ADHD & Executive Dysfunction

Child Neurology CME
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DISCLOSURES

None
ADHD
(Attention Deficit Hyperactivity Disorder)

ask me about my attention deficit disorder or pie or my cat. a dog. i have a bike. do you like tv? i saw a rock. hi.
ADHD

“one of the best-researched disorders in medicine, and the overall data on its validity are far more compelling than for many medical conditions”

(AMA Council on Scientific Affairs, 1998)
ADHD – OLD DEFINITION

- a behavior disorder accompanied by chronic problems in not paying enough attention to what others are saying, hyperactivity and impulsivity
ADHD – NEW DEFINITION

- These impairments are **situationally variable**, **chronic**, and significantly interfere with functioning in many aspects of the person’s daily life.

*Thomas E Brown, PhD*
ADHD - DSM IV CRITERIA

- ≥ 6 of 9 inattentive and/or ≥ 6 of 9 hyperactive/impulsive symptoms
- 3 subtypes: predominantly inattentive, predominantly hyperactive/impulsive, combined type
- Symptoms must
  - persist for ≥ 6mo
  - be maladaptive & inconsistent w/ developmental level
  - present in ≥ 2 settings (school, home, etc)
  - present before 7yo
    - Might not be recognized until after 7yo when school/work becomes more challenging (esp in inattentive subtype)
  - cause significant impairment in social, academic or occupational fxn
  - not be attributable to another physical, situational or mental disorder
## ADHD – DSM IV CRITERIA

<table>
<thead>
<tr>
<th>Inattentive</th>
<th>Hyperactive/Impulsive</th>
<th>Hyperactivity symptoms</th>
<th>Impulsivity symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.) inattentive to details/careless mistakes</td>
<td>1.) fidgets w/ hands/feet, squirms in seat</td>
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<tr>
<td>2.) difficulty sustaining attn</td>
<td>2.) difficulty remaining seated</td>
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<td>3.) not listen when spoken to directly</td>
<td>3.) runs about/climbs excessively (adolesc w/ subjective restlessness)</td>
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<td>4.) not follow through/finish tasks</td>
<td>4.) difficulty playing/engaging in leisure activities quietly</td>
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<td>5.) difficulty organizing</td>
<td>5.) “on the go,” “driven by motor”</td>
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<td>6.) avoids/dislikes tasks requiring sustained attn</td>
<td>6.) talks excessively</td>
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<tr>
<td>7.) loses things</td>
<td>7.) blurts answers before questions completed</td>
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<tr>
<td>8.) easily distracted</td>
<td>8.) difficulty awaiting turn</td>
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<td>9.) forgetful</td>
<td>8.) interrupts/intrudes on others</td>
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ADHD DSM 5 CHANGES

• **Autism spectrum disorders** can now be classified with comorbid ADHD
  – Previously excluded by criteria that could not be attributed to another mental disorder
• “Neurodevelopmental” not “disruptive” to reflect brain developmental correlates
• ≥ 6/9 symptoms over the past 6mo
  – From either/both inattentive or hyperactive/impulsive list
• ≥ 5 symptoms for adults (>17yo) & description of symptoms more tailored to adults
  – DSM symptoms originally developed in children & symptoms/pattern may change w/ age & context
  – Can see age related decline in # of symptoms
• No “subtypes,” now “presentations”
  – Appendix: restricted inattention subtype worth further study
• Symptoms present by 12yo (not 7yo)
  – Multiple studies since 1994 show no difference between child identified by 7yo vs later in regards to course, outcome, severity, or tx response
“Typically, symptoms vary depending on context within a given setting. Signs of the disorder may be minimal or absent when the individual is receiving frequent rewards for appropriate behavior, is under close supervision, is in a novel setting, is engaged in especially interesting activities, has consistent external stimulation (e.g. via electronic screens), or is interacting in one-on-one situations (e.g. the clinician’s office).”
ADHD DSM 5 SHORTCOMINGS

• Retains behavioral focus. Not reflect underlying cognitive difficulties/executive dysfunction.

• Not address important role of emotions or impaired motivation. No symptoms included to reflect difficulty in modulating experience and expression of emotions.

• Not recognize the importance of problems in regulating sleep and alertness which have been identified in research on ADHD in children and adults.
ADDITIONAL CLINICAL CONSIDERATIONS

• DSM symptom cluster req’d but somewhat simplified description

• Display variable executive function deficits

• Poor regulation of attn gives appearance that child can pay attn when he/she “wants to”
  – e.g. studies baseball cards for hours but can’t focus on math homework

• Poor self perception & difficulty w/ self-external appraisal
  – can → positive & negative illusory bias (unrealistic optimism - ability to complete a project at the last minute – or pessimism – will always be blamed for problems)

• May develop demoralization & low self esteem 2/2 persistent impairments of untreated ADHD
  – Depression vs demoralization: 1° psych disorder vs untreated ADHD
  – Anxiety: 1° psych disorder vs untreated ADHD? Important to assess prior to starting stimulant
ADHD EPIDEMIOLOGY

- Most commonly dx pedi neurobehavioral disorder
  - affects 4-12% school-aged children
- M/F Ratio
  - Children M > F
  - Adults M = F
  - Likely due to ↓ rates aggression/disruptiveness in girls, so not referred until later
- DSM IV Subtypes:
  - Inattentive 20-30%
  - Hyperactive/impulsive < 15%
  - Combined 50-75%
    - most common, most severe, greatest risk of comorbidities
- Comorbidities common
  - anxiety disorders, depression, bipolar, ODD, conduct disorder, learning disabilities, substance abuse
ADHD PATHOPHYSIOLOGY

- **Heterogenous disorder** with multiple contributing factors:
  - genetic, neuroanatomical, neurochemical, environmental

- **Catecholamine dysregulation**:
  - DA (dopamine) and NE (norepinephrine) in prefrontal cortex (PFC) & fronto subcortical pathways

- **Functional & structural neuroimaging**:
  - smaller anterior cingulate cortex (ACC) & dorsolateral prefrontal cortex (DLPFC)
  - delay in dvmnt cortical thickness (pattern of dvmnt btwn ADHD & controls similar, but delayed in ADHD)
  - DLPFC, ACC & parietal areas remain thinner in ADHD adults
  - ↑ disorganization of white matter tracts emanating from PFC
  - attenuated frontostriatal activity on go/no go test (needed for inhibitory control & attn)
  - ↑activation nonfrontostriatal regions (ACC, parietal) vs controls
  - *stimulant tx shown to improve ACC & DLPFC activation*

- **Genetic**:
  - heritability 75% (1 indicates entirely genetically influenced, 0 is no genetic influence) vs depression/anxiety/asthma < 50%
  - likely polygenetic; evidence for candidate genes include DA recept’s, DA transporter, DA β-hydroxylase, SNAP25 gene

- **Environmental**:
  - maternal smoking during pregnancy, severe early deprivation
  - *ordinary variations in child-rearing do not contribute to ADHD*

