

ADHD Overview and Update

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Origin of ADHD

- Evolutionary/societal advantages?
 - Past – could risk-taking, reactivity, novelty seeking offer valuable survival advantages?
 - Present – are different thinking styles important in solving the large problems we face today?
 - Future – will this cognitive style be better suited to manage high stimulus environment?

Etiology of ADHD

- Abnormality in the dopamine and noradrenaline systems
- Affects motor and processing parts of the brains (frontal lobe, basal ganglia, anterior cingulate gyrus, prefrontal cortex, parietal cortex and cerebellum)
- Genetic/heritable contribution
- Causal relationship with low birth weight - even in full term infants
- Substance exposure in utero
- Brain injury (any cause)
- Early deprivation
- Preterm birth
- Environmental exposures (Organophosphate pesticides, technology?)

Prevalence

- Increasing rates in US
- Twice as common in boys
- Prevalence somewhere between 6-9%
- Within US, huge differences by state and even county
- Why is it more common?
 - actual increase
 - effects of technology
 - increased awareness
 - decreased support at school
 - “medical-industrial complex”
 - pressure to perform

Impact in Childhood

- Social challenges/interpersonal difficulties – *peer rejection*
- Academic problems – lower achievement, lower graduation rates
- Strained parent-child relationships
- Behavioral problems - aggression
- Emotional problems – low self-esteem, anxiety, depression,
- Accidents
- Substance use

Impact in Adulthood

- higher rates of traffic and other accidents
- more marital difficulties and divorce
- higher rates of unemployment/job instability
- antisocial and criminal behavior
- obesity
- attempted and completed suicide
- lower educational attainment
- lower household income attained

Executive Functioning

- Neurologically-based skills involving mental control and self-regulation
- Necessary for control of behavior and the attainment of chosen goals. (Stanford marshmallow experiment)
- Includes attentional control, inhibitory control, working memory, reasoning, problem solving, and planning
- Gradually develops across the lifespan of an individual
- Can be learned
- ADHD is just one medical issue that causes a deficit in executive functioning
 - Can you name others?

The other “A”SD – ADHD Spectrum Disorder

- Executive functions include a number of skills
- There is a range of normal within each skill
- Perceived cut-offs are subjective
- Imperfect wording of diagnostic criteria
- Process of diagnosis dichotomizes a continuous variable – the risk is this leaves some out of treatment.



Diagnosis

- Onset of symptoms before 12 years
- 6 months duration
- 2 or more settings
- **Clinically significant impairment**
- Not explained by other disorder
- 6 symptoms of inattention or hyperactivity or a combination

DSM-5 Changes

- Adolescents >17 and adults need minimum of 5 symptoms (not six)
- Age of onset of symptoms increased to 12 years (previously 7 years)
- Need for symptoms across settings is emphasized (but also provides more examples of symptoms across life span)
- No more subtypes - replaced with specifiers
- Autism is no longer exclusion criteria
- Categorized as a neurodevelopmental disorder

How is the diagnosis made?

- ADHD is a *clinical* diagnosis
- Does an MRI or CT scan help with diagnosis?
 - No. Imaging does not help.
- Are there other medical tests that help make the diagnosis?
 - No. In some cases, iron, magnesium, lead and thyroid hormone levels may be checked.
- Do rating scales can “make” the diagnosis?
 - No. They help elicit symptoms and compare different settings.
- If symptoms improve with stimulants does this *make* the diagnosis?
 - No.
- Does the diagnosis require psychological testing?
 - No but can be helpful if low cognitive ability or learning disorder.

Symptom Overlap

Differential Diagnosis

- Other disruptive behavior disorders (CD, ODD)
- Anxiety disorders
- Mood disorders
- Developmental speech and language disorders
- Reactive attachment disorder
- Substance abuse
- Trauma
- Sleep problems
- Medications (bronchodilators, anti-histamines, corticosteroids)

Common comorbidities

- Language or Learning problem (25-35%)
- ODD (55-85%)
- Substance abuse (20-40%)
- Conduct (10-20%)
- Anxiety (33%)
- Tic disorder (50%)
- Mood disorders
- Sleep problems

Multimodal Treatment of Attention-Deficit/Hyperactivity Disorder Study (MTA)

- 600 children, 7-9 y/o
- Four treatment groups
 1. Intensive medication management (stimulants and other medications as needed; algorithmic adjustments; general advice and readings);
 2. Intensive behavioral treatment alone (parent training; structured teacher consultation; full time summer treatment program; half time classroom behavioral specialist)
 3. Combined treatment
 4. Routine community care (the control group).

