How ADHD Develops, Sometimes gets Worse & Sometimes gets Better

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What is essential problem in ADHD?

- **Old**: behavior problems & not listening
- **New**: developmental impairment of the brain’s management system: EF

- Aspects of brain’s EF don’t come online in usual time frame.
- And don’t work consistently

TE Brown, Yale Medical School, 2013
Executive Functions

- Wide range of central control processes of the brain
- Connect, prioritize, and integrate cognitive functions—moment by moment
- Like conductor of a symphony orchestra

TE Brown, Yale Medical School, 2013
<table>
<thead>
<tr>
<th>Question</th>
<th>Category</th>
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<tr>
<td>Will you do it?</td>
<td>Motivation/Activation</td>
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<tr>
<td>How will you do it?</td>
<td>Planning/Organizing</td>
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<tr>
<td>When?</td>
<td>Timing/Remembering</td>
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“Will you do it and, if so, how and when?”  
(Lezak, 2004)

TE Brown, Yale Medical School, 2013
Characteristics of ADHD Symptoms

- **Dimensional, not “all-or-nothing”**
  - Everyone sometimes has some impairments in these functions; in ADHD: chronic, severe impairment

- **Situational variability: “If I’m interested”**
  - Most persons with ADHD have a few activities where ADHD impairments are absent

ADHD looks like willpower problem, but it isn’t!

T.Brown, Attention Deficit Disorder: The Unfocused Mind in Children & Adults (2005)
The Mystery of ADHD: Situational Variability of Symptoms

- Why focus for this, but not that?
  “If it really interests me” (attraction)

- Why focus then, but not now?
  “If I feel the gun to my head” (fear)
Brown’s Model of Executive Functions Impaired in ADHD

Executive Functions

Organizing, prioritizing, and activating to work

1. Activation

Focusing, sustaining focus, and shifting focus to tasks

2. Focus

Regulating alertness, sustaining effort, and processing speed

3. Effort

Managing frustration and modulating emotions

4. Emotion

Utilizing working memory and accessing recall

5. Memory

Monitoring and self-regulating action

6. Action

Average genetic contribution of ADHD based on twin studies

- **ADHD Genetics: Heritability Coefficient**

<table>
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<th>ADHD</th>
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<th>Asthma</th>
<th>Schizophrenia</th>
<th>Height</th>
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Average genetic contribution of ADHD based on twin studies

Continuing Brain Development in Late Childhood and Adolescence

- Between 6-15 years, **extreme growth** (to 80%) occurs at the collosal isthmus that supports associative relay, while considerable **synaptic pruning** occurs.

- **Brain myelination increases 100%** during the teenage years.

- **Dopamine (DA)**, **norepinephrine (NE)**, and **serotonin (5-HT)** **transmitter systems** in the brain **continue to develop** into one’s 20s.

Executive Functions: Development and Demands

- EF capacity develops through childhood, into adolescence, and beyond; it is not fully present in early childhood.
- Environmental demands for EF increase with age, from preschool through adulthood.
- EF impairments often are not noticeable by age 12 yrs!

TE Brown, Yale Medical School, 2013
When Are ADHD Impairments Noticeable?

- Some are obvious very early and are noticeable in preschool years
- Some are not noticeable until middle elementary or junior high
- Some are not apparent until child leaves home to go to college or later

TE Brown, Yale Medical School, 2013
Brain differences underlying ADHD (temporary and/or longer term)

1. Delay in unfolding of brain development that supports executive functions
2. Impaired white matter connections between brain regions
3. Impaired control of oscillations that coordinate brain region communications
4. Inadequate release/reloading of transmitter chemicals at synapses

TE Brown, Yale Medical School, 2013
Cortex Maturation in ADHD vs NC

- MRI studies of 40K cortex sites in 223 youths with ADHD vs matched controls
- Brain maturation was delayed ~3yrs in specific regions in ADHD youths vs NC
- Frontal areas of cortex slower in ADHD
- Medial PFC developed lagged 5 yrs

(Shaw, et al, PNAS, Nov, 2007)
Strutural Brain Differences in Persistent vs Remitted ADHD

MRI comparisons of persons with remitted vs persistent ADHD at 24 yrs indicated increased medial PFC cortical thinning in those with persistent ADHD while cortical thinning gradually began to thicken in those whose ADHD sx remitted, making their cortical thickness more similar to TDC. (Shaw, Malek, Watson, et al. 2013)
Is ADHD Brain Wired Differently?

