

Selecting effective treatments for ADHD: What, Where, and Why



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Learning Objectives



- ☞ Brief overview of ADHD
- ☞ Review long-term outcomes in ADHD.
- ☞ Discuss the need for effective treatments in ADHD.
- ☞ Identify empirically-supported treatments for ADHD.



Brief Overview of ADHD

- ADHD affects 5-10% of children and ~4% of adults.
 - 5 million children in US alone!
- DSM-V diagnosis: requires 6/9 inattentive sx's and/or 6/9 hyperactive/impulsive sx's
- Affects mostly boys: 9:1 in clinic samples, 3:1 in community
- Impaired social relationships, emotional lability, learning disorders are common

DSM 5 changes to ADHD dx

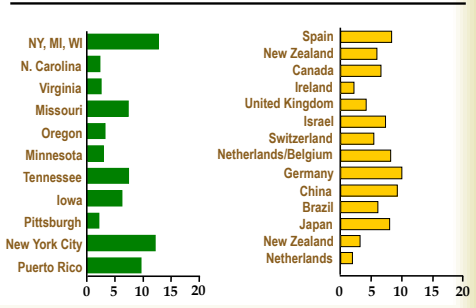


- 1. Conceptual separation from ODD and CD-now a neurodevelopmental disorder rather than a disruptive behavior or impulse control disorder.
- 2. Replaces DSM subtypes with dimensional specifiers of current presentation (for past 6 months)
- 3. Change age of onset criterion to 12 years.
- 4. Eliminate autism/PDD as exclusionary criterion
- 5. Requires symptoms and impairment in at least two different settings
- 6. Gives examples of symptoms adapted for adolescents/adults (e.g., poor time management, doesn't pay bills, keep appointments, return calls)

ADHD looks remarkably similar all over the world...

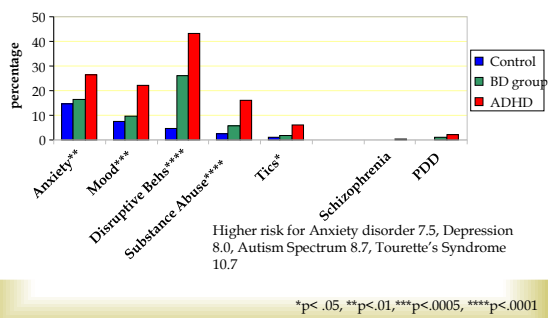


ADHD: Worldwide Prevalence (5-10%)



Faraone SV et al. World Psychiatry 2003;2:104-113.

Psychiatric comorbidity is the rule not the exception

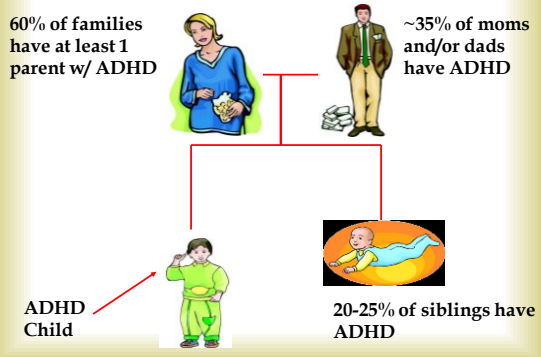


There are strong genetic underpinnings in ADHD



"Your son has a very short attention span, Mr. Clayton"

ADHD often runs in families...



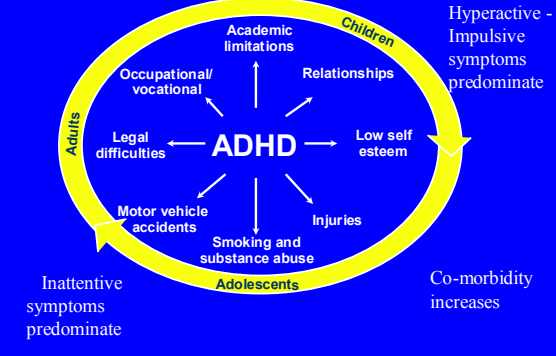
Consistent neurobiological differences in ADHD

