ADHD and Stimulant Prescribing:

Best Practices to Keep Your Patients and Your License Safe

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Slides available at

DrJonathanTerry.com/KCOMADHD

What is your differential diagnosis?

A 33-year-old male with no past medical history presents to clinic with a chief complaint of difficulty concentrating.

Write down 10 items in your differential diagnosis

Question 1

- Which of the following adverse events have been reported with atomoxetine in adults?
  - A-Sexual side effects
  - B-Stevens-Johnson syndrome
  - C-Bradycardia
  - D-Hypotension
  - E-None of the above

Question 2

- A diagnosis of ADHD in adults must include?
  - A-Retrospective history of ADHD symptoms before the age of 12 years
  - B- History of school failure
  - C- History of motor vehicle accidents
  - D- History of failed multiple marriages
  - E- History of substance abuse

Question 3

- Which of the following statements about bupropion is true?
  - A-It should not be used in youth with a history of seizure disorder
  - B-It should not be used in youth with a history of eating disorder
  - C-It can be associated with serum sickness
  - D-it has off-label use for ADHD
  - E-All of the above

Question 4

- Which 2 of the following instruments are useful in diagnosing adult ADHD?
  - A-CAARS
  - B-CARS
  - C-BAARS
  - D-WRAADS
  - E-CARBS

Question 5

- Which of the listed disorders is the most common co-morbidity with ADHD in children?
  - A-Learning disorders in Math
  - B-Learning disorders in expressive language
  - C-Oppositional defiant disorder
  - D-Separation anxiety disorder
  - E-Gender Identity Disorder of Childhood

Teaching Points

ADHD is a *clinical* diagnosis in both youth and adults

There are several subtypes that have different presentations

The drugs of choice are psychostimulants and atomoxetine, but there are several other medications that can be effective

Clinical Characteristics

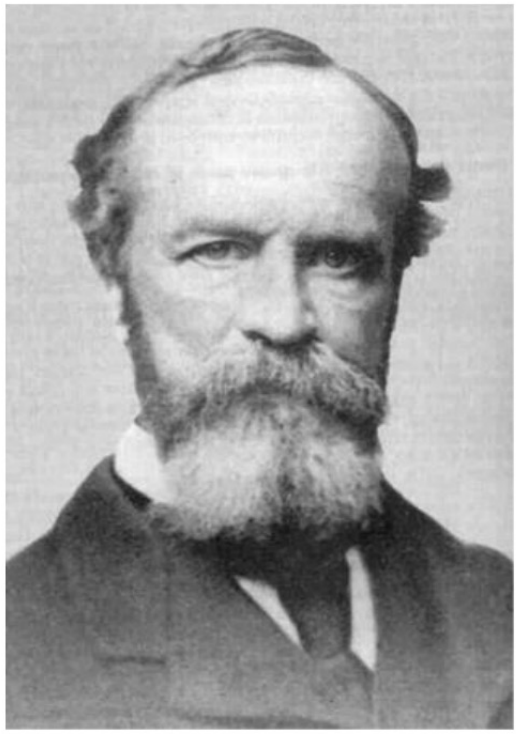
some combination of severe inattention, hyperactivity, and impulsivity that begins in childhood, and often persists into adult yrs.

Must cause functional impairment across settings, and must be developmentally relevant

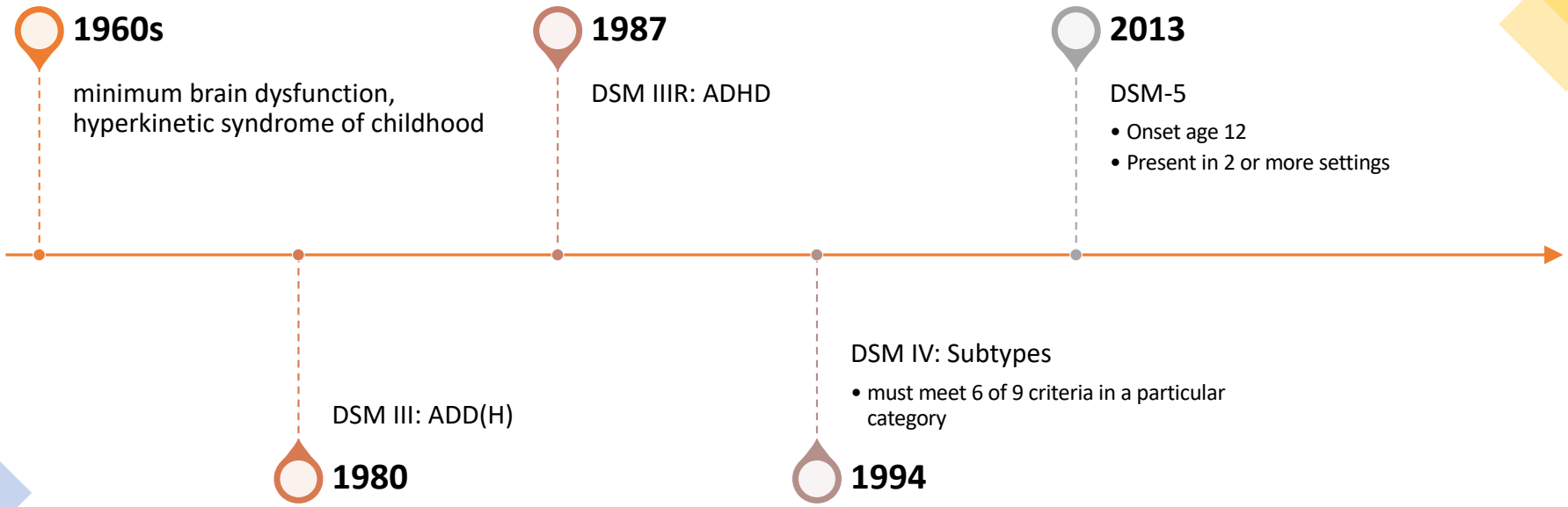
some symptoms should be present before age 7-12

History of ADHD

- William James (1890)
"There is a normal type of character, for example, in which impulses seem to discharge so promptly into movements that inhibitions get no time to arise. These are the 'dare devil' and mercurial temperaments overflowing with animation and fizzling with talk."



History


1960s
minimum brain dysfunction, hyperkinetic syndrome of childhood
1980
DSM III: ADD(H)
1987
DSM IIIR: ADHD
1994
DSM IV: Subtypes
• must meet 6 of 9 criteria in a particular category
2013
DSM-5
• Onset age 12
• Present in 2 or more settings

Epidemiology

3-7% of school-age children

boys 4-9x > girls

The Cognitive Process of Attention

- ADHD is a genetic, neurobiological disorder that affects one's ability to regulate impulse control, motor activity, and attentiveness.

Cognitive Process of Attention:

- Detecting a stimulus (focusing).
- Processing the detecting information.
- Sustaining attention to the relevant stimulus.
- Inhibiting involuntary shifting (distractibility).
- Organizing a response to the stimulus.

