

New developments in the research and treatment of ADHD

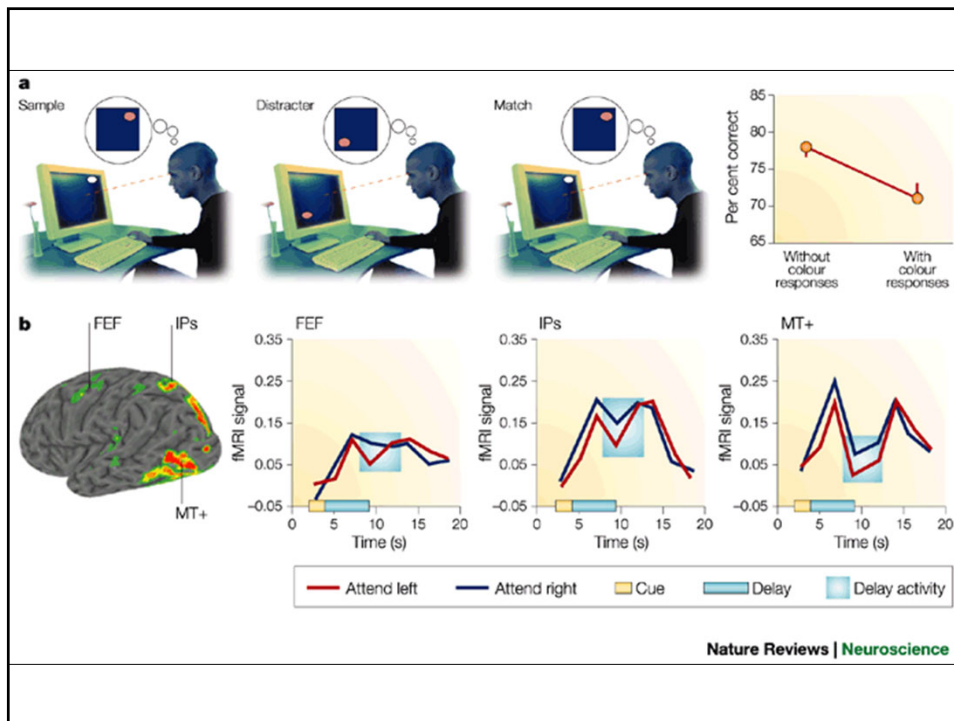
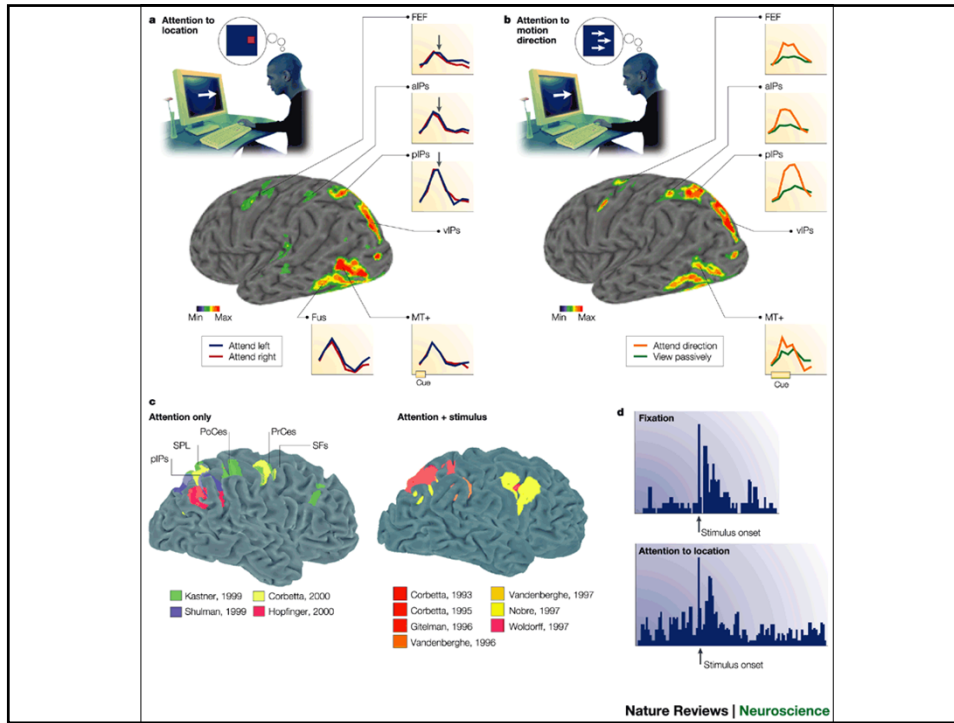
Steven R. Pliszka, M.D.
Professor and Vice Chief
Chief, Division of Child
and Adolescent Psychiatry