(Postgrad Med.2010.122.97, CNS Drugs.2009.23 Suppl 1.33, JAACAP.2010.49.884)
FH: Not “does anyone have ADHD” but “who in family has ADHD?”
ANATOMY OF ADHD

Figure 1. Brain structures implicated in ADHD. Interacting neural regions have been implicated in ADHD. In particular, the dorsal anterior midcingulate cortex (daMCC), dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC), parietal cortex, striatum, and cerebellum—all key elements of cognitive/attention networks—have also been found to display functional abnormalities in multiple studies of ADHD.
ADHD – Prefrontal Cortex

• PFC volume on right smaller in ADHD
• PFC uses representational knowledge (i.e. working memory) to
  – guide overt responses (movement)
  – guide covert responses (attention)

• PFC lesions
  – ↓ ability to sustain attn (particularly over a delay)
  – ↓ ability to gate sensory input

J Clin Psychiatry. 2006. 67(suppl 8)
Fig. 2. The prefrontal cortex (PFC) is very sensitive to its neurochemical environment. The catecholamines are released in the PFC according to an arousal state, based on the relevance of the stimuli occurring in the environment. Either too little or too much catecholamine release impairs PFC function. Moderate levels of noradrenaline (NA) engage postsynaptic $\alpha_{2A}$-receptors to improve PFC function, while high levels engage $\alpha_1$ and $\beta_1$ which impair PFC function. Animal studies suggest that therapeutic doses of stimulants improve PFC function by increasing endogenous NA and dopamine (DA) stimulation of $\alpha_{2A}$ and $D_1$ receptors, respectively.
DA & NE in Prefrontal Cortex

- PFC rich in D1 receptors
- Stim of D1 leads to inverted U-shaped dose-resp influence on WM and attn regulation processes of PFC
- Modest D1 stim are essential to PFC fxn; high D1 impair WM

- NE improves PFC fxn via postsynaptic alpha 2A receptor at both cognitive & cellular level
  - Improves WM, attn regulation, behavior inhibition, planning
  - alpha-2 recept stim increases delay-related firing, the cellular mechanism of WM and behavior inhibition
  - alpha-2A recept stim increases “signal” in PFC
  - blocking alpha-2 recept w/ yohimbine markedly reduced delay-related firing -> impairs WM & impulse control
  - yohimbine infusions in PFC have been shown to induce locomotor hyperactivity

- High levels NE release impair PFC fxn via alpha-1 recept
  - phenylephrine impairs WM when infused into rats
  - at cellular level, alpha-1 recept stim suppresses delay-related neuronal firing
  - alpha-1 antagonists (prazosin) protect PFC cognitive abilities, preventing stress-induced PFC impairment
ADHD – Anterior Cingulate

• Roles in cognitive & emotional processing

• **Cognitive division:**
  – Strong reciprocal interconnections w/ lateral PFC, parietal, premotor & suppl motor
  – Role in **attention processing/executive fxn** via
    • Modulating stimulus selection (i.e. focusing attn)
    • Mediating response selection
  – Monitoring competition, complex motor control, motivation, novelty, error detection, working memory
  – Anticipation of cognitively demanding tasks

• **Affective division**
  – Connected to amygdala, periaqueductal gray, nucleus accumbens, hypothalamus, anterior insula, hippocampus, orbitofrontal
  – Outflow to autonomic, visceromotor, endocrine systems
  – Assesses **salience of emotional & motivational info** & regulation of emotional responses
**ACC – Cognitive & Affective Divisions**

![Diagram showing the cognitive and affective divisions of the ACC](image)

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*Fig. 2. Meta-analysis of activations and deactivations during cognitive and emotional studies.* Activations (a) and deactivations (b) are shown in 2-D spatial coordinates. The cognitive division is activated by Stroop and Stroop-like tasks divided attention tasks, and complex response selection tasks. It is deactivated (i.e., shows reduced blood flow or MR signal) by emotional tasks. The affective division is activated by tasks that relate to affective or emotional content, or symptom provocation. It is deactivated by cognitively demanding tasks. A direct comparison within the same subjects supports the cognitive versus affective distinction. The orange triangle indicates the activation of the cognitive division during the cognitive Counting Stroop. The same group of subjects activated the affective division (blue diamond) while performing the Emotional Counting Stroop. Although matched normal controls activated the cognitive division during the Counting Stroop (yellow triangle), subjects with attention-deficit/hyperactivity disorder failed to activate the region. Abbreviation: CC, corpus callosum.

ACC Activation

Figure 3. Anterior cingulate cognitive division activates in the normal control group but not in the ADHD group during the counting Stroop. The coronal slices (\(y = +21\) mm) for the control and ADHD groups show the KS statistical map data (for interference blocks minus the neutral blocks of scan one) superimposed on the group averaged Talairach and Tournoux (1988) transformed high-resolution structural scans. These coronal slices pass through the ACCd activation depicted in Figure 5 for the normal control subjects in the present study (represented by the anterior green triangle in Figure 5). The ACcd showed significantly higher activity in the normal control group during the interference blocks minus the neutral blocks (\(p = 6.0 \times 10^{-5}\)). In contrast, while the ADHD group did display significant activity in a frontostriato-insular-thalamic network (as evidenced by the bilateral insular activation seen in this slice and in Table 2b), they did not show significant activation anywhere in cingulate cortex.

Normal controls activate ACC during cognitive task but ADHD do not.

Decreased Frontal Volume – Sup Frontal & ACC

Figure 2. Cortical Parcellation. This is a cartoon representation of the cortical parcellation system. The upper left drawing is a lateral view, the lower left drawing is a sagittal view, and the middle and right drawings are axial views. Overall frontal lobe volume reduction is shown in blue. The significant reduction in superior frontal gyrus cortex (F1) and anterior cingulate gyrus cortex (CGa) is shown in darker blue.

DLPFC & ACC Volume Decrease

Nucleus Accumbens (NAc): Red
Dorsolateral Prefrontal Cortex (DLPFC): Blue
Anterior Cingulate Gyrus (CGa): Blue

of the nucleus accumbens and anterior cingulate gyrus. (Lower left panel) In red, the volume increase in the nucleus accumbens (NAc) and in blue, a volume decrease in the dorsolateral prefrontal cortex (DLPFC) and the anterior cingulate gyrus (CGa). (NAC and CGa are abbreviations derived from

Figure 3. Three-Dimensional (3-D) Isosurface Representation of the Right Anterior Cingulate Gyrus. This figure compares the average volumes of the control participants ($n = 18$) and persons with ADHD ($n = 24$) in the right anterior cingulate represented as 3-D isosurfaces (in both 3a and 3b). The pink color represents areas where the ADHD group has a larger isosurface than controls. The purple color represents areas where the control group has a larger isosurface than persons with ADHD. The greatest difference between the two groups is in the pregenual part of the anterior cingulate gyrus (CGa; BA 24/32) observed most clearly in 3b. These changes are also observed in the dorsal part of the anterior cingulate gyrus. Given that the control volumes are larger than those in ADHD, it is not possible to visualize all of the differences between the two groups. To make visible the maximal effect in the pregenual CGa, we set the purple on the right figure (3b) in transparency and allowed visualization of the underlying smaller CGa in ADHD (pink). The tool used for the creation of this figure is Surface Volume Visualizer (SVV) developed by the MGH Center for Morphometric Analysis.