It’s About Executive Function

Executive function can be divided into the following tasks:

- Working memory - where we select bx responses from past successes
- Motor control - planning movements and inhibiting non-planned ones
- Regulating emotions - such as frustration tolerance and reactivity
- Motivation - controls starting tasks and persisting until completion
- Planning - ability to organize, develop and implement a plan of action

Executive functions are controlled in three areas of the brain:

- Frontal lobe - pre-frontal cortex and pre-motor cortex in particular
- Basal ganglia - control gaiting and initiating/inhibiting all events
- Cerebellum - controls coordinating brain activity/events

The core problem in ADHD seems to be with response inhibition

ADHD Through Development

- **Infants**
  - more active in utero
  - more sleeping and feeding difficulties
  - increased colic and crying
  - more difficult temperaments
  - associated with maternal cigarette and etoh use, low birth weight and brain injuries in utero

- **Preschool**
  - mean age of onset for H type is 4.21 years
  - mean age of onset for C type is 4.88 years
  - difficulty sitting still and being read to, noncompliance, temper tantrums
  - parents state they need to child-proof the home, must provide more supervision, have difficulties with babysitters and day care settings

ADHD Through Development

School Age

- school accentuates problems: high rates of off-task behaviors, noncompliance, temper tantrums
- at risk for learning/academic problems: 3x more likely to be retained, often children retained as “immature”
- poor social skills; at risk for social rejection
- hyperactive types (98%) and combined types (82%) usually meet criteria and are impaired by age 7yo
- By late childhood, 30-50% develop sx of conduct disorder such as fighting, stealing, truancy

Adolescence

•50-70% continue to have poor attention, impulse control, although hyperactivity diminishes

•many inattentive types (?20-30%?) may not become impaired and met criteria until middle school

•30% drop out of high school compared to 10% for normal controls; 5% of ADHD students go to college vs 41% of normal controls

•increased risk for car accidents, substance abuse, juvenile delinquency

•25-35% of ADHD children will be referred to juvenile court at least one time

Adulthood

- difficulties with attention, impulsivity, organization, but not hyperactivity (may be subjectively restless)
- more likely to quit jobs, to be seen by employers as less capable
- lower SES than unaffected siblings
- low self-esteem, increased divorce rates
- increased risk for adult psychopathology including depression, suicide
- 40% of ADHD children have inadequate social adjustment in adulthood

Heterogenous condition, many causes

- **Final common pathway: prefrontal / frontal dysregulation**
  - factors include:
    - brain structure / functional abnormalities
    - family / genetic factors
    - prenatal / perinatal factors
      - Maternal smoking and alcohol use
    - neurotoxins
    - psychosocial stressors and combined factors

Genetics

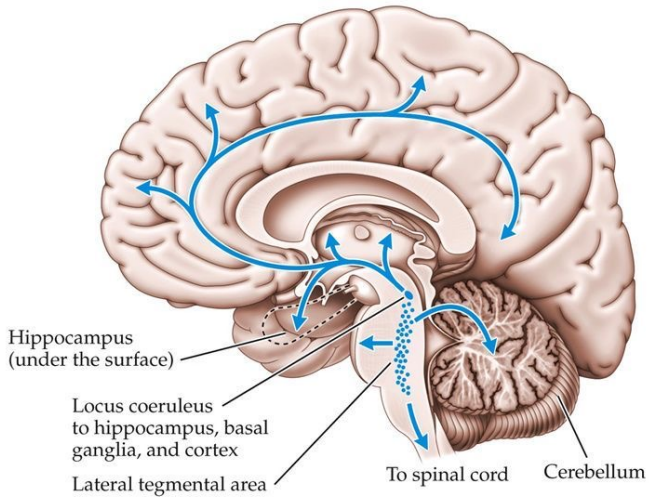
- 81% of identical twins vs 29% of fraternal twins (Levy)
- Biederman has conducted several showing genetic links
  - 20 - 30% of parents of a child with ADHD have ADHD themselves
  - 57% of children with one parent with ADHD have ADHD
  - 32% of siblings of a child with ADHD have ADHD
  - ADHD is 5x more likely if you have a close relative with ADHD
- Hyperactive/impulsive, adopted children resemble biological parents much more strongly than adoptive parents (Cantwell)
- Recent studies have shown a link with the D4 receptor gene with 7-repeat allel (Faraone) as well as D2 receptor (Comings) and the DAT1 (pre-synaptic dopamine transporter) gene

Genetics, cont.

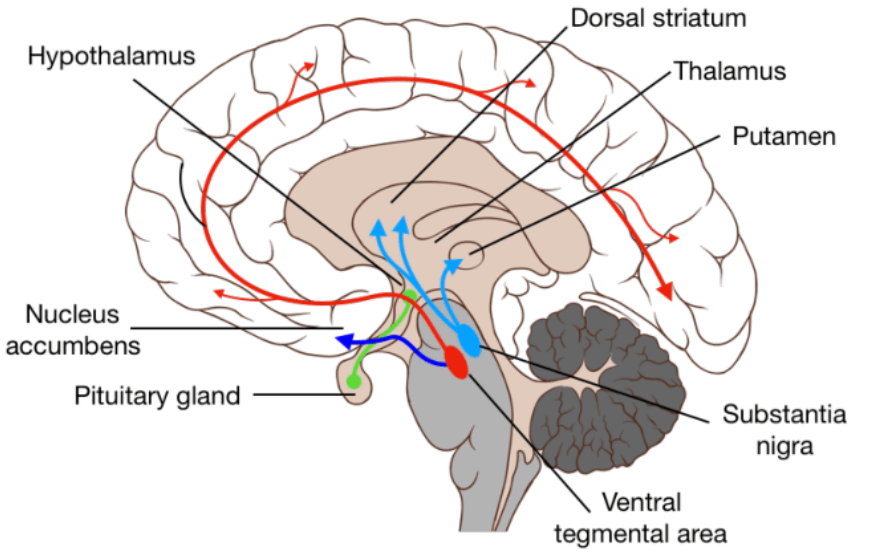
- DA2 dopamine gene (Blum et al., 1996; Comings et al., 1991)
- DAT1 dopamine transporter gene (Cook et al, 1995; Cook, Stein and Leventhal, 1997; Gill et al., 1997)
- - 70% higher in ADHD adults (Dougherty et al., 1999; Krause et al., 2000)
- DRD4-7 (dopamine receptor gene 4 - 7 repeat allele) over-represented in ADHD patients (Lahoste et al., 1996)
  - D4 located in dorsolateral prefrontal cortex
  - affects post-synaptic sensitivity, primarily in frontal and prefrontal regions that are associated with attention and executive fx. (Swanson et al 1997)
  - associated with high novelty seeking behavior (Benjamin et al 1996)
  - affects response to psychiatric drugs (Van Tol et al 1992)
  - D4 is agonized by both dopamine and noradrenaline
- SNAP 25 docking protein variation, involved in pre-synaptic release of DA, may not respond to methylphenidate, only amphetamines.