The MTA Cooperative Group. A 14-month Randomized Clinical Trial of Treatment Strategies for Attention-Deficit/Hyperactivity Disorder. Arch Gen Psychiatry 1999; 56: 1073-1086.

MTA results at 14 months

- Combination treatment and medication management are superior to behavior management and community care. (Arch Gen Psychiatry. 1999)
- Combination treatment is better for certain areas of functioning: (Arch Gen Psychiatry. 1999)
 - oppositional/aggressive symptoms, anxiety symptoms, reading achievement, parent-child relations, and social skills.
- Combination treatment allowed lower doses of medication than medication treatment alone group (Greenhill *et al.* JAACAP. 2001)

MTA at 8 years

- No outcome differences between original treatment groups
- MTA group as a whole was functioning significantly less well than the non-ADHD classmate sample.
- Sustained improvement is achievable, but not normalization.
- Behavioral, socio-economic, or intellectual advantage or best response to treatment have the best prognosis.

Molina et al. The MTA at 8 Years. J. Am. Acad. Child Adolesc. Psychiatry 2009; 48(5): 484-500.

Preschool ADHD Treatment Study (PATs)

- NIMH funded multi-center randomized efficacy trial
- 3-5.5 yo with severe ADHD unresponsive to 10 week psychosocial intervention
- 37/279 patient parents said behavioral treatment resulted in satisfactory improvement.

Greenhill et al. Efficacy and Safety of Immediate Release Methylphenidate Treatment for Preschoolers with ADHD. J. Am. Acad. Child Adolesc. Psychiatry 2006; 45(11): 1284-1293.

PATS – What was learned about Medications in preschoolers?

- Stimulants are generally effective
- Lower doses provided better balance of benefits and side effects
- Lower response rates compared to older children
- Higher rates of side effects

Greenhill et al. Efficacy and Safety of Immediate Release Methylphenidate Treatment for Preschoolers with ADHD. *J. Am. Acad. Child Adolesc. Psychiatry* 2006; 45(11): 1284-1293.
Riddle et al.

PATS at 6 yrs

- ADHD diagnosis is stable over time - 89.9% still meeting diagnostic criteria
- Patients with comorbid ODD or conduct disorder had higher rates of ADHD.
- Girls experienced a steeper symptom decline (but girls' baseline symptoms more severe).
- Some indication of long-term benefit based on parent ratings

Preschool ADHD (PATS) 6-Year Follow-up. J. Am. Acad. Child Adolesc. Psychiatry 2013; 52(3): 263-278.

Psychosocial and Complementary Treatments



ADHD Treatment

Psychosocial and CAMs



Psychoeducation

- Information about the illness, symptoms and treatments
- Tailored for kids or caregivers
- Understand how symptoms may affect everyone
- Opportunity to let them know they are not alone but also think about who they want to share what information with
- Provide hope that and reassurance that there are treatments that work
- Start conversation what treatment might look like – duration, time commitment, etc.
- Identify who will be involved and their roles

Behavioral Therapies

- Behavior Management Training (Incredible Years, “Triple P” aka Positive Parenting Program)
- Formerly “Parent Management Training”
- Good evidence base for ADHD and disruptive behaviors
- Common elements:
 - Praise – off-sets negative interactions, improves behavior, builds self-esteem
 - Positive reinforcement – promotes desired behavior with tangible rewards
 - Stimulus management/environmental strategies – identify triggers and stressful circumstances; reduce distractions; visual aides and organizational tools
 - Problem solving – helps with critical thinking, consider outcomes of different choices, develops perspective taking, self-efficacy
 - Time out – goal is self-directed use
 - Calm discipline and consistent consequences