- ☞ Brain structure
 - ☞ Smaller total volume
 - ☞ Thinner cortex, particularly frontal/parietal regions
- ☞ Brain Function
 - ☞ Aberrant activation during cognitive tasks
- ☞ Brain connectivity
 - ☞ Reduced connectivity in resting state & task positive networks
- ☞ Brain electrophysiology
 - ☞ Aberrant cortical activity
- ☞ Both developmental delay and maturational deviation are implicated

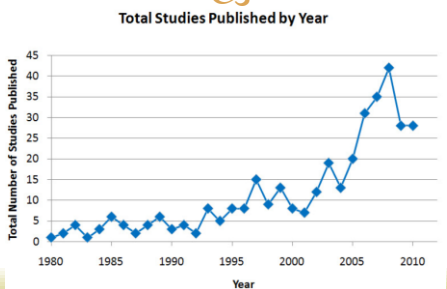
Environmental Etiologies

- Prenatal Injuries (10-15%)
 - Total pregnancy complications
 - Fetal exposure to alcohol and/or tobacco
 - Prematurity with minor brain hemorrhages
- Postnatal Brain Damage (3-5%)
 - Head trauma, brain hypoxia, or infection
 - Lead poisoning in preschool years
 - Survival from acute lymphoblastic leukemia (ALL)
- Post-natal Streptococcal Bacterial Infection
 - triggers auto-immune antibody attack of basal ganglia

ADHD across development



Long-term outcome in ADHD

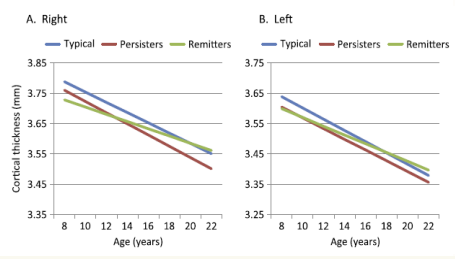


ADHD persistence/remission



- Diagnostic remission is highly variable (ranges from 30-70%)
- Impairment continues for 60-80%
- Childhood characteristics associated with persistence
 - ADHD severity & impairment
 - Treatment
 - Increased psychiatric comorbidity
 - Poor family functioning (parental psychiatric disorder, family conflict)
- Related Qs:
 - What are there pathways out of ADHD?
 - If so, what can we do to help someone get on the right pathway?

Cortical thinning in frontal regions and ADHD persistence



Shaw et al 2013

ADHD in adulthood

- Lower educational levels and employment status
 - ~30% drop out of high school
 - Relatively few adults with ADHD attempt college (20%) and even fewer graduate (5%)
 - Fired from more jobs, lower job performance
- Social impairment continues
 - Fewer close friends, more trouble keeping friends
 - More sexually active (greater number of partners, treated for more STDs)
 - More often parents relative to age-matched peers
- Higher incidence of substance abuse, antisocial personality disorder, and not mood or anxiety disorders
- Severity of Conduct Disorder predicts most of the bad outcomes.

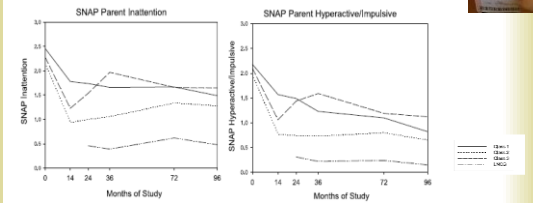
Economic burden of ADHD

- Review of 19 studies: National annual incremental costs of ADHD \$143 to \$266B (Doshi et al 2012)
- Adults: Total cost \$105-\$194B, largest for productivity and income losses (\$87B-\$138B)
- Children: Total cost \$38-\$72B, largest for health care (\$21-44B) and education (\$15B-\$25B).

Good outcomes happen too...