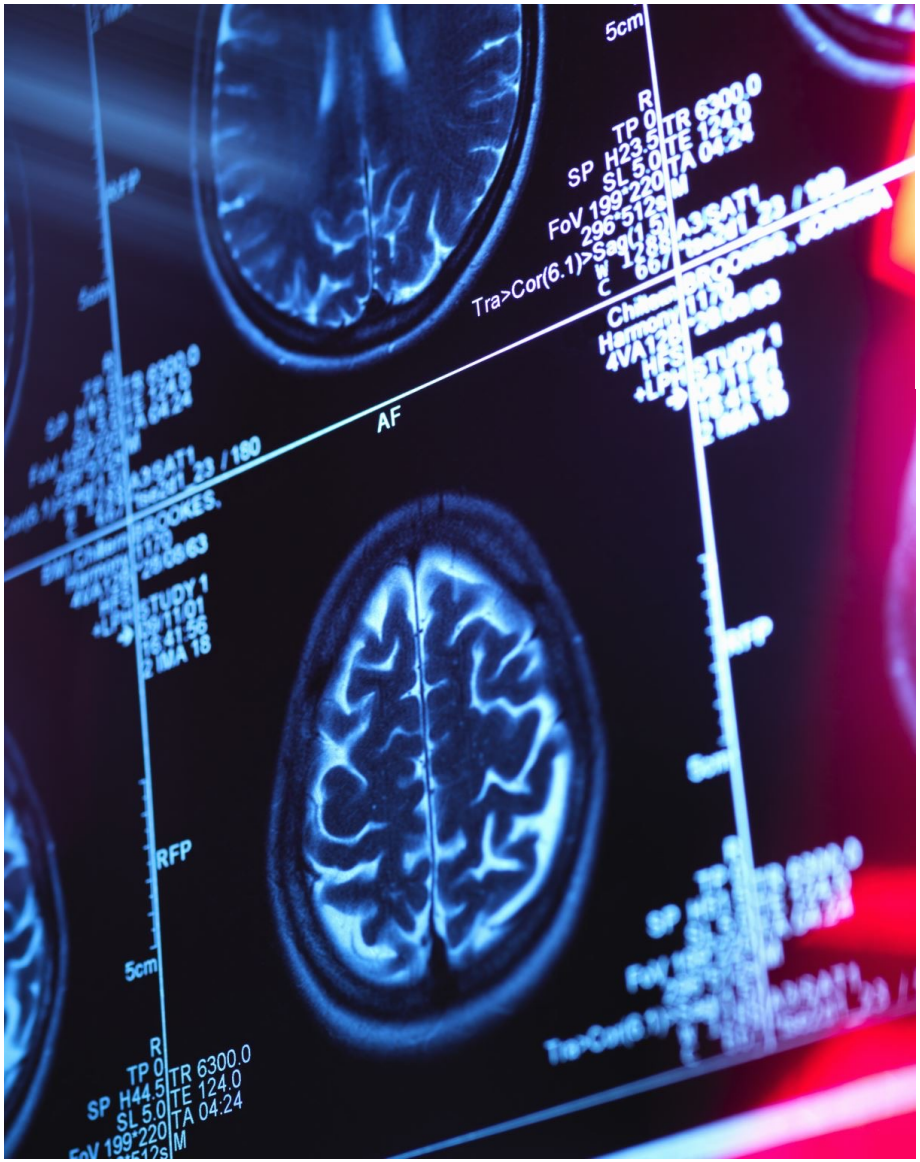
Noradrenergic Pathways in the Brain

Noradrenergic fibers from the locus coeruleus project broadly



BIOLOGICAL PSYCHOLOGY 7e, Figure 4.5





Neuroimaging

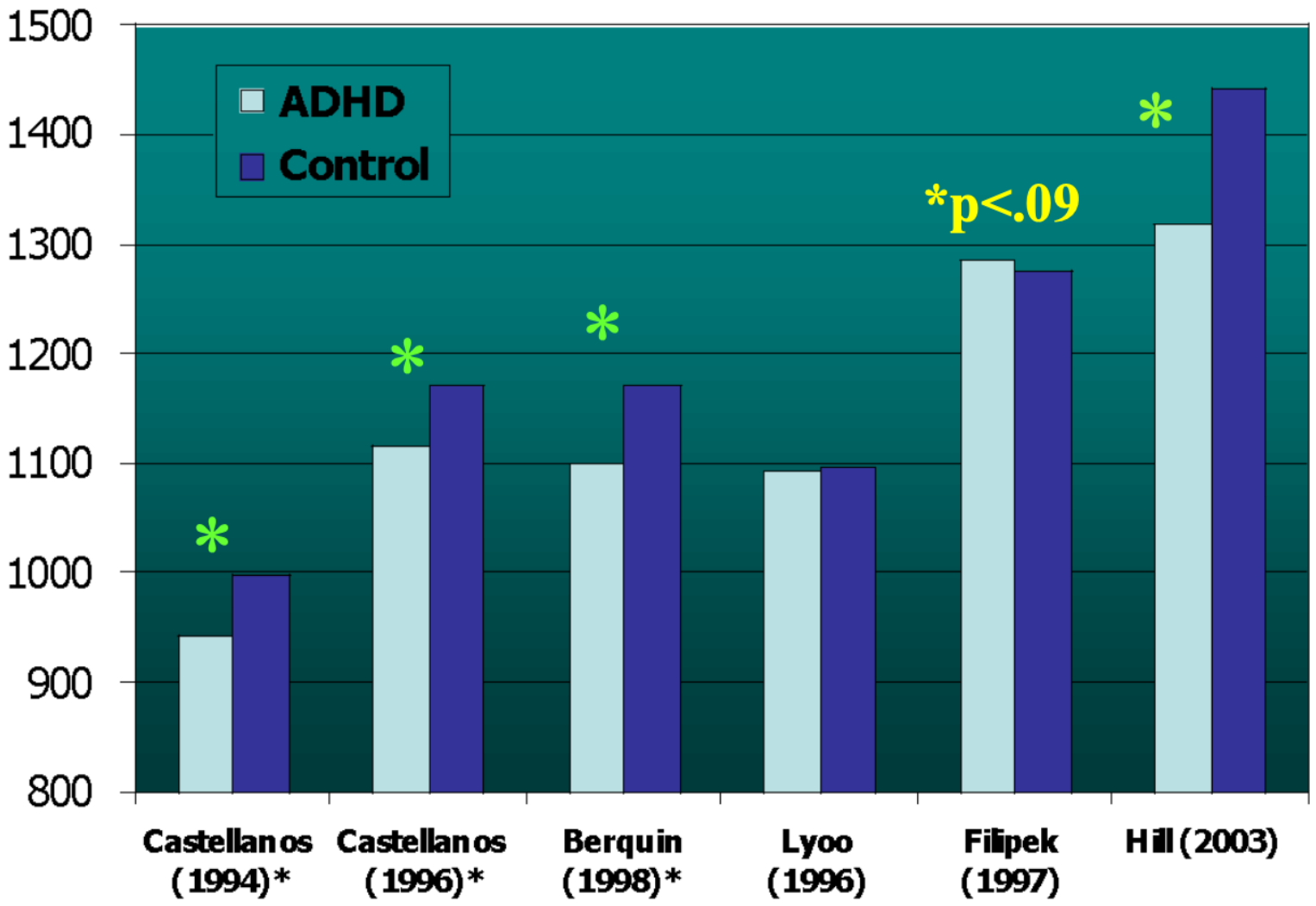
- MRI
  - Loss of the normal L > R asymmetry, smaller brain volumes of specific structures, esp. L caudate, smaller white matter vol of R frontal lobe
    - PFC, BG--both rich in DA receptors
      - 5-10% decrease in volume
    - Decreased volume of anterior-superior hemisphere
  - 5% decrease in R cerebellar volume, 4% reduction in intracranial volume; Unaffected siblings: up to 9% decrease in selected prefrontal and occipital areas