CBT for ADHD

- Growing evidence base
- Improvement in both functional domains and symptom management
- Improves knowledge of ADHD and acceptance of treatment, social behavior, self-esteem and core symptoms (Mongia et al. Current Psychiatry. 2012)
- Worse outcomes if co-morbid ODD/CD
- Better outcomes if co-morbid depression/anxiety
- Modules:
 - Information – Psychoeducation: information about symptoms and treatments
 - Self-assessment - Coping with distractibility : honest appraisal of challenges and identification of coping strategies
 - Cognitive restructuring - Adaptive thinking : evaluates perceived impairments and corrects maladaptive automatic thoughts
- Availability/access is a problem

School and Academic Interventions

- Discuss with child and parents what is to be shared with school
- Accommodations can be formalized with 504/IEP
- Stimulus management
- Test taking accommodations
- Study Skills – Organizational aides, assistance planning assignments
- Frequent breaks
- Physical activity
- Consider psycho-educational testing if cognitive challenges or possible learning disorder

Social Deficits in ADHD

- Most children with ADHD struggle socially (50-70%)
- Problems start early, usually by age 7
- Children with ADHD have higher rates of stigmatization, rejection and victimization
- Fewer friends, lower quality friendships (F > M)
- Define “friendship” differently – “fun” and “entertaining” versus emotional support and security
- More likely to engage in impulsive and inappropriate behaviors
- More likely to be bullied and engage in bullying
- Higher rates of substance abuse, academic problems (lower achievement, school refusal) and emotional problems (aggression, anxiety) are associated with poor *peer* functioning
- To improve peer-peer functioning, programs needs to be longer-term (12-14 weeks), include homework and involve parents

How ADHD affects socializing

- Trouble making friends
ADHD link: doesn't get social cues, don't realize their behavior affects others, interrupts others, trouble filtering
What you can do: role play; you be child and demonstrate some of behaviors; talk about other ways to handle situations
- Loses friends quickly
ADHD link: can be very demanding, intense and therefore, tiresome to other kids, difficult taking turns and waiting
What you can do: group activities (normative or therapeutic) where he/she can "practice" being with others, waiting, taking turns, etc.
- Struggles in conversations
ADHD link: lose track of topic, get distracted, misinterpret things, interject random thoughts
What you can do: record conversations and then play back and discuss what could be done differently
- Overreacts to situations
ADHD link: low frustration tolerance, lashes out at others, poor emotional control leading to age-inappropriate tantrums and melt-downs
What you can do: identify triggers and signs of frustration; teach skills to manage emotions and increase awareness through emotional coaching
- Isn't reliable
ADHD link: trouble with planning and follow-through; unreliable in managing home/school responsibilities or in tasks where others are counting on them (e.g. group projects)
What you can do: help him/her take initiative in dividing work up; teach study skills and find effective tools for helping them keep track of things and monitor progress along the way

Omega 3 fatty acids

- Essential poly-unsaturated fatty acids (PUFAs)
- Lower blood levels in patients with ADHD compared with age-matched controls
- Most research on ω -3 but may be ω -3/ ω -6 ratio
- Important for brain function and development
- 25 studies included in most recent meta-analysis (Konigs et al. 2016)
- Results are mixed, but encouraging
- Can be used in addition to prescribed medications and may allow for lower dose of stimulant
- Most effective for mild ADHD
- Well tolerated
- Reasonable alternative to (prescribed) psychotropic medications

Dietary (elimination) strategies

- For some, may be mild benefit from elimination of food color from diet.
- Sugar ?
- Can't hurt
- Studies inconclusive

Sonuga-Barke et al. Nonpharmacological Interventions for ADHD: Systematic Review and Meta-Analyses of Randomized Controlled Trials of Dietary and Psychological Treatments. *Am J Psychiatry* 2013;170(3): 275-289.

Physical Exercise (Rommel et al. JAACAP 2013)

- May improve executive functioning
- Improves behavioral symptoms associated with ADHD.
- Can't hurt
- Enough evidence to consider addressing in school accommodations and class schedule
- Mechanism unclear but may stimulate neurogenesis and alter gene expression.

