

Advances in the Management of ADHD

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Sources:

Barkley, R. A., Murphy, K. R., & Fischer, M. (2008) *ADHD in adults: What the science says*. New York: Guilford

Barkley, R. A. (2006) *Attention deficit hyperactivity disorder: A handbook for diagnosis and treatment (3rd ed.)*. New York: Guilford Publications

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- Speaking Fees and Expenses:
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Objectives – To Review

- The major advances in understanding the nature of ADHD as a disorder of self-regulation
- The implications of viewing ADHD as a disorder of executive functioning that disrupts self-regulation
- The latest developments in the science-based treatment of ADHD, including both proven and unproven treatments.

What is ADHD?

The Current Clinical View

A disorder of age-inappropriate behavior:

- **Inattention (Executive Functioning ?)**
 - At least 6 types of attention – not all are impaired
 - Arousal, alertness, selective, divided, span of apprehension, & persistence
 - Poor persistence toward goals or tasks
 - Impaired resistance to responding to distractions
 - Deficient task re-engagement following disruptions
 - Impaired working memory (remembering so as to do)
- **Hyperactivity-Impulsivity (Poor inhibition)**
 - Impaired verbal and motor inhibition
 - Impulsive decision making; impatient or cannot wait
 - Greater disregard of future (delayed) consequences
 - Excessive task-irrelevant movement and verbal behavior
 - Fidgeting, squirming, running, climbing, touching
 - Restlessness decreases with age, becoming more internal, subjective by adulthood

Advances in Theory

- ADHD is a disorder of inhibition and self-regulation
- Self-regulation arises from the brain's executive system
- The EFs serve to organize behavior across time so as to direct it toward probable future events
- This system involves at least 5 functions that appear to be forms of self-directed private action
 - Inhibition (preventing the prepotent response) and interference control (resistance to distraction)
 - Nonverbal working memory (sensing to the self)
 - Verbal working memory (private self-speech)
 - Emotional and motivational self-regulation
 - Planning and problem-solving (private play to the self)

Developmental Transitions in Behavioral Control from the EFs

- External → Mental (private)
- Others → Self
- Temporal now → Anticipated future
- Immediate → Delayed gratification

Understanding ADHD

- ADHD Creates a “Time Blindness” or “Temporal Neglect Syndrome” (Myopia to the Future)
- Those with ADHD Live in the Moment
- Its a Disorder of:
 - Performance, not skill
 - Doing what you know, not knowing what to do
 - The when and where, not the how or what
 - Using your past at the “point of performance”

The point of performance is the place and time in your natural settings where you should have used what you know but did not
- Its Not an Attention Deficit but an Intention Deficit Disorder (Inattention to mental events & the future)