Durston, et al (2004): *J Amer Acad Child Adol Psychiatry*; 43(3); 332-340

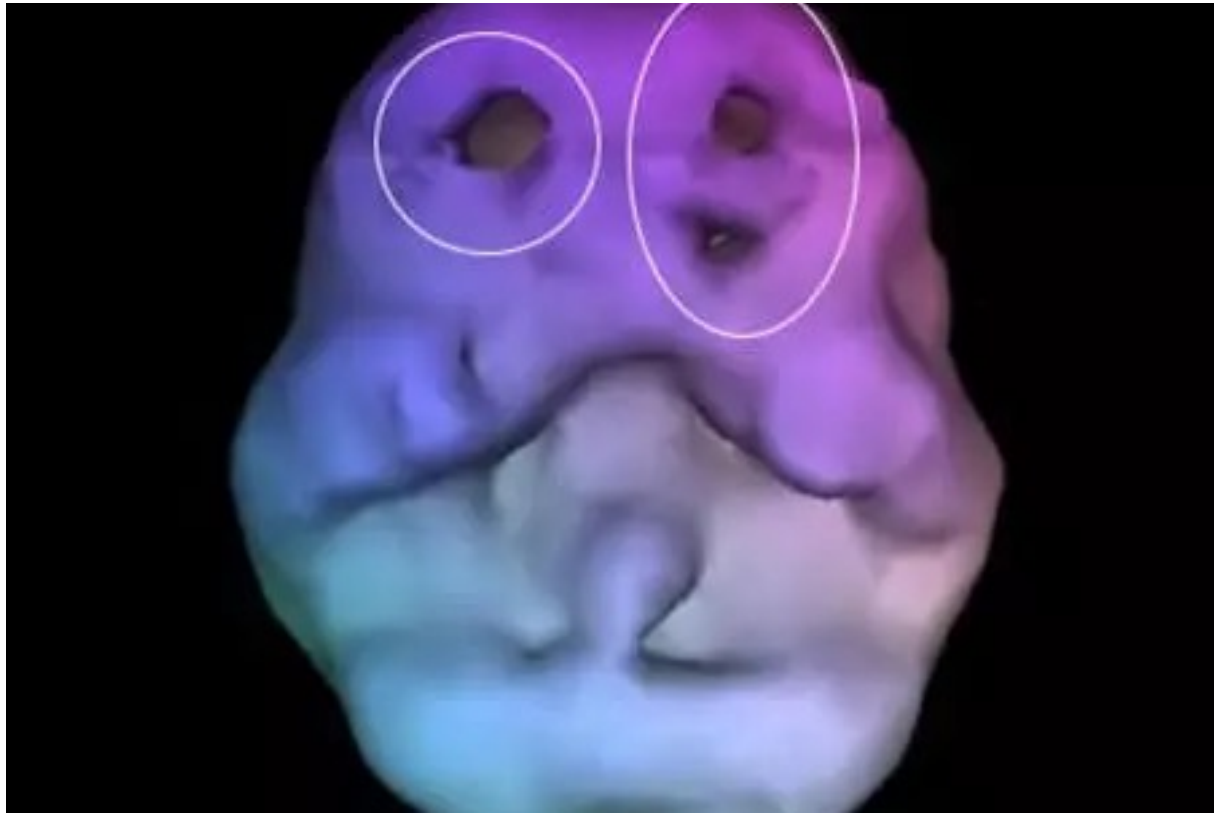
Essential Research

- Functional studies (PET, SPECT, quantitative EEG, etc.)
- Frontal lobes - multiple modalities show decreased activity in the frontal lobes during concentration
  - The difference in females is the most profound
  - Subjects had increased theta waves (slow waves) during concentration in their frontal lobes (Lubar)
- Limbic regions - had increased activity with decrease frontal lobe activity on SPECT (Amen)
- Parietal lobes - increased activity vs controls (Amen)
- Chabot et al. found 11 distinct patterns on QEEG associated with ADHD, some of which predicted good response to certain meds, but poor response to other ones

ADHD Whole Volume Brain Studies



*p<.05



SPECT

Co-Existing Conditions

- 30-50% of ADHD may be **co-morbid** with other dx
  - **Oppositional Defiant Disorder (ODD)-** Pervasive pattern of negativistic, defiant, disobedient, and hostile behaviors toward authority figures
  - **Conduct Disorder (CD)-** Repetitive pattern of violating the basic rights of others/ major age-appropriate social norms or rules are violated
  - **Mood disorders (depression/bipolar disorder)-** check family history!
    - Poor outcome in co-morbid teens (higher risk for suicide)
  - **Anxiety Disorders-** 25% or more
  - **Learning Disorders-** up to 60% in non-PCP settings
    - Especially Reading Disorder

The Public Health Case

Earlier age at first intercourse (15.4yo vs 16.5yo)	More unintended teen pregnancies (38% vs 4%)	Four times higher STD's
2-3x more MVA's, 9x more traffic tickets	Greater use of medical services, especially ER's	2-3x more arrests, 9x more convictions in teens
2x higher substance use disorders	60-70% rates of ADHD in prisoners (3 studies) and 30-40% rates in one other study	Treatment of ADHD resulted in increased rehab, fewer parole violations and earlier parole in one study

Why do we treat ADHD?

1. Prevention of academic/occupational failure.
2. Decrease the risk of substance use disorders.
3. Safety while driving and to prevent accidents and impulsive aggression.
4. Improve social skills and social functioning.
5. Improve relationships and prevent divorce.
6. Maintain parental/care taker sanity and to prevent physical abuse of the child.

Let’s go back to our patient

A 33-year-old male with no past medical history presents to clinic with a chief complaint of difficulty concentrating.

What might lead you to think about ADHD?

Adult ADHD

Still regarded as “controversial”, despite presence of continued morbidity in 30-40% of children diagnosed, and 50% + of teens transitioning to young adulthood; Prevalence in adults = 4-5% (Rostain, 2008)

Diagnosis is primarily clinical

- Useful tools include Connors Adult ADHD Rating Scales (CAARS), and Wender-Reimherr Adult ADD Scale (WRAADS)
- Self-assessment, Adult ADHD Self Report Scale (NYU)
  - http://www.med.nyu.edu/psych/assets/adhdscreen18.pdf
- DSM is only partially useful
  - Valid for children and teens only
  - Some items irrelevant for adults : “runs/climbs excessively; difficulty playing quietly”
  - Adult dx “relies” on ADHD NOS, or “Residual type”

Diagnostic Considerations in Adults

Ruling out of underlying conditions	DSM-5	ASRS
UTox	Pregnancy Test	Family history (sudden death)
Height, Weight	Risks vs. benefits	NO Dx by med trial

Adult ADHD Self-Report Scale (ASRS-v1.1) Symptom Checklist

Patient Name		Today's Date	

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.	Never	Rarely	Sometimes	Often	Very Often
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?					
3. How often do you have problems remembering appointments or obligations?					
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?					

Part A

7. How often do you make careless mistakes when you have to work on a boring or difficult project?					
8. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?					
9. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?					
10. How often do you misplace or have difficulty finding things at home or at work?					
11. How often are you distracted by activity or noise around you?					
12. How often do you leave your seat in meetings or other situations in which you are expected to remain seated?					
13. How often do you feel restless or fidgety?					
14. How often do you have difficulty unwinding and relaxing when you have time to yourself?					
15. How often do you find yourself talking too much when you are in social situations?					
16. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?					
17. How often do you have difficulty waiting your turn in situations when turn taking is required?					
18. How often do you interrupt others when they are busy?					

Part B

Treatments

Established Treatments

- Psychostimulants (1st line)
- Atomoxetine (1st line)
- Bupropion (2nd line)
- Tricyclic antidepressants (TCAs: 2nd line)
- Guanfacine extended release, recently FDA approved as Intuniv, for ages 6-17

Probable Efficacy

- Alpha-2 agonists (clonidine, guanfacine)
- Modafinil

Treatments, cont.