Concepts of Attention

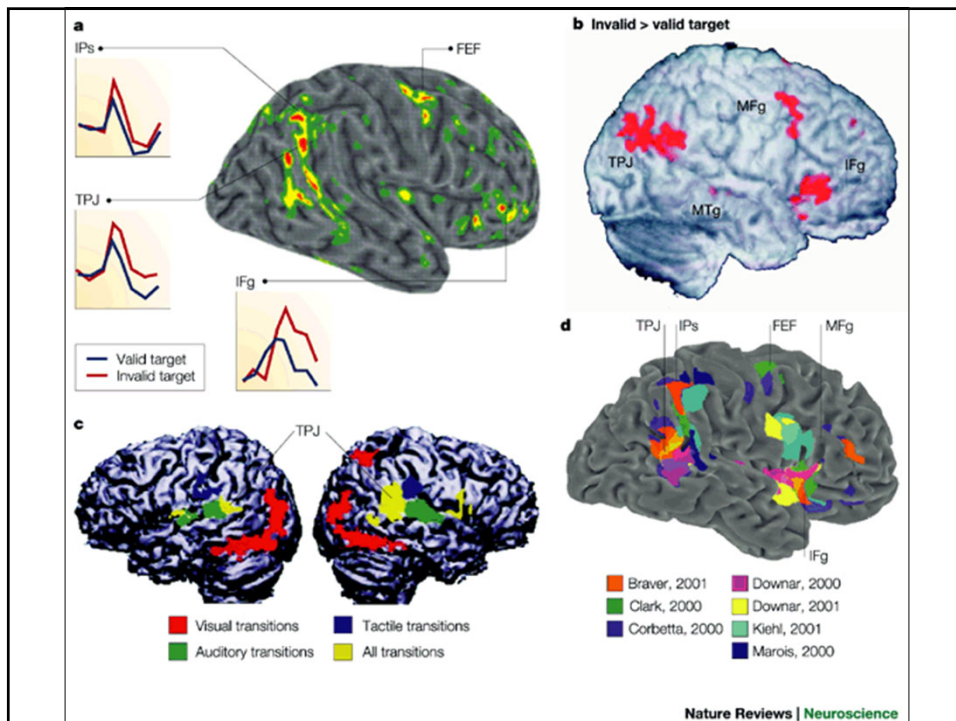
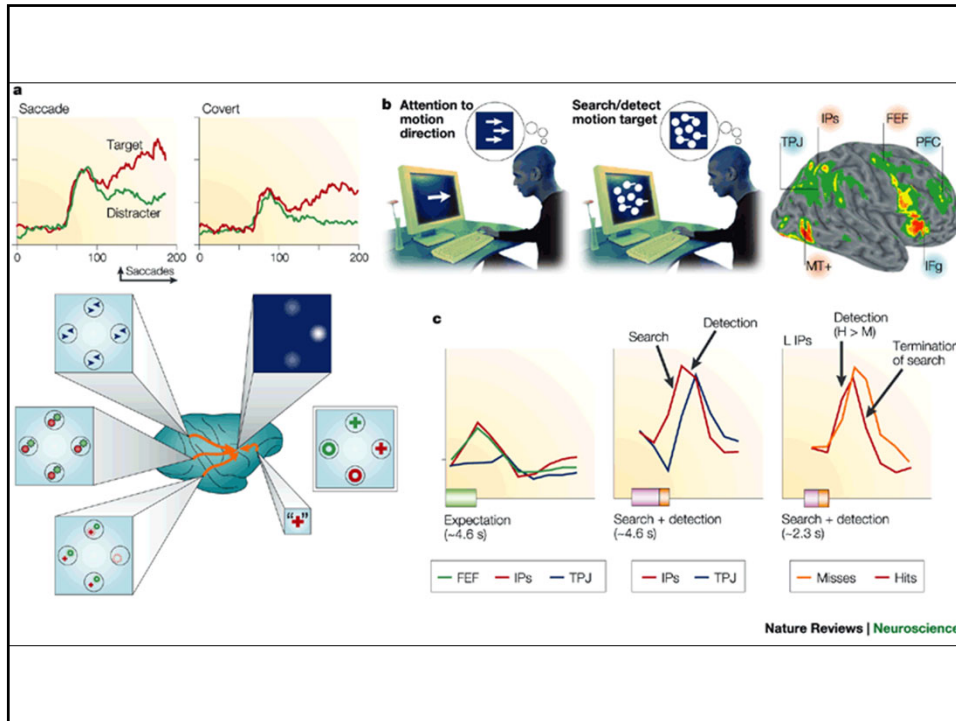
- “Bottom Up” –Capture of Attention by external stimulus
- “Top down” Directed attention enhances sensory perception
- “Paying attention” - suggests effort and energy involved
- Does attention = motivation?
Consciousness?