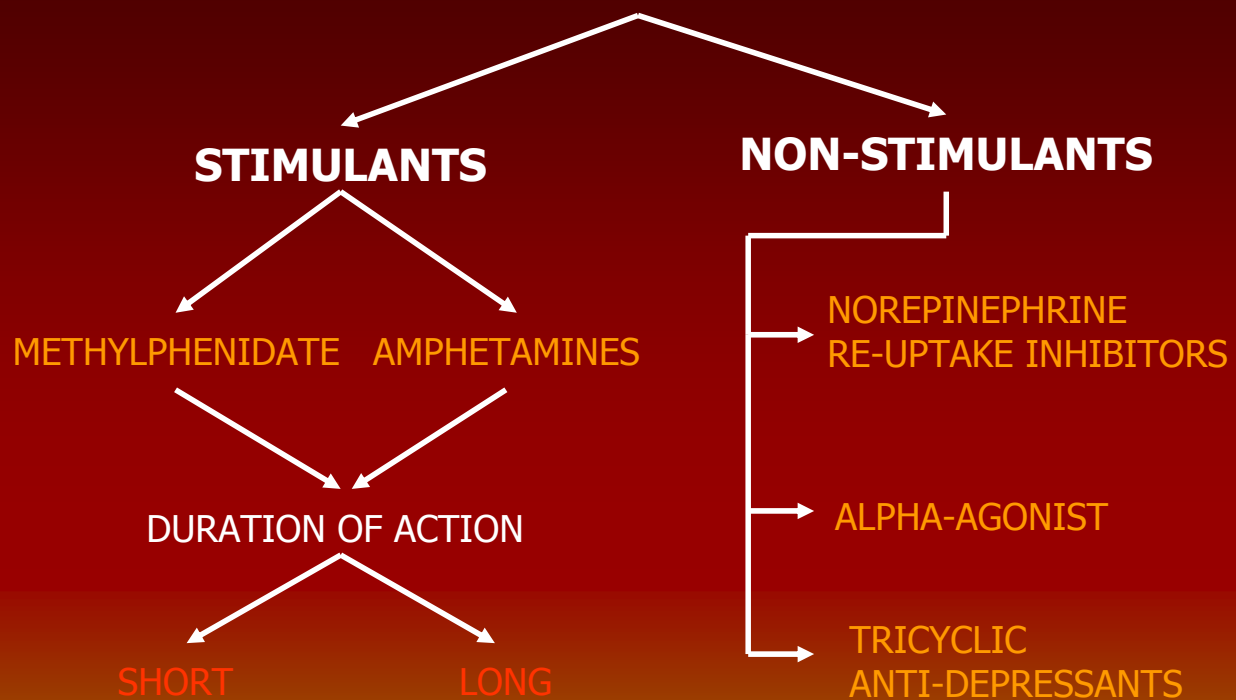
Implications for Treatment

- Teaching skills is inadequate
- All treatments are at the point-of-performance
- Medications may be essential for most (not all) cases – it is a form of neuro-genetic therapy
- While ADHD creates a diminished capacity, does this excuse accountability? (No!, the problem is time and delays -- not consequences)
- Behavioral treatment is essential but does not generalize or endure after removal
- The compassion and willingness of others to make accommodations are vital to success
- A chronic disability perspective is most useful

Reverse Engineer the EFs

- Externalize important information
 - lists, posters, signs, other cues of critical reminders and post at the point of performance
- Externalize time periods related to tasks
 - use timers, clocks, counters, that signal time's passing
- Break up future tasks into many small steps
 - do 1 step each day; keep the E-R-Os close in time
- Externalize sources of motivation
 - Quick praise, token/point systems, tangible rewards
- Permit more external manipulation of task components
 - manualize the problem as much as you can

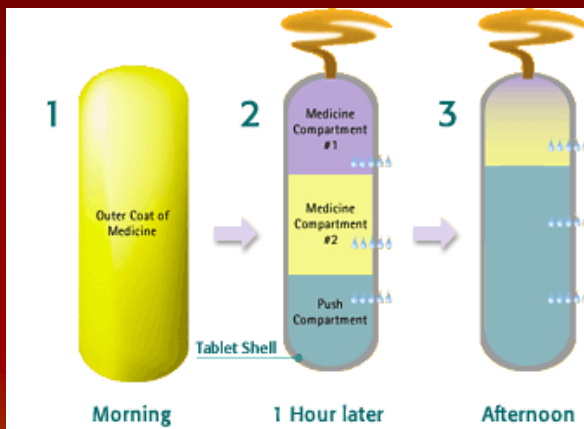
ADHD MEDICATIONS



Advances in Medications

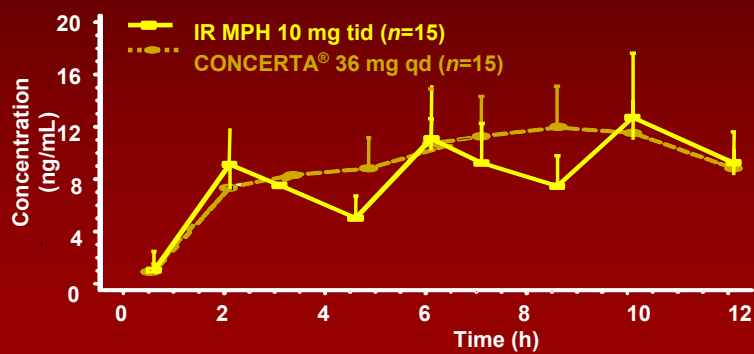
- Psychopharmacology
 - New stimulant delivery systems
 - Pills, pumps, pellets, and patches (e.g., Concerta, Medadate CD, Ritalin LA, Focalin XR and Adderall XR, Daytrana)
 - Non-abusable formulations (Vyvanse – novel prodrug amphetamine binding formula)
 - Better understanding of preschooler stimulant response
 - New noradrenergic medications
 - Strattera – highly selective NE reuptake inhibitor; first FDA approved non-stimulant for ADHD in children and adults;
 - Also Wellbutrin – not as selective an NE reuptake blocker
 - Decreasing use of tricyclic anti-depressants
 - Demonstrated efficacy of anti-hypertensives
 - (e.g., Catapres, Tenex)

