



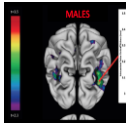
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Chief Editor:



UNDERGRADUATE and MEDICAL SCHOOL:

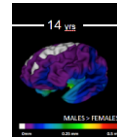
University of North Dakota

PSYCHIATRY RESIDENCY: Menninger

CHILD FELLOWSHIP: Duke

RESEARCH: NIMH

RCHSD: 2014



To explore the **path mechanisms**, and influences on brain development in health illness through longitudinal studies combining brain imaging, genetics, and **psychological/behavioral** assessments.



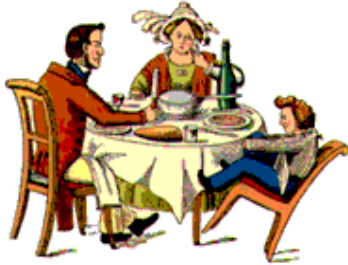
Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Disclosures

- No Financial Disclosures



The Story of Fidgety Phil Heinrich Hoffman - 1884



Let me see if Philip can
Be a little gentleman
Let me see, if he is able
To sit still for once at table:
Thus Papa bade Phil behave;
And Mamma look'd very grave.
But fidgety Phil,
He won't sit still;
He wriggles and giggles,
And then, I declare
Swings backwards and forwards
And titlts up his chair,
Just like any rocking horse;

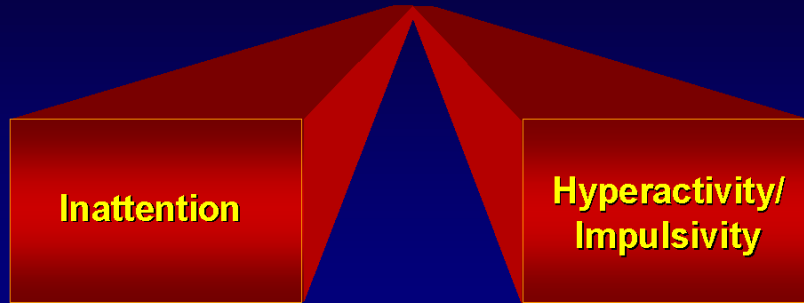
The Story of Johnny Head-In-Air



As he trudg'd along to school,
It was always Johnny's-rule
To be looking at the sky
And the clouds that floated by;
But what just before him lay,
in his way,
Johnny never thought about;
So that everyone cried out -
"look at little Johnny there,
Little Johnny Head-In-Air!"

Definition of ADHD

Developmental Disorder of



American Psychiatric Association. 1994;78-85.

DSM-V Diagnosis of ADHD

- 6/9 symptoms required for each subtype
- Clear impairment (social, academic, or occupational)
- [impairment by age 7 in DSM-IV removed]
- **Impairment** present in more than 1 setting
- Not accounted by another condition (e.g., autism, psychosis, depression, ...)

ADHD: Hyperactive / Impulsive Sx

Often...

- fidgets or squirms
- can't stay seated
- restless (subjective in adolescents)
- loud, noisy
- always “on the go”
- talks excessively
- blurts out
- impatient
- intrusive

ADHD: Inattention Sx

Often ...

- careless errors, inattentive to detail
- sustains attention poorly
- *appears* to not be listening
- follows through poorly on obligations
- disorganized
- avoids or dislikes sustained mental effort
- loses needed objects
- easily distracted
- forgetful

Problems with ADHD Dx

- Observer-based (rater bias)
 - Yet moderately to highly reliable, especially for hyperactivity symptoms *in childhood*
- Appropriateness of symptom cut-offs for adolescents/adults unclear

