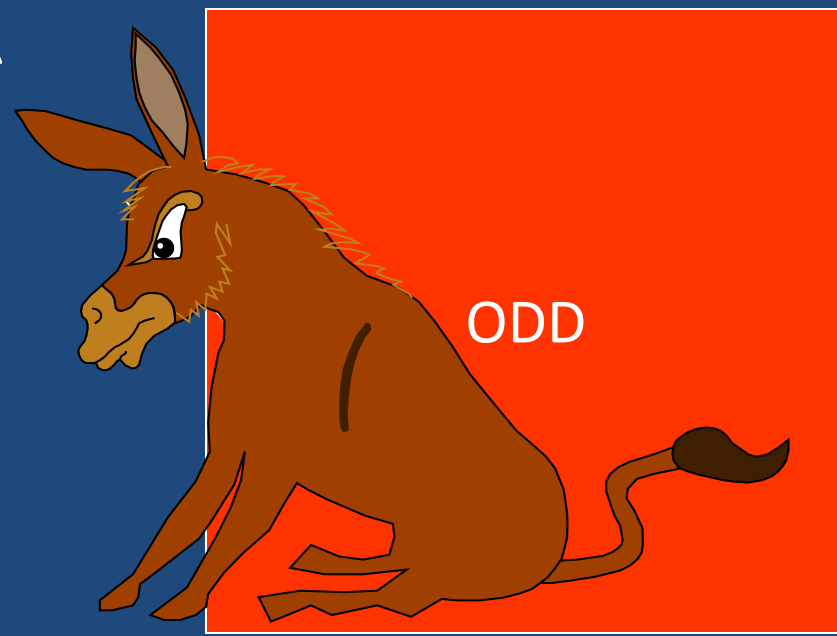
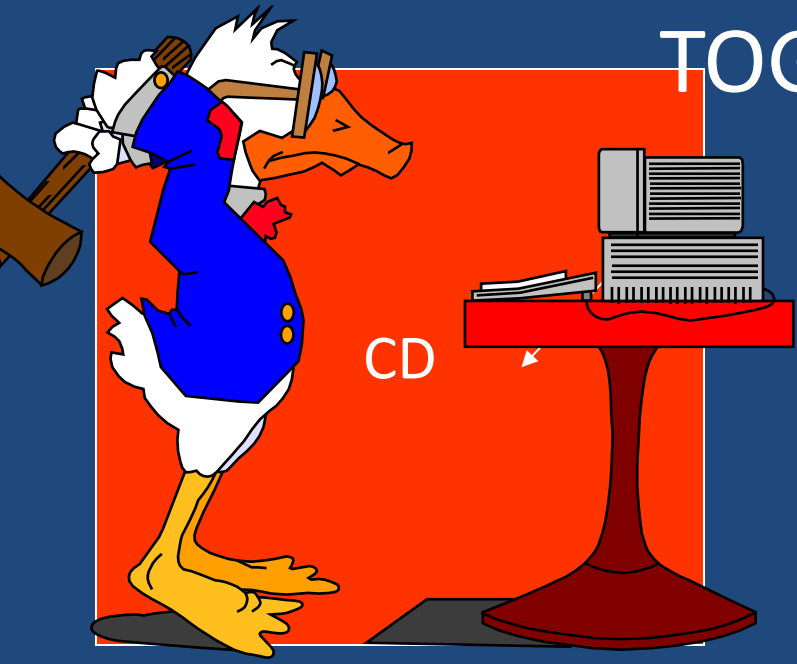
Mean heritability of ADHD = 0.75