MPH Activates Dorsal Ant Midcingulate Cortex

- DOUBLE BLIND placebo control.
- fMRI at baseline and again at week 6. OROS MPH showed higher daMCC activation at 6wks vs placebo. N=21 adults with ADHD.

*Figure 4. Individual-level dorsal anterior midcingulate cortex (daMCC) analyses confirmed that the methylphenidate osmetic-release oral system (OROS) and placebo groups did not differ at baseline, but the methylphenidate OROS group showed higher daMCC activation at 6 weeks. Specifically, although there was no main effect of treatment group ($F_{1,19}=2.2; P=.15$) or scan ($F_{1,19}=0.03; P=.87$), there was a significant predicted treatment group × scan interaction ($F_{1,19}=5.2; P=.04$), and a 2-tailed unpaired t test confirmed that at 6 weeks, the mean (SD) daMCC percentage functional magnetic resonance imaging (fMRI) signal change was higher in the methylphenidate OROS group (1.95% [1.4%]) than in the placebo group (0.74% [0.65%]) (mean difference, 1.2%; $t_{19}=2.47; P=.02$). Error bars represent SE; asterisk, significant difference during scan 2 at $P<.05$ level.*

MPH Activates Dorsal Ant Midcingulate Cortex

- DOUBLE BLIND placebo control.
- fMRI at baseline and again at week 6. OROS MPH showed higher daMCC activation at 6wks vs placebo. N=21 adults with ADHD.

ADHD – What’s in a Name?

• Not really about ability to “pay attention”
  – Name leads to confusion for parents
  – No problem w/ attn during preferred activities

• Actually about self-regulation
  – Therefore affects all areas of life
  – Regulating attn, motivation/level of arousal, emotion, frustration tolerance

• Skills/performance deficit vs volitional
  – Observers make incorrect/judgmental attributions about causes of behavior
  – All children want to succeed!
ADHD & EXECUTIVE FUNCTIONS

• **Executive Function:**
  – Refers to brain circuits that prioritize, integrate & regulate other cognitive functions
  – Provide the mechanism for self-regulation
• **Neuropsych/Psychometric Test Model**
  – e.g. Stop-Signal Task, Tower of Hanoi, Wisconsin Card Sorting
  – Only a percentage of ADHD pt’s have impaired EF
• **“Real world” model** of complex interacting deficits
  * (Russell Barkley, Thomas Brown)
  – ADHD is an impairment in development of EF or of brain’s self-regulatory mechanisms
  – All pt’s with ADHD have EF impairments

EF: Definitions

- **Self regulation:**
  - Any action directed at the self that is used to modify behavior so as to alter the likelihood of a later consequence
  - ADHD = SRDD (self-regulation deficit disorder)

- **EF:**
  - A specific type of action directed at oneself for the purposes of self regulation
  - EF = SR (each EF is a type of SR)

- ADHD = SRDD = EFDD  
  
* (Barkley, 2012)*
EF: Definitions

• Contemporary view of EF often overfocused on “cold,” cognitive constructs
  – Response inhibition, working memory, set shifting, sustained attention

• Must also encompass the more widespread deficits
  – Behavioral, social, emotional, economic, occupational, moral/ethical

(Barkley, 2012)
# EF: Definitions

**Barkley**

<table>
<thead>
<tr>
<th>1. Self-directed Attn</th>
<th>2. Self-Restraint/Inhibition</th>
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<tbody>
<tr>
<td><strong>Self-awareness</strong></td>
<td><strong>Impulse control</strong> (motor, verbal, cognitive, emotional)</td>
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<td><strong>Self-monitoring</strong></td>
<td>Contemplated behavior is not kept private</td>
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<tr>
<td><em>Appear unaware of social cues (knowledge &amp; insight about oneself &amp; impact of behavior on other’s)</em></td>
<td>Delayed gratification</td>
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<td></td>
<td>Inhibit prepotent response &amp; interrupt ongoing response</td>
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<td></td>
<td><em>Appear selfish, impulsive, irrational, hyperactive</em></td>
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<tr>
<td><strong>Nonverbal WM</strong></td>
<td><strong>Verbal WM</strong></td>
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<tr>
<td>Holding events in mind (using imagery)</td>
<td>Internalization of language</td>
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<tr>
<td>Sense of past &amp; future (temporal myopia)</td>
<td>Reading comprehension</td>
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<tr>
<td>Hindsight, foresight, sense of self across time</td>
<td>Ability to use self-talk for self-guidance</td>
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<tr>
<td>Cross temporal organization of behavior</td>
<td>Self description/ reflection/ instruction/ questioning</td>
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<tr>
<td><em>Appear late for appointments/deadlines, unprepared, disorganized, forgetful</em></td>
<td>Rule-governed behavior</td>
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<td></td>
<td><em>Appear to ignore rules and directions, don’t follow through on plans, poor reading comprehension, can’t prioritize</em></td>
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## EF: Definitions

### Barkley

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<tr>
<td><strong>Emotional regulation</strong></td>
<td><strong>Problem-solving</strong></td>
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<tr>
<td>Ability to self-generate emotions</td>
<td>Goal-directed innovation</td>
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<tr>
<td>Decision-making about risk/benefit trade-offs</td>
<td>Ability to generate new strategies when faced with obstacle to a goal</td>
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<tr>
<td>Appear <em>quick-tempered, easily frustrated</em></td>
<td>Cognitive flexibility</td>
</tr>
<tr>
<td><strong>Internal/self-motivation</strong></td>
<td><em>Appear inflexible and “rigid,” give up on goals in face of obstacles, likely fall back on overlearned automatic behaviors</em></td>
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<tr>
<td>Persistence towards tasks &amp; goals</td>
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<tr>
<td>Generate intrinsic motivation for task without immediate reward</td>
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<td>Appear <em>lazy</em></td>
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<td><strong>Regulation of arousal</strong></td>
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<tr>
<td>Appear <em>bored, in “a fog,” daydreamy, apathetic</em></td>
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ADD symptoms reflect kinks in the brain’s “executive functions,” which manage learning, perception, judgment, and so on. Dr. Brown organizes executive functions into six clusters (above). Impairments in these clusters tend to show up together in persons with ADD, and to respond together to ADD medication.
EF: Methods of Assessment
Psychometric Tests

EXAMPLES:
- Wisconsin Card Sorting
- Stroop
- Trail Making Test
- Tower of London
- Stop Signal
- Delis-Kaplan Executive Function System/DKEFS (includes battery of several subtests)
EF: Methods of Assessment
Psychometric Tests