ADHD Developmental Trends by Age

Symptoms of ADHD decline and change from childhood to adulthood

- Clinicians should consider impact on QOL

Children



Adults

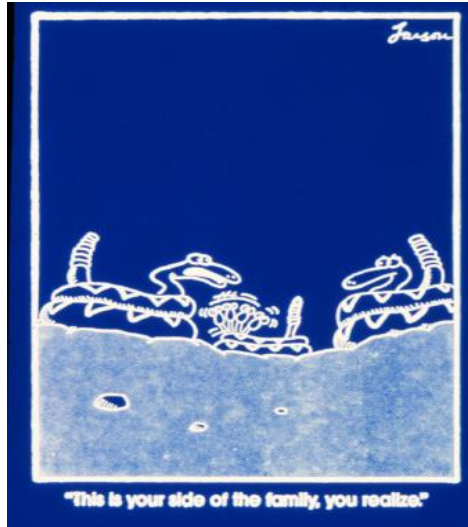
Motoric Hyperactivity
Aggressiveness
Low Frustration Tolerance
Impulsiveness
Easily Distracted
Inattentiveness
Shifts Activities
Easily Bored
Impatient
Restlessness

Is ADHD Real?

1. True
2. False

Is ADHD Real?

Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder



“This is your side of the family, you realize”

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Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Converging Evidence for the Genetic Basis for ADHD

Heritable Factors

+

?

ADHD



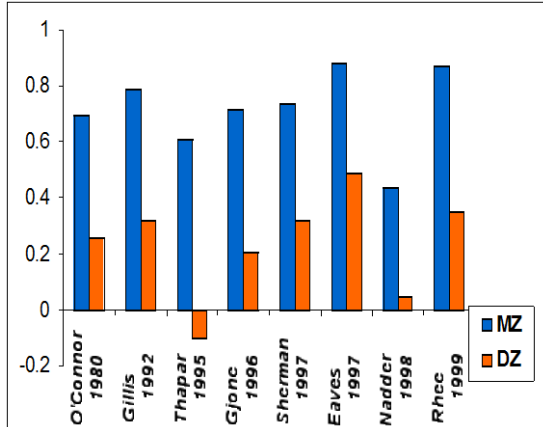
- Adoption Research
- Family Aggregate Studies
- Twin Studies
- Molecular Genetics

Goodman, Stevenson. *J Child Psychol Psychiatry*. 1989;30:691-709.
Faraone, Biederman. *Biol Psychiatry*. 1998;44:951-958.
Swanson et al. *Neurosci Biobehav Rev*. 2000;24:21-25.

Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Twin Concordances in ADHD

- All studies consistent regardless of criteria or country
- Heritability ~ 70%
- MZ/DZ > 2 suggests multiple genes and/or contrast effects

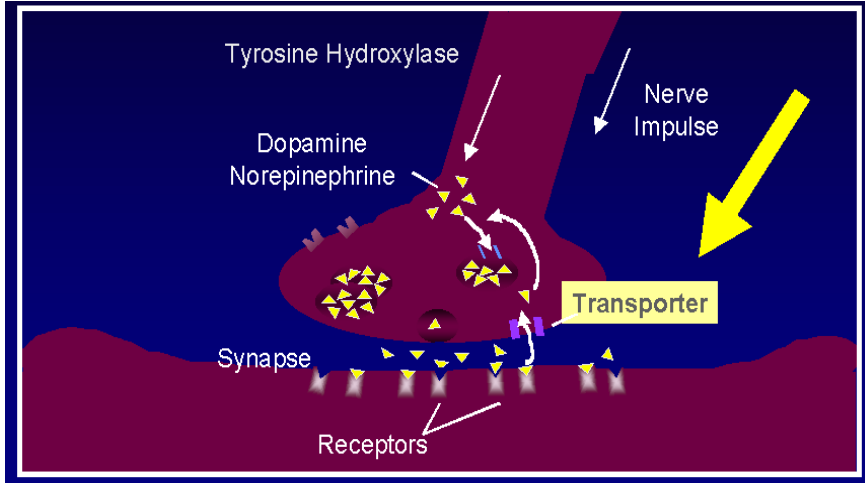


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When it was an advantage to have adult ADD



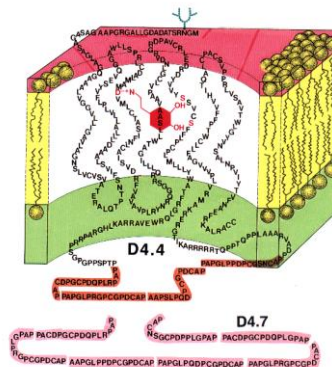
Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder



Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

DRD4 & ADHD

- 7-repeat allele association replicated > 6 studies
- 7-repeat less effective transducer?
- Associated w/ normal neuropsychological profile in ADHD (Swanson)



Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Genetics of ADHD

- Genes replicated at least once
 - DRD4
 - DRD5
 - DAT
 - 5HT1B
 - 5HTT
 - SNAP-25
 - COMT
 - MAO
 - Others ...
- No single gene causes ADHD
- Genes are of small effect
- Not currently of clinical utility (September 13, 2013)

Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

What is the neurobiological basis of ADHD?