Heritability

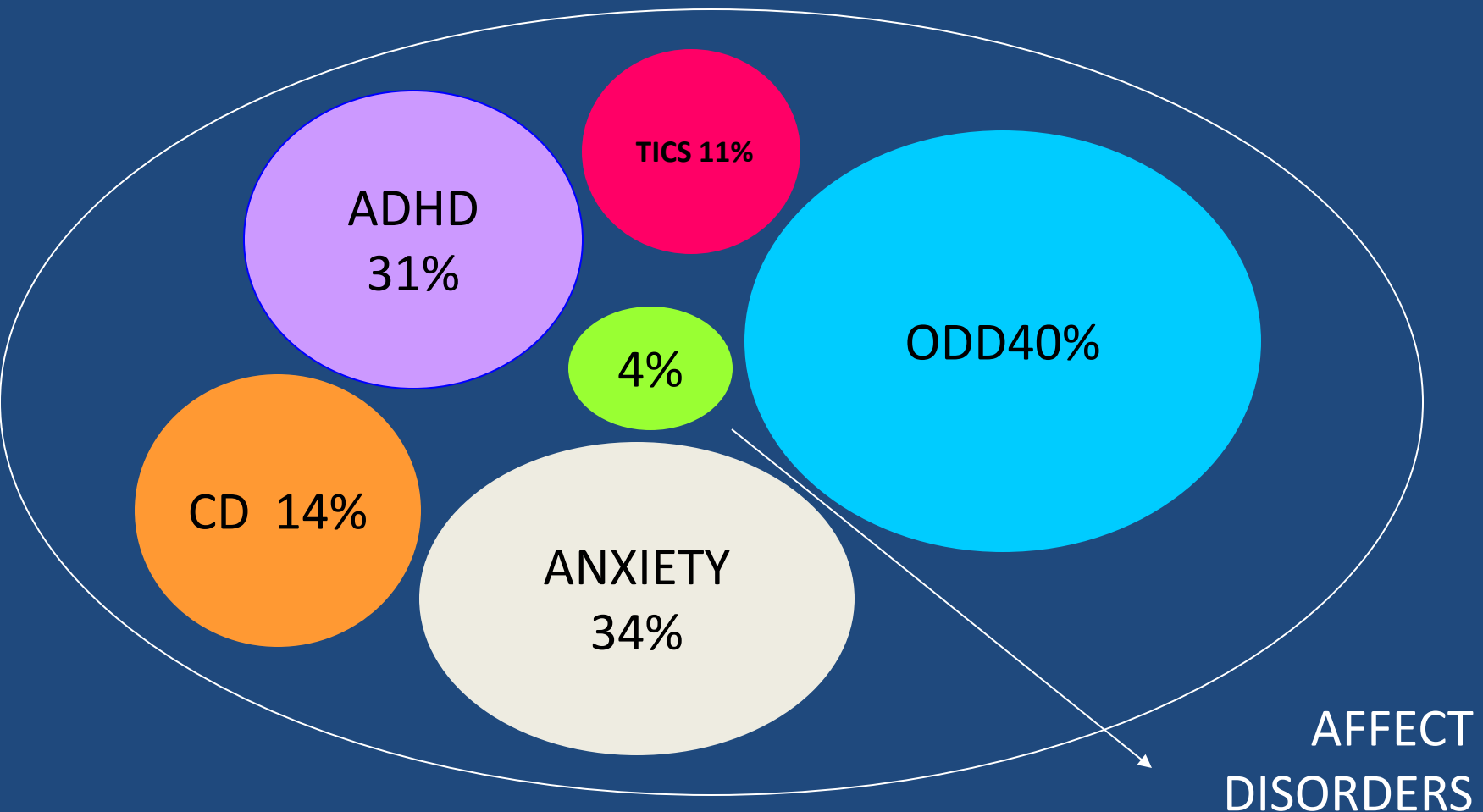
Faraone SV et al. *Biol Psychiatry*. 2005;57:1313-1323.



ALONE OR TOGETHER



Comorbidity in children



- **CO-MORBIDITIES (literature review)**

- ADHD frequently is comorbid with other psychiatric disorders (Pliszka et al., 1999). **54-84% of children and adolescents with ADHD** may meet criteria **for oppositional defiant disorder (ODD)**; a significant portion of these patients will develop conduct disorder (Barkley, 2005; Faraone et al., 2000).
- **25% to 35% of patients with ADHD will have a coexisting learning or language problem** (Pliszka et al., 1999), and anxiety disorders occur in up to one-third of patients with ADHD (Biederman et al., 1991; MTA Cooperative Group, 1999b; Pliszka et al., 1999; Tannock, 1998).