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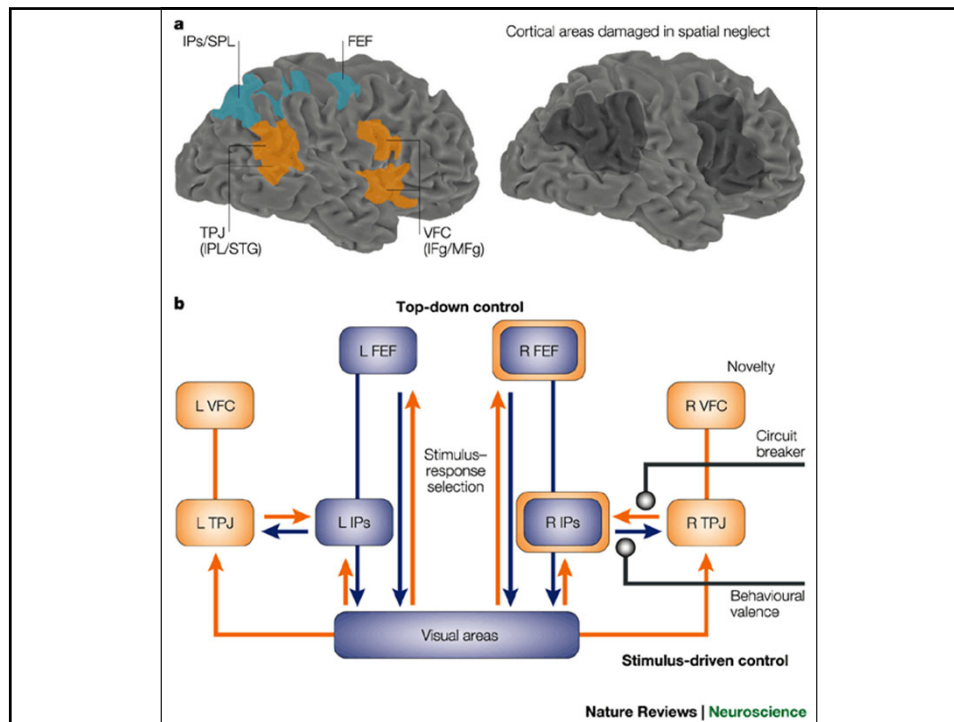
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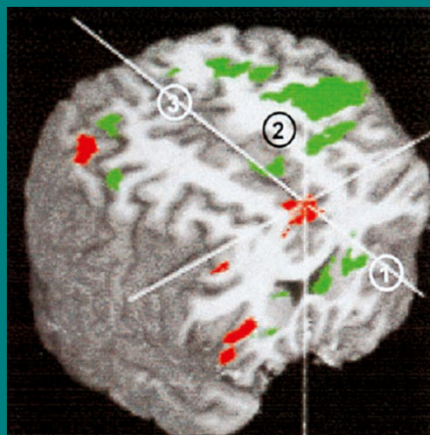
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Imaging Inhibitory Control

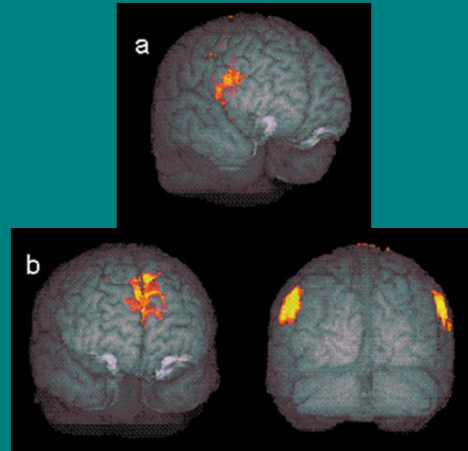


- ACC: performance monitoring
- DLPFC: implementation of control
- Double Dissociation (Macdonald et al., 2000)
- Parietal lobe: motor/attentional
- Lateralization

Garavan et al 1999

SST Activation Patterns

- Successful Inhibition
 - Stop trial where subject does not press button
 - Increase in Right DLPFC (a)
- Unsuccessful Inhibition
 - Stop trial where subject presses the button
 - Increase in ACC and Parietal lobe (b)



Rubia et al., 2003

Participants

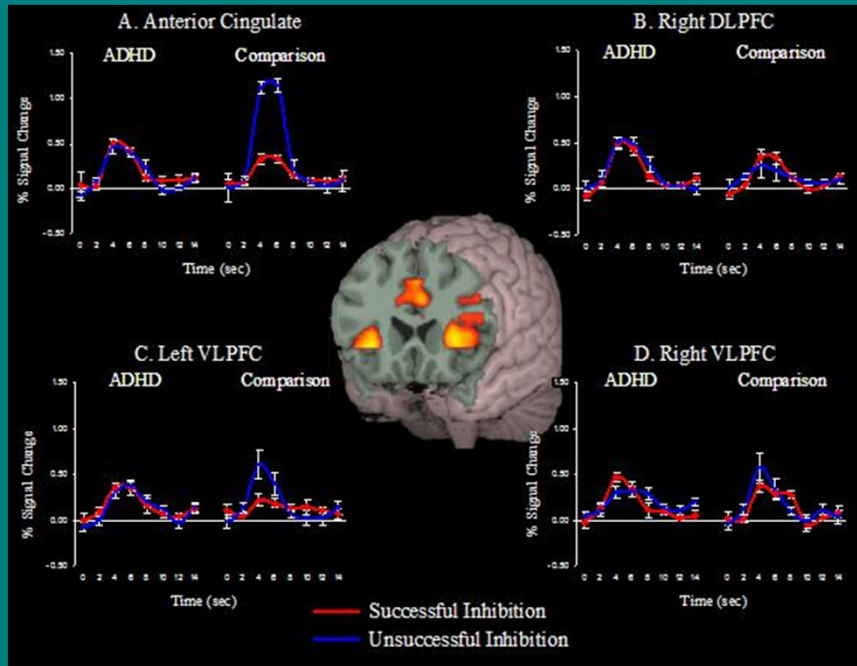
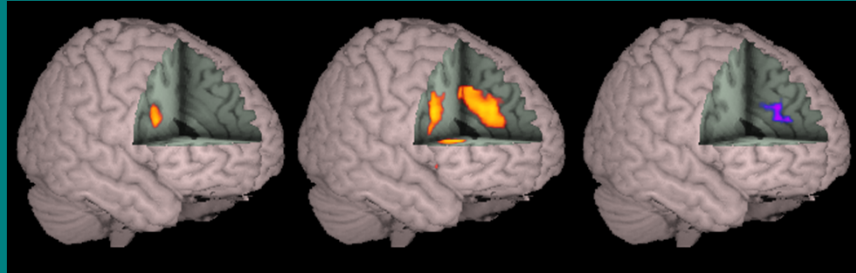
- 17 children with ADHD
- 15 healthy comparison subject
- Without chronic medical illness; anxiety or affective disorder, or reading/learning disability
- All children were not medicated (24 hours)