CEOs w/ ADHD +/- dyslexia
 Richard Branson (Virgin)
 Ted Turner (Turner Broadcasting)
 Bill Hewlett (Hewlett-Packard)
 Henry Ford (Ford Motor Co)
 Bill Gates (Microsoft)
 David Neelman (Jetblue)
 John Chambers (Cisco)
 Steve Jobs (Apple)
 Walt Disney
 Charles Schwab
 Malcolm Forbes
 Andrew Carnegie

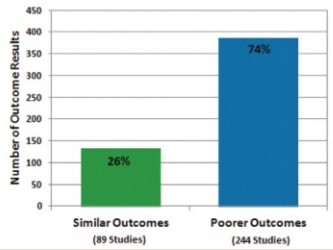
Reconciling the difference- Is it luck?



Class 2 had better scores at baseline : symptom severity, conduct problems, learning problems and IQ, social skills, favorable family environment (fewer breakups, stable financial situation).
Molina et al., 2009

Reconciling the difference- Is it treatment?

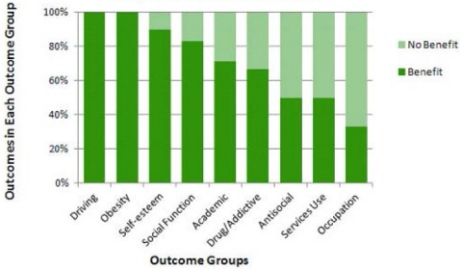
Untreated Participants with ADHD
compared with non-ADHD participants



Shaw et al., 2012

Treatment makes a difference

Treatment Benefit by Outcome Group
compared with untreated ADHD



Motor Vehicle Driving Risks

(100% treatment benefit)

Assessed via self-report, driving records, lab testing, driving simulators, and BTW tests (Barkley studies)

- Poorer steering, more false braking, and slower reaction times to significant events
- Rated as using fewer safe driving habits
- More likely to drive before licensing
- More accidents (and more at faults) (2-3 vs. 0-2)
 - % with 2+ crashes: 40 vs. 6;
 - % with 3+ crashes: 26 vs 9
- More citations (Speeding - mean 4-5 vs. 1-2)
- Worse accidents (\$4200-5000 vs \$1600-2200)
 - (% having a crash with injuries: 60 vs 17%)
- More Suspensions/Revocations (Mean 2.2 vs 0.7)
 - (% suspended: 22-24 vs. 4-5%)

Social-Emotional Impairments

(~80% treatment benefit)

Assessed via parent ratings, peer sociometrics, and videotaped interactions of ADHD children with others

- Increased parent-child conflict & stress
 - especially ODD/CD subgroup
- Peer Relationship Problems (50%+)
 - Less sharing, cooperation, turn-taking
 - More talking, commanding, intrusive, hostile
 - Most serious in ODD/CD subgroup
- Poor Emotional Control
 - More anger, frustration, hostility (ODD/CD)
 - Less self-regulation of emotional states

Sexual-Reproductive Risks

(~80% benefit)

Assessed via self-reports:

- Begin Sexual Activity Earlier (15 vs 16 yrs.)
- More Sexual Partners (18.6 vs. 6.5)
- Less Time with Each Partner
- Less Likely to Employ Contraception
- Greater Risk of Teen Pregnancy (38 vs. 4%)
- Less likely to have custody of offspring (54% vs 11%)
- Higher Risk for STDs (16 vs. 4%)

Educational Outcomes

(~70% benefit)

Assessed by self-report and high school transcripts:

- More grade retention (25-45% vs. 10-15%)
- More are suspended (40-60% vs. 20%)
- Greater expulsion rate (10-18% vs. 5-8%)
- Higher drop out rate (30-40% vs. 1-5%)
- Lower Class Ranking (69% vs. 50%)
- Lower GPA
- Fewer enter college 20-25% vs. 75-80%)
- Lower college graduate rate (5 vs. 35%)

Antisocial Activities (~50% benefit)