Concerta: A New Delivery System

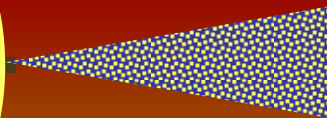


- Concerta uses OROS technology to create an osmotic pump
- Activated by water absorption in the stomach and intestinal track
- Pressure delivers a continuous flow of liquid methylphenidate
- Lasts 10-12+ hours
- Same effects and side effects as regular methylphenidate

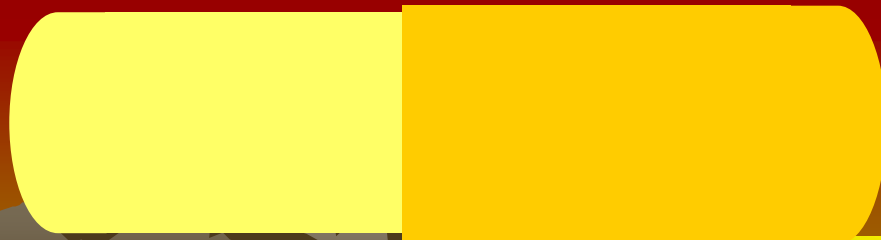
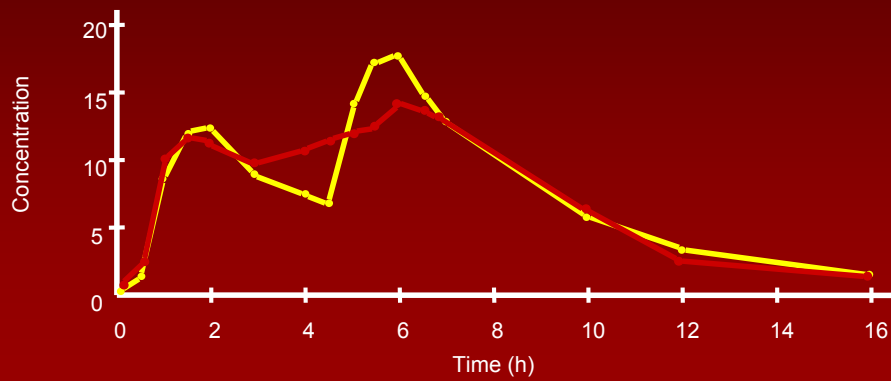
MPH OROS (Concerta[®])



Outer Coat of Medicine
(22% Immediate Release)