The prevalence of **mood disorder in patients with ADHD** is more controversial, with studies showing up to 33% of patients with ADHD meeting criteria for a depressive disorder (Pliszka et al., 1999). The prevalence of mania among patients with ADHD remains a contentious issue (Biederman, 1998; Klein et al., 1998).

- Biederman and colleagues (Biederman et al., 1992) found that 16% of a sample of ADHD patients met criteria for mania, although a chronic, irritable mania predominated.
- Comorbidity in adult ADHD patients is similar to that of children, except that antisocial personality replaces ODD or CD as the main behavioral psychopathology and mood disorders increase in prevalence (Biederman, 2004). **Clinicians should be prepared to encounter a wide range of psychiatric symptoms in the course of managing patients with ADHD.**

Diagnosis approach: Neurocognitive and behavioral disorder

- In order to assess :
- Executive and cognitive functions.
- To measure Inhibition, intelligence, memory
- Ej: CPT Continuous Performance Task/Test –Conners
- Test of Variables of Attention or **TOVA**

Intake-anamnesis

Clinical diagnosis

Questionnaires

Neuro-cognitive tests

CONNERS TEST

ADHD inattentive
hiperqactive - compulsive
combined

Hyperactivity/Impulsivity
Learning Problems

General Psychopathology
Inattention

Executive Functioning
Aggression

Peer Relations
Family Relations

Oppositional Defiant Disorder
Conduct Disorder

What are the potential consequences of ADHD?

ADHD

Adults with ADHD may be:

- 3x to be currently unemployed
- 2x to have problems keeping friends
- 47% more likely to have trouble paying bills
- 2x more likely to have been arrested
- 2x more likely to have been divorced
- 2x likely to rarely or never use birth
- 4x likely to have contracted a sexually transmitted disease
- 78% more likely to be addicted to tobacco
- 2x more likely to have been involved in 3 or more car crashes

Lifetime Course of ADHD Symptoms: Inattention Domain

Childhood

Difficulty sustaining attention
Doesn't listen
No follow-through
Can't organize
Loses important items

Adulthood

Difficulty sustaining attention (meetings, readings, paperwork)
Paralyzing procrastination
Slow, inefficient
Poor time management
Disorganized

Adler L, Cohen J. *Psychiatr Clin North Am.* 2004;27:187-201; American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, text revision. Washington, DC: American Psychiatric Association; 2000:85-93; Weiss MD, Weiss JR. *J Clin Psychiatry.* 2004;65:27-37.

Lifetime Course of ADHD Symptoms: Hyperactivity-Impulsivity Domain

Childhood

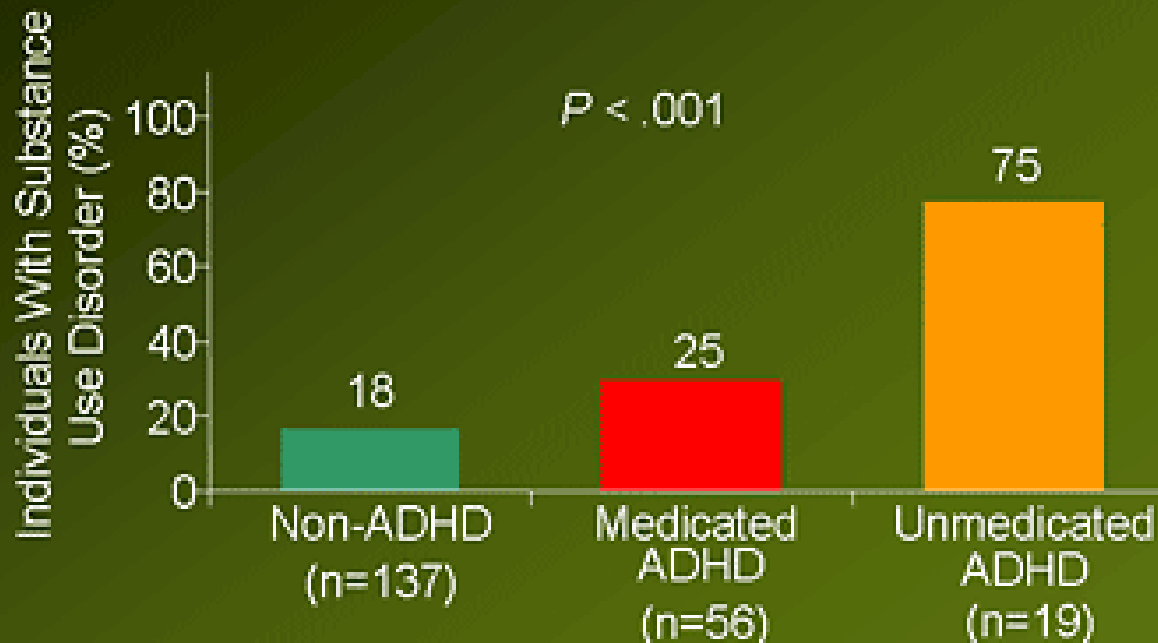
Squirming, fidgeting
Can't stay seated
Can't wait turn
Runs/climbs excessively
Can't play/work quietly
On the go/driven by motor
Talks excessively
Blurts out answers
Intrudes/interrupts others

