

Living Well with ADHD: Scientific Guideposts to Improved Outcomes

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Outline

- What is ADHD?
 - Provisionally defined by DSM-5 diagnosis
- Is ADHD a serious mental disorder?
 - It can be – but outcomes can also be excellent
- What have we learned about the brain in ADHD?
 - Delayed maturation
- What are challenges of living with ADHD?
 - Avoiding irreversible errors
- Essentials of psychoeducation

DSM-5 ADHD

Hyperactive/Impulsive Symptoms

Often...

- fidgets or squirms
- can't stay seated
- restless (subjective in adolescents)
- loud, noisy, diff playing quietly
- always “on the go”
- talks excessively

- blurts out
- impatient
- intrusive

**6 or more present
over 6 months;**

5 if age \geq 17 y

DSM-5 ADHD

Inattention Symptoms

Often ...

- careless errors, inattention to detail
- sustains attention poorly
- *appears* to not listen
- poor follow through on obligations
- disorganized
- avoids/dislikes sustained mental effort
- loses needed objects
- easily distracted
- forgetful

**6 or more present
over 6 months;**

5 if age \geq 17 y

Conditions that co-occur with ADHD

- Most common:
 - Specific learning disorders
 - Oppositional defiant disorder
 - Anxiety disorders
 - Depressive disorder
- These commonly co-occur with ADHD – may be missed
- ADHD symptoms might be secondary

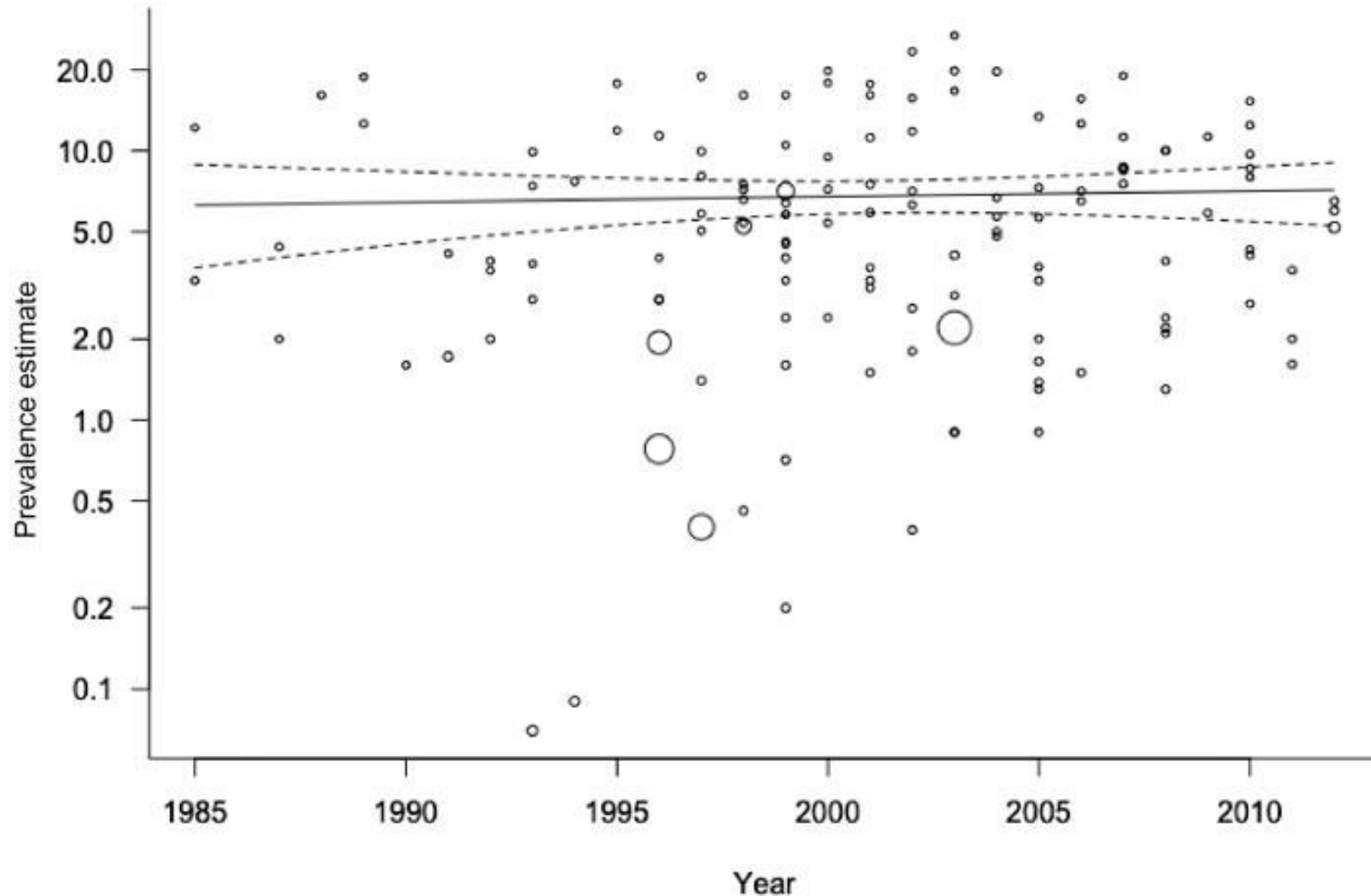
Conditions that could be confused for ADHD