1. Frontal
2. Striatal
3. Cerebellum
4. All of the above

Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Anatomic Brain Imaging In ADHD

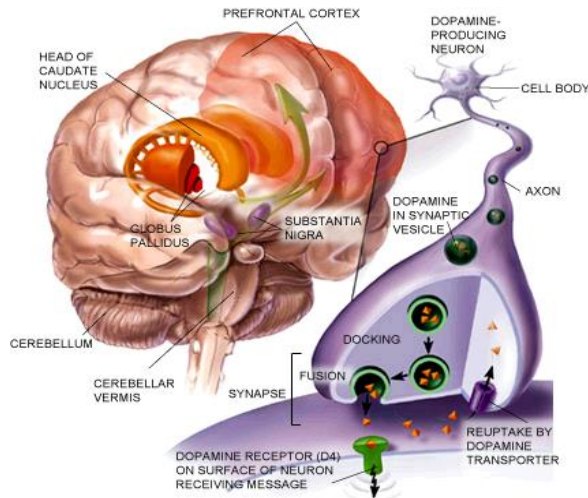


"You're a right-brained sort of person, Mr. Sommersby—very creative, artistic, etc.... Unfortunately, I think I also see why you're having trouble figuring out your gas mileage."

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Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Brain Regions Implicated in ADHD



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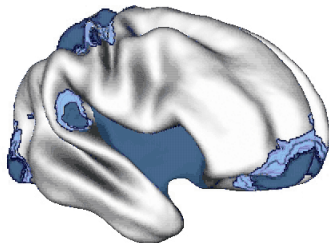
Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Frontal Lobes = “CEO” or “Executive”

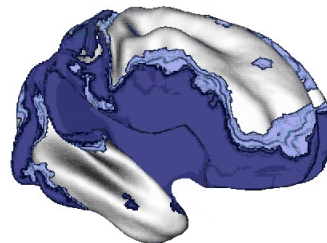
- Inhibiting
- Sustaining
- Initiating
- Shifting or Stopping
- Prioritizing
- Organizing
- Strategizing

Age of attaining peak cortical thickness for the ADHD and healthy control groups: ADHD has “shift to the right”

AGE: 6



ADHD



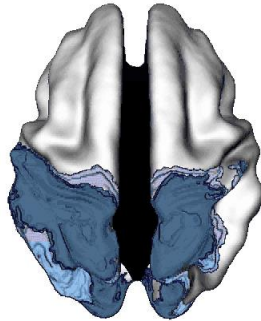
HEALTHY CONTROLS

The darker colors indicate regions where a quadratic model was not appropriate and thus a peak age could not be calculated, or that the peak age was estimated to lie outside the age range covered

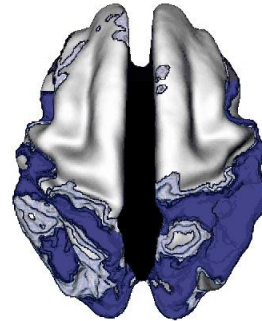
Shaw et al. Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation. *PNAS*, 104(49): 19649-19654

Age of attaining peak cortical thickness for the ADHD and healthy control groups: ADHD has “shift to the right”

