Neuropsychology of Attention Deficit Hyperactivity Disorder (ADHD)

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Disclosures

Lundbeck–Advisory Board and Research Support

FDA- Research Support
What is a Neuropsychologist?

- Doctoral training in psychology
- Specialized coursework
- Postdoctoral training (two years)
- Has probably done and can do ‘regular psychologist’ things
- Additional specialized training in assessment of cognitive functioning
- Diagnoses abnormality in cognitive functions
- Does lots of testing!
What is a Neuropsychological Evaluation?

• A neuropsychological evaluation is a comprehensive assessment of cognitive and behavioral functions using a set of standardized tests and procedures.
Neuropsychological evaluations may:

- Confirm or clarify a diagnosis
- Provide profile of strengths and weaknesses for educational, vocational, or other services
- Document changes in functioning since prior examinations, including effects of treatment
- Clarify what compensatory strategies would help
- Result in referrals to other specialists
Why all the testing?
Neuropsychological evaluations typically include:

• Intelligence (IQ)
• Attention / organization
• Fine motor
• Academic achievement
• Memory
• Mood
• Parent / teacher questionnaires (assessing mood, behavior, strengths)
Researchers: Scope of Inquiry

• Parallels between ADHD symptoms and presumed cognitive deficits and frontal lobe disorders

• Higher-order cognitive processes thought to be sub-served by the frontal lobes such as:
  – inhibitory control
  – attentional regulation
  – working memory

• Constructs grouped under the rubric of executive function (EF)
Cannot react and respond to information appropriately.

Believed to be a shortage of dopamine and noradrenaline.

RESPONSIBLE FOR: Planning, Motivation, Social functioning, Speech.

FRONTAL LOBE
The part of the brain involved in ADHD.

Works more slowly in ADHD. Has a shortage of neurotransmitters.
Interest in Executive Functions

*5 articles in 1985

*14 articles in 1995

501 articles by 2005

-Bernstein & Waber
Executive Function, 2007
What are Executive Functions?

Orchestration of basic cognitive processes during goal-oriented problem-solving:

the “CONDUCTOR”
Executive Functions

Functions of the “Orchestra”

- Perception
- Attention
- Language processes
- Visual-spatial processes
- Memory
- Sensory Inputs
- Motor Outputs
- Knowledge & Skills
- Social
- Non-social

Functions of the “Conductor”

- Inhibit
- Shift Flexibly
- Modulate Emotions
- Initiate
- Working Memory
- Plan
- Organize

Development of Executive Functions

Plan/Organize/Monitor 3-32 yrs

Emotional Modulation 3-???

Verbal Working Memory 2-13 yrs

Nonverbal Working Memory 3-24 mo

Inhibit 0-???
Assessment of EFDs

• Neuropsychological Testing

• Checklists
A large meta-analysis domains of **executive functioning** deficits in ADHD

<table>
<thead>
<tr>
<th>Domains of Executive Functioning</th>
<th>Meta-analytic Effect Size ($d$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Set shifting</td>
<td>0.50</td>
</tr>
<tr>
<td>Working memory (verbal)</td>
<td>0.45</td>
</tr>
<tr>
<td>Working memory (spatial)</td>
<td>1.00</td>
</tr>
<tr>
<td>Planning</td>
<td>0.55</td>
</tr>
<tr>
<td>Inhibition</td>
<td>0.60</td>
</tr>
</tbody>
</table>

### Neuropsychological Tests

<table>
<thead>
<tr>
<th>Neuropsychological Test</th>
<th>Executive Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color Word (D-KEFS)</td>
<td>Inhibition</td>
</tr>
<tr>
<td>Trails Making (D-KEFS), IED (CANTAB), Letter-Number Test (WAIS)</td>
<td>Set Shifting</td>
</tr>
<tr>
<td>Stockings of Cambridge (CANTAB)</td>
<td>Planning/Organizing</td>
</tr>
<tr>
<td>Symbol Search (WAIS/WISC)</td>
<td>Task Monitoring, Initiating</td>
</tr>
<tr>
<td>Digit Span, Arithmetic, Letter-Number Test (WAIS/WISC)</td>
<td>Working Memory</td>
</tr>
<tr>
<td>Coding (WAIS)</td>
<td>Initiating</td>
</tr>
<tr>
<td>Matrix (WAIS)</td>
<td>Inhibition, Spatial Working Memory</td>
</tr>
</tbody>
</table>
Inhibition