Computer training

- Small studies thus far
- Some indication of improvement, often targeting existing specific neuropsychological deficits (working memory)
- Improvement on student self-rating, parent and teacher ratings not consistent
- School-based interventions promising concept
- Need additional larger studies

Amonn, et al. Evaluation of computer-based neuropsychological training in children with ADHD. *NeuroRehabilitation* 2013:32(3).
Klingberg T, et al. Computer training of working memory in children with ADHD—a randomized controlled trial 2005:44(2).
Steiner N, et al. Computer-based attention training in the schools for children with ADHD: a preliminary trial. *Clinical Pediatrics* 2011:50(7).
Rabiner DL, et al. A randomized trial of two promising computer-based interventions for students with attention difficulties. *J Abnorm Child Psychol* 2010: 38(1).

ADHD Treatment

Psychotropic Medications



Stimulants

- Act on dopamine and noradrenaline pathways.
- Most effective medication choice
- Can start with either a methylphenidate or an amphetamine product
- Amphetamines FDA approved $>$ or $=$ 3 yo
- Methylphenidates FDA approved $>$ or $=$ 6 yo
- Similar efficacy
- Side effects may be more pronounced with amphetamine products. (Efron et al. Peds 1997)
- May have protective effect on comorbid disorders (depression, anxiety) and functional outcomes (family functioning, repeating a grade) (Biederman et al. Peds 2009; Pliszka S. JAACAP 2007)

Immediate Release Stimulants

Name	Duration of Action
Methylphenidate (Ritalin, Methylin)	4-6 h
D-methylphenidate (Focalin) *2x potency of methylphenidate	4-6 h
Mixed amphetamine salts (Adderall)	4-6 h
D-amphetamine (Zenzedi, ProCentra)	4-6 h

Micromedex, accessed 5/4/12.

Long Acting Stimulants

Name	Mode of Delivery	Duration of Action
Ritalin SR, Metadate ER, Methylin ER	Gradual release	4-8 h
Metadate CD	30% IR, 70% 3 h later	7-9 h
Ritalin LA	50% IR, 50% 4 h later	7-9 h
Quillivant XR	20% IR, 80% gradual release	8-10h
Focalin XR	50% IR, 50% 4 h later	Up to 12 h
Concerta	22% IR, pump	Up to 12 h
Daytrana patch	Gradual release	3-5 h after removal
Adderall XR	50% IR, 50% 4 h later	8-12 h
Dexedrine spansule	50% IR, 50% gradual	10 h
Vyvanse	Activated in GI tract	10 h

Micromedex, accessed 5/4/12.

Stimulant Side Effects – Common

- Decreased appetite
- Insomnia
- Headaches and stomachaches
- Emotional lability/aggression
- Slowing in growth velocity - weight and height
- Increased heart rate (5 bpm) and blood pressure

Screening and Monitoring of Cardiac Issues

- Physical exam is recommended before initiating stimulant treatment
- Prescribing doctor should ask about history of palpitations, syncope, chest pain, exercise intolerance, family history of sudden death under age 35
- Patients with known cardiac issues should be referred to cardiology before a stimulant trial.
- During treatment, blood pressure and heart rate are monitored at each appointment.

Perrin et al. Cardiovascular Monitoring and Stimulant Drugs for Attention-Deficit/Hyperactivity Disorder. Pediatrics 2008; 122(2): 451-453.

Stimulants and Substance Abuse

1. Does ADHD increase the risk of substance use disorders?

Yes - ADHD diagnosis increases the risk of substance use and nicotine dependence. (Charach *et al.* JAACAP. 2011)

2. Does stimulant treatment increase the risk of stimulant abuse later in life?

No - Treatment with stimulants does NOT increase risk of stimulant use or abuse later in life (Wilens *et al.* JAACAP. 2008)

3. Does stimulant treatment for ADHD delay or prevent substance abuse?

We don't know.

ADHD treatment and Risk of Substance Use Disorders

- Early stimulant treatment *may* reduce or delay the onset of substance use disorder. (Wilens *et al.* APAM. 2008)
- Early stimulant treatment may NOT matter - recent follow up data from the MTA revealed no harm or benefit from medication treatment in regard to rates of adolescent substance abuse. (Molina *et al.* JAACAP. 2013)

Abuse and Diversion of Stimulants

- Stimulant misuse rates of 5-9% through 12th grade and 5-35% in college-age individuals
- If suspicions, consider lisdexamfetamine (Vyvanse) or atomoxetine (Strattera)
- ADHD medications used for adolescents with active substance abuse are not as effective.