Adulthood

Inefficiencies at work
Can't sit through meetings
Can't wait in line
Drives too fast
Self-selects very active job
Can't tolerate frustration
Talks excessively
Interrupts others
Makes inappropriate comments

Adler L, et al. *Psychiatr Clin N Am.* 2004;27:187-201; American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed, text revision. Washington, DC: American Psychiatric Association; 2000:65-83; Weiss MD, et al. *J Clin Psychiatry.* 2004;65:27-37.

Substance Use Disorders in ADHD Teens Growing Up: Overall Rate of Substance Use Disorder



Biederman J et al. *Pediatrics*. 1999;104:e20

SUMMARY FOR ADHD APPROACH

- ADHD IS NOT A SCHOOL PROBLEM... IS A LIFE PROBLEM

*.1 Evaluation of the preschooler, child, or adolescent for ADHD should consist of **clinical interviews** with the parent and patient, obtaining information about the patient's school or day-care functioning, evaluation for co-psychiatric disorders, and review of the patient's medical, social, and family history*

2. *If the patient's medical history is unremarkable, **laboratory or neurological test are not indicated***

- 3, *Psychological and neuropsychological **tests are not mandatory for the diagnosis** for ADHD, **but** should be performed if the patient's history suggests low general cognitive ability or low achievement in language or mathematics relative to the patient's intellectual ability*

.4 The clinician must evaluate the patient with ADHD for the presence of co-morbid psychiatric disorders .

- The clinician **must integrate the data obtained with regard to co-morbid symptoms** to determine :
 - a) whether the patient **meets criteria for a separate co-morbid** disorder in addition to ADHD ,
 - b) whether the **co-morbid disorder is the primary disorder** and the patient's inattention or hyperactivity/impulsivity is directly caused by it
 - c) whether the co-morbid symptoms do not meet criteria for a separate disorder but **represent secondary symptoms** stemming from the ADHD .

.5

A well thought-out and comprehensive treatment plan should be developed for the patient with ADHD