Self-report for lifetime occurrences

Antisocial Activities	ADHD %	Control %
Stolen Property	85	64
Stolen Money	50	36
Disorderly Conduct	69	53
Assaulted with Fists	74	52
Assaulted with a Weapon	22	7
Carries Concealed Weapon	38	11
Illegal Drug Possession	51	42*
Illegal Drug Sales	24	20*
Breaking and Entering	20	8
Sets Fires	15	6
Runaway from home	31	16

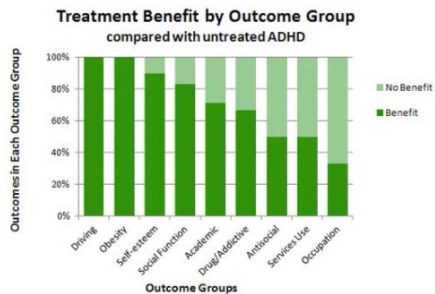
*=Not Significantly different

Employment Problems

(~30% benefit)

- More likely to be fired
 - (55 vs. 23%; Mean 1.1 vs. 0.3 jobs)
- Change jobs more often (2.7 vs. 1.3 over 2-8 years since leaving high school)
- More ADHD/ODD symptoms on the job
 - As rated by current supervisors
- Lower work performance ratings
 - As reported by current supervisors
- Lower social class (SES) (Hollingshead System)
- By 30s, 35% self-employed

Treatment makes a difference



Bringing ADHD into focus

1. Proper diagnosis
 - ☞ ADHD, co-morbid conditions
 - ☞ Need for accommodations
2. Education
 - ☞ Knowledge of existence/causes of ADHD
 - ☞ Perceptions of normal/abnormal behavior developmental context
 - ☞ Knowledge of resources & treatment options
 - ☞ Implement strategies and effect change within family/school environments where feasible.
3. Unimodal & Multimodal treatments
 - ☞ Select necessary components based on child's needs
4. Accommodations
 - ☞ Advocate for these based on child's needs




Diagnostic Q & A




- ☞ Is inattention a cardinal symptom for ADHD only?
- ☞ What % of cases are diagnosed in primary care settings (i.e. by a pediatrician)?
- ☞ What % of pediatricians use DSM criteria in making an ADHD diagnosis?
- ☞ How much time on average does a pediatrician spend per visit?
- ☞ Most common grades in which ADHD is diagnosed (hint: there are three!)

Diagnostic Q & A




- ☞ **Is inattention a cardinal symptom for ADHD only?**
 - ☞ Inattention is like fever, it's indicative of lots of disorders but non-specific to any one disorder.
- ☞ **What % of cases are diagnosed in primary care settings (i.e. by a pediatrician)?**
 - ☞ ~50% of ADHD cases are identified and treated within primary care settings.
- ☞ **What % of pediatricians use DSM criteria in making an ADHD diagnosis?**
 - ☞ 25% of pediatricians use the DSM-IV diagnostic criteria or AAP guidelines for ADHD dx.

Diagnostic Q & A



- ☞ **How much time on average does a pediatrician spend per visit?**
 - ☞ Pediatricians receive limited mental health training & spend on average 12-20 minutes per visit.
 - ☞ Diagnosis typically based solely on parent (and sometimes teacher) report
- ☞ **Most common grades in which ADHD is diagnosed (hint: there are three!)**
 - ☞ ADHD most commonly diagnosed in 1st, 4th, 6/7th

Should you get a neuropsychological assessment?

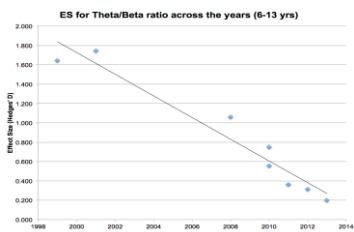


<p>Yes:</p> <ul style="list-style-type: none"> ☞ Qs re: impairments in the context of cognitive function ☞ Clarify diagnostic questions within context of cognition ☞ Assist with treatment planning/educational accommodations 	<p>Not necessary:</p> <ul style="list-style-type: none"> ☞ If the question is primarily diagnostic, no cognitive questions (i.e., ADHD but no significant learning/ processing issues) <ul style="list-style-type: none"> ☞ "Is the child having a hard time learning in school for reasons other than behavior?" ☞ When the child is in crisis and unstable or extremely depressed
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'Newer' is not always better



FDA permits marketing of first brain wave test to help assess children and teens with ADHD
July 15, 2013



ES=Effect Size, the degree of difference between ADHD and non-ADHD individuals.