Wilens TE, Adler LA, Adamson J, et al.
Misuse and diversion of stimulants
prescribed for ADHD: a systematic review
of the literature. *J Am Acad Child Adolesc
Psychiatry* 2008; 47:21–31.

Stimulants, Tics and ADHD (Cochrane Review. 2011)

- 60% of patients with tics have ADHD
- stimulants do not worsen tics in most people with tic disorders
- Stimulant may exacerbate tics
- If a tic disorder is present or if tics get worse with stimulant, consider alternative medications or focus on non-medication strategies

Atomoxetine (Strattera)

- Noradrenergic reuptake inhibitor
- Taken once or twice a day
- Increased to maximum dose in 2-3 steps, depending on response and side effects.
- Can take up to 6 weeks for full effects to be seen
- FDA approved for children ≥ 6 years old
- Can be helpful for anxiety in some cases
- In terms of response, side effects and missed doses, can feel like a stimulant in some

Atomoxetine Response

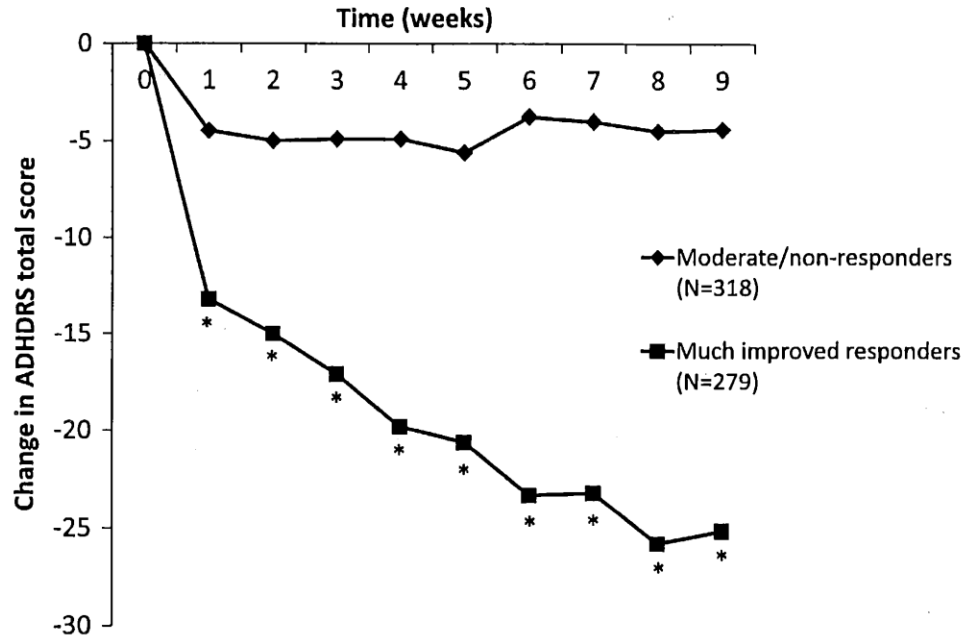


Fig. 1 Temporal course of changes in the Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator Administered and Scored (ADHD-RS total score). Unlike moderate/nonresponders (filled diamonds), much improved responders (filled squares) experienced sharp decreases (i.e., improvements) in the ADHD-RS total score within the first 1 to 4 weeks, with continued divergence at later time points. * $p < .001$ at each time point across response groups by week.

Newcorn et al. Clinical Responses to Atomoxetine in Attention-Deficit/Hyperactivity Disorder. *J. Am. Acad. Child Adolesc. Psychiatry* 2009; 48 (5): 511-518.

Atomoxetine side effects

- Stomach aches, cramps, diarrhea
- Sedation or insomnia
- Slowed growth (height and weight)
- Not recommended if structural cardiac abnormalities, cardiomyopathy, or rhythm abnormalities
- Rare liver toxicity
- FDA “Black Box” warning for suicidal thinking (risk of 4/1000 in a large controlled study); no completed suicides

Alpha agonists (guanfacine, clonidine)

- Better for hyperactivity than inattention
- Most common side effect is sedation (clonidine > guanfacine)
- Affects blood pressure (↓) and heart rate (↓ or ↑)
- Can take a while to work (4-6 weeks)
- Risk of serious side effects if cardiac problems, given with stimulants or over dosed
- Narrow dose range, potent medicines (“small” doses) and doesn’t take much to “overdose”