- Posttraumatic stress disorder
- Reactive attachment disorder
- Autism spectrum disorder – or traits
- Mood disorders
 - Depressive disorder
 - Disruptive mood dysregulation disorder
 - Bipolar disorder
- Substance use disorders
- Sleep disorders (obstructive sleep apnea & sleep deprivation)

Diagnosing ADHD

- Imperfect but acceptable
 - One of the most reliable diagnoses in psychiatry
- Diagnosing complex conditions is always challenging
 - Particularly when we don't understand the causes
- Awareness of ADHD in popular culture has increased dramatically
- Worldwide prevalence has not changed

ADHD Prevalence Estimates Across 3 Decades



Polanczyk et al., Int J Epidemiology, 2014

Clinical and Functional Outcome of Childhood Attention-Deficit/Hyperactivity Disorder 33 Years Later

Rachel G. Klein, PhD; Salvatore Mannuzza, PhD; María A. Ramos Olazagasti, PhD; Erica Roizen, MS; Jesse A. Hutchison, BA; Erin C. Lashua, MA; F. Xavier Castellanos, MD

Outcome	Probands	Comparisons	χ^2	P
Incarcerated	36%	12%	22.4	<.001
Deceased	7.2%	2.8%	3.8	.05
Conduct disorder	62%	26%	35.1	<.001
Antisocial personality disorder	33%	4%	38.2	<.001
Alcohol-related disorder	45%	41%	0.44	.51
Substance use disorder	56%	38%	8.9	.003
Nicotine dependence	60%	31%	23.2	<.001
Any mood disorder	59%	43%	1.1	.30
Any anxiety disorder	18%	21%	.2	.67

Cause and Age of Death Related to Physical Conditions

Cause of death	Probands (n)	Age @ death	Comparisons (n)	Age @ death
Cancer	2	37, 37	2	42, 43
Diabetes (diabetic coma)	1	38	0	
AIDS	0		1	33
Cardiac arrest	1	38	0	
Total related to medical conditions	4		3	

Ramos Olazagasti et al., J Am Acad Child Adolesc Psychiat, 2013

Cause and Age of Death Unrelated to Physical Conditions

Cause of death	Probands (n)	Age @ death	Comparisons (n)	Age @ death
Suicide	3	21, 30, 30	0	
Overdose (alcohol or drugs)	1	39	1	26
Homicide	2	22, 40	0	
Occupational (pilot; fire fighter)	2	30, 40	0	
Hit by a car	1	16	0	
Fell from a roof	1	24	0	
Terrorist attack on 9/11	0		1	36
Unknown	1	34	0	
Total unrelated to medical conditions	11		2	

Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study

Søren Dalsgaard, Søren Dinesen Østergaard, James F Leckman, Preben Bo Mortensen, Marianne Giørtz Pedersen

- N=1.9 million Danes included 32,061 w/ADHD. During 25 million person-years, 5580 people died.
- Mortality rate was 5.85 among those w/ADHD vs. 2.2 per 10,000 person-years.
- Mostly from unnatural causes, especially **accidents**.
- Even after excluding individuals with oppositional defiant disorder, conduct disorder, and substance use disorder, ADHD remained associated with increased mortality, and was higher in girls and women than in boys and men.

Dalsgaard et al., The Lancet, 2015

Serious Transport Accidents in Adults With Attention-Deficit/Hyperactivity Disorder and the Effect of Medication

A Population-Based Study

Chang et al., JAMA Psychiatry, 2014

- A total of 17,408 patients with ADHD in Sweden were observed for serious transport accidents from 1/1/06 to 12/31/09
- **Risk of serious accidents was increased by 47% in men and 45% in women**
- In males with ADHD, medication was associated with a significant 58% reduction in risk
 - Unclear why a significant protective effect was not detected in females

Stimulant ADHD medication and risk for substance abuse

Chang et al., J Child Psychol Psychiatry 2014

- In 26,249 men and 12,504 women w/ADHD, medications for ADHD were not associated with increased rate of substance abuse.
- Actually, the rate of substance abuse during 2009 was **31% lower** among those prescribed ADHD medication in 2006, even after controlling for covariates.
- Also, the **longer the duration of medication, the lower the rate** of substance abuse.
- Similar risk reductions were suggested among children.