Inhibition in 15 Healthy Children

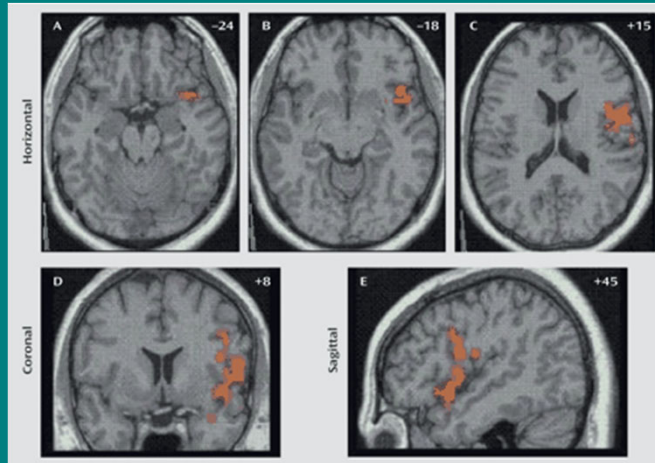
Successful

Unsuccessful

Contrast

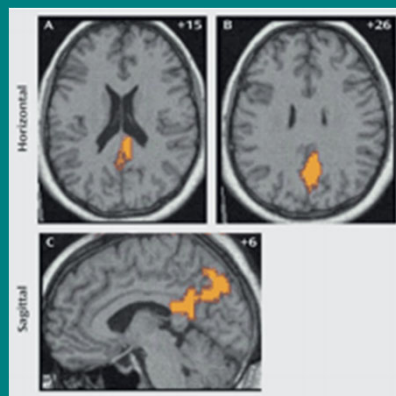


Rubia et al. AJP June 06: SST



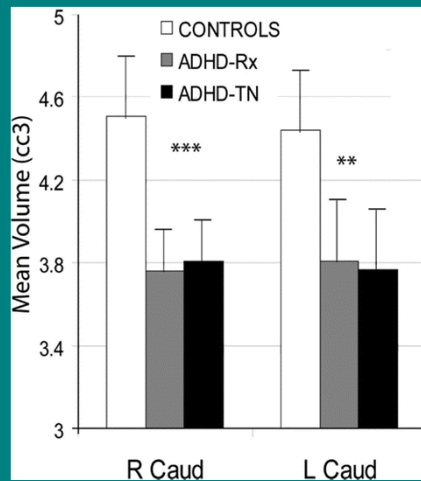
Orange: Controls > ADHD during successful inhibition