- Ability to control impulses and stop one’s own behavior at the appropriate time
- Test
  - Color Word (D-KEFS)
- BRIEF examples
  - Interrupts or disrupts group activities
  - Has trouble putting on the brakes
  - Says/does things impulsively without thinking
  - Makes decisions that get them into trouble

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<thead>
<tr>
<th>red</th>
<th>blue</th>
<th>red</th>
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<tbody>
<tr>
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<td>blue</td>
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<td>red</td>
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</table>

### Color Word

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<tr>
<th>red</th>
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<tr>
<td>green</td>
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</tr>
<tr>
<td>blue</td>
<td>green</td>
<td>red</td>
</tr>
</tbody>
</table>

Set Shifting

- Ability to move from one situation, activity, or part of a problem to another as the condition demands

- Test
  - Trails Making (D-KEFS)
  - Intra-Extra Dimensional Shift Set (CANTAB),

- BRIEF examples
  - Tries the same approach even when it does not work
  - Has trouble moving from activity to activity
  - Resists accepting a different solution
  - Experiences anxiety, or extreme anger when things change

Trails Making

- Switch between connecting the numbers and letters
- Begin at number 1 and draw a line from 1 to A, A to 2, 2 to B, B to 3 and so on until you reach the end

Planning/Organizing

• Ability to manage current and future oriented task demands within the situational context

• Test
  – Stockings of Cambridge (CANTAB), TOWER tasks

• BRIEF examples
  – Starts tasks without the right materials
  – Has trouble prioritizing or organizing activities
  – Starts homework or chores at the last minute
  – Underestimates the time to finish tasks

Stockings Of Cambridge

• Use the balls in the bottom to copy the pattern in the top

Task Monitoring

• Ability to check work and assess performance during or after finishing a task to ensure a goal is finished

• Test
  – Symbol Search (WAIS/WISC)

• BRIEF examples
  – Does not check work for mistakes
  – Makes careless errors
  – Fails to catch one’s errors while completing a task
  – Does not problem solve during a task

Symbol Search

- One of these shapes is in this group of shapes over here, so draw a line through the shape.
- Neither of these shapes is in this group of shapes over here, so draw a line through the NO box.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>NO</td>
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<td>NO</td>
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<tr>
<td></td>
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<td></td>
<td>NO</td>
</tr>
</tbody>
</table>

Initiating

• Ability to begin a task and independently generate ideas, responses, or problem solving strategies

• Test
  – Coding, Symbol Search, and Matrix (WAIS/WISC), Color Word and Trails Making (D-KEFS)

• BRIEF examples
  – Lies around the house a lot (couch potato)
  – Has good ideas but does not get the job done
  – Needs extensive reminders to begin a task
  – Has trouble getting started on tasks

Self Monitoring

• Ability to keep track of the effect of one’s behavior on others and attend to one’s behavior in a social context
• TEST examples: careless errors (process approach)
• BRIEF examples
  – Does not notice when behavior causes negative reactions
  – Becomes too wild or silly
  – Does not notice when others get mad until it is too late
  – Makes inappropriate sexual comments

Working Memory

• Ability to hold information in one’s mind for purpose of generating a response or completing a task

• Test
  – Digit Span, Letter Number, and Arithmetic (WISC/WAIS)

• BRIEF examples
  – When given three things, remembers only the first or last
  – Forgets to hand in homework
  – Forgets what they are doing in the middle of things
  – Has trouble remembering things, even for a few minutes

Definition of EFD

• In our previous work, individuals with $\geq 2$ impaired measures (across any domain) have showed particularly poor functional outcome

  – 2 or more tests has face validity in terms of what a neuropsychologist would need to conclude that an EF impairment exists

  – Operationally defined EFD as impairments in 2 or more tests
Impact of EFDs on Children with ADHD

- Examined psychometrically defined EFDs in children with and without ADHD and EFDs
- Included male and female (mean age=12.3-13.7 years old) probands from two longitudinal family studies of ADHD

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>103</td>
<td>121</td>
</tr>
<tr>
<td>Female</td>
<td>122</td>
<td>138</td>
</tr>
<tr>
<td>N</td>
<td>125</td>
<td>159</td>
</tr>
</tbody>
</table>

Impact of EFDs on Children with ADHD

Impact of EFDs on Children with ADHD

Impact of EFDs on Children with ADHD

Repeated School Grade

- Control: 8%
- Control + EDFs: 12%
- ADHD: 19%
- ADHD + EDFs: 42%

Impact of EFDs on Children with ADHD

- Using the psychometrically defined method, significantly more children with ADHD had EFDs than controls.
- Neuropsychological impairments in children with ADHD have implications for functional outcome above and beyond the diagnosis itself.
- Children with ADHD and EFDs had an increased risk for grade retention and a decrease in academic achievement, relative to ADHD alone.

