"New Directions in ADHD and Autism: Assessment and Treatment"

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Learning Objectives

- ADHD: Basic condition & impairments
- Autism Spectrum Disorders: Basic condition & impairments
- Attention: Relationship between attention problems, executive functioning and autism spectrum disorders
- Assessment: reliable & valid approaches, especially attention, within ASD
- Treatment: planning and novel approaches

Social Emotional NeuroScience Endocrinology (S.E.N.S.E.) lab

TABLE 1 Descriptive Statistics

<table>
<thead>
<tr>
<th>Measure</th>
<th>ADHD</th>
<th>Control</th>
<th>Univariate F</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOADQF</td>
<td>1.37</td>
<td>1.33</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>SD</td>
<td>1.27</td>
<td>1.33</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>TOADQc</td>
<td>2.86</td>
<td>2.84</td>
<td>p &lt; .0001</td>
</tr>
<tr>
<td>SD</td>
<td>2.86</td>
<td>2.84</td>
<td>p &lt; .0001</td>
</tr>
<tr>
<td>StroopW</td>
<td>47.48</td>
<td>46.27</td>
<td>p &lt; .0001</td>
</tr>
<tr>
<td>SD</td>
<td>7.48</td>
<td>7.55</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>StroopWC</td>
<td>42.74</td>
<td>40.53</td>
<td>p &lt; .0001</td>
</tr>
<tr>
<td>SD</td>
<td>6.97</td>
<td>7.39</td>
<td>&lt; .0001</td>
</tr>
</tbody>
</table>

- Symptoms of ADHD persist into adulthood.
- Many areas of executive functioning appear intact, but aspects of attention were significantly impaired in adults with ADHD.

Neuropsychological Functions in ADHD

COGNITION
Average-Above IQ

MOTOR
Hyperactivity
Motor Impersistence

PERCEPTUAL
Emotions Nuances

SOCIAL
Interupt

LANGUAGE
Talkative

MENTAL
Executive
ATTENTION
Establishing
Sustaining
Distractibility

SENSORY
Auditory

ENDOCRINOLGY (S.E.N.S.E.) lab

Neuropsychological Functions in ADHD

- Processing Affective Stimuli in Children with Attention-Deficit Hyperactivity Disorder*

<table>
<thead>
<tr>
<th>Variable</th>
<th>ADHD (SD)</th>
<th>Control (SD)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial Emotion</td>
<td>84 (17)</td>
<td>94 (96)</td>
<td>-0.87</td>
<td>0.39</td>
</tr>
<tr>
<td>Reading-Related</td>
<td>10.9 (3.2)</td>
<td>10.5 (3.5)</td>
<td>1.01</td>
<td>0.32</td>
</tr>
<tr>
<td>Verbal Go/No-Go</td>
<td>1.46 (0.87)</td>
<td>1.16 (1.12)</td>
<td>1.21</td>
<td>0.24</td>
</tr>
<tr>
<td>Matching Figures</td>
<td>7 (0.8)</td>
<td>7.07 (0.68)</td>
<td>0.45</td>
<td>0.66</td>
</tr>
</tbody>
</table>

*ADHD = 37 (28 boys, 10 girls); Control = 37 (29 boys, 8 girls); Matching Figures Test.
EEG Study PARTICIPANTS

- **Inclusion**: 25 children ages 8 to 12 with typical development (11) or ADHD - combined type (14) were enrolled.
- **Diagnosis**:
  - DSM-IV criteria (APA, 2000) and clinical evaluation,
  - Diagnostic Inventory Schedule for Children (DISC) (Shaffer, et al., 1996),
  - Conners’ Parent Rating Scale (Conner’s, 2001) hyperactivity and inattention scores >70
- **Estimated IQ**: Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999).
- **Medication**: Stimulant medication withheld 24 hours.