AGE: 5



ADHD



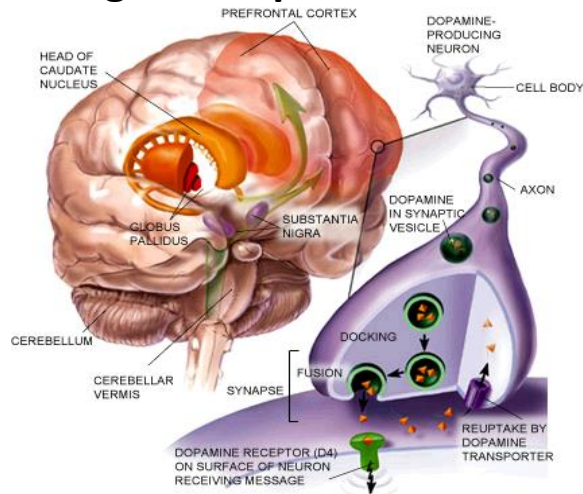
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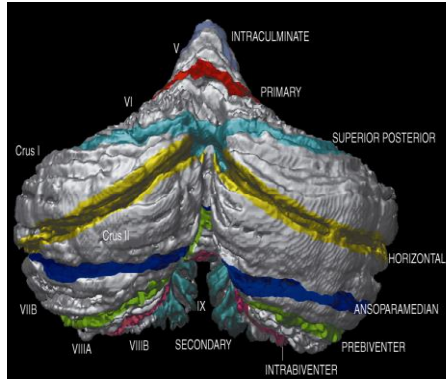
Myths and Misconceptions in Attention Deficit/Hyperactivity Disorder

Brain Regions Implicated in ADHD



The Unique Cerebellum! (among our gross anatomic measures)

- Least heritable
- Latest to reach adult volume
- Most sexually dimorphic (male >female, surviving TCV covariate)



ADHD Brain Imaging: Conclusions

- Brain smaller (4%), esp frontal lobe (8%)
- Basal Ganglia smaller (~ 6%)
- Cerebellum smaller (12%), esp posterior-inferior vermis (15%)
- Not currently of routine diagnostic value.
- Developmental *trajectories* may be most informative.

What is the best strategy for determining optimal medication management?

1. Fair fight
2. Guess and check
3. Mg/kg
4. Pharmacogenetics

Medicines Can:

- Increase
 - focus/ability to sustain attention
 - accuracy of work
 - following of rules better
 - “thinking before acting”
- Decrease
 - fidgetiness/activity level
 - impulsivity
 - aggression

Medicines Can't:

- Teach good behavior
- Teach skills they missed
- Teach dealing with feelings
- Motivate the child

Pharmacotherapy



Stimulants

Methylphenidate HCl
Amphetamine

Antidepressants

Tricyclic antidepressants
Bupropion

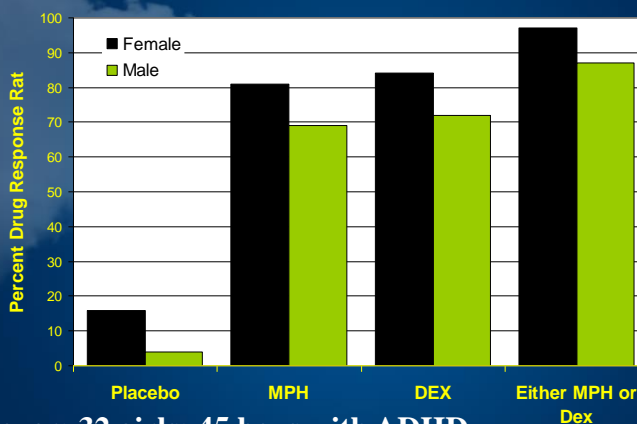
Antihypertensives

Clonidine
Guanfacine

ADHD and Stimulants

- Methylphenidate and Amphetamine
 - 70% have positive response to first stimulant tried
 - 90% if second tried
 - Safe and effective if used appropriately

Stimulant efficacy in ADHD



Crossover: 32 girls; 45 boys with ADHD

One size does not fit all

- Individualized dosing = key
- Head-to-Head comparisons
- Feedback from teachers, parents, and student critical to adjust dosage

“Fair Fight” Treatment Strategy

- Compare Methylphenidate product (e.g. Concerta) to Dextroamphetamine product (e.g. Adderall XR) – one month trial of each
- Start low (Concerta 18mg, Adderall 5mg), increase dosage each week (Concerta + 9mg, Adderall + 5mg)
- Stop if side effects!
- After the two months have patient choose which medicine and which dosage works best

Thank You!

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