Rubia et al. AJP June 06: SST

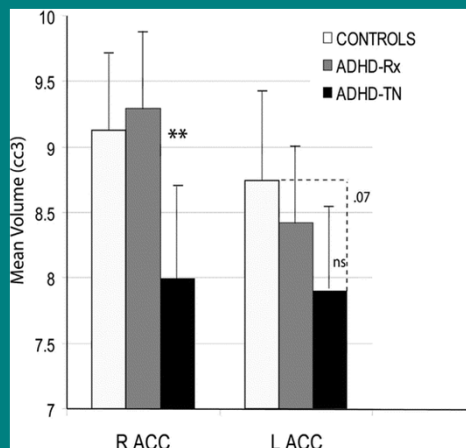


Orange: Controls > ADHD during unsuccessful inhibitions

Semrud Clikeman et al. Neurology 67: 1023 2006

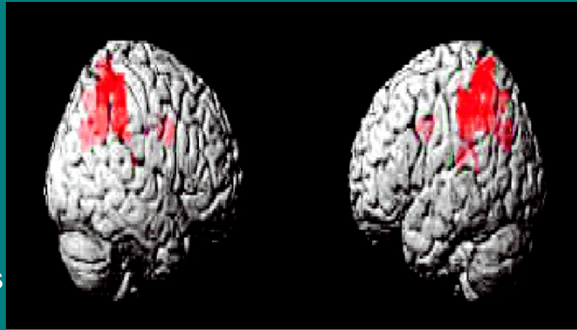


Semrud Clikeman et al. Neurology 67: 1023 2006



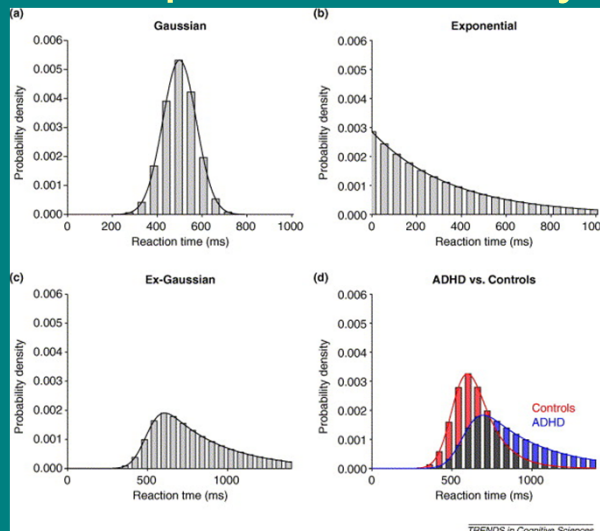
Tamm et al. AJP 163:1033 2006

- 14 adolescents with ADHD, 12 controls
- Performed an oddball task- press button 1 for common stimuli (circles), button 2 for rare stimuli (triangles)
- Rare stimuli activates parietal attentional areas



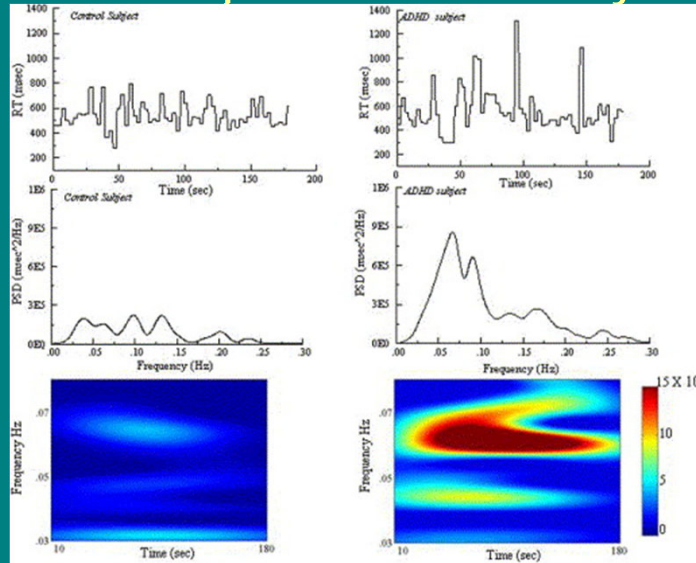
Areas of activation greater in controls vs. ADHD

Response variability

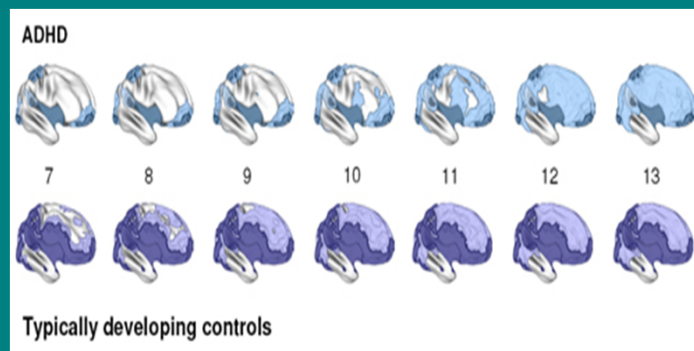


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Response Variability



Brain maturation in ADHD



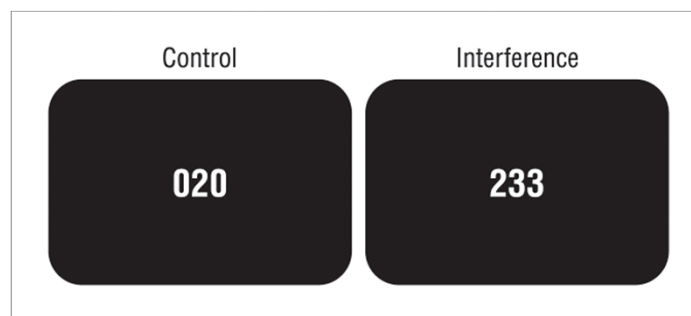
Shaded areas represent greater cortical maturation, note how ADHD average brain at age 8-11 shows less development (less thickening)

Shaw et al., 2007, www.nimh.nih.gov

Imaging Treatment Response

- Bush et al. Archives Gen Psych 65:102, 2008
- 21 unmedicated adults with ADHD randomized to MPH OROS or PBO
- FMRI at baseline and endpoint, subjects performed Multisource Interference Task