NICE* Guidelines

- Diagnosis should be made **when** symptoms of hyperactivity, impulsivity and inattention
 - Meet DSM-5 or ICD-10 criteria
 - **Are associated with at least moderate psychological, social and/or educational or occupational impairment ... in multiple settings**
 - Are persistent and trait-like

Atkinson & Hollis, 2010

*National Institute for Clinical Excellence

Assessment → Diagnosis → Treatment

- When to diagnose?
- **Impairment** is the key question
 - If a child is chronically failing to keep up...
 - Likely to internalize: “I am a failure,” “I hate school,” “My teachers don’t like me...”
 - Oppositional defiant disorder, conduct disorder, mood & substance use disorders ... all are potential consequences
 - We can’t be certain of causal relationships ... but these may be consequences of untreated ADHD

Psychoeducation

- The essential component of all treatment
 - What ADHD is and is not
 - ADHD is not voluntary or intentional
 - Causes are mostly genetic/neurodevelopmental
 - Not “bad parenting”
 - Although calm, effective parenting does help

Goals of treatment

- Outcomes are variable, from excellent to awful
 - Risk of death significantly increased
 - Accidents, overdose, homicide, suicide
 - Addiction ...
- Even when outcome is excellent, development is delayed, particularly socially
- Crucial to differentiate reversible from irreversible mistakes
- Reversible mistakes = Learning opportunities

Irreversible errors

- **Irreversible errors** change (or end) lives
 - **Death** (motor vehicle or other accident; suicide, overdose, homicide)
 - **Addiction** is forever
 - Tobacco is most common; cannabis, alcohol, ...
 - Incurable **viral infections**
 - HIV, HPV, Herpes type 2, Hepatitis C,...
 - Being arrested for **serious crimes** (felonies)
 - Having children prematurely

Adolescence

- The major risks associated with ADHD occur/begin in adolescence
- Intervention in adolescence is often futile
- Goal is to establish a therapeutic alliance before ... and then be able to maintain it through adolescence and young adulthood
- Fundamental behavioral principles of rewarding appropriate behaviors and ignoring negative behaviors, whenever possible, are counter-intuitive
- That's why they take training & practice

Medications

- Every parent wonders: *Will giving my child medications **damage his or her brain?***
- Are we certain these medications are ***completely safe?***

Safety of Medications

- *Will giving my child medications damage his or her brain?*
- THERE IS NO EVIDENCE in humans or non-human primates, that usual doses of stimulant medications produce measurable adverse effects on brain
- Not the same as proof of absolute safety, which can never be assured

Developmental Trajectories of Brain Volume Abnormalities in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder

	Mean (SD)	
	Patients With ADHD (n = 152)	Controls (n = 139)
Total cerebral volume	1059.4 (117.5)	1104.5 (111.3)
Total gray matter	700.9 (77.3)	727.9 (74.3)
Total white matter	358.5 (53.5)	376.6 (49.8)
Frontal gray matter	217.3 (24.9)	225.2 (22.5)
Parietal gray matter	116.6 (13.0)	122.0 (12.9)
Temporal gray matter	174.0 (18.5)	181.6 (18.2)
Occipital gray matter	62.5 (9.6)	66.5 (10.5)
Frontal white matter	135.8 (21.4)	141.9 (18.5)
Parietal white matter	70.6 (10.4)	74.9 (9.8)
Temporal white matter	74.4 (11.0)	77.6 (10.6)
Occipital white matter	30.3 (5.5)	32.2 (5.9)
Caudate	10.4 (1.1)	10.8 (1.0)
Cerebellum	124.1 (12.3)	129.8 (12.7)

Effects were greatest in the 49 children who had never been treated with stimulant medication.

Figure 1. Predicted Unadjusted Longitudinal Growth Curves for Total Cerebral Volumes for Patients With ADHD and Controls