Possible efficacy

- Omega 3-6-9 Fatty Acids
  - For excellent review, see Freeman, et al. Jnl Clin Psychiatry 2006

Effective, but impractical: MAOIs

Likely ineffective

- SSRIs
- Caffeine
- St. John's Wort

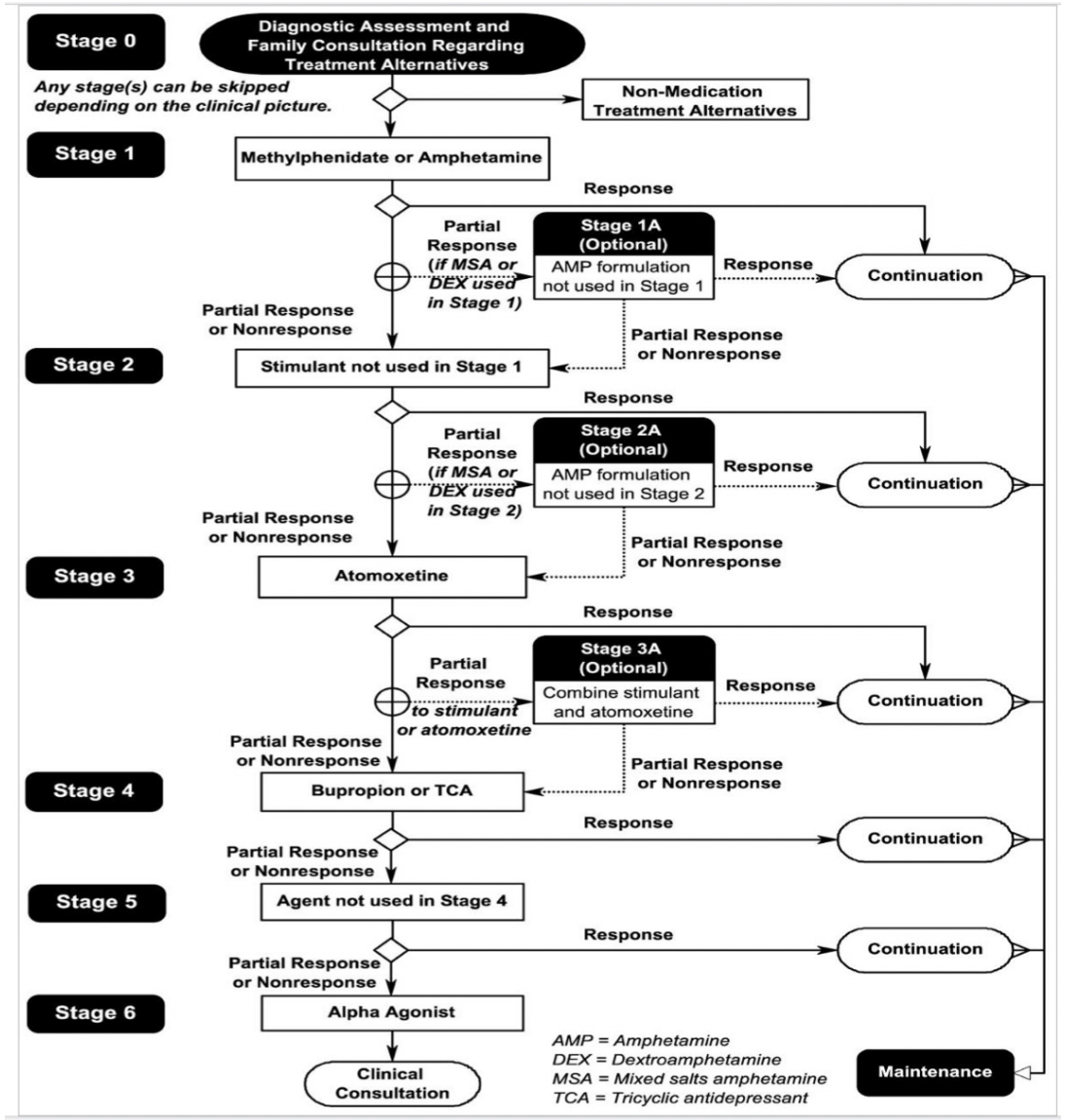
Adult

Wilens, et al, 2004

Table. Medications Used in Adults With Attention-Deficit/Hyperactivity Disorder

Medication	Daily Dose, mg*	Daily Dosage Schedule	Common Adverse Effects
Stimulants			
Methylphenidate	20-100	Twice to 4 times	Insomnia Decreased appetite/weight loss Headaches Edginess
Amphetamine			
Dextroamphetamine and mixed amphetamine salts†	10-60	Twice to 3 times	Insomnia Decreased appetite/weight loss Headaches Edginess Mild increases in pulse/blood pressure
Magnesium pemoline	75-150	Once or twice	Insomnia Decreased appetite/weight loss Headaches Edginess Abnormal liver function test results
Noradrenergic agents			
Atomoxetine	40-120	Once or twice	Sleep disturbance Gastrointestinal tract distress, nausea Headache Mild increases in pulse/blood pressure
Antidepressants			
Tricyclics			
Desipramine; imipramine	100-300	Once or twice	Dry mouth Constipation Vital sign and electrocardiographic changes
Nortriptyline	50-200	Once or twice	Dry mouth Constipation Vital sign and electrocardiographic changes
Bupropion	150-450	Once or twice	Insomnia Risk of seizures (in doses >6 mg/kg) Contraindicated in bulimia

*Denotes typical daily doses, which may exceed US Food and Drug Administration–approved dosing.
†US Food and Drug Administration approved for adults with attention-deficit/hyperactivity disorder.


Stage 0
Diagnostic Assessment and Family Consultation Regarding Treatment Alternatives
Any stage(s) can be skipped depending on the clinical picture.
Non-Medication Treatment Alternatives
Stage 1
Methylphenidate or Amphetamine
Response
Partial Response (if MSA or DEX used in Stage 1)
Stage 1A (Optional)
AMP formulation not used in Stage 1
Response
Continuation
Partial Response or Nonresponse
Partial Response or Nonresponse
Stage 2
Stimulant not used in Stage 1
Response
Partial Response (if MSA or DEX used in Stage 2)
Stage 2A (Optional)
AMP formulation not used in Stage 2
Response
Continuation
Partial Response or Nonresponse
Partial Response or Nonresponse
Stage 3
Atomoxetine
Response
Partial Response to stimulant or atomoxetine
Stage 3A (Optional)
Combine stimulant and atomoxetine
Response
Continuation
Partial Response or Nonresponse
Partial Response or Nonresponse
Stage 4
Bupropion or TCA
Response
Continuation
Partial Response or Nonresponse
Stage 5
Agent not used in Stage 4
Response
Continuation
Partial Response or Nonresponse
Stage 6
Alpha Agonist
Clinical Consultation
AMP = Amphetamine
DEX = Dextroamphetamine
MSA = Mixed salts amphetamine
TCA = Tricyclic antidepressant
Maintenance

Stimulants

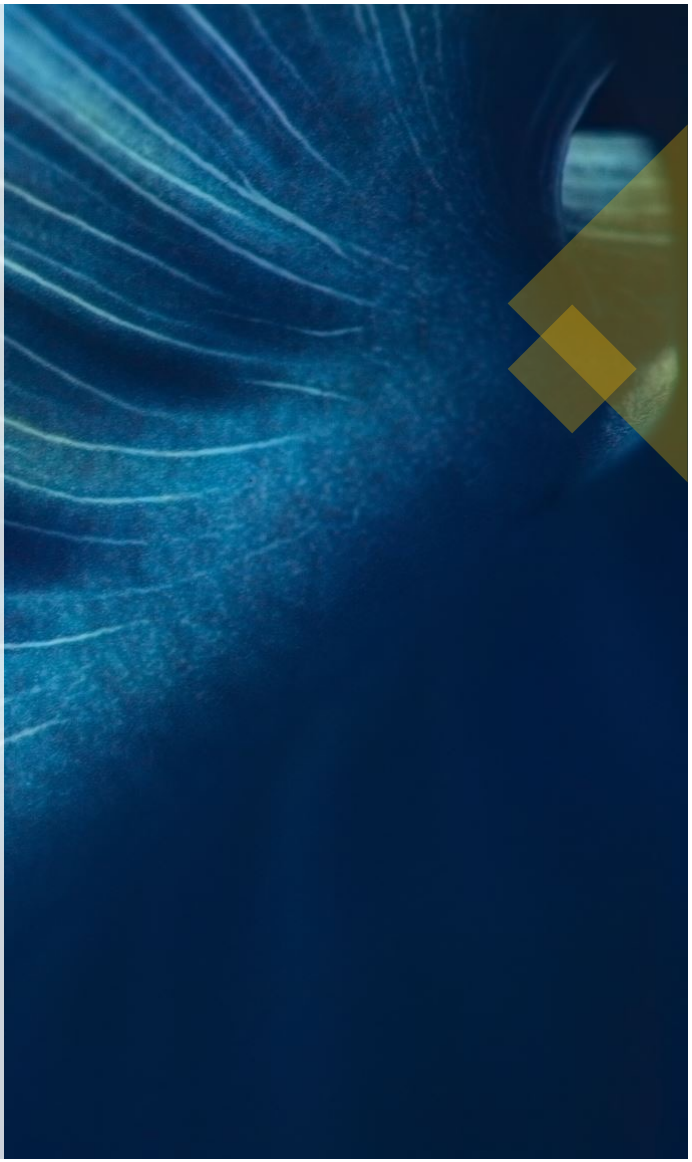
- “stimulate” certain areas of the brain to focus better
  - FDA classifies a substance as “psychostimulant” if nucleus accumbens is activated
- in use for “behavioral disorders” in children since 1930’s
- many studies to document safety and efficacy
- 70-85% response rate
  - do not use this to confirm diagnosis!