Multi-Source Interference Task trial examples

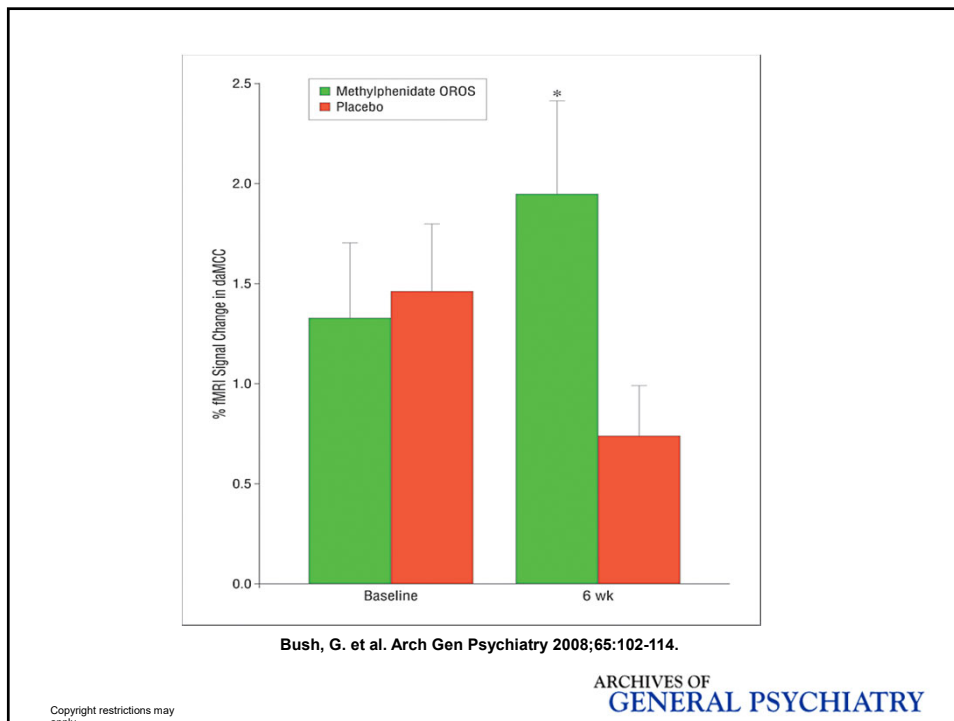
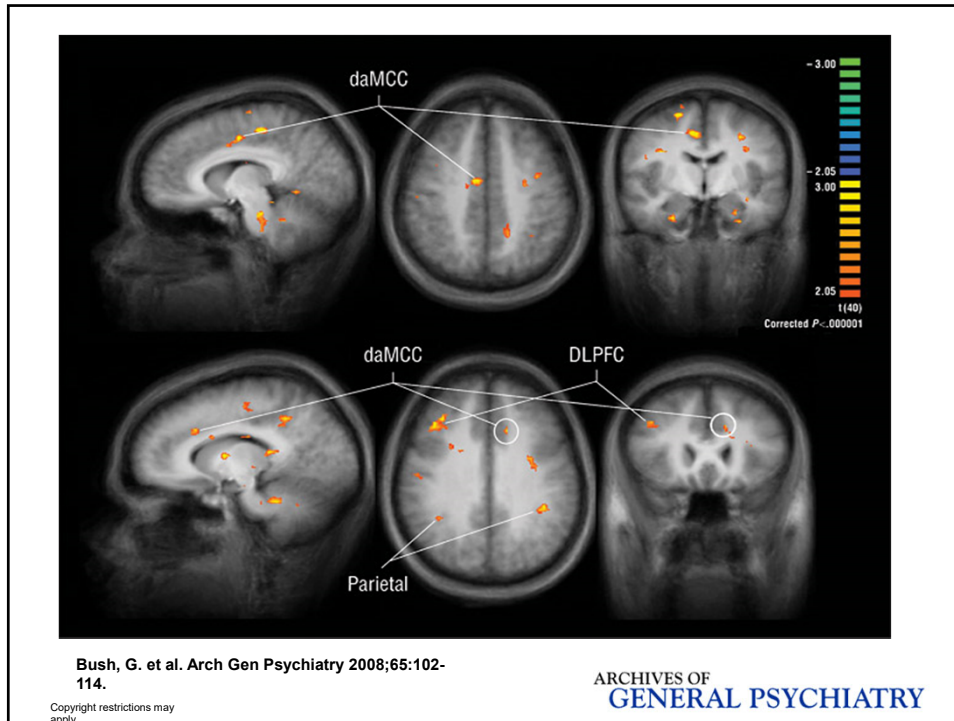


Bush, G. et al. Arch Gen Psychiatry 2008;65:102-114.