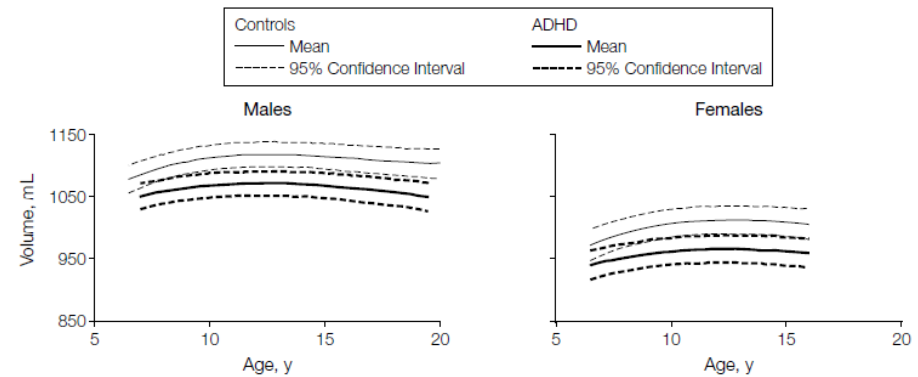
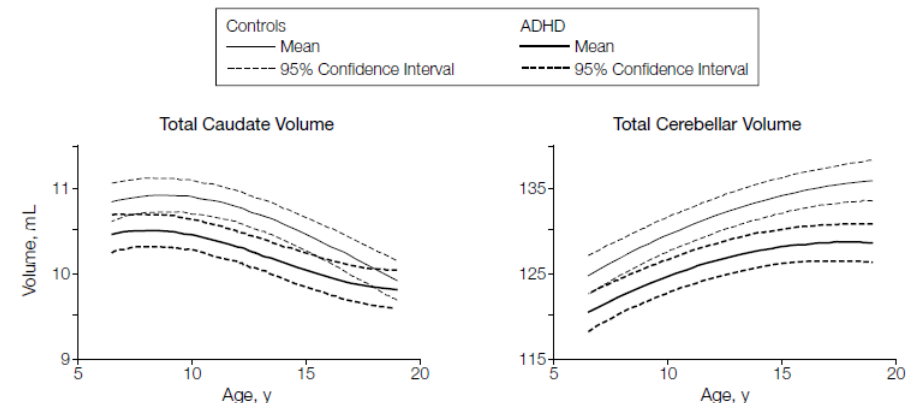
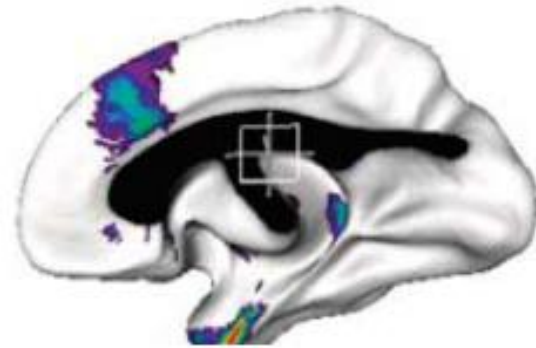
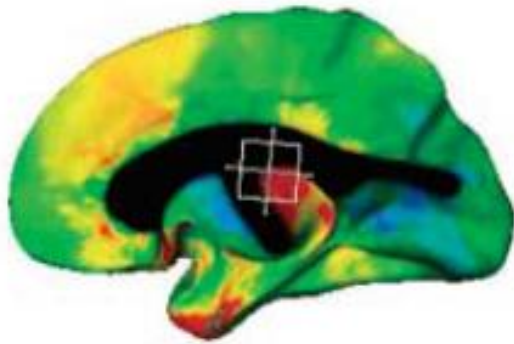


Figure 2. Predicted Unadjusted Longitudinal Growth Curves for Total Caudate and Cerebellar Volume for Patients With ADHD vs Controls



Longitudinal Mapping of Cortical Thickness and Clinical Outcome in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder

Philip Shaw, MD; Jason Lerch, PhD; Deanna Greenstein, PhD; Wendy Sharp, MSW; Liv Clasen, PhD; Alan Evans, PhD; Jay Giedd, MD; F. Xavier Castellanos, MD; Judith Rapoport, MD 2006