Stimulants

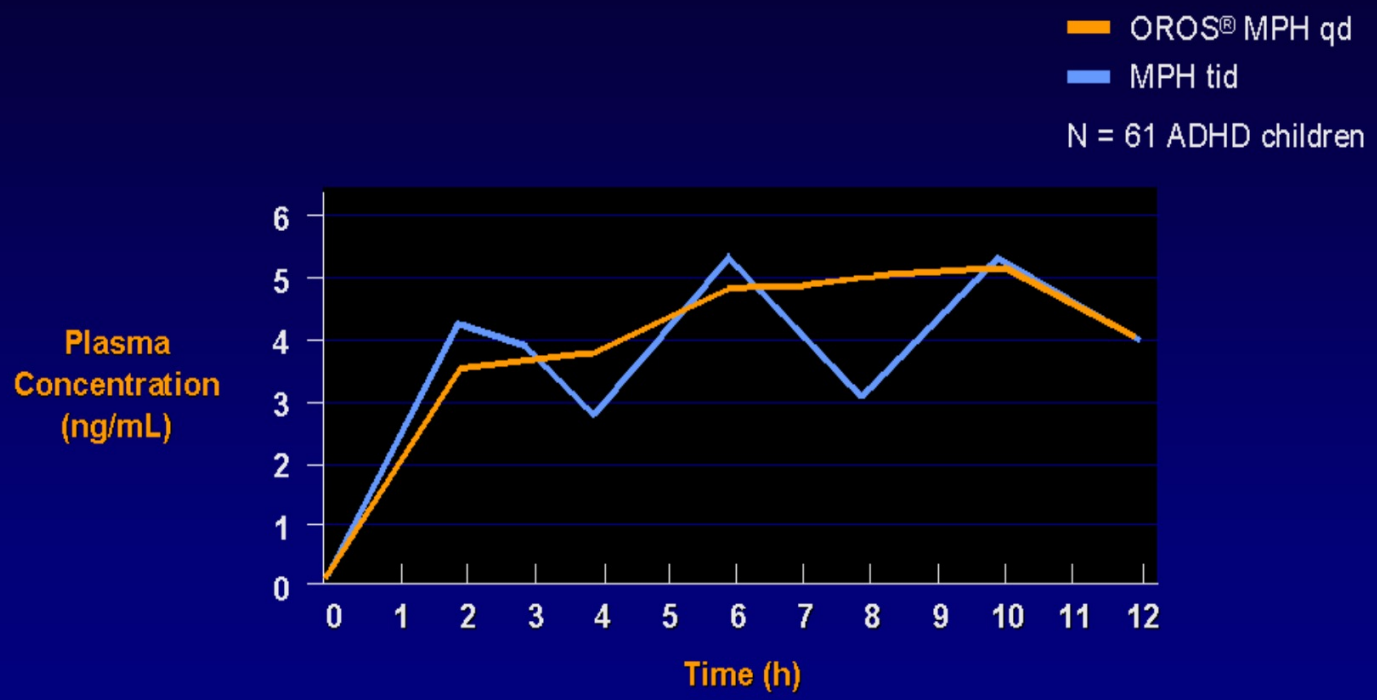
benefits: improved focus, concentration, attention span; reduced hyperactivity, impulsivity, and fidgeting

side effects: irritability, stomachache, headache, dysphoria, zoned-out effect, appetite suppression, sleep problems, height velocity slow-down (<10%)

Amphetamine formulations may produce more sleep/ appetite problems, especially at higher doses



OROS® Methylphenidate HCl qd (Concerta™) Versus Methylphenidate HCl tid (Ritalin®)



Swanson JM et al. Comparison of efficacy and safety of Concerta™ (methylphenidate HCl) with Ritalin® and placebo in children with ADHD. Presented at Region IX and X Annual Meeting of the Ambulatory Pediatric Association; February 12-13, 2000; Carmel, CA.

Atomoxetine (Strattera®)

- Atomoxetine *(not to be confused with Tamoxifen)*
  - Michelson, et al (2001) : n=297, ages 8-18, 71 % male; 67% ADHD-CT; 8-week randomized prospective controlled study
  - Participants were moderately -to-severely impaired prior to tx.
  - Results showed superior response to placebo (65% response rate)
    - ADHD symptoms
    - Measures of social and family functioning
- Total database (Lilly) of several million pediatric and adult patients with ADHD
- Common side effects: Dizziness, drowsiness, dyspepsia, decreased appetite
- Less common, but not rare (>2%)
  - Depression, tremor, early AM awakening, pruritus (generalized itching)
- Adult patients: Possible Sexual dysfunction; No abuse potential (no activation of dopamine in nucleus accumbens)

Guanfacine

- Guanfacine extended release (Intuniv)
  - Released in U.S. Nov 2009; FDA indicated for ADHD (6-17y.o.)
  - Alpha-2a agonist, non-stimulant; non-schedule II
  - T ½ = 17 hours (5 hours to Cmax)
  - Dose range 1-4 mg total daily dose
    - consider 0.05-0.08 mg/kg/day (max 0.12 mg/kg/day)
    - 1mg QD to start, then increase by 1mg weekly, if needed, to 4mg QD
  - Common side effects: **drowsiness, dyspepsia, fatigue
    - Monitor BP and HR for hypotension and bradycardia
- CYP3A4/5 substrate
  - Use cautiously when other medicines are used (potential additive CNS effects, drug interactions)
  - Assess cardiac function with good history

Clonidine

alpha-2 adrenergic agonist

may have role for H-I symptoms and aggression (not inattention)

- special utility in DD population

placebo-med differences have been found in small controlled studies

side effects often limit its usefulness

- CV, sedation

Dose:

- Start with 0.05 mg @ HS
- Typical range is 0.05-0.2 mg, BID-QID
- max daily dose 0.9 mg

Must monitor BP, other CV parameters

- Possible bradycardia
- rebound tachycardia and HTN
  - children between doses
  - if d/c'd abruptly
- *if tx'd for more than 1 month, d/c at a rate of 0.05 mg q3-7 days*

Bupropion

- Bupropion (Wellbutrin / Zyban)
  - Minimal 5-HT effects
  - Inhibits NE, DA uptake
  - May have special use with comorbid depression or substance abuse
  - 1 open and 3 controlled studies in children
    - not quite as robust an effect as stimulants
- Side effects
  - skin rash
  - seizures (lower with SR preparation)
    - 0.3%-0.4%; risk increases with doses> 450 mg Total Daily Dose
  - psychosis, agitation
  - sleep problems
  - appetite suppression
    - May have paradoxical beneficial effect on appetite when combined with stimulants
- Callaghan, *JAACAP*, July 1999