EEG to assess functional connectivity of Frontal & Visual Cortex

- **Rationale**: pathophysiological models suggest impaired functional connectivity of attention networks in ADHD
- **EEG recorded while children performed cross-modal (visual/auditory) task**
- **Power spectra of EEG in theta (3-5 Hz) and alpha (8-12 Hz) calculated for 1-sec interval after cue and before target while subject prepared to discriminate expected target**

Cross-Modal Paradigm

- **Symbolic visual cues validly or invalidly signaled the modality of an upcoming target**
  - 75% valid and 25% trials
- **Maintain fixation and use cue to prepare for upcoming target**
- **Press button right hand for Visual Target (red vs. blue target) or Auditory Target (high vs. low tone)**

Mazaheri, Mangun, Corbett (2010), Biological Psychiatry

**Behavioral Performance**
Both groups showed significant cuing effects for visual targets

![Graph showing behavioral performance](image)
Conclusions of EEG ADHD Study

- The functionally connectivity suggests top-down drive (i.e., midline theta) to perceptual areas (occipital alpha) setting the state of the brain to be prepared for the oncoming stimuli.
- In TD this connectivity may involve the normal functioning of the frontal-parietal attention network.
- This frontal-parietal attention network is disordered in ADHD children supporting the long-standing idea of a fundamental deficit in attentional control.

Autism DSM-IV Criteria

Qualitative impairment < 3-years in:

1. Social Interaction
   - Impaired nonverbal behavior,
   - Failure peer relationships,
   - Lack of shared enjoyment,
   - Lack social-emotional responsivity
2. Verbal & Nonverbal Communication
   - Delay, lack, repetitive, stereotyped
   - Lack ability to initiate or sustain conversation
   - Stereotypic & repetitive use
   - Lack make-believe or imitative play
3. Restricted/Repetitive/Stereotyped Behavior
   - Preoccupation with stereotype & restricted patterns
   - Inflexible routines
   - Repetitive motor
   - Preoccupation parts of objects

Comprehensive Neuropsychological Study

Three groups of children with Autism, ADHD, and Typical Development

- Attention & Response Control
- Executive functioning
- Memory
- Emotion processing
Neuropsychological Functions in Autism Spectrum Disorder (ASD)

- Motor Planning
- Incoordination
- PIQ > VIQ
- Emotions
- Faces
- Social
- Joint Attention
- Relationships
- Pragmatics
- Language
- Receptive
- Expressive
- Prosody
- Memory
- Rote
- Multimodal
- Procedural
- Executive
- Set Shifting
- Perseveration
- Mental Flexibility
- Attention
- Selective
- Shifting
- Distractibility
- Sensory
- Auditory
- Visual
- Tactile
- Cognition
- 70% < 70 IQ

Frontostriatal System
- Region developmentally vulnerable to neurodevelopmental disorders (ADHD & ASD)
  - Dorsolateral Prefrontal Cortex: executive decisions
  - Anterior Cingulate: mediating intentionality, aspects of directed attention
  - Lateral Orbitofrontal: inhibitory control, self-monitoring
  - Supplementary Motor: mediating intentional and complex movement
  - Basal Ganglia: selecting, amplifying wanted actions, inhibiting unwanted actions

Attention & Inhibition in ADHD and Autism
- Inattention and arousal may underlie some of the primary neuropathological functioning in autism (Courchesne et al., 1989; Dawson et al., 1989; Wainwright-Sharp & Bryson, 1993)
- Deficits in various aspects of attention have been associated with subtypes of autism (Bonde, 2000)

ADHD Symptoms in Autism
- Sturm, et al., 2004:
  - 95% = inattention, 86% = behavioral dysregulation, 50% = impulsivity
- Frazier, 2001:
  - 83% of children with PDD met full diagnosis for ADHD
- Yoshida & Uchiyama, 2004:
  - Majority met criteria for ADHD; 57% with autism and 85% with Asperger & PDD-NOS

Differential Diagnosis: ADHD or ASD?
- Differentiating can be challenging (Barkley, 1990; Clark et al., 1999; Gillberg, 1992; Pennington & Ozonoff, 1996; Roeyers et al., 1998).
- Increased identification of autism in ADHD may be a contributing factor in increased prevalence of ASD (Charman & Baird, 2002; Keen & Ward, 2004)
- Many children w/ASD often misdiagnosed or initially diagnosed with ADHD (Jensen, Larrieu, & Mack, 1997; Keen & Ward, 2004; Perry, 1998).
**Or Both?**

- A separate diagnosis of ADHD in PDD can provide clinical utility, guide treatment and encourage research into comorbidity (Ghaziuddin, Tsai, & Alessi, 1992).
- ADHD with ASD is critical to recognize because of the impact of associated problems with these disorders (Kadesjo & Gillberg, 2001).
- Possible exponential risk associated with comorbidity (Goldstein & Schwebach, 2004).