• **Low to moderate reliability**
  – Limited utility for detecting PFC injury
  – Frontal lobe injuries & ADHD: few impaired on tests, but are impaired on rating scales & direct observation in natural settings

• **Poor ecological validity (extent to which indicate real world impairment)**
  – Poor correlation with more ecologically valid means of assessing EF in everyday life
  – When study children with frontal lobe lesions, TBI and ADHD
  – Single EF test shares 0-10% of variance with EF ratings/observations; best combination of tests shares only 9-20% of variance

• **Low, often nonsignificant predictive validity**
  – Poorly predict impairment in various major life activities: occupational & educational functioning, driving, criminal conduct, etc

(Barkley 2012)
EF: Methods of Assessment
Psychometric Tests

• May have some role in evaluating basic, low level cognitive EF components

• Deficient:
  – Social nature & purposes of EF
  – Cross-temporal regulation of behavior (tests given over very short time period)
  – Complexity & hierarchical nature of goal-directed behavior in natural settings
  – Emotional regulation & motivational components

(Barkley, 2012)
EF: Methods of Assessment
Rating Scales & Interviews

• Clinical Interview
• Direct observations of human action in natural settings
• Rating scales completed by pt or others (family, teachers)
EF: Methods of Assessment
Rating Scales & Interviews

- EF rating scales
  - Behavior Rating Inventory of Executive Functioning (BRIEF)
  - Barkley Deficits in Executive Functioning Scale
EF: Methods of Assessment
Rating Scales & Interviews

- **Adaptive behavior scales**
  - Vineland Adaptive Behavior Inventory, Adaptive Behavior Assessment System, Scales of Independent Behavior Revised
- **Social Skills Rating Scale**
- **Impairment scales**
  - Child Behavior Checklist (CBCL), Behavior Assessment System for Children-2 (BASC), Barkley Functional Impairment Scale-Children & Adolescents
- **Clinical interview** regarding functioning/impairment in:
  - Education, work, family, social relationships, criminal record, driving record, etc
EF Interview

- Emotionally dysregulated?
  - React easily, poor frustration tolerance, “Everything is great! Everything is terrible!”

- Intrinsic motivation?
  - Procrastinate & avoid homework & undesired activities

- Typical “punishments” & rewards don’t work
  - Don’t seem to care if promise reward/punishment in the future & not affected by past punishments

- Difficulty with transitions

- Poor social awareness; seem unaware of effect on others

- Teachers report don’t work to potential (performance deficit, not knowledge deficit)
Working Memory (WM) Interview

- Do remember what read at top of page when get to the bottom?
- If give list of instructions, how many steps completed before forget their place
  - “Go upstairs, put backpack away, change into play clothes, brush teeth and come back downstairs.”
- **Reading comprehension**
  - Distinguish from developmental reading disability
- **Math**
  - Difficulty with multiple steps
  - Distinguish from dyscalculia
- **Written expression** very difficult
  - (relies on multiple components of EF)
EF: Methods of Assessment
Neuropsych Testing

• Careful when reading patients’ neuropsych test reports!

• Review the data (psychometric tests vs Rating Scales; DKEFS vs BRIEF)
  – not just the summary conclusions
• Railroad foreman, explosion caused tamping iron to propel through skull; frontal lobe devastated

• “He is fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint of advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operation, which are no sooner arranged than they are abandoned in turn for others appearing more feasible. In this regard, his mind was radically changed, so decidedly that his friends and acquaintances said he was ‘no longer Gage.’” (Harlow 1868)
Phineas vs “Johnny”

1) Irreverent
2) Indulging at times in the grossest profanity
3) Little deference for his fellows
4) Impatient of restraint of advice when it conflicts with his desires
5) Pertinaciously obstinent
6) Capricious and vacillating
7) Devising many plans of future operation, which are no sooner arranged than they are abandoned in turn for others appearing more feasible.

1) Talks back to teachers
2) Verbally impulsive
3) Poor social awareness
4) Doesn’t listen/follow rules
5) Oppositional
6) Emotionally dysregulated
7) Doesn’t follow through; many unfinished projects
EF in ADHD

• Not absolute loss of EF abilities (vs severe brain injury), but less developed
  – Appear less mature, age-inappropriate

• Disorder of performance, not knowledge!

• Careful of attributional thinking
Approach to EF Deficits

- **Externalize information**
  - Physical/visual cues in immediate context vs nag to “try harder to remember”

- **Externalize motivation**
  - “no matter how great the plan or mental map constructed to attain a goal, no self-powered, acting entity is going anywhere without a source of fuel”

(Barkley, 2012)
Approach to EF Deficits

- Externally represent or remove gaps in time
  - Small daily tasks vs project due in 1 month
- Intervene at point of performance in natural settings
  - “that place and time in the natural setting of the person’s life where they are failing to use what they know – they are failing to engage effectively in EF (self-regulation).”
- Approach EF deficits as chronic conditions
  - Symptom breakthrough & crises likely to occur
  - Do not withdraw treatments expecting permanent change

(Barkley, 2012)
• If a child *could* do well, he *would* do well.
  – Challenging behavior occurs when the demands of the environment exceed a kid's capacity to respond adaptively.
  – If have to skills for adaptive behavior, won’t exhibit challenging behavior

• Your explanation guides your intervention.
  – If attribute challenging behavior to lagging skills & unsolved problems, then typical reward/punishment not ideal approach.

• Whether of the natural or adult-imposed variety, consequences do not teach lagging cognitive skills or help kids solve problems.

-Dr. Ross Greene, Lost at School
# ASSESSMENT OF LAGGING SKILLS & UNSOLVED PROBLEMS (Rev. 11-12-12)

**Child’s Name:** ________________  **Date:** ________________

**Instructions:** The ALSUP is intended for use as a *discussion guide* rather than as a freestanding check-list or rating scale. It should be used to identify specific lagging skills and unsolved problems that pertain to a particular child or adolescent. If a lagging skill applies, check it off and then (before moving on to the next lagging skill) identify the specific expectations the child is having difficulty meeting in association with that lagging skill (unsolved problems). A non-exhaustive list of sample unsolved problems is shown at the bottom of the page.