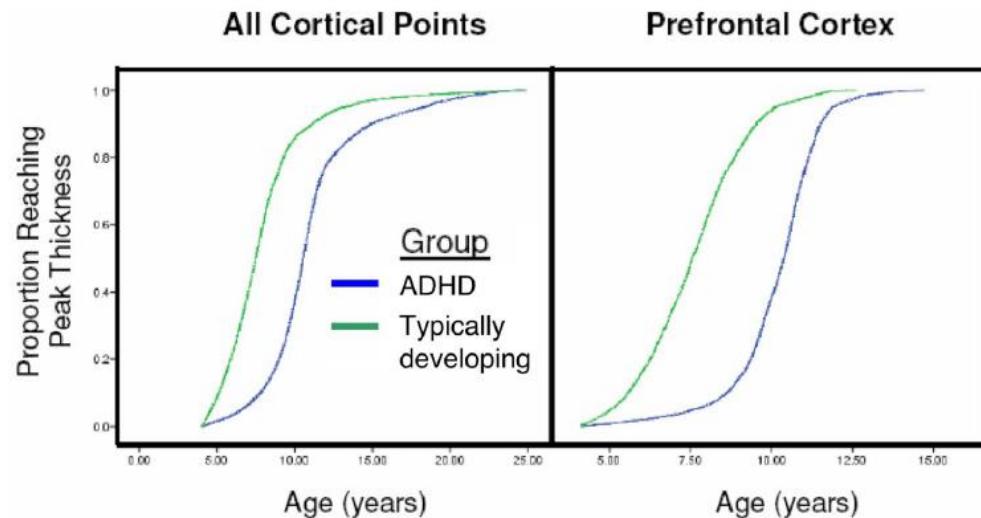
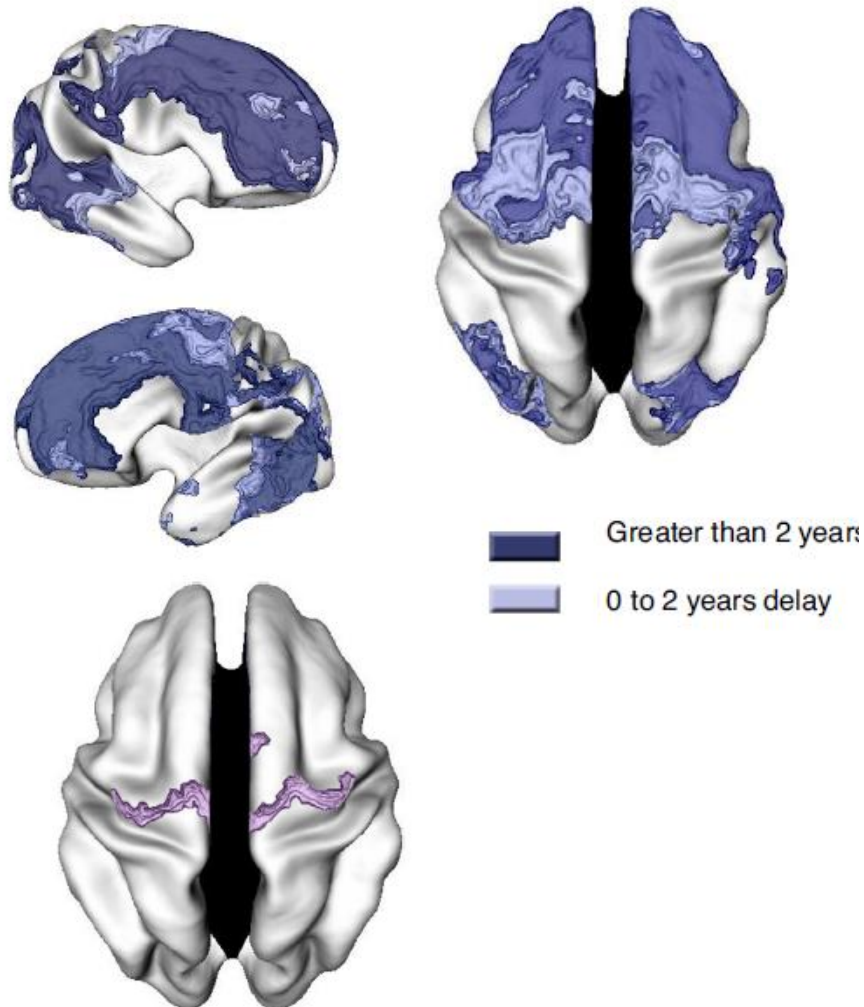


cortical thickness ... the distance between 40.962 linked vertices

Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation

P. Shaw^{†‡}, K. Eckstrand[†], W. Sharp[†], J. Blumenthal[†], J. P. Lerch[§], D. Greenstein[†], L. Clasen[†], A. Evans[§], J. Giedd[†], and J. L. Rapoport[†]

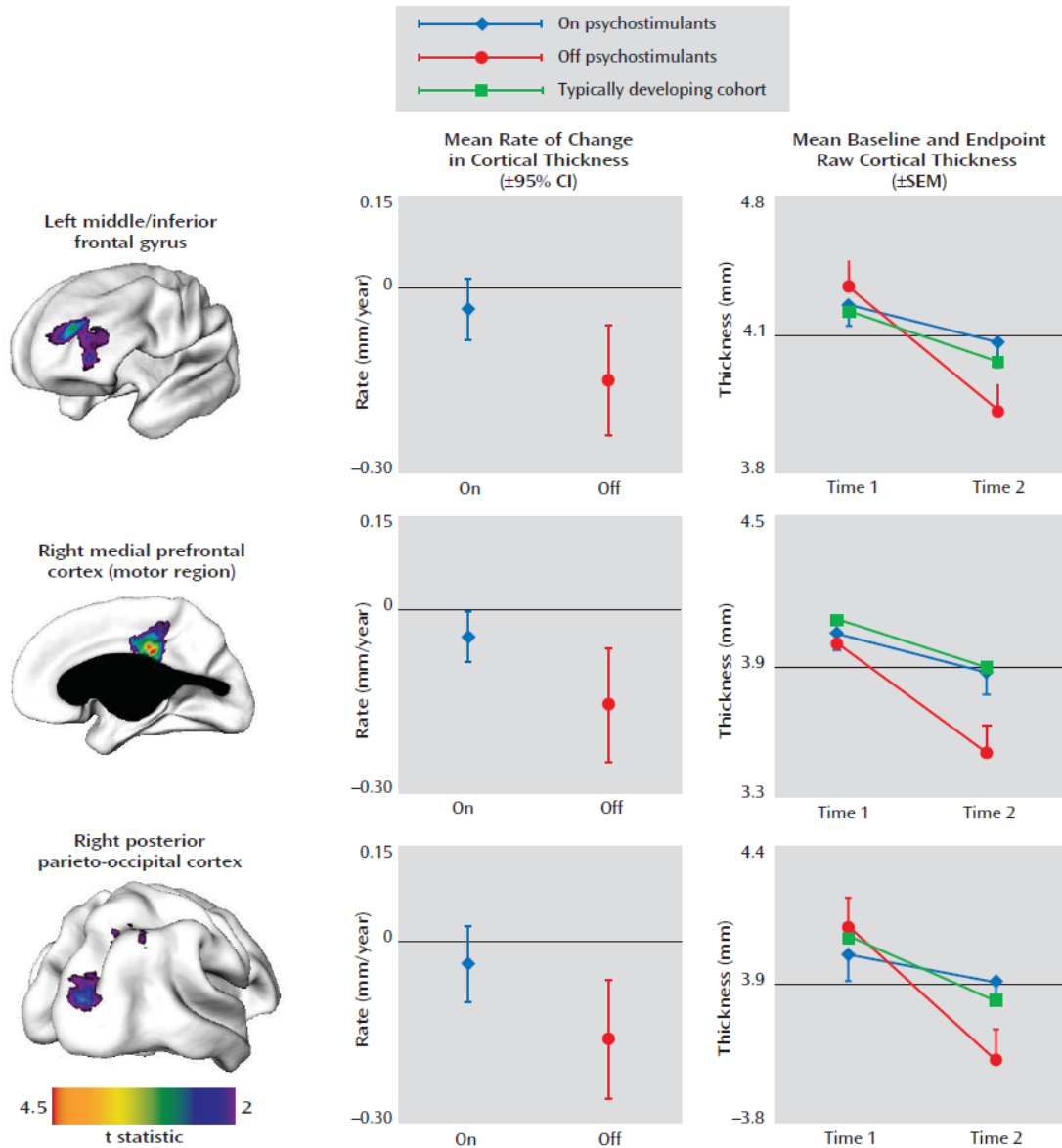
Proceedings National Academy
Sciences USA, 2007