## Impact of EFDs on Adults with ADHD

- Examined psychometrically defined executive function deficits (EFDs) in adults using traditional neuropsychological tests

### Table: Comparison of Groups

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Control + EDF</th>
<th>ADHD</th>
<th>ADHD + EDF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>122</td>
<td>23</td>
<td>147</td>
<td>66</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>29.3 ± 8.4</td>
<td>35.4 ± 8.8</td>
<td>34.6 ± 10.4</td>
<td>40.0 ± 10.3</td>
</tr>
<tr>
<td><strong>Gender (% male)</strong></td>
<td>55 (45%)</td>
<td>11 (48%)</td>
<td>80 (54%)</td>
<td>33 (50%)</td>
</tr>
</tbody>
</table>

Impact of EFDs on Adults with ADHD

Impact of EFDs on Adults with ADHD

Special Classes in School

- Control: 1%
- Control + EFDs: 4%
- ADHD: 11%
- ADHD + EFDs: 21%

Impact of EFDs on Adults with ADHD

Extra Help in School

- Control: 19%
- Control + EFDs: 35%
- ADHD: 42%
- ADHD + EFDs: 61%

Impact of EFDs on Adults with ADHD

Repeated School Grade

Control: 2%
Control + EFDs: 22%
ADHD: 17%
ADHD + EFDs: 32%

Can self-reported behavioral scales assess executive function deficits? A controlled study of adults with ADHD

Prevalence of EFDs in 194 Adults with ADHD

Self-Report EFDs
N=67

Psychometric EFDs
N=28

N=71 ADHD with neither EFD

BRIEF Scores in Adult ADHD

Biederman, Fried,, et al unpublished data
Social Adjustment Scale:
>65 Significant Problem

- No EFD
- Psychometric EFD
- Self-Report EFD
- Combined EFD

p<0.01 vs. No EFD and Psychometric EFD
p<0.001 vs. No EFD and Psychometric EFD
Lifetime GAF

- No EFD
- Psychometric EFD
- Self-Report EFD
- Combined EFD

p < 0.05 vs. all groups
CLINICAL CORRELATES OF WORKING MEMORY DEFICITS IN YOUTH WITH AND WITHOUT ADHD: A CONTROLLED STUDY
Background
What is Working Memory?

• The ability to hold information in memory for short time periods for use in complex tasks
• Dysfunction has been associated with academic deficits
• Predicts academic achievement
Background
Working Memory and ADHD

• Working Memory (WM) and ADHD are both associated with educational deficits
• WM deficits are prevalent in children with ADHD
• Literature is lacking on the contribution of WM deficits to academic dysfunction in children with ADHD
Main Aim:

• To assess the clinical correlates of WM deficits in ADHD

• Compared the functional outcomes of WM deficits using data from children with and without ADHD

• Hypothesis: WM deficits will be more prevalent in children with ADHD relative to controls, and individuals with WM deficits will have more impairments in academic functioning than individuals with ADHD without WM deficits
Subjects

• Youth of both sexes from longitudinal, case-control family studies at MGH (Biederman, 1992; Biederman, 1999)
• Participants aged 6-18 years

<table>
<thead>
<tr>
<th>ADHD</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 259</td>
<td>N= 222</td>
</tr>
</tbody>
</table>

Biederman et al. (1992). Further evidence for family-genetic risk factors in attention deficit hyperactivity disorder. Patterns of comorbidity in probands and relatives in psychiatrically and pediatriically referred samples, Arch Gen Psychiatry, 49(9), 728-38

## Assessment Procedures

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Abbreviation</th>
<th>Function</th>
</tr>
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<tbody>
<tr>
<td>Kiddie Schedule for Affective Disorders and Schizophrenia- Epidemiological Version</td>
<td>K-SADS-E</td>
<td>Psychiatric Functioning</td>
</tr>
<tr>
<td>Child Behavior Checklist</td>
<td>CBCL</td>
<td>Dimensions of Psychopathology</td>
</tr>
<tr>
<td>Social Adjustment Inventory for Children and Adolescents</td>
<td>SAICA</td>
<td>Psychosocial Functioning</td>
</tr>
<tr>
<td>Moos Family Environment Scale</td>
<td>FES</td>
<td>Family Functioning</td>
</tr>
<tr>
<td>DSM-IV Global Assessment of Functioning</td>
<td>GAF</td>
<td>Overall Lifetime Functioning</td>
</tr>
</tbody>
</table>
## Intellectual Functioning