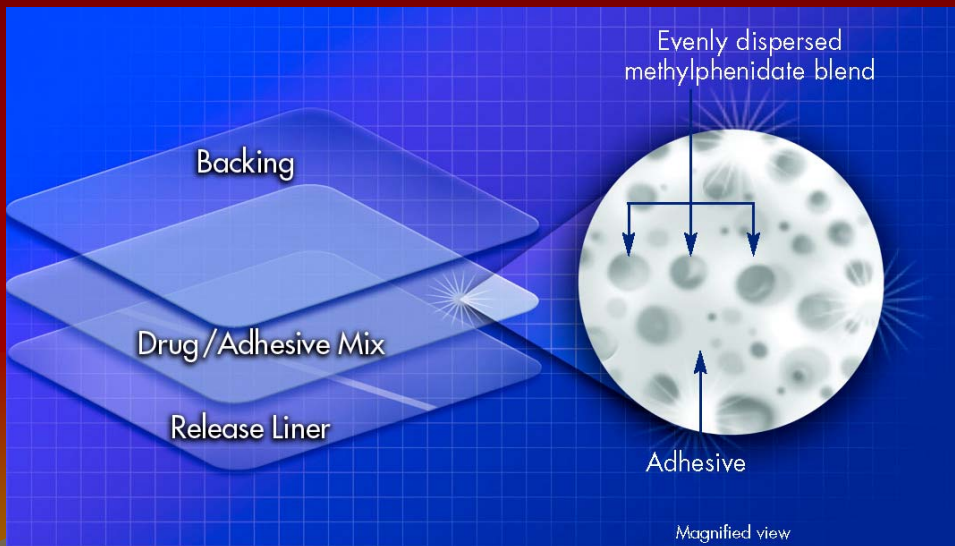


Pulse Delivery System (Diffucaps, Microtrol, SODAS)



Daytrana DOT Matrix™ Transdermal Technology

- Methylphenidate is mixed with adhesive

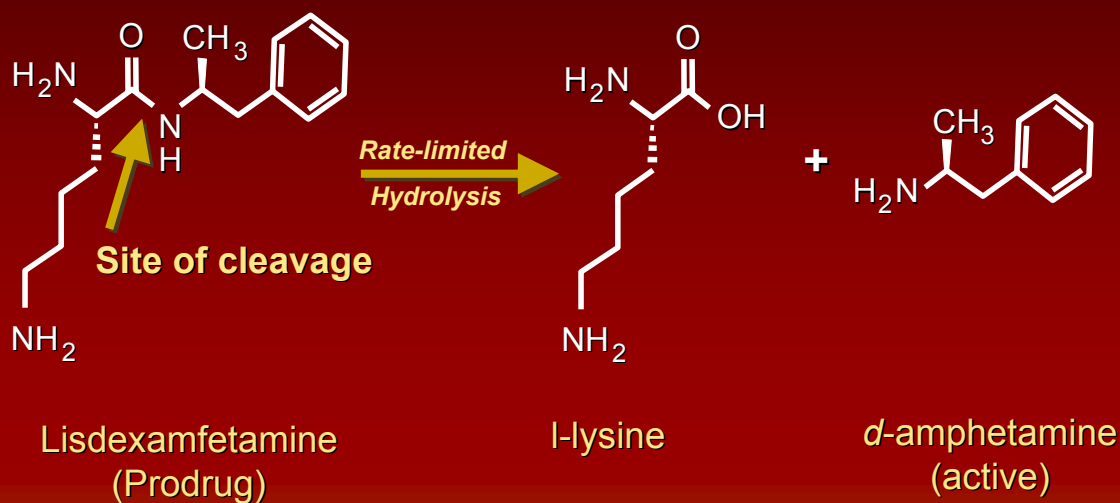


DOT Matrix is a trademark of Noven Pharmaceuticals, Inc.

What Is Vyvanse™?

- A long-acting, prodrug stimulant
- Once-daily medication indicated for the treatment of ADHD
 - The efficacy and tolerability of Vyvanse were evaluated in children aged 6 to 12 years
- Capsules available in multiple dosage strengths
 - 30 mg
 - 50 mg
 - 70 mg
- Can be taken with or without food
- Can be dissolved in water

Chemical Structure of Vyvanse™



- Vyvanse is a prodrug that is therapeutically inactive until it is converted to active *d*-amphetamine in the body

Stimulants in Preschoolers

- PATS study examined 303 preschoolers (3-5.5 years old) 165 of whom entered drug trial (all received prior parent training)
- Used doses of 2.5, 5, & 7.5 mg MPH given 3x daily for 9 weeks (best dose was 14.2 mg/day₊₈)
- Study found smaller effect sizes (.4-.8) than in school-age children, 22% normalized (vs. 55%)
- Possibly greater side effects
 - Over 8% could not tolerate drug (vs. 3% of school age)
 - Otherwise, side effects were similar to school-age children (insomnia, poor appetite, weight loss most common, some had emotional outbursts)
 - Some delayed growth, 50% less in weight gain, 20% less in height gain during acute treatment period
- Medications considered safe for use with preschoolers but with increased risk of side effects and decreased degree of change relative to older children

Journal of the American Academy of Child and Adolescent Psychiatry, 2006, 45 (11), 1275+