Special considerations

Motor tics

Depression

Anxiety d/o (children w/ co-morbid anxiety may improve on MPH, according to MTA study)

Seizure d/o

Children under 6 years old may be safely treated, starting with methylphenidate, once all psychosocial treatments have been implemented

- PATS (Pre-school ADHD Treatment Study) is one of many to document safety and efficacy
- Young children may be more sensitive to side effects
- Consider weight-based dosing for children under 25 kg: 1mg/kg/day (MPH); 0.5 mg/kg/day (AMPH)

Methylphenidate Formulations

Brand	Type	Dosage forms (mg)	Est. duration (hrs)	Max daily dose [mg] *Range 0.3-1.0mg/kg/day*
Generic	IR	5,10,20	2.5 - 4	[60]
Ritalin	IR	5,10,20	2.5 - 4	[60]
	SR	20	6 - ?	
	LA***	20	8-10	
Methylin	IR*	5,10,20	2.5 - 4	[60]
	ER	5,10,20	6 -8	
Focalin	IR	2.5,5,10	3-5	[20-30]
	XR***	5, 10, 15, 20	8-10	
Metadate	ER	10,20	6-8	[60]
	CD***	20	8 -12	
Concerta	ER	18, 27,36,54	10 - 12	[72]
Daytrana	patch	10, 15, 20, 30	9-12	[30]

[ ] Some patients may tolerate higher doses.
* Available in chewable tablets and liquid
*** May be sprinkled on food
Chart adapted from Glen R. Elliott, PhD, MD

Amphetamine Formulations

Brand	Type	Dosage forms (mg)	Est. duration (hrs)	Max daily dose (mg) *Range 0.15-0.5 mg/kg/day*
Generic	IR	5,10,20	3-6	40 *
Dexedrine	IR	5,10	4-5	40 *
	Spansules**	5, 10, 15	5-9	
Adderall	IR	5, 7.5, 10, 12.5, 15, 20, 30	4-6	40*
	XR**	5-30 mg , (in 5-mg increments)	8-10	
Vyvanse	Lisdex-amfetamine	20, 30, 40, 50, 60, 70	8-12	70

*Some patients will tolerate higher doses. **may be sprinkled on food
Chart adapted from Glen R. Elliott, PhD, MD

Match the formulation with the needs of the patient

1

Have to know when patient "needs" the psychostimulant (e.g., early in AM for school only, or including homework, peer activities, week-ends)

2

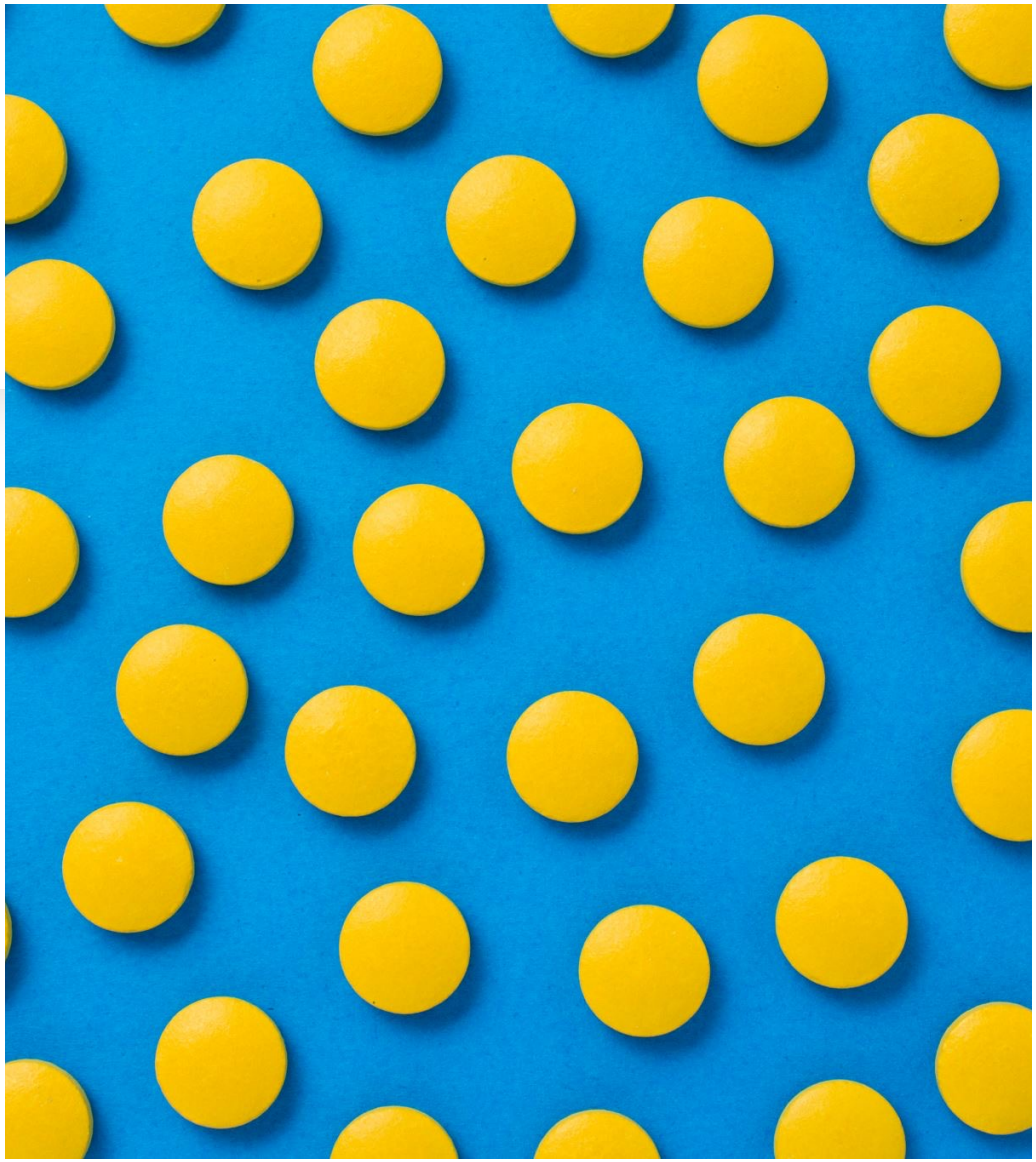
Parent and teen sometimes have definite preferences for one or another, and so do HMOs

3

Train family/patient to observe efficacy and side effects through the day and into the evening

How to initiate dosing

- Generally not by weight, unless patients are less than 25 kg (0.3- 1mg/kg/d for MPH)
  - (0.15 - 0.5 mg/kg/d for AMPH)
- Titrate to efficacy or intolerable side effects: start at 5 mg MPH or 2.5 mg AMP
  - Increase by 5 mg MPH, or 2.5 mg AMP every 3-5 days to first target dose, decided upon by doctor and family
  - Get weekly reports and adjust upward, checking for side effects and efficacy



Fine Tuning

- Must have accurate info about performance “over the day”; use scales and listen to observers: titrate as needed
- Can combine short and long-acting preparations
  - if dysphoric at days end, add MPH to Concerta at the end of the school day (no later than 3:30PM); Dex to Dex-spansules at the start of the day because of delayed effect of spansules
- If only partial efficacy with stimulants, can “mix and match” with other anti-ADHD drugs (e.g., clonidine / guanfacine, bupropion, atomoxetine TCAs)
- Inform family, and be vigilant about checking for additive sympathomimetic side effects

Common Errors

- Failure to increase dosing slowly to maximum if no side effects (MTA study showed lower dosing in community sample
- Beginning with a dose that is too high
  - “Start low and go especially slow” with patients who are developmentally delayed
- Not assessing the duration of action; (may need to “bunch up “ dosing with IR formulations)
- Failure to use another psychostimulant if the first or second trial fails
- Failure to use input from others