## LAGGING SKILLS

- Difficulty handling transitions, shifting from one mindset or task to another
- Difficulty doing things in a logical sequence or prescribed order
- Difficulty persisting on challenging or tedious tasks
- Poor sense of time
- Difficulty maintaining focus
- Difficulty considering the likely outcomes or consequences of actions (impulsive)
- Difficulty considering a range of solutions to a problem
- Difficulty expressing concerns, needs, or thoughts in words
- Difficulty understanding what is being said
- Difficulty managing emotional response to frustration so as to think rationally
- Chronic irritability and/or anxiety significantly impede capacity for problem-solving or heighten frustration
- Difficulty seeing the “grays”/concrete, literal, black-and-white, thinking
- Difficulty deviating from rules, routine
- Difficulty handling unpredictability, ambiguity, uncertainty, novelty
- Difficulty shifting from original idea, plan, or solution

## UNSOLVED PROBLEMS

| ________________ | ________________ | ________________ | ________________ |}
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</table>
Interventions shown to Aid Executive Function Development in Children 4–12 Years Old

Adele Diamond¹ and Kathleen Lee¹
¹University of British Columbia and Children’s Hospital, Vancouver, BC Canada


- Computerized cognitive training
- Martial arts, mindfulness
- Aerobic exercise/ sports
- School-based programming

- Those with poorest scores show greatest gains
- Demanding/ adaptive measures most effective
- Children as young as 4-5 may benefit
  - Possibly greatest benefits to ages 8-12
Figure 1.
A teen working at a CogMed© game.
Evidence for working memory training in ADHD is growing.
REFRAMING ADHD

• EDUCATE FAMILIES about ADHD & EF
  – Can greatly impact how others approach the pt
• EDUCATE THE PT
  – Impacts ability to self-advocate
  – Learn to be active participant in treatment decisions
  – Impacts self-esteem
• Redirect attributional thinking
  – Not “wouldn’t” but “couldn’t”
  – Not “lazy” or “doesn’t care” but deficit in skills/performance/cognitive development
  – Not “irresponsible,” when forgetful/misses appt’s/loses things
• Manage expectations
• Discuss how to support the pt in implementing skills
Pharmacotherapy for ADHD

- **Stimulants (FDA approved)**
  - Methylphenidate
  - Amphetamine compounds
- **Atomoxetine (FDA-approved)**
- **Antihypertensives (FDA-approved)**
  - Guanfacine extended-release
  - Clonidine extended-release
- **Antidepressants**
  - Bupropion
  - Tricyclics
- **Modafinil**
- **Research**
  - Natural agents
  - Combined
  - Anti-Alzheimer's/cog enhancing agents

*(Wilens & Spencer, Postgraduate Medicine, 2010)*
ADHD OUTCOME & PROGNOSIS

• ADHD should be viewed as chronic condition across the lifespan
• If no longer meet full DSM diagnostic criteria as get older, not equivalent to remission
  – Symptoms/impairment in adolescents/adults obscured by compensatory strategies, learned avoidance of ADHD-sensitive tasks, poor self report
  – Typical DSM IV symptoms differ/subthreshold in adolescents/adults: inner restlessness, impulsive decision making, poor focus in meetings, etc
ADHD OUTCOME & PROGNOSIS

• ADHD pt’s have ↑ risk/rates:
  – smoking & substance abuse (SA), w/ SA more severe & longer lasting
  – psychosocial deficits (poor self esteem, fewer friends, social rejection)
  – hospitalizations for accidental injuries; teen pregnancies
  – driving problems (speeding violations, accidents)
  – academic difficulties (repeated grades, delinquency, need for special ed)
  – employment & family/marital problems

(Postgrad Med.2008.120.48.)
ADHD OUTCOME & PROGNOSIS

• Adherence to stimulant tx shown to:
  – ↓ risk for anxiety & depressive disorders
  – ↓ risk SA (studied in adolescent girls, no difference in SA when followed into adulthood)
  – ↓ rate of school failure/repeated grades
  – ↓ rate of smoking to control levels
  – improve self-esteem & peer relations
  – improve driving

• Overall costs (treated & untreated):
  – estimated addtl cost of ADHD (vs controls) in U.S. is $31.6 billion (including costs for pt and family member health care and work-lost)

RESOURCES FOR PROVIDERS

- ADHD Toolkit (nichq.org)
- www.schoolpsychiatry.org
- Russell Barkley Fact Sheets on ADHD, EF, Classroom Accommodations (www.russellbarkley.org/factsheets)
- Ross Greene, PhD
  - “The Explosive Child”
  - www.livesinthebalance.org (resources for parents to work on challenging behavior)
- www.ADHDMedicationGuide.com
TO:

RE: , DOB

Tues,

To Whom It May Concern:

____ was evaluated in the MGH Pediatric Cognitive-Behavioral Neurology Clinic on ______ and diagnosed with Attention Deficit Hyperactivity Disorder (likely inattentive, hyperactive/impulsive, combined type). He has evidence for associated deficits in working memory and executive functions (e.g. adaptive problem-solving, organization, time-management, set-shifting, emotional/motivational regulation), with poor frustration tolerance. He is being started on stimulant medication (_____ ) with slow titration up in dosage to help manage his ADHD, but he will require school accommodations as well to insure that he is able to access the curriculum and make academic and social progress.

To address the ADHD, in-classroom accommodations should be made, such as preferential seating, eye contact by teacher when giving instructions, one instruction at a time, short work periods, frequent work breaks, and extra time for coursework, homework and tests if needed. A separate quiet room for test taking should be made available when needed. He should be graded on his knowledge of the subject matter and not penalized for organization, neatness or careless errors.

To address the executive dysfunction, training in executive function and study skills (organization, time management, test preparation) will be necessary. This can be accomplished in an Academic Strategies class or in the Learning Resource Room. The use of organizers and time management aids should be implemented, and a system put in place to insure that he is recording his assignments correctly and has all necessary supplies/books both at home and at school. It is important that ______’s parents and teachers have frequent communication.

These accommodations can be made part of an IEP or 504 plan. If needed, the school should perform a CORE evaluation to determine additional details of the various accommodations that will be implemented. If a CORE evaluation will be scheduled in the future, we do recommend implementation of some of the basic accommodations outlined above in the interim, given ______’s confirmed diagnosis of ADHD and executive dysfunction and potential for falling behind in school.

We would ask that the enclosed Vanderbilt Assessment forms be filled out by ______’s teacher(s) based upon their assessment of him prior to starting stimulant medication (prior to _____), and again after 1-2 month(s) on the medication. These forms will be reviewed at ______’s follow-up visits.

Please feel free to contact us if you have any further questions.

Sincerely,

M. Zelime Ward, MD
Pediatric Neurology Attending
THANK YOU!!
ADHD TREATMENT

Probably the most effective drug I could recommend for your child's problems is Ritalin.

Mum! Dad said that if strange men offer me drugs, I should just say 'No'.