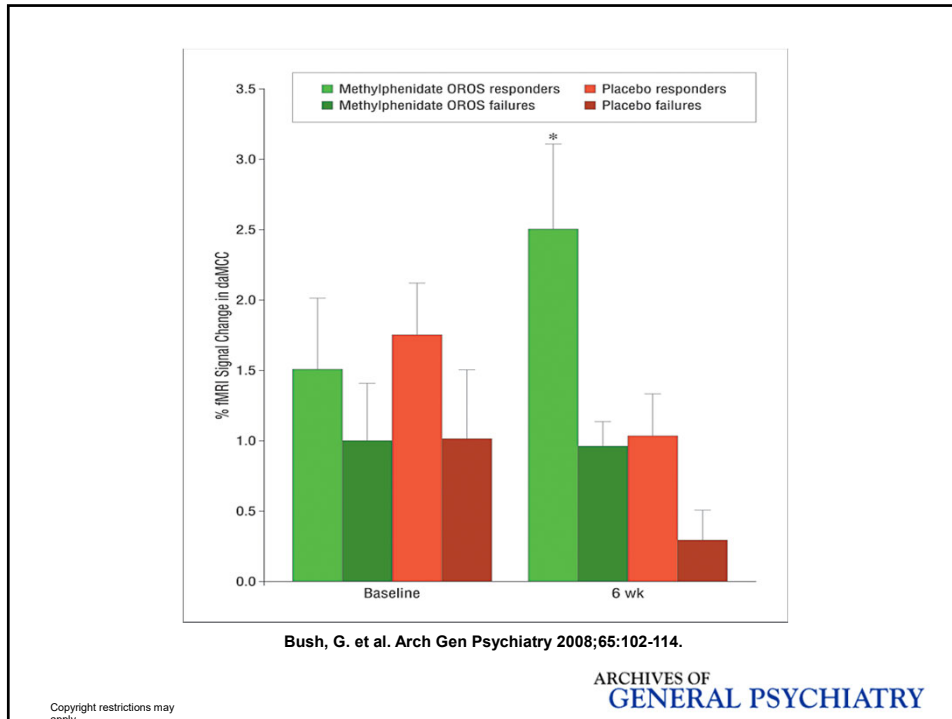
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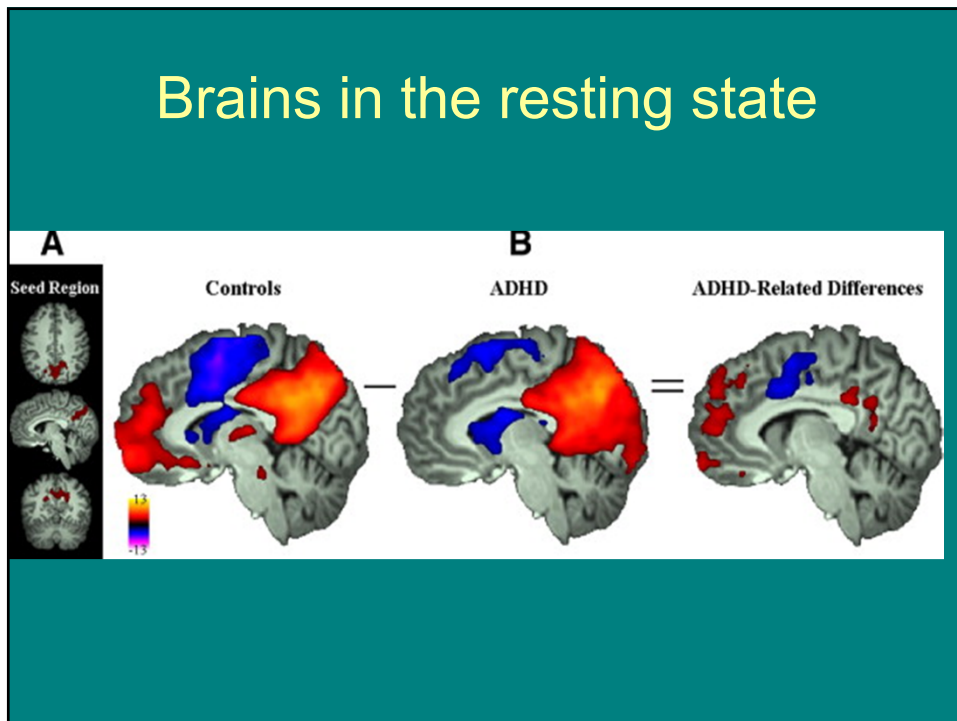
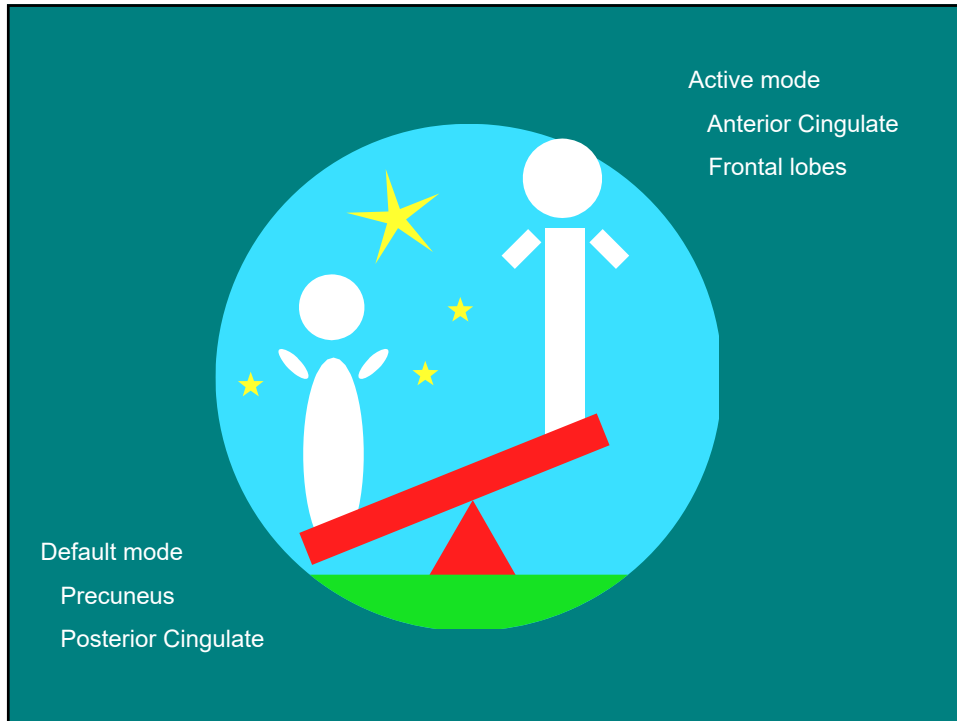
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Resting attention