The Bottom Line:

EEG currently does not have sufficient sensitivity or specificity for use in clinical practice to diagnose ADHD or any other psychiatric disorder.

Not for learning disabilities.

Not for substance abuse.



Not for Anxiety.

Not for Autism!

Not for ADHD!

Not for Depression.

Bringing ADHD into focus



- ✓ Proper diagnosis
 - ✓ ADHD, co-morbid conditions
 - ✓ Need for accommodations
- 1. Education
 - Knowledge of existence/causes of ADHD
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- 2. Unimodal & Multimodal treatments
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Education



Books (rather than the internet) are a fantastic resource, recommended reading:



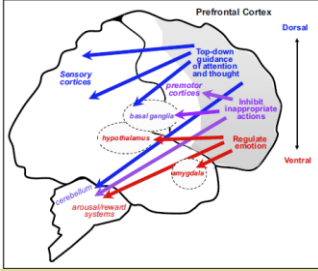
- Parent/Client Support Groups (CHADD, ADDA, Independents)
- Teacher Education About ADHD
- Parent training classes

Bringing ADHD into focus

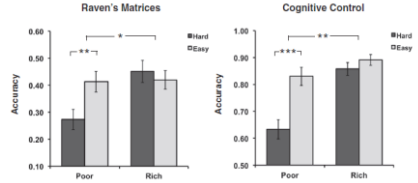


- ✓ Proper diagnosis
 - ✓ ADHD, co-morbid conditions
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1. Unimodal & Multimodal treatments
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Brain-based model of management



But first a digression...



- The brain is a limited capacity system Mani et al., 2013
- Increased attentional/emotional demands affect problem solving & intelligence
- Reducing cognitive demands promotes better decisions

Multimodal treatment approaches

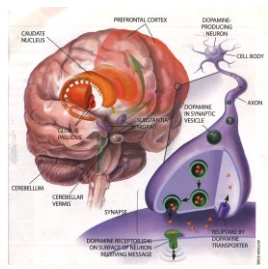
- ☞ To target core ADHD symptoms: medications (non-pharmacological treatments alone do not fare well).
- ☞ To target other impairments (oppositional behaviors, family conflict, anxiety, depression, social skills): psychosocial treatment/therapy.
- ☞ To target educational impairments: cognitive remediation and educational accommodations.



Multimodal treatment approaches

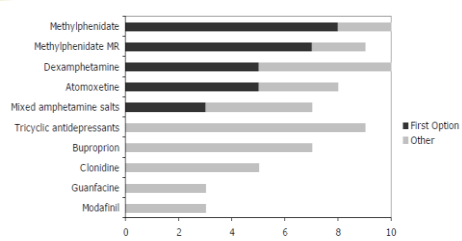
- ☞ Effect of multimodal treatment vs medication alone is small (20% increase in rate of excellent response) on ADHD symptoms alone.
- ☞ But benefits on other areas of functioning are well-documented.
- ☞ Benefit greater for younger (<6yrs) and older (>16 yrs) children.

Medication therapy to address neurochemical deficits



From R. Barkley, *Scientific American*, Sept. 1998, p. 47

Front line pharmacological treatments



70% of subjects respond to any given stimulant

Well documented ST effects....