Structural brain differences in ADHD

- Slight but consistent global decreases in volume of entire brain; thickness of nearly entire cortex is reduced
- Developmental trajectory is **delayed** across most of the cortex
- Effect greatest in the **prefrontal cortex**
 - Brain areas most involved in executive function, i.e., **self-regulation**

Psychostimulant Treatment and the Developing Cortex in Attention Deficit Hyperactivity Disorder



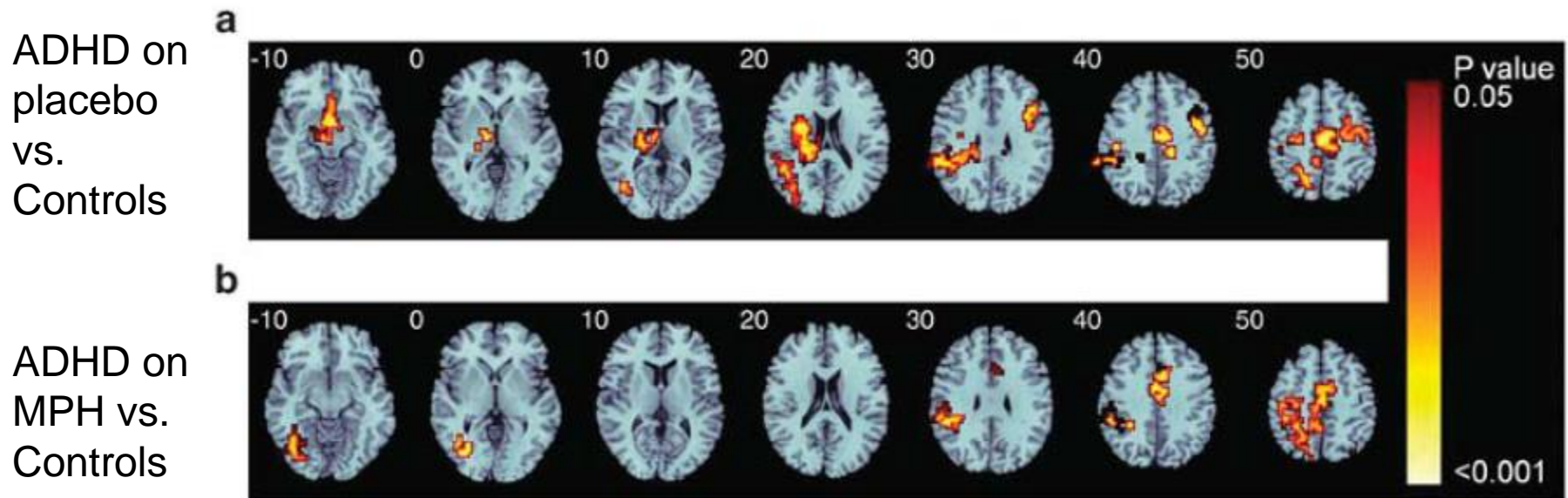
Shaw et al., 2009:

Two scans per child:
19 not taking meds vs. 24 treated

Contrasted to 294 TDC
(620 scans)