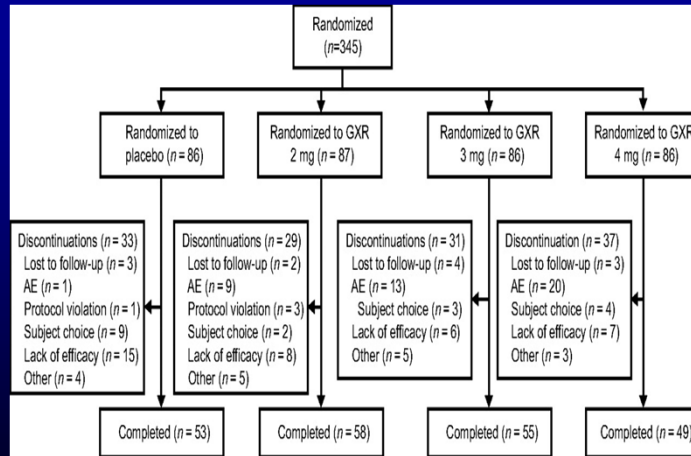
- Brain has two major modes of activity
 - “Resting”- in fact brain is active- many random thoughts, daydreaming
 - “Active”- when performing a task
- Even when engaged in a task, people shift between the modes
- Precuneus of the brain (middle of the parietal lobes) is active during default mode
- The teeter-totter brain

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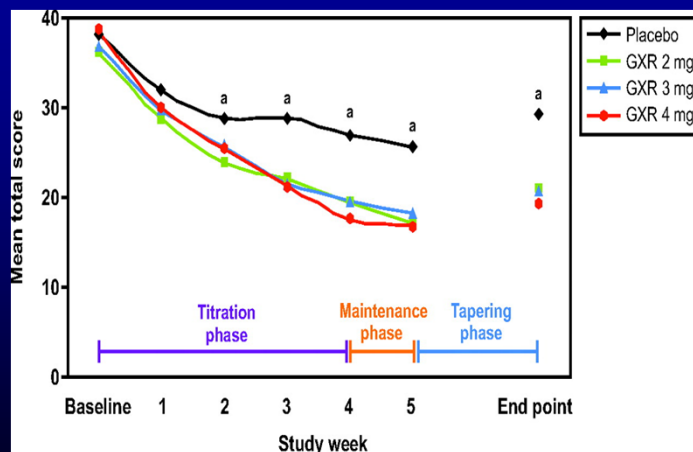
Guanfacine Extended Release



Biederman, J. et al. Pediatrics 2008;121:e73-e84



ADHD-RS-IV: mean total score according to randomized dose

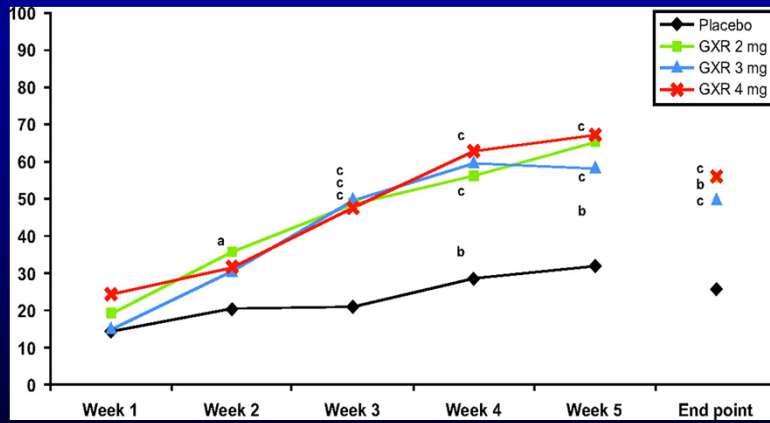


Biederman, J. et al. Pediatrics 2008;121:e73-e84



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Percentage of subjects with improvement in CGI-I scores

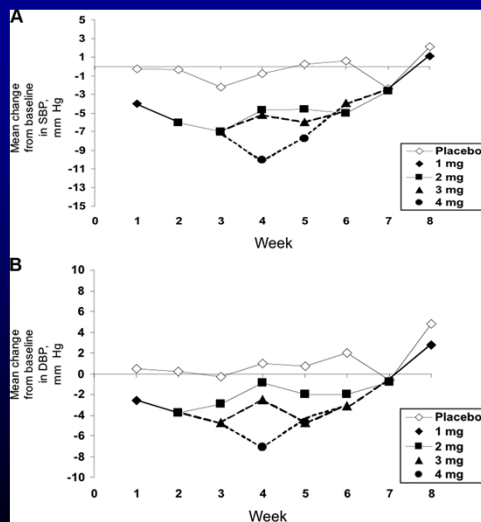


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Mean change from baseline in SBP according to actual GXR dose



Biederman, J. et al.
Pediatrics 2008;121:e73-
e84

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