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Subtest</th>
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<tbody>
<tr>
<td>WRAT-R</td>
<td>Reading &amp; Arithmetic</td>
</tr>
<tr>
<td>Full Scale IQ</td>
<td>Block Design + Vocabulary</td>
</tr>
<tr>
<td>Freedom from Distractibility Factor (Working Memory)</td>
<td>Digit Span, Digit Coding, Arithmetic</td>
</tr>
</tbody>
</table>

- Wide Range Achievement Test-Revised (WRAT-R)
FFD Proxy

• The significant correlation of .72 between the Freedom of Distractibility Factor and the Working Memory Index of the WISC-IV renders the use of FFD factor scores an appropriate proxy for WM index.
WM Deficit Classification

1. Subjects with FSIQ of 120 or less who had Freedom from Distractibility (FFD) score 1 SD (15 points) lower than FSIQ
2. Any subject with FFD ≤ 85
3. Subjects with full IQ ≥ 120 with a FFD 1.5 SDs (22.5 points) below full IQ.
Results

• Significantly more youth with ADHD had WM deficits than controls (31.9% vs. 13.7%, P<0.05)

<table>
<thead>
<tr>
<th>Within Group Comparisons:</th>
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<tbody>
<tr>
<td>ADHD</td>
</tr>
<tr>
<td>WM Deficits</td>
</tr>
<tr>
<td>N=88</td>
</tr>
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</table>
# Results: Socio-Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ADHD Groups</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WM Deficits N=88</td>
<td>No WM Deficits N=188</td>
<td>p</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Age</td>
<td>11.2 (± 3.1)</td>
<td>10.8 (± 3.2)</td>
<td>0.3</td>
</tr>
<tr>
<td>SES</td>
<td>2 (± 1)</td>
<td>1.8 (± 1)</td>
<td>0.3</td>
</tr>
<tr>
<td>Male</td>
<td>52 (59.1%)</td>
<td>86 (± 45.7%)</td>
<td>0.053</td>
</tr>
<tr>
<td></td>
<td>WM Deficits N=33</td>
<td>No WM Deficits N=208</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Age</td>
<td>12.2 (± 4)</td>
<td>11.8 (± 3.2)</td>
<td>0.5</td>
</tr>
<tr>
<td>SES</td>
<td>1.8 (± 0.9)</td>
<td>1.6 (± 0.7)</td>
<td>0.1</td>
</tr>
<tr>
<td>Male</td>
<td>20 (60.6%)</td>
<td>100 (48.1%)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*No significant within group pairwise comparisons for age, sex, SES, or intactness of family*
Results: Working Memory Deficit Rates

ADHD Subjects
- 68% No WMD
- 32% WMD

Control Subjects
- 86% No WMD
- 14% WMD
Results: School Deficits

ADHD

Extra Help: ADHD+WM > ADHD

Repeat Grade: ADHD+WM > ADHD

Special Class: ADHD+WM > ADHD

Controls

Extra Help: Controls + WM > Controls

Repeat Grade: Controls + WM > Controls

Special Class: Controls + WM > Controls

Codes: # = p<0.05, * = p<0.01, **=p<0.001
CBCL: Competence and Problems Scores

Scores

<table>
<thead>
<tr>
<th>Activities</th>
<th>Social</th>
<th>School</th>
<th>Total Competence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD + WM</td>
<td>ADHD + WM</td>
<td>ADHD + WM</td>
<td>ADHD + WM</td>
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<tr>
<td>ADHD</td>
<td>ADHD</td>
<td>ADHD</td>
<td>ADHD</td>
</tr>
</tbody>
</table>

Internalizing | Externalizing | Total

Scores

Internalizing | Externalizing | Total

ADHD + WM | ADHD + WM | ADHD

Codes: # = p<0.05, *= p<0.01, **=p<0.001
WRAT Arithmetic and Reading Score Comparison

Codes: ** = p < .001
Conclusions

- WM deficits among ADHD children significantly increased the risk for:
  - Grade retention
  - Placement in special classes
  - Lower academic achievement in reading and math
- Academic dysfunction could not be accounted for by differences in the clinical features of ADHD or by patterns of comorbidity
- No statistical evidence that WM deficits affected any other functional outcomes
- Findings provide support for selectively detrimental effect of WM deficits on cognitive and academic functioning in youth with ADHD