**DSM-IV Criteria**

Although the manual identifies short attention span, impulsivity and hyperactive behavior as part of the of the associated features of autism, a diagnosis of ADHD cannot be provided "if the symptoms of inattention and hyperactivity occur exclusively during the course of a pervasive developmental disorder" (APA, 1994; 2000).

**PDD Can Evolve into ADHD**

Fein et al., 2005

- 11 cases presented (3 in detail) that progress from prototypical of PDD to ADHD
- **Theoretical speculations:**
  - Comorbidity
  - Subtype of severe ADHD
  - Attentional features more difficult to remediate
  - Kinsborne (1991) attentional features core and ADHD and ASD lie on a continuum
  - PDD-ADHD subtype

**Corbett & Constantine (2006).**

Autism and ADHD: Assessing attention and response control with the IVA. Child Neuropsychology, 12, 1-14

**GOALS:**

1. Assess symptoms of ADHD (i.e., inattention and impulsivity) in children with ASD using a standardized measure
2. Assess the utility of a neuropsychological measure designed to facilitate the diagnosis of ADHD in being able to identify ADHD across diagnostic groups
3. Compare neuropsychological data to a parent report measure

**IVA**

**Attention & Response Control**

(Sandford & Turner, 2000)

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**Visual Attention (VA) & Auditory Attention (AA)**

**Visual Response Control (VRC) & Auditory Response Control (ARC)**

**500 Trials**

**Over 13 Minutes**

**IMPULSIVITY**

| 1st Block measures impulsivity by creating a response set to a ratio of 5.25 targets (“1”) to one foil (“2”) – 84% of trials |

**INATTENTION**

| 2nd Block measures inattention by reversing ratio, presenting 5.25 foils (“2”) to one target (“1”) - 16% of trials |
GOALS:
1. Assess symptoms of ADHD (i.e., inattention and impulsivity) in children with ASD using a standardized measure, IVA (Sanford & Turner, 2000).
2. Assess the utility of a neuropsychological measure designed to facilitate the diagnosis of ADHD in being able to identify ADHD across diagnostic groups.

**IVA Attention Quotients Across Groups**

**IVA Attention Quotients Across Groups**

**Integrated Visual Auditory CPT**

Respond when you see/hear a 1, do not respond when you see/hear a 2.

<table>
<thead>
<tr>
<th>Target</th>
<th>Foil</th>
<th>1.5 sec</th>
<th>&lt;157 ms</th>
</tr>
</thead>
</table>

*Impulsivity: 1st Block*
Ratio of 5.25 targets (1) to one foil (2) 84% of trials

*Attention: 2nd Block*
Ratio of 5.25 foils (2) to one target (1) 16% of trials

Counterbalanced two-block pattern repeated 5 times for a total of 500 trials.
IV A Attention Quotients Across Groups

DFA for IVA and Conners
84.4% of original grouped cases correctly classified

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Predicted</th>
<th>Group</th>
<th>Membership</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>TYP</td>
<td>ADHD</td>
<td>ASD</td>
</tr>
<tr>
<td>TYP</td>
<td>73.3</td>
<td>20.0</td>
<td>6.7</td>
</tr>
<tr>
<td>ADHD</td>
<td>0.0</td>
<td>93.3</td>
<td>6.7</td>
</tr>
<tr>
<td>ASD</td>
<td>6.7</td>
<td>6.7</td>
<td>86.7</td>
</tr>
</tbody>
</table>

Summary
- **ATTENTION**: ASD & ADHD showed comparable deficits
- **INHIBITION**: ASD < ADHD < Typical
- **DFA**: The IVA shows good ability to discriminate the groups
- **IVA combined** with parent report improved diagnostic accuracy in ADHD

<table>
<thead>
<tr>
<th>DOMAIN</th>
<th>ADHD</th>
<th>ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response Inhibition</td>
<td>Core to ADHD</td>
<td>Spared Impaired*</td>
</tr>
<tr>
<td>Working Memory</td>
<td>Inconclusive</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Flexibility Shifting</td>
<td>Inconclusive</td>
<td>Impaired</td>
</tr>
<tr>
<td>Planning</td>
<td>Inconclusive</td>
<td>Impaired</td>
</tr>
<tr>
<td>Fluency</td>
<td>Inconclusive</td>
<td>Inconclusive</td>
</tr>
</tbody>
</table>