- New model shifts focus from local brain abnormalities to dysfunction in broader distributed network organization.  
  (Cortese, Kelly, Chabernaud, et al., 2012)
- DTI shows evidence for white matter (“subway”) pathology & disrupted connectivity in ADHD  
  (Konrad & Eichoff, Human Brain Mapping, 2010)

TE Brown, Yale Medical School, 2013
Gray & white matter Differences in Persistent vs Remitted ADHD

- fMRI comparison of adults w/persistent vs remitted ADHD showed clear differences in functional connectivity btwn the 2 grps (Mattfeld, Gabrieli, et al. 2014)

- DTI comparison of adults w/ADHD 33 yrs earlier vs controls showed persistent decrease in white matter connections for both current and remitted ADHD vs NC (Cortese, Imperati, Zhou, et al. 2013)
Chemical Dynamics of Brain also contribute to impairments of ADHD

- Not due to overall “imbalance of chemicals” (not too much/too little salt in soup)
- But to inadequate release and/or reloading of transmitter chemicals in countless infinitesimal network junctions
- Except for “messages” re priority interests or fear of imminent unpleasantness

TE Brown, Yale Medical School, 2013
A Chemical Problem

- ADHD is fundamentally a chemical problem
- Most effective treatment is to change the chemistry with medication
- Unless the problematic chemistry is changed, other interventions are not likely to be very effective
In the Human Brain

- 100 billion neurons
- each one linked to >1000 others
- in complex sub-systems
- that have to “talk to each other”
- using low voltage electrical impulses
- that have to jump across gaps
- so fast that 12 can cross in 1/1000 sec.
Chemicals Jump the Gaps

- Inside brain >50 different chemicals are continuously made
- every neuron system uses 1 of them
- stored in little vesicles near tip of neuron
- when electrical impulse comes, mini-dots of that chemical are released,
- cross the gap, fire next neuron, then reload in fractions of a second
Message
Zips in
Releasing transmitter
Mechanisms of Action of Stimulant Medications

Increasing release of dopamine (AMPH)

Slowing reuptake of dopamine (MPH and AMPH)
Medications for ADHD

- Evidence for safe and effective
- Effective dose not based on age, wt or severity of sx
- Require titration and monitoring to “fine tune” to individual sensitivity and time frames for schedule and tasks
Time Frames and Rebound

If sustained feeling/acting excessively:

- “wired” or racy
- irritable
- serious, loss of “sparkle”

During the time dose is active, dose is probably too high

If these effects occur as med is wearing off, problem is more likely to be “rebound”, ie dropping too fast.

TE Brown, 2002
How do ADHD Impairments of EF Usually Respond to Medication?

- This wide range of cognitive impairments responds to medication treatment in 70-90% of cases in children, adolescents and adults.
- Symptom improvement varies from modest to very dramatic.
- Adverse effects are usually transient, not significant.
Set Realistic Expectations for Tx Medications do not cure ADHD!

- Cannot realistically promise “there will be no problematic effects” for any medication for any disorder.
- Cannot realistically promise that medication will effectively treat ADHD. ~80% success rate w/stims
- Close prescriber-patient collaboration is essential for “fine-tuning”
How ADHD sometimes gets worse

1. Being required to undertake new challenges without adequate support
2. Being repeatedly or harshly criticized for failures they cannot control
3. Co-occurring emotional, cognitive, or behavioral problems, eg drugs or alcohol, anxiety, depression
How ADHD sometimes gets worse

4. Environmental adversities, persistent family stresses, eg poverty, violence
5. Bodily changes of aging & menopause
6. Lack of appropriate diagnosis and treatment
How ADHD Sometimes Improves

1. Brain development may be delayed, then catch up
2. Ongoing interaction with supportive family members, teachers, friends
3. After completing basic schooling, finding work that fits interest & skills
4. Stable relationship with a partner with mutual support and compensations
How ADHD Sometimes Improves

5. Co-occurring disorder may improve, eg, stopping excessive etoh or drugs

6. Developing **compensatory strategies** to compensate for ADHD impairments

7. **Getting adequate** assessment and effective treatment
Key Points

1. Essential problem in ADHD is developmental impairment of EF
2. Those with ADHD usually can focus well for some tasks, though not for most others.
3. Inherited brain differences underlie ADHD.
4. Brain developmental delays & environmental stresses can worsen ADHD
5. Adequate treatment with meds and supports can improve it.

TE Brown, Yale Medical School, 2013
A Useful Resource

Understood.org
free objective information from experts
In understandable English or Spanish
24/7
Books by Thomas E. Brown, Ph.D. (www.DrThomasEBrown.com)

- “Smart but Stuck: Emotions in Teens and Adults with ADHD” – 2014
- “A New Understanding of ADHD in Children and Adults: Executive Function Impairments” – 2013
- “Attention Deficit Disorder: The Unfocused Mind in Children and Adults” - 2005