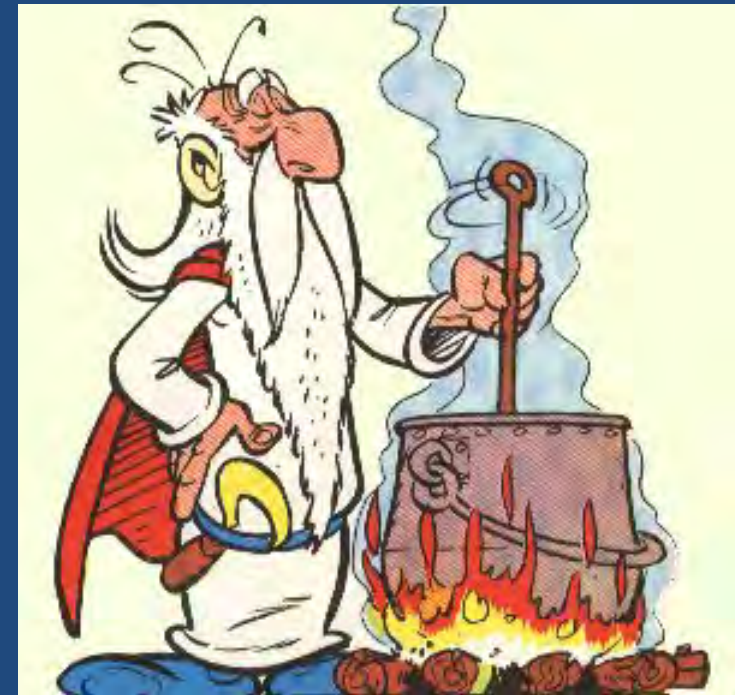
The patient's treatment plan should take account of **ADHD as a chronic disorder** and may consist of psychopharmacological and behavior therapy .

Should **include parental and child psycho-education about ADHD and its various treatment options** (medication and behavior therapy), linkage with community supports, and additional school resources as appropriate .

The treatment plan **should be reviewed regularly** and modified if the patient's symptoms do not respond .