TABLE 1
Selected Reviews of Psychostimulant Treatments for Attention Deficit/Hyperactivity Disorder

Study (Year)	Drugs	No. of Studies	Subjects	Response Rate	Placebo Response	No. of References
Barkley (1977)	DEX	15	915	74%	29%	159
	MPH	14	866	77%	23%	
	PEM	2	105	73%	27%	
Ginsman-Klein (1980)	PE	8	417	59%	—	308
	DEX	6	235	Moderate	Low	
	MPH	18	528	69%	24%	
Ginsman-Klein (1987)	PEM	4	228	69%	23%	82
	MPH	25	777	NA	NA	
	PEM	1	20	NA	NA	
Hinshaw (1991)	MPH	10	187	Situation*	NA	82
Jacobson (1990)	MPH	136	NA	NA	NA	175
Wolens (1992)	MPH	37	1,113	73%	2-23%	121
Schacht (1993)	MPH	18	531	Recp ^a	26% Attention	88
Swanson (1993)	[Review of 341 reviews]			0.8 SD	30%	22
Richters (1995)	[Concept paper]			NA	NA	153
Spencer (1996a)	STIM-P	5	144	Mild-to-obst	NA	329
	STIM-L	140	5,603	70%	23-27%	
	STIM-T	7	122	70%	NA	
	STIM-A	9	230	54%		
Greenhill (1997)	MPH	15	236	70%	20%	229
	SR	7	181	73%	20%	
	DEX	2	2	High	Low	
	PEM	1	22	75%	20%	
McManer (1998)	MPH	54	NA	NA	NA	570
	PE	63	NA	NA	NA	
	DEX	18	NA	NA	NA	
	PEM	5	NA	NA	NA	

And long term effects...

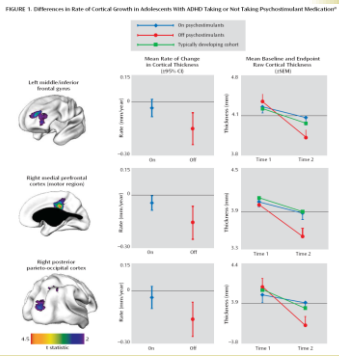


- ~70% of children treated with medication displayed favorable response and better long-term outcome
- No difference between MPH and D-AMPH although slightly more side effects with D-AMPH
- No gender differences

Barberesti et al. 2012

Medications may help brain development

- Meds are related to highly focal (rather than global) changes
- Suggests med effects facilitate use of neural circuits
- Consistent with more normalized white matter density with meds (Castellanos et al., 2002)



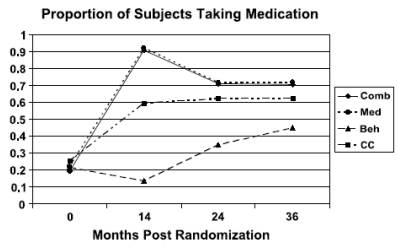
And on brain functions in ADHD



- Brain structure: 6/6 studies found meds associated with attenuation of structural abnormalities.
- Brain function: 19/20 studies found attenuation of control vs ADHD differences in striatum (9/15), anterior cingulate (10/16), and prefrontal cortex (9/15).
- Brain connectivity: 3/3 studies show increased connectivity with meds.
- Not one study found association of medication with worse brain outcomes!

Spencer et al., 2013

But treatment adherence is an issue



(Mis)Perceptions and misattributions contribute to adherence issue



- ☞ Parental hesitation to give their child medications is one of the strongest predictors of untreated ADHD.
- ☞ Improvements in academic performance and social interactions encourage continued tx (Ahmed et al., 2013).
- ☞ Therapy typically ceased due to side effects (appetite suppression, weight loss, sleep disturbance), concerns about potential for addiction, growth stunting, stigma.
- ☞ Adolescents may not accurately perceive the benefits of medication, leading to noncompliance (Pelham et al., 2013)

Treatment implications

- Medication is the gold standard of treatment in ADHD.
- Evidence for beneficial long-term effects mounting.
- Qs still to be answered:
 - How to predict response/optimal dose?
 - Which medication for whom and when?
 - Would better compliance = better outcomes?
 - Are growth trajectories different in populations according to medication history?