Strattera (atomoxetine)

- Exclusive noradrenergic reuptake inhibitor
- Unscheduled (not Schedule II); no abuse potential
- Approved in US January 2003 by FDA; tested in more than 6,000 cases worldwide
- Used with more than 4.5 million patients to date
- Effective for kids, teens, and adults with ADHD
- Equal efficacy with methylphenidate for new, medication naïve cases; slightly lower success rates in children previously on stimulants
 - But effect sizes are somewhat smaller .6-.8 vs. .7-1.0
- 75%+ positive response rate in new cases, 55% in previous stimulant treated cases
- Sustained response demonstrated for up to 3 years
- Increasing improvement with time on drug
- Can be given once daily (in AM) or split (AM/PM)

Antihypertensive Drugs: Clonidine and Guanfacine

- Not FDA approved for use with ADHD
- Consider as last choice agents; both require EKG monitoring; can be combined with stimulants
- May be most optimal for aggressive-explosive behavior and severe hyperactivity
- Both Alpha2 adrenergic agonists but may work in ADHD by affecting norepinephrine
- Both improve ADHD, ODD, & CD symptoms but not as effective as stimulants;
 - guanfacine better for comorbid tic disorders
- Cause sedation (more for clonidine) and rebound hypertension; Clonidine may improve sleep problems associated with ADHD or stimulants

Advances in Family Treatment

- Parent Education About ADHD
 - The first critical step in treatment
 - Adopt a “parents are shepherds” perspective
- Learning the value and limitations of parent training
 - Changes defiance and parent-child conflict, not ADHD
 - Works best in younger children
 - (<11 yrs., 65-75% respond)
 - Modestly useful for teens
 - (25-30% show reliable change)
- Incorporate teen in treatment and use Problem-Solving, Communication Training
 - (30%+ show reliable change)
 - Best to combine it with above PT to reduce drop outs

More Treatment Advances

- Teacher Education About ADHD
- Classroom Behavior Management
 - Designing prosthetic classrooms
 - Very effective but no generalization or maintenance after withdrawal
 - Mild to moderate intensity of treatment is as good as high intensity treatment
- Special Education Services (IDEA, 504)
- Regular Physical Exercise
 - A coping or compensatory tool
- Residential Treatment (5-8%)
- Parent/Family Services (25+%)
- Parent/Client Support Groups (CHADD, ADDA, Independents)

Experimental Psychosocial Treatments (in need of further research)

- Biofeedback (EEG) (Lubar, Univ. of Tennessee)
 - Numerous positive clinical studies but all suffer serious flaws in their methods
 - 2 randomized trials found no real benefits
- CogMed – cognitive training of working memory (Torkel Klingberg, Karolinska Institute, Stockholm)
- Time Management and Organization Training for School (Abikoff, NYU Medical School)
- After School Supplemental Training for Teens (Smith, Univ. of South Carolina)
- Group Cognitive Behavioral Training of Adults with ADHD (Safren, Harvard Medical School; Ramsay & Rothstein, Univ. of Pennsylvania)

Unproven Therapies

- Elimination Diets – removal of sugar, additives, etc. (Weak evidence)
- Megavitamins, Anti-oxidants, Minerals (No compelling proof or have been disproved)
- Omega 3 Fatty Acids (Fish Oil) – one recent study with mixed results (better at home, no effect at school)
- Sensory Integration Training (disproved)
- Chiropractic Skull Manipulation (no proof)
- Play Therapy, Psycho-therapy (disproved)
- Self-Control (Cognitive) Therapies for Children (disproved)
- Social Skills Therapies for Children (in clinic)
 - Better for Inattentive (SCT) Type and Anxious Cases

Conclusions

- ADHD is probably a disorder of self-regulation and executive functioning that leads to impaired organization of behavior across time toward future goals
- This leads to conceptualizing treatment as a means of accommodating the EF deficits
- ADHD and its EF deficits largely result from neuro-genetic factors
- Many advances in treatment occurred in the past decade, especially in medications and delivery systems, as well as in refining psychosocial treatments
- ADHD is among the most treatment responsive disorders in psychiatry and can be successfully managed leading to improved life course and outcomes