Emma Malester 2005
Pharmacotherapy for ADHD

- **Stimulants (FDA approved)**
  - Methylphenidate
  - Amphetamine compounds
- **Atomoxetine (FDA-approved)**
- **Antihypertensives (FDA-approved)**
  - Guanfacine extended-release
  - Clonididine extended-release
- **Antidepressants**
  - Bupropion
  - Tricyclics
- **Modafinil**
- **Research**
  - Natural agents
  - Combined
  - Anti-Alzheimers/cog enhancing agents

(Wilens & Spencer, Postgraduate Medicine, 2010)
ADHD MEDICATION

• Awareness of what is helped by stimulants vs what is not

• Higher order EF not as responsive to stimulants
  – So will still need a “surrogate frontal lobe”
  – But important to teach child to develop good habits/problem-solving so don’t fall off cliff when get to college (demands↑ as supports/structure↓)

• Practice regulating use of their meds/taking correctly or can’t expect them to do it in college
STIMULANT MEDICATIONS

- Work to increase intrasynaptic catecholamines (DA & NE)
- AMP vs MPH
- 65-75% pt’s show clinical response to a stimulant; ↑’s to 85% if tried both MPH & AMP
  - Studies show 25% resp to MPH, 25% to AMP, 50% to both; currently unable to predict how/who will respond
Fig. 1 Overlapping but distinct putative mechanisms of action of a methylphenidate (MPH) and b amphetamine (AMF) at the dopamine synapse. VMAT2 vesicular monoamine transporter 2.
STIMULANT DOSING

• “Linear” dose-response curve to stimulants
  – ↑symptom reduction w/ ↑’ing doses

• Start at lowest dose & titrate up Q3-7 days
  – Titrate up to max tolerable for symptom control;
    not titrated according to mg/kg guidelines; each pt
    has individual dose-resp curve
  – Use objective measure to monitor sx improvement

• long-acting now preferred to short-acting for
  – ease administration
  – ↑adherence
  – (youngest pt’s/preschool may prefer short-acting
    for smaller doses)

ADHD and Methylphenidate: Dose Effects on Attention in Clinic and Classroom

Rapport, et al. 1987
## STIMULANTS: Duration of Action & Max Dose

<table>
<thead>
<tr>
<th>Duration Action</th>
<th>MPH-based</th>
<th>AMP-based</th>
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</thead>
<tbody>
<tr>
<td></td>
<td><em>(max 2mg/kg/day except dex-MPH &amp; MPH patch 1mg/kg/day)</em></td>
<td><em>(max 1.5mg/kg/day except Vyvanse 1mg/kg/day)</em></td>
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<tr>
<td><strong>Short-acting</strong></td>
<td>[3-5hr] Ritalin, Methylin, Focalin (dex-MPH)</td>
<td>[4-6hr] Dexedrine (dextro-AMP), Dextrostat</td>
</tr>
<tr>
<td><strong>Intermediate-acting</strong></td>
<td>[3-8hr] Ritalin SR, Metadate ER, Methylin ER</td>
<td>[6-8hr] Adderall (AMP mixed salts), Dexedrine spansules</td>
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<tr>
<td><strong>Intermediate/long-acting</strong></td>
<td>[8-10hr] Metadate CD, Ritalin LA</td>
<td></td>
</tr>
<tr>
<td><strong>Long-acting</strong></td>
<td>[10-12hr] Focalin XR, Concerta (OROS MPH), Daytrana patch, Quillivant XR (new liquid formulation)</td>
<td>[8-12hr] Adderall XR, Vyvanse (prodrug lisdexamphetamine)</td>
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</tbody>
</table>

*Dosing may exceed FDA approved limits.*
## SUPPLEMENTAL TABLE 3  FDA-Approved Medications: Dosing and Pharmacokinetics

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<thead>
<tr>
<th>Medication</th>
<th>Brand</th>
<th>Initial Titration Dose</th>
<th>Frequency</th>
<th>Time to Initial Effect</th>
<th>Duration, h</th>
<th>Maximum Dose (per FDA guidelines)</th>
<th>Available Doses</th>
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<tr>
<td>Mixed amphetamine salts</td>
<td>Adderall&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.5–5.0 mg</td>
<td>QD–BID</td>
<td>20–60 min</td>
<td>6</td>
<td>40 mg</td>
<td>5.0, 7.5, 10.0, 12.5, 15.0, 20.0, and 30.0-mg tablets</td>
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<tr>
<td></td>
<td>Adderall XR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>10</td>
<td>40 mg</td>
<td>5-, 10-, 15-, 20-, 25-, and 30-mg capsules</td>
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<tr>
<td>Dextroamphetamine</td>
<td>Dexedrine&lt;sup&gt;a&lt;/sup&gt;/Dextrostat</td>
<td>2.5 mg</td>
<td>BID–TID</td>
<td>20–60 min</td>
<td>4–6</td>
<td>40 mg</td>
<td>5- and 10-mg (Dextrostat only) tablets</td>
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<tr>
<td></td>
<td>Dexamfetamine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg</td>
<td>QD–BID</td>
<td>≥ 60 min</td>
<td>≥ 6</td>
<td>40 mg</td>
<td>5-, 10-, and 15-mg capsules</td>
</tr>
<tr>
<td>Lisdexamfetamine</td>
<td>Vyvanse</td>
<td>20 mg</td>
<td>QD</td>
<td>60 min</td>
<td>10–12</td>
<td>70 mg</td>
<td>20-, 30-, 40-, 50-, 60-, and 70-mg capsules</td>
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<td>Methylphenidate</td>
<td>Concerta</td>
<td>18 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>12</td>
<td>54 mg (≤ 13 y); 72 mg (≥ 13 y)</td>
<td>18-, 27-, 36-, and 54-mg capsules</td>
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<tr>
<td></td>
<td>Methyl ER</td>
<td>10 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>8</td>
<td>60 mg</td>
<td>10- and 20-mg tablets</td>
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<td>Methylin</td>
<td>5 mg</td>
<td>BID–TID</td>
<td>20–60 min</td>
<td>3–5</td>
<td>60 mg</td>
<td>5-, 10-, and 20-mg tablets and liquid and chewable forms</td>
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<tr>
<td></td>
<td>Daytrana</td>
<td>10 mg&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Apply for 9 h</td>
<td>60 min</td>
<td>11–12</td>
<td>30 mg</td>
<td>10-, 15-, 20-, and 30-mg patches</td>
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<tr>
<td></td>
<td>Ritalin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 mg</td>
<td>BID–TID</td>
<td>20–60 min</td>
<td>3–5</td>
<td>60 mg</td>
<td>5-, 10-, and 20-mg tablets</td>
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<td>Ritalin LA</td>
<td>20 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>6–8</td>
<td>60 mg</td>
<td>20-mg capsules</td>
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<tr>
<td></td>
<td>Ritalin SR</td>
<td>20 mg</td>
<td>QD–BID</td>
<td>1–3 h</td>
<td>2–6</td>
<td>60 mg</td>
<td>10-, 20-, 30-, 40-, 50-, and 60-mg capsules</td>
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<tr>
<td></td>
<td>Metadate CD</td>
<td>20 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>6–8</td>
<td>60 mg</td>
<td>10-, 20-, 30-, 40-, 50-, and 60-mg capsules</td>
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<tr>
<td>Dexamphetamine</td>
<td>Focalin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.5 mg</td>
<td>BID</td>
<td>20–60 min</td>
<td>3–5</td>
<td>20 mg</td>
<td>2.5-, 5.0-, and 10.0-mg tablets</td>
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<tr>
<td></td>
<td>Focalin XR</td>
<td>5 mg</td>
<td>QD</td>
<td>20–60 min</td>
<td>8–12</td>
<td>30 mg</td>
<td>5-, 10-, and 20-mg tablets</td>
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<tr>
<td>Atomoxetine</td>
<td>Stratter&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.5 mg/kg per d, then increase to 1.2 mg/kg per d; 40 mg/d for adults and children at &gt; 154 lb, up to 100 mg/d</td>
<td>QD–BID</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>1.4 mg/kg</td>
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<tr>
<td></td>
<td>Intuniv</td>
<td>1 mg/d</td>
<td>QD</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>4 mg/d</td>
<td>1-, 2-, 3-, and 4-mg tablets</td>
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<tr>
<td></td>
<td>Kapvay</td>
<td>0.1 mg/d</td>
<td>QD–BID</td>
<td>1–2 wk</td>
<td>At least 10–12 h</td>
<td>0.4 mg/d</td>
<td>0.1- and 0.2-mg tablets</td>
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QD indicates daily; BID, twice daily; TID, three times daily.