Use , bad use and abuse of medications in ADHD



STIMULANT ACTIONS



Better capability to sustain attention

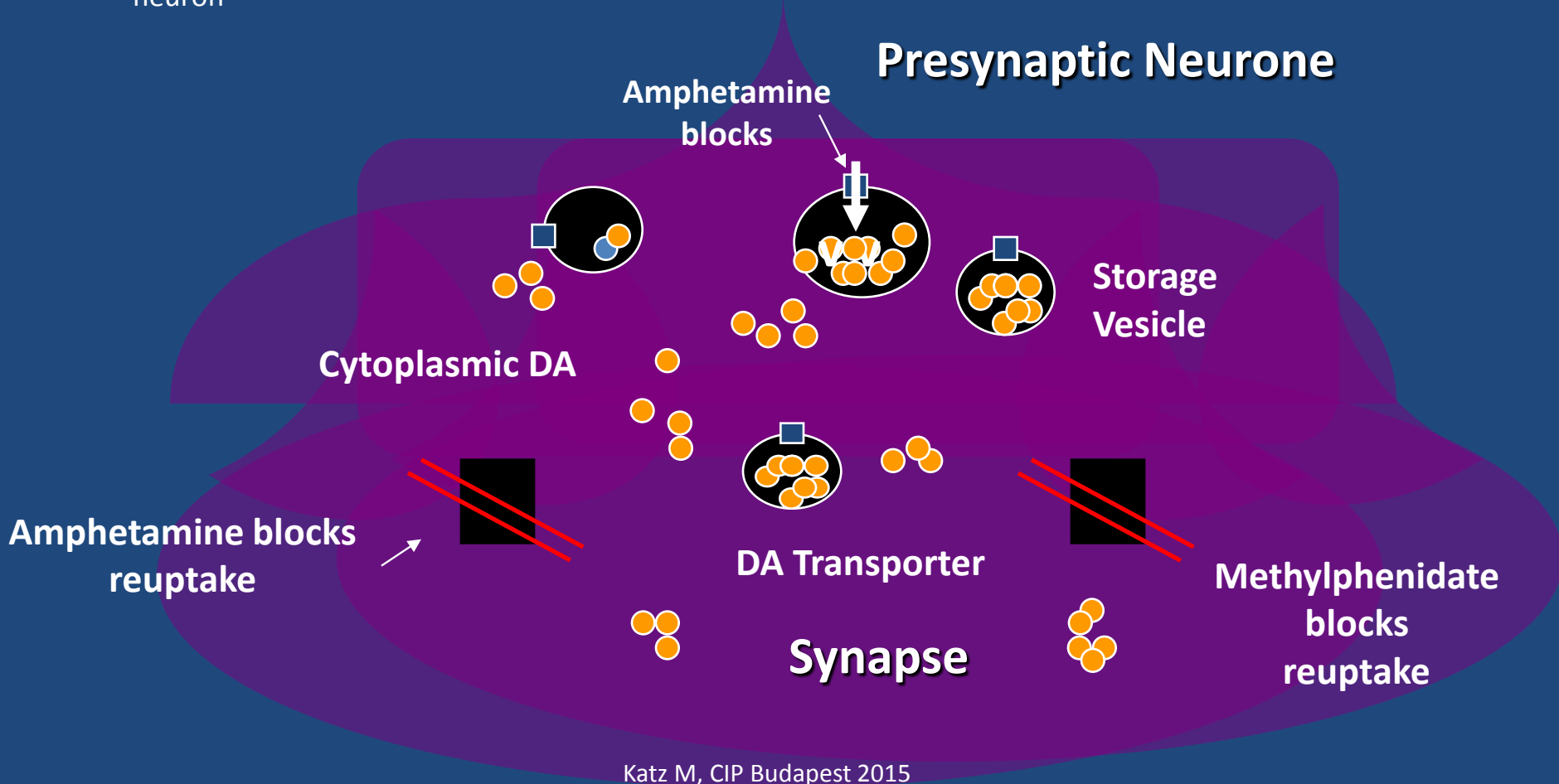
Improve Inhibition
and impulsiveness

Less aggressiveness
Better social interaction
Compliance

Social capabilities
Academic accuracy
Academic efficiency

DEXMETHYLPHENIDATE, RACEMIC- METYLPHENIDATE, AMPHETAMINE - BASED PRODUCTS

Well known inhibitors of catecholamine reuptake. Increases trans-synaptic concentrations of the neurotransmitters dopamine and noradrenaline by inhibiting the action of the respective neurotransmitter transporter proteins (DAT-NET) responsible for moving these transmitters back into the presynaptic neuron



ADHD: MTA Results

- All treatment arms found to be effective on an absolute basis

Medication management
alone

Medication management
plus behavioral treatment

*Nearly equally effective
and superior to both:*

- Behavioral treatment alone
- Community-based treatment

MTA, Multimodal Treatment Study of
Children With ADHD.

MTA Cooperative Group. *Arch Gen Psychiatry*. 1999;56:1073-1086.

- 6 *During a psychopharmacological intervention for ADHD, the patient should be **monitored for treatment-emergent side effects***

- 7 *If a patient with ADHD has a robust response to psychopharmacological treatment and subsequently shows **normative functioning** in academic, family, and social functioning, then psychopharmacological **treatment of the ADHD alone is satisfactory***

- 8 *If a patient with ADHD has a **less than optimal** response to medication, has a comorbid disorder, or experiences stressors in family life, then **psychosocial treatment in conjunction with medication treatment is often beneficial***

Patients *should be assessed periodically* to determine
9 if there is continued need for treatment or if
symptoms have remitted. Treatment of ADHD
should continue as long as symptoms remain
present and cause impairment

10 Patients treated with medication for ADHD should
have *their height and weight monitored*
throughout treatment.

ATOMOXETINE: FDA + for adult ADHD: affects the regulation of norepinephrine by acting as a potent inhibitor of the pre-synaptic norepinephrine transporter. Is not a controlled medication

Why Nonstimulant Treatments for ADHD?

Problems with the stimulants

- Schedule II drugs (abuse liability, diversion, medicolegal concerns)
- 30% do not adequately respond or cannot tolerate stimulant treatment
- Short duration of action (compliance, embarrassment)
- Side effect profile adversely impacting sleep, appetite, mood, and anxiety
- Concerns about cardiovascular effects, growth suppression, and tic development

Dulcan M et al, for the Work Group on Quality Issues of the American Academy of Child and Adolescent Psychiatry. *J Am Acad Child Adolesc Psychiatry.* 1997;36:95S-121S;
Greenhill LL et al, for the Work Group on Quality Issues of the American Academy of Child and Adolescent Psychiatry. *J Am Acad Child Adolesc Psychiatry.* 2002;41:26S-49S; Spencer T et al. *J Am Acad Child Adolesc Psychiatry.* 1996;35:409-432.

Manuel Katz MD, MPH
Katzmanuel@gmail.com



and... thank you for your **attention**