Methylphenidate Normalizes Fronto-Striatal Underactivation During Interference Inhibition in Medication-Naïve Boys with Attention-Deficit Hyperactivity Disorder

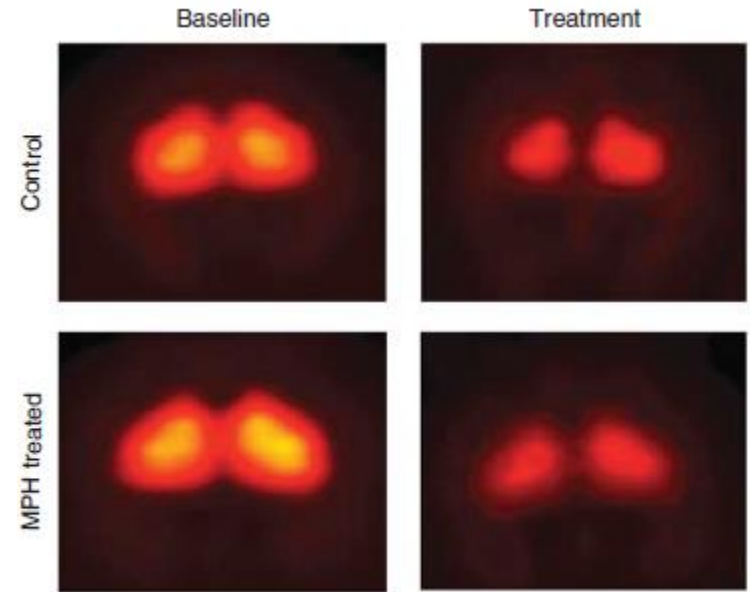
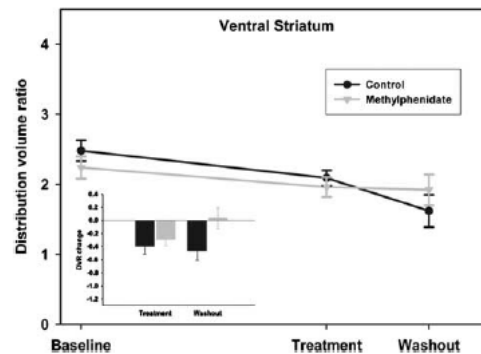
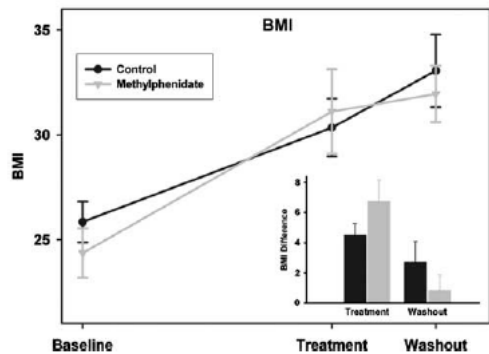
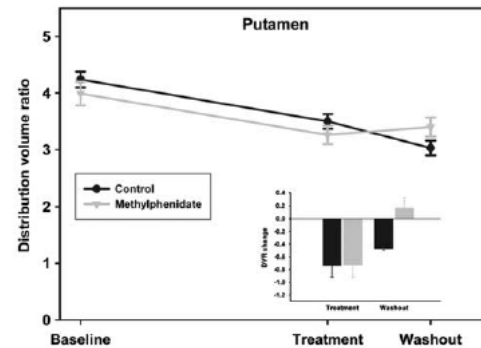
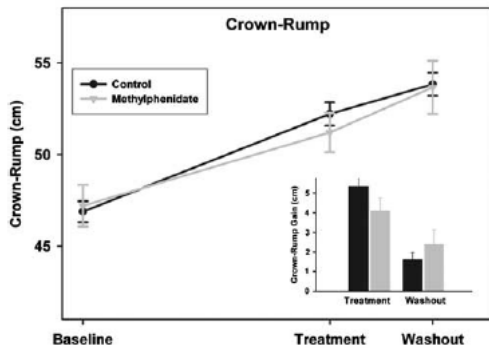
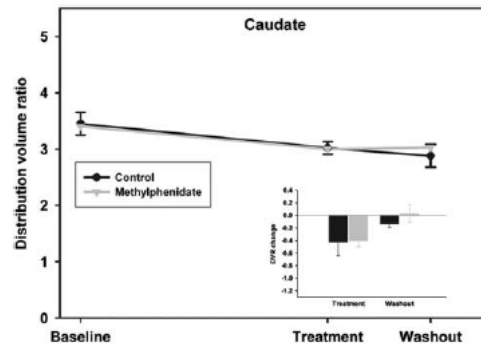
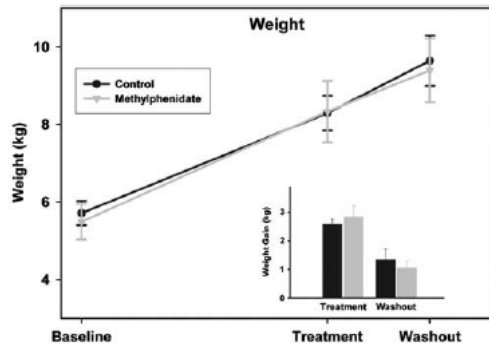
Rubia et al., 2011



“MPH significantly normalized the fronto-striatal underfunctioning in [12] ADHD patients relative to [13] controls during interference inhibition, but did not affect medial frontal or temporal dysfunction. MPH appears to have a region-specific upregulation effect on fronto-striatal activation.”