* Available in a generic form.

* Dosages for the dermal patch are not equivalent to those of the oral preparations.
STIMULANT “PROFILES”

- **Single “Camel Hump:”**
  - Ritalin, Focalin, Adderall, Dexedrine tablet

- **Double “Camel Hump:”**
  - Adderall XR, Focalin XR, Ritalin LA (all 50:50)

- **Ascending:**
  - Concerta (22:78), Metadate CD (30:70), Daytrana, Vyvanse, Dexedrine Spansule

- **Flat:**
  - Ritalin SR (but in wax-based matrix so only small amt absorbed & inconsistent delivery), Methylin ER

(Slide adapted from Dr. Jefferson Prince)
### ADHD Medication Guide

#### Methylphenidate Derivatives – Long Acting/Extended Release

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<tr>
<th>Product</th>
<th>Strength 1</th>
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<th>Strength 3</th>
<th>Strength 4</th>
<th>Strength 5</th>
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<td>Concerta® †</td>
<td>18 mg</td>
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<td>Focalin® XR ‡</td>
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<td>Methylfin® ER</td>
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<td>Ritalin® SR</td>
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#### Methylphenidate Derivatives – Short Acting/Immediate Release

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<th>Strength 3</th>
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<tbody>
<tr>
<td>Focalin®</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>10 mg</td>
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<tr>
<td>Ritalin®</td>
<td>5 mg</td>
<td>10 mg</td>
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<tr>
<td>Methylfin®</td>
<td>5 mg</td>
<td>10 mg</td>
<td>20 mg</td>
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<tr>
<td>Methylfin® Chewable §</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>10 mg</td>
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<tr>
<td>Methylfin® Solution §</td>
<td>5mg/5ml</td>
<td>10mg/5ml</td>
<td></td>
</tr>
</tbody>
</table>

*Disclaimer: The ADHD Medication Guide was created by Dr. Andrew Adesman of the North Shore-LIJ Health System. The North Shore-Long Island Jewish Health System is not affiliated with or the owner of any of the brands referenced in this Guide.

The Guide should not be used as an exclusive basis for decision-making. The user understands and accepts that if the health system were to accept the risk of harm to the user from use of this Guide, it would not be able to make the Guide available because the cost to cover the risk of harm to all users would be too great. Thus, use of this ADHD Medication Guide is strictly voluntary and at the user’s sole risk.

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ADHD Medication Guide*

Amphetamine Derivatives – Long Acting/Extended Release

- Vyvanse® (lisdexamfetamine) 20mg, 30mg, 40mg, 50mg, 60mg, 70mg
- Adderall XR® (mixed amphetamine salts) 5mg, 10mg, 15mg, 20mg, 25mg, 30mg
- Dexedrine Sustained Release® (a amphetamine) 5mg, 10mg, 15mg

Amphetamine Derivatives – Short Acting/Immediate Release

- Adderall® (mixed amphetamine salts) 5mg, 7.5mg, 10mg, 12.5mg, 15mg, 20mg, 30mg
- Dextroamphetamine 5mg, 10mg
- ProCentra® (Bubblegum Flavor) 5mg/5ml

Non-Stimulants

- Intuniv® (guanfacine, extended release) 1mg, 2mg, 3mg, 4mg
- Kapvay® (clonidine, extended release) 0.1mg
- Strattera® (atomoxetine) 10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg

Medication Administration Key

† Must be swallowed whole
¥ Can be dissolved in liquid
§ Chewable
+ Capsule can be opened and medication sprinkled on applesauce

AGES FOR WHICH MEDICATIONS HAVE AN FDA INDICATION FOR TREATMENT OF ADHD.

<table>
<thead>
<tr>
<th>Tab</th>
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<th>6-12</th>
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*Disclaimer: The ADHD Medication Guide was created by Dr. Andrew Adesman of the North Shore-LIJ Health System. North Shore-Long Island Jewish Health System is not affiliated with the owner of any of the brands referenced in this Guide.

The ADHD Medication Guide is a visual aid for professionals caring for individuals with ADHD. The Guide includes only medications indicated for the treatment of ADHD by the FDA. In clinical practice, this guide may be useful to assist patients in identifying medications previously tried, and may allow clinicians to identify ADHD medication options for the future. Medications have been arranged on the card for ease of display and comparison, but dosing equivalency cannot be assumed. Practitioners should refer to the FDA-approved product information to learn more about each medication. Although every effort has been made to depict each medication in its actual size and color, we cannot guarantee that there are not minor distortions in the final image. This guide is accurate as of January 11, 2012. For updates, visit www.ADHDMedicationGuide.com.

- Future revisions of the ADHD Medication Guide can be viewed at www.ADHDMedicationGuide.com
- Laminated copies of the ADHD Medication Guide can be obtained at: www.ADDWarehouse.com
- For questions or comments, contact Dr. Andrew Adesman at ADHDMedGuide@NShS.edu
STIMULANT PEARLS

• **MPH**
  - Not affected by food
  - Duration does *not* ↑ with ↑ dose
  - Often need dose ↑ in first 6-12mo, even without growth
  - Low bioavailability (20-25%) & genetic polymorphisms may → ultra slow metab
    • Dex-MPH & Daytrana patch have higher bioavailability

• **AMP**
  - Vit C ↓ absorption, alkalinizing agents (antacids) ↑ absorption
  - Fatty food slows absorption
  - Duration can ↑ with ↑ dose
  - Higher (75%) & more consistent bioavailability
  - Vyvanse (*lisdexamfetamine*) has longer ½-life
    • If minor rxm to adderall (just don’t feel good) but good clinical resp, change to LDX might give same efficacy w/out SE
STIMULANT PEARLS

• Pay attn to profiles
  – Do need 50% in am or ascending profile?
• Can use long-acting BID
• Add IR onto long-acting
  – “boost” in the morning
  – For homework
  – On weekends if sleep in too late
• Long-acting for younger children
  – Sprinkles: Ritalin LA, Metadate CD, Focalin XR, Adderall XR
  – Liquid Quillivant: if need to titrate to exact dose that can’t achieve with sprinkles
STIMULANT PEARLS

