The Neuroscience of Attention Deficit Hyperactivity Disorder: Implications for Treatment

Steven R. Pliszka, M.D.
Professor and Chief
Division of Child and Adolescent Psychiatry
UTHSCSA

Objectives

• Describe the neuroanatomy and neurophysiology of the developing brain in children and adolescents
• Describe the differences in the neuroanatomy and neurophysiology associated with Attention Deficit Hyperactivity Disorder (ADHD)
• Discuss the impact that the current knowledge of neurobiology in children and adolescents has on current treatment strategies in ADHD

Multifaceted Neurology of ADHD

• Neuroanatomy
• Attention Networks
• Cerebellar networks
• Reward processes
• Default network
• Connectivity

Cortical thickness over time

BIOL PSYCHIATRY 2013;74:599–606
How do stimulants effect brain growth?

- 43 patients with ADHD, mean age 12 yrs, 40 taking stimulants at baseline
- 19 patients stopped taking medication (reasons not specified)
- 19 off stimulants compared to 24 on stimulants at age 16
- Small numbers in each group exposed to alpha agonists and antidepressants
ADHD neurobiology

Meta-analysis of fMRI data

Rubia et al., Biological Psychiatry

Meta-analysis of stimulant effects (single dose)

Cerebellum in ADHD

Mulder, Durston et al., JAACAP Jan 2008

Reward Processes in ADHD

Ventral Tegmental/Nucleus Accumbens

Money

Beauty

Sports cars

Reward music

Happiness

Hunger

Arrested development

Ventral striatum and Reward
Ventral striatum and Reward

Default Mode Network

Active mode
Anterior Cingulate
rIFG, rMFG

Brains in the resting state

Default mode
Precuneus
Posterior Cingulate
VM PFC

Differences in Resting State

MPH and the default mode network (DMN)

• 24 children with ADHD (age 9-15 years), 24 age matched controls.
• FMRI with Go/No Go task
• ADHD children scanned on and off medication
• All subjects did low and high reward.

• Castellanos et al. Biol Psychiatry 63: 332, 2008

Brains in the resting state
MPH and the default mode network

Functional Connectivity

Cool (blue) colors represent deactivation of the DMN.

Tomasi & Volkow, Biol Psychiatry 71:442, 2010

247 ADHD
304 Controls

Functional scans

Meta-analysis

More connected to limbic, less to DMN

Emotional Processing in ADHD


Subliminal fearful faces presented during fMRI

Age and IQ matched control and adolescent with ADHD

Emotional Processing in ADHD

Connectivity between PFC and amygdala on y axis

Are these deficits unique to ADHD?

During an impulse control task (in bipolar subjects without ADHD):
- Bipolar children have less ACC activation than controls
- Bipolar adults have more ACC activation than controls


Other issues

- Genome Wide Association Studies (GWAS) have not:
  - Confirmed genes found in earlier candidate gene studies
  - Found genes of major effect in spite of high heritability (~.7-.8)
- CNVs more numerous in ADHD with developmental disabilities
- Possible that early experience shapes brain development (epigenetics)

Implications for Clinicians

- No single neurological lesion that defines ADHD.
- Neurological dysfunction detected by current technology (EEG, etc) would be found in any disorder that impairs attention/impulse control.
- How do tell ADHD from _____? Not really a relevant question.

Using a chronic treatment model

- Reduce symptoms with stimulant medication- not a bad thing- no need to be constantly looking for “alternatives”
- Brain differences vs. brain damage
  - Asthma as a model
    - Effort is to ADHD as exercise is to asthma
- Good and bad stigma

Behavioral Approaches

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Behavioral Approaches

- Behavioral approaches are mostly adjunctive
- Time consuming
- Differences in outcome
  - IQ
  - Family
  - Lack of aggressive comorbidity