Psychosocial treatments to address psychiatric co-morbidity & interpersonal difficulties

- ☞ Parent skills training
- ☞ Behavior therapy
- ☞ Empirically supported for comorbid disorders: Cognitive-behavioral therapy, Dialectical behavior therapy (mood and anxiety disorders)



Family environment and parenting



- ☞ Family environment strongly linked to comorbidities, particularly disruptive behavior and anxiety disorders
- ☞ Family conflict and cohesion in particular play a large part in the development and maintenance of co-morbidities
- ☞ Effects of parent psychiatric diagnoses secondary to the effects on family environment.
- ☞ Number and type of co-morbidities predictive of impairment and later functioning.

Parenting and psychiatric co-morbidity

- ☞ Transactional nature of child problems and family functioning hard to capture
- ☞ Positive parenting protects against conduct problems (Chronis et al., 2007).
- ☞ Child disruptive behavior exerts a greater influence on parenting practices than parenting behavior did on child symptoms (Burke et al., 2008)

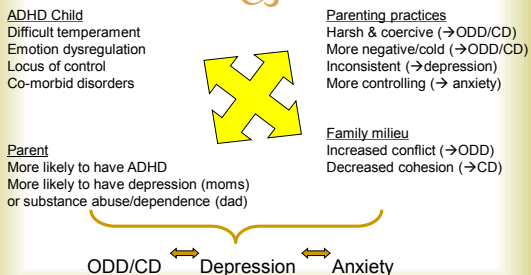


Combined therapy leads to greatest improvement in overall functioning



- BT combined with meds showed significant improvement over meds alone in : aggressive/oppositional behavior, internalizing symptoms, teacher reported social skills and parent-child relations and reading scores.
- Greater improvements in constructive parenting (e.g., warmth, positive reinforcement, setting the stage and behavior management) than meds alone.

Theoretical model of family factors



Adding psychosocial treatments to the mix



- Need to weigh the advantages with additional resources needed for therapy
- Assess/Treat parent psychiatric conditions
- Parent skills training (consistency, positive parenting), Reduce family conflict/break cycle of coercion
- Consider developmental level of child, which may affect outcome:
 - Parent Training in Child Management: Children (<11 yrs., 65-75% respond), Adolescents (25% respond)
 - Family Therapy for Teens: Problem-Solving, Communication Training (30% respond)

Cognitive training and Educational Therapy to address executive functioning difficulties

What are Executive Functions?

3

1. Help to select and achieve goals

- Planning/prioritization-setting appropriate ST & LT goals, correct valuation of predicted reward and punishment
- Time management-accurate assessment of how much time is needed to accomplish necessary work
- Organization-keeping track of assignments/exams
- Working memory-keep the end goal in mind
- Cognitive Flexibility-adapting to dynamic situations
- Metacognition-self-monitor work

What are Executive Functions?

3

2. Help to guide actions to achieve goals

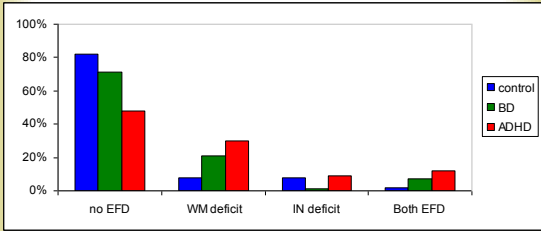
- Goal-directed persistence-cognitive engagement depends on social and motivational salience.
- Sustained attention-managing boredom, distraction
- Response inhibition-delay gratification
- Emotional control-tolerate frustration
- Task initiation-speed/accuracy tradeoff

ADHD and executive functions

- ADHD conceptualized as a disorder of Executive Functioning (EF) (Barkley, 1997)
 - Planning, organizing, working memory and inhibition
- Non-EFs such as processing speed, motor coordination, language, visual-motor integration, learning and memory are also affected.
- Deficits in cognitive functioning well-documented, however, they are 'neither necessary nor sufficient to cause all cases of ADHD' (Willcutt et al., 2005)