Guanfacine

	Starting dose	Maximum dose	Half life	FDA
Guanfacine	<45kg, 0.5 mg qhs; >45 kg, 1 mg qhs	2 mg (27-40 kg); 3 mg (40-45 kg); 4 mg (>45 kg)	14 h	Not approved
Guanfacine extended release (Intuniv)	1 mg daily	4 mg	16 h	Approved 6-17yo

Pliszka S. AACAP Work Group on Quality Issues. Practice Parameter. J. Am. Acad. Child Adolesc. Psychiatry 2007; 46(7):894-921.

Clonidine



	Starting dose	Maximum dose	Half life	FDA
Clonidine	<45kg, 0.05 mg qhs >45 kg, 0.1 mg qhs	0.2 mg (27-40 kg); 0.3 mg (40-45 kg); 0.4 mg (>45 kg).	12 h	Not approved
Clonidine extended release (Kapvay)	0.1 mg qhs; doses greater than 0.1 mg should be bid	0.4 mg	12-16 h	Approved 6-17yo

Pliszka S. AACAP Work Group on Quality Issues. Practice Parameter. J. Am. Acad. Child Adolesc. Psychiatry 2007; 46(7):894-921.

Bupropion

- Brand name: Wellbutrin
- **Not FDA approved for pediatric use**
- Combined dopaminergic/noradrenergic mechanism of action
- Consider when primary treatments have failed or in patients with co-occurring mood disorders, substance abuse, or smoking.

Micromedex, accessed 5/4/12.

Bupropion

- Common side effects include insomnia, appetite decrease, tics increase (less common than stimulants)
- Risk of seizures increases with doses > 450 mg/day
- Narrow dose range (300-450 mg/day; 3-6 mg/kg/day)
- Maximum of 150 mg per dose.

Kratochvil CJ, Daughton JM. Review of ADHD Pharmacotherapies: Advantages, Disadvantages, and Clinical Pearls. *J. Am. Acad. Child Adolesc. Psychiatry* 2009; 48: 240-248.



Case 1



- 8 year old boy
- mom is requesting he see the psychiatrist to be evaluated for ADHD
- behavioral problems starting in preschool. Teachers told mom he was hyperactive, aggressive, and did not listen.
- Currently, he is still restless, “on the go”, “gets into everything”, bothers the family dog, needs frequent redirection, messy, forgetful, and irritable.
- Socially he is falling behind

Case 1



- Normal pregnancy and infancy.
- Family history of ADHD in an older sister and an aunt with bipolar.
- Family recently moved from out of state because the parents are divorcing.
- A trial of MPH 10 mg daily ineffective just before moving out of previous state.
- Not on any medications right now.

Case 1



- Vanderbilt supports ADHD at school and home.
- Teachers note he is a happy and well-adjusted kid despite ADHD symptoms.
- Further screening for depression negative (SMFQ)

Case 2

- 3 year old girl
- Daycare is reporting behavioral problems, including hitting and biting. Patient has been asked not to return to daycare.
- Aggression often happens when she wants something or is frustrated.
- You notice it's difficult to understand her speech, but parents understand everything.

Case 2

- She is very active and difficult to contain.
- There is an older brother diagnosis with ADHD who has improved with methylphenidate.
- Father lost his job 5 months ago
- Parents have a history of conflict with each other.

Case 3

- 9 year old boy
- Mom and step-dad report he is defiant, refuses requests, does not respect family rules (stays out playing with neighborhood friends longer than allowed)
- Frequently fights with sister but not peers or teachers
- He is very bright, but grades are variable.
- Parents feel he mentally checks out.

Case 3

- Patient says parents favor his sister and the rules at home are unfair. He sees no problems with himself at all.
- You feel he is likeable, well-spoken, engages appropriately.
- Parents are angry. They want a medication to fix this. Mom shares that bio father was manipulative and verbally abusive with a history of legal difficulties for drugs and violent behavior.

Case 3

- Referred for counseling and behavior management training. Therapist reports Mom viewed patient as turning into bio Dad.
- Therapist coached a different view of patient, encouraged positive time, and consistent limits (they had been favoring other sib).
- Defiance improved.