Intradimensional/Extradimensional Shift (IED)
- **IED** measures discrimination & reversal learning under conditions where participant is required to shift attention to changing patterns of visual stimuli
- The shift requires that the participant learn and respond to a new rule (e.g., shapes are no longer correct, lines are correct)
- Analogous to category shifts such as WCST
Intra-Extra Dimensional Shift
(Corbett unpublished)

Spatial Span

• A test of visual attention and short-term memory, and span for spatial items in much the same way as “digit span” for verbal items
• Participant is required to tap out a prescribed pattern of increasing length and complexity
• Analogous to the Corsi blocks

Stockings of Cambridge

• The task measures planning and behavioral inhibition.
• Top row is the model with three colored balls, bottom row moved to match the top
• Task is to move the balls to make the rows look like the model in a prescribed number of moves
• Analogous to Tower tasks

CANTAB
Stockings of Cambridge and Spatial Span

Corbett & Glidden (2000) Child Neuropsychology
Processing Affective Stimuli in Children with ADHD

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>ADHD</th>
<th>TYPICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>M</td>
<td>1</td>
</tr>
<tr>
<td>SD</td>
<td>SD</td>
<td></td>
</tr>
</tbody>
</table>

- PICTURE OF AFFECT
  - ADHD: 0.76, SD: 0.10
  - TYPICAL: 0.89, SD: 0.06
  - t: 6.39, p: 0.000

- PROSODY
  - ADHD: 0.84, SD: 0.17
  - TYPICAL: 0.94, SD: 0.06
  - t: 3.17, p: 0.002

N = 37
26 boys, 11 girls
N = 37
19 boys, 18 girls
Summary

- ADHD:
  - Executive functioning: inhibition
  - Attention: greater impairment usually than ASD and TYP
  - Emotion: Greater impairment in complex emotions rather than basic
  - Short-Term Memory: mild-to-moderate difficulty

<table>
<thead>
<tr>
<th></th>
<th>TYPICAL N = 25</th>
<th>ADHD N = 25</th>
<th>ASD N = 25</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MEAN</td>
<td>SD</td>
<td>MEAN</td>
</tr>
<tr>
<td>FACIAL EXPRESS</td>
<td>1.0</td>
<td>0.03</td>
<td>1.0</td>
</tr>
<tr>
<td>PROSODY HAPPY</td>
<td>0.9</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>FACES IMMED</td>
<td>12.1</td>
<td>3.2</td>
<td>11.5</td>
</tr>
<tr>
<td>FACES DELAY</td>
<td>12.1</td>
<td>2.4</td>
<td>11.1</td>
</tr>
</tbody>
</table>

Emotion Recognition Faces and Prosody

- Autism Spectrum Disorder:
  - Executive functioning: broader more severe deficits
  - Attention & Inhibition: greater impairment in presence of ADHD symptoms
  - Emotion: Greater impairment in emotion identification especially on basic emotions (e.g., prosody happy)
  - Short-Term Memory: generally intact
Discussion

- **SYMPTOMS:**
  - Need to evaluate ADHD symptoms in ASD and vice versa
  - Identify + and -
- **DIAGNOSTIC ACCURACY:**
  - Diagnose both when warranted
- **PHENOTYPES:**
  - Evaluating subtypes may be more useful for understanding the disorders
  - Endophenotypes to guide research
- **COMORBIDITY:**
  - Critical to Exponential risks and associated problems

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**DSM–V ASD Proposed changes**

1. Autistic disorder, Asperger's, childhood integrative disorder, and PDD-NOS be folded under term "ASD" with a single set of criteria and severity ratings.
2. Three domains become two:
   - Social/Communication Deficits
   - Fixated Interest and Repetitive Behaviors

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**DSM–V ADHD Proposed Changes**

1. Change age onset 7 to 12
2. Change 3 subtypes to 3 current presentations
3. Add 4th presentation for restrictive inattentive
4. Change wording to accommodate lifespan relevance
5. Remove PDD from exclusion criteria
6. Information obtained from 2 different informants
7. Adjust cut point for diagnosis in adults

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**SENSE Team**

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- Danica Chandra Denton, MD
- Dina Hany Ghoneim, MD
- Julia Evans, M.A.

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- Lily Wang, Ph.D.
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**Collaborators**

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- Sasha Key, Ph.D.
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- David Zald, Ph.D.