Chronic Treatment with Extended Release Methylphenidate Does Not Alter Dopamine Systems or Increase Vulnerability for Cocaine Self-Administration: A Study in Nonhuman Primates

Gill et al. & Porrino, 2012



DA D2/D3 receptor binding at baseline and after 1 year MPH or placebo treatment (n=8/group)

Gill et al. 2012 Conclusions

- “long-term administration of MPH to juvenile nonhuman primates produced no significant alteration in the regulation of the dopamine systems as measured with PET, or significantly altered growth. **These data support the hypothesis that MPH administered in formulations used therapeutically in children does not have obvious long-term effects.**
- In addition, there was no evidence for an increased vulnerability to the reinforcing effects of cocaine in adolescence as a result of MPH treatment.
- The absence of any significant long-term developmental, neurobiological, or behavioral consequences provides **further support that the use of these medications to treat ADHD will not negatively impact children either during or after treatment.**”

So are they safe?

- Q: Are we **certain** these medications are completely safe?
- A: All medications have risks, but usual therapeutic doses of stimulants in school-age children or older appear to be among our safest medication options
- Starting low, using lowest effective dose, and monitoring for adverse effects still key

Maintaining the treatment alliance

- ADHD is a potentially life-long condition
 - Particularly burdensome when academic environments are inflexible
- Maintaining therapeutic alliance through adolescence is extremely challenging
 - Childhood acquiescence → adolescent autonomy
- Need to lay groundwork for this transition from the first encounter with the family

Predict the future

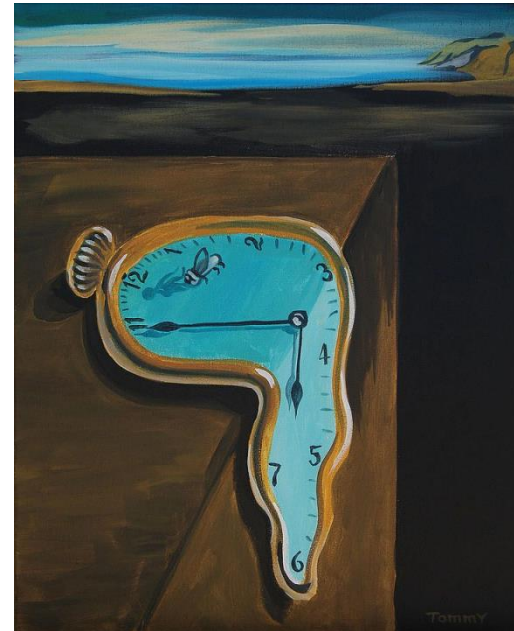
- At some point, between ~ ages 10 and 12, ALL CHILDREN with ADHD, even if they have responded optimally to medication, will wonder if they still need it
- At first, this doubt is expressed tentatively
- → it soon hardens into a declaration: “You can’t make me take that pill!”

Respecting autonomy

- As soon as doubt/concern about medication is raised by child, parents should notify physician
- Clinician should discuss with child (without parents)
 - Validate possibility medication may not be needed currently
 - Brain maturation is increasing; combination with environmental supports may be sufficient this year ...
 - You may not need the medication – at least right now
 - Propose a trial discontinuation up to 2 weeks
 - Better if > 1 month of school has elapsed; optimal near end of school year
 - Timing is up to the child

Trial discontinuation

- Child/adolescent decides when to stop taking stimulant medication
 - The patient now has to monitor results – not necessarily immediate
 - Take two weeks:
 - Do you notice time passing more slowly?
 - Do your teachers seem more boring?
 - Are you more forgetful or impulsive?
- If so, you can resume medication without anyone's permission – if you decide it is sometimes helping you



Trial discontinuation

- Anecdotally, I found that children always transitioned from being ordered to take medication to deciding that it sometimes (or often) helped
- Then tailor medication to their changing needs
 - If a dose that was tolerated well now produces adverse effects, start by **lowering** the dose
 - Puberty → slowed hepatic metabolism
- Each person has to figure out their “owner’s manual”
- Clinician’s job is to define the limits of what is safe
 - Make recommendations
 - But we have no control – make this a virtue

In conclusion: Treatment of ADHD

- Can be tremendously rewarding for all concerned
- Requires patience, long-term perspectives and optimism
- Maintaining therapeutic alliance through adolescence is challenging and crucial
- Prevent **irreversible errors** so that brain maturation can continue to diminish the gap