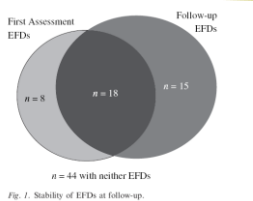


Executive function deficits occur with greater frequency (~50% in ADHD)



Executive function deficits are highly stable & associated with impairment

- ~70% continued to show EF deficits 7 yrs later
- WM performance was highly stable
- Decreased educational and occupational attainment
- Lower SES
- Increased traffic violations & legal infractions
- Higher rate of comorbidities



Biederman et al 2007

Cognitive training



- Cogmed Working Memory Training Program (Klingberg et al., 2002; 2005)-resulted in improvement on visual & verbal WM, nonverbal reasoning, & inhibition.
 - Gains maintained at 3 mo follow up.
 - Increased brain activity in frontal & parietal regions linked to WM (Olesen et al., 2004).
- Recent studies have replicated the positive effects of WM training at school (Holmes et al., 2009) and at home (Beck et al., 2010) in independent samples of children with ADHD (ages 7-17).
- Recent review suggests effects are more specific to WM and not as effect on improving ADHD symptoms.

Treatment implications

- ‘Exercising’ the neural circuits involved in executive functions may reduce impairment in ADHD.
- Educational therapy for explicit training of Efs
- Cognitive exercises show promise as effective interventions for slowing cognitive decline in the elderly, needs more exploration for ADHD.
- More research demonstrating positive, lasting benefit of psychosocial txs in ADHD is needed.

Bringing ADHD into focus



- ✓ Proper diagnosis
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 - ✓ Need for accommodations
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 - ✓ Knowledge of existence/causes of ADHD
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 - ✓ Unimodal & Multimodal treatments
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1. Accommodations
 - Advocate for these based on child’s needs

Educational accommodations

- Preferential seating
- Test taking in quiet environment
- Provision of lecture notes
- Reduce work load-quality not quantity
- Multi-modal learning
- Flexible format expression of knowledge
- Extra breaks off the clock (note: not extended time)
- Assistive technology (if warranted)
- Necessary for EAs on college board exams so encourage their use when appropriate

Why not extended time accommodation on tests?

- High school students w/ & w/o ADHD: similar performance on speed and # of test items accessed (Lewandowski et al., 2012)
 - Made more errors on some reading tasks (decoding, comprehension)
 - Extra time helpful to review and double check answers
- On Nelson-Denny Reading Test, college students w/ & w/o ADHD scored exactly the same on standard, 1.5x and 2x conditions.
 - At 1.5x and 2x, ADHD sig outperformed TD students at standard time in items attempted and answered correctly. Percent correct did not differ.
 - ET may confer an unfair advantage for ADHD

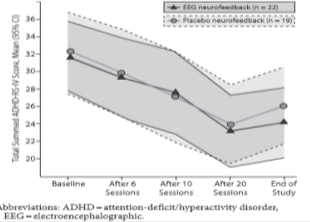
Alternative treatments?

- Managing Diet (e.g., sugar, additives, health supplements, etc.)
 - Megavitamins, Anti-oxidants, Minerals
- Sensory Integration Training
- Chiropractic Skull Manipulation
- Play Therapy
- Mindfulness/Meditation
- EEG Neurofeedback



Improvement tends to be a placebo effect...

Figure 2. Mean Total Summed Scores and 95% Confidence Intervals for the ADHD Rating Scale IV (ADHD-RS-IV) Over Time As Rated by the Investigator and Shown by Treatment Group



Abbreviations: ADHD = attention-deficit/hyperactivity disorder, EEG = electroencephalographic.

Van Dongen-Boomsma et al., 2013

Summary and Conclusions



- ☞ For most, ADHD is a lifespan disorder associated with many enduring negative outcomes
- ☞ Treatment is a key factor in mitigating the bad outcomes
- ☞ Studies of brain function and development suggest
 - ☞ Reduce competing demands for attention/emotion regulation
 - ☞ Exercise key brain circuits for better outcomes
- ☞ Treatment modalities/accommodations should be used based on child's needs