• Check serum MPH level \( \text{want} < 50-60\text{ng/mL} \) if only partial resp to max dose MPH w/ no side effects
  – MPH has low bioavailability & might not be absorbing
  – If level low normal, can increase dose or consider patch

• Daytrana Patch:
  – much better bioavailability than po
  – Approved for 9hr wear but can wear up to 16hr
  – Remove approx 3hr prior to desired off time
  – Takes longer for onset
    • Can put on in morning while still sleeping. Study showed improved symptoms in morning & kids \text{still ate breakfast}
  – “Pink” under the patch is ok
    • if notable skin rxn try topical benadryl or hydrocortisone prior to applying patch
    • Rotate sites
COMMON STIMULANT SE’S

• **Sleep problems:**
  – IMPORTANT to document any sleep issues (VERY common) prior to initiation of stimulants
  – If long-acting → intermediate acting (i.e. concerta → metadate CD)
  – Consider melatonin, alpha-agonist, amitriptyline

• **HA:** consider problem might be ↓ fluid intake

• **Abd discomfort:** take with food (but careful with AMP)
COMMON STIMULANT SE’S

• Transient ↑ in tics
  – Often abate with time
  – NOT contraindicated
  – Start low & go slow
  – TACT (Treatment of ADHD & Tics) Study:
    • Double-blind placebo controlled trial showed no difference in tic exacerbation w/ MPH, clonidine or placebo; combo MPH + clonidine best for both ADHD & tics.
    • Tic severity ↓ in all Rx groups vs placebo (clonidine + MPH > clonidine > MPH alone > placebo).

(Neurology 2002.58.527)
COMMON STIMULANT SE’S

• Dysphoric rxn (irritability, mood)
  – Timing: during med effect or rebound/withdrawal?
  – Alter formulation of same stimulant vs change to another stimulant or non-stimulant
  – For very young (4-6yo), wait a few yrs & try again
  – If just “edgy,” 1st consider change in formulation/stimulant or consider adjunct beta-blocker (propranolol) or alpha-agonist

• Appetite suppression
  – Don’t force feed
  – Encourage frequent snacks & eating when med not effective – breakfast, after school snack, dinner
  – Focus on total calories per day
  – Don’t obsess over mild weight loss
  – Long term studies show total height not lost
  – Consider adjunct periactin or nortriptyline if needed; drug holidays
STIMULANT SIDE EFFECTS

- **Infrequent SE’s:**
  - Incre HR/BP (should only see very slight ↑SBP, not much DBP)
  - Dizziness
  - Growth suppression
  - Hallucinations/mania (confirm taking correct dose)
  - Notable ↑tics

- **If SE intolerable**, often alleviated by Δ to different formulation of same stimulant or Δ to alternate stimulant (MPH to AMP or vice versa)
STIMULANTS AND CV CONCERNS

- Rate sudden death in kids on stimulants not shown to exceed base rate in population
- Obtain pt & FH of CV disease
  - Severe palpitations, CP, fainting, exercise intolerance not accounted for by obesity
  - WPW, strong hx sudden death, HOCM, long Qt
  - Postop Tetralogy of Fallot, coronary artery abnorm’s, subaortic stenosis are known problems requiring special consideration
- If no significant hx, do not need screening EKG or echo
- If concern, refer to cardiology for possible EKG or echo

(NEJM.2011.365.1896; JAACAP.2007.46.894)
Non-Stimulant Review

- **Non-stimulants**: often less effective than stimulants & delayed onset action; good if stimulant non-response/adverse effects or as adjunctive for partial response (indicated below)
  - **atomoxetine** (FDA approved): selective NE reuptake inhib (NRI); start 0.5mg/kg/day x 2wk, then ↑ 1.2mg/kg/day; consider for ADHD w/ anxiety, tics, substance abuse
  - **α-adrenergic agonists** (FDA approved): guanfacine ER (Intuniv) & clonidine ER (Kapvay); consider for ADHD w/ tics, anxiety, sleep disturbance, emotional dysregulation, ODD
  - **Non-FDA approved but demonstrated benefit**: buproprion (NE & DA reuptake inhib), TCA’s (imipramine, nortriptyline), modafinil (for arousal/motivation), melatonin (for sleep)

- **School & home based interventions**:  
  - Medication can be ineffective for more complex executive fxn deficits; school accommodations (504 plan or IEP), extended time on tests, preferential seating, organizers, daily progress reports, tutors, home/classroom behavioral interventions, social skills remediation
Atomoxetine: When to Use

• Better for inattention than hyperactivity
• Monotherapy (higher likelihood of response as first start)
• Stimulant nonresponders
• Stimulant partial responders (monotherapy, adjunctive therapy-no drug interactions with stimulants)
• Adverse effects to stimulants
• Concerns of stimulant diversion
• Comorbid ADHD plus
  – Oppositional disorder
  – Anxiety
  – Tics
  – Substance abuse

*Slide from Dr. Timothy Wilens, MGH Pediatric Psychiatry*
Atomoxetine: Dosing & SE’s

Dosing (Wilens’ method):
- Start at 0.5 mg/kg/day for two weeks
- Then increase to 1.2 mg/kg/day.
- After six weeks if partial response, increase to 1.8-2 mg/kg/day
- Start QHS b/c often sleepy initially but resolves in 1-2wk so change to QAM (more effective in am)
- BID dosing best & can help w/ GI discomfort but QD ok

• Adverse effects:
  - Rare hepatic injury (2 cases): advise, LFTs NOT required
  - Suicidality (0.37% vs 0%): black box
  - Somnolence, appetite suppression, GI upset/dyspepsia, blood pressure/pulse (adults), sexual dysfunction (adults), irritability
  - Potential drug interactions (lower dose if using with p448 inhibitor)

Slide from Dr. Timothy Wilens, MGH Pediatric Psychiatry
Alpha Agonists: When to Use

• Monotherapy
• Stimulant or nonstimulant nonresponders
• Medication partial responders (adjunctive therapy)
  – Studied with stimulant coadministration (N=5 studies)
• Adverse effects to stimulants or nonstimulants
• Comorbid ADHD plus
  – Oppositional disorder
  – Anxiety
  – Tics
  – “Emotional dysregulation” (needs to be studied)
• Potentially younger children (needs to be studied)
Extended-release Clonidine

- **BID** Dosed preparation FDA approved for pediatric ADHD (Kapvay)
  - Tablet (0.1 and 0.2 mg)
  - Start at 0.1 mg qHS; increase 0.1 mg/week

- **QD** Dosed preparation FDA approved for adult hypertension (Nexiclon) but NOT ADHD
  - Chewable tablet form (0.17 mg; 0.26 mg)
  - Oral suspension (0.09 mg/cc)
  - UPDATE 2013: Nexiclon no longer being distributed