Practice Guidelines

- In children who have good primary care, other diagnostic tests are not *routinely* indicated
  - EEGs indicated only if a history of seizure d/o or clinically significant lapses in consciousness exists
  - Continuous Performance Tests (CPT's) are useful in research settings only
    - measures of vigilance / distractibility which have low odds ratios in differentiating children with and without ADHD

Serious Side Effects of Psychostimulants

Sudden cardiac death

- Anecdotal, but not irrelevant
- Cases thus far have been primarily in patients with pre-existing cardiac conduction defects
- Ask about history of sudden tachycardia, fainting, and family history of sudden cardiac death prior to initiating

30+ cases of psychosis or formal hallucinations: discontinue the medication

Growth Suppression (MTA 2004, 2009) effects are likely to be made up in late teens or by drug holidays; especially at risk, those with nausea and vomiting

- Plot heights every 3 months to ensure proper growth velocity

Tics

- Mild or moderate tics occur in a significant number of patients with or without ADHD pharmacotherapy
  - 5-18% of schoolchildren will experience a simple or complex tic in their lifetime
- Tics during ADHD treatment may improve even while psychostimulants are used; discontinue only if serious
- **Lipkin et al**, in a review of 122 children treated with stimulant medication found 9% developed transient tics and <1% developed chronic tics
- Many children with tics and ADHD can tolerate stimulants without an increase in tics
  - **Law & Schachar (1999):** 12-month study, 91 children
    - MPH treatment did not produce significantly more tics than placebo in children with or without mild-to-moderate preexisting tic disorder
  - **Gadow et al (1999):** 24-month study, 34 children with ADHD and tic disorder or Tourette's syndrome
    - stimulant treatment was effective in controlling ADHD symptoms without adversely affecting tics

Tics, Continued

Tics are usually transient

- Rarely do patients develop a chronic tic disorder

When tics do occur or are worsened

- Decrease dose
- Switch to another stimulant
- Add adjunctive drug to treat tics
  - Clonidine / guanfacine
- Try nonstimulant medication
  - Atomoxetine
  - Modafinil

When to refer

- Diagnostic Uncertainty
- Severe comorbidity
- Difficult side effects
- Failure of stimulants
- Developmental delays
- Mania or psychosis

References

- Slides 22 and 23 are courtesy of H. Brent Solvason, MD, PhD; previous lectures by Shahank V. Joshi, MD (Stanford University) and Jessica R. Oesterheld (Tufts)
- Stein MT: Attention-Deficit/Hyperactivity Disorder: The Diagnostic Process From Different Perspectives; *Pediatrics,* Nov 2004; 114: 1453 - 1457.
- MTA Cooperative Group
  National Institute of Mental Health Multimodal Treatment Study of ADHD Follow-up: Changes in Effectiveness and Growth After the End of Treatment**;** *Pediatrics*, Apr 2004; 113: 762 - 769.
- Arnold LE: Methylphenidate vs. Amphetamine: A Comparative Review, in: Greenhill and Osman (*eds)* Ritalin, Theory and Practice, Liebert, NY, 2000
- Greenhill, L. L., Pliszka, S. R., Dulcan, M. K., & and the Workgroup on Quality Issues. (2002). Practice Parameter for the Use of Stimulant Medications in the Treatment of Children, Adolescents and Adults. *Supplement to Journal of the American Academy of Child and Adolescent Psychiatry, 41*(2), 26S-49S**.**
- Joshi SV, et al: Stimulants, atomoxetine, and other agents used to treat ADHD, in: Steiner, Handbook of Mental Health Interventions in Children and Adolescents: An Integrated Developmental Approach, 2004; SF, Jossey-Bass
- Joshi SV: Teamwork: The therapeutic alliance in pharmacotherapy with children and teenagers, in: Martin A & Bostic J (eds.), *Child & Adolescent Psychiatry Clinics of North America*, 15 (2006), pp239-262
- Pliszka, S. R., and the Texas Consensus Conference Panel on Medication Treatment of Childhood Attention-Deficit/Hyperactivity Disorder. (2000). The Texas children's medication algorithm project: Report of the Texas consensus conference panel on medication treatment of childhood attention-deficit/hyperactivity disorder. Part I,II. *J Am Acad Child Adolesc Psychiatry* **(***JAACAP) 39,* **908-927.**
  - **Revision and update of the above in Pliszka et al. : *JAACAP*. 2006 Jun;45(6):642-57**
- Pliszka SR, and the AACAP Work Grp on Quality Issues: Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2007 Jul;46(7):894-921
- Rostain AL: ADHD in Adults-Evidence based recommendations for management, Postgraduate Medicine, 120(3), pp 27-38, Sept 2008

References

- Schulz KP: Neurobiological models of ADHD: A brief review of the empirical evidence. *CNS Spectrums,* 5(6) pp.34-44 June 2000
- Robin AL: ADHD in Adolescents: Diagnosis and Treatment (1998); NY Guilford Press
- Rugino, TA & Samsock T.C.(2003). Modafinil in children with attention-deficit hyperactivity disorder; *Pediatric Neurology* 29 (2), 136-142
- Plizska S: "The Comprehensive Treatment of Attention and its Disorders", The 9th Ann Symposium on Developmental Approaches to Psychopathology- Stanford Univ Med Center, Stanford, CA (April 2006)
- Greenhill, LL, et al. A Randomized, Double-Blind, Placebo-Controlled Study of Modafinil Film-Coated Tablets in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder, *JAACAP*, 45(5), May 2006
- Biederman, J et al: Efficacy and safety of modafinil film-coated tablets in children and adolescents with attention-deficit/hyperactivity disorder: results of a randomized, double-blind, placebo-controlled, flexible-dose study. *Pediatrics*. 2005 Dec;116(6):e777-84
- Heiligenstein E, Conyers LM, Berns AR, Miller MA, Smith MA (1998) : Preliminary normative data on DSM-IV attention deficit hyperactivity disorder in college students. *J Am Coll Health*; 46:185–188
- Castellanos FX, Lee PP, Sharp W, et al. (2002): Developmental trajectories of brain volume abnormalities in children and adolescents with attention-deficit/hyperactivity disorder. *JAMA*;288:1740-1748.
- Freeman MP, et al. (2006): Omega-3 Fatty Acids: Evidence Basis for Treatment and Future Research in Psychiatry. J Clin Psychiatry 67:12, December
- McGough JJ & Barley RA (2004): Diagnostic controversies in adult attention deficit hyperactivity disorder; *American Journal of Psychiatry,* 161 (11); 1948-1956
- Wilens TE, Faraone SV, Biederman J (2004): Attention-Deficit/ Hyperactivity Disorder in Adults ; *JAMA,* 292(5): 619-623
- Richardson AJ (2004): Long-chain polyunsaturated fatty acids in childhood developmental and psychiatric disorders; *Lipids* ;39(12):1215-22.
- Vaidya CJ, et al: Selective effects of MPH in ADHD: An fMRI study. *Proc Nat Acad Sci USA,* 95:14494-14499, 1998

Resources

- Classroom strategies and modifications
  - www.schoolpsychiatry.org
- Parent Education and Empowerment
  - www.parentshelpingparents.com
  - www.schwablearning.org / www.greatschools.net
  - www.chadd.org
  - www.aacap.org (Amer Acad of Child & Adol Psychiatry: Facts for Families)
  - *www.parentsmedguide.org* (antidepressants)
  - www.add.org
- NAMI (www.nami.org)

ADHD and Stimulant Prescribing:

Best Practices to Keep Your Patients and Your License Safe

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