ADHD and Autism Spectrum Disorder

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Roadmap for today’s talk

ADHD

Overlap with ASD

Current Research
Inattention cluster

- **Inattention** cluster – inability to sustain attention, or to stick to tasks or play activities, to remember and follow through on instructions/rules, and to resist distractions
Hyperactivity/impulsivity cluster

• **Hyperactivity/impulsivity cluster** – under control of motor behavior, poor ability to inhibit behavior, and inability to delay a response or defer gratification
  - **Hyperactivity** – relates to the under control of motor behavior (i.e., fidgeting, squirming, running around aimlessly, and being “driven by a motor”)
  - **Impulsivity** – relates to the inability to inhibit immediate reactions to stimuli (i.e., blurting out or interrupting others, difficulty waiting for ones turn)
# Subtypes

**Table 8.1** | Diagnostic Criteria for **Attention-Deficit/Hyperactivity Disorder** *(continued)*

Specify whether:

- **Combined presentation**: If both Criterion A1 (inattention) and Criterion A2 (hyperactivity-impulsivity) are met for the past 6 months.
- **Predominantly inattentive presentation**: If Criterion A1 (inattention) is met but Criterion A2 (hyperactivity-impulsivity) is not met for the past 6 months.
- **Predominantly hyperactive-impulsive presentation**: If Criterion A2 (hyperactivity-impulsivity) is met but Criterion A1 (inattention) is not met for the past 6 months.

Specify if:

- **In partial remission**: When full criteria were previously met, fewer than the full criteria have been met for the past 6 months, and the symptoms still result in impairment in social, academic, or occupational functioning.

Specify current severity:

- **Mild**: Few, if any, symptoms in excess of those required to make the diagnosis are present, and symptoms result in no more than minor impairments in social or occupational functioning.
- **Moderate**: Symptoms or functional impairment between “mild” and “severe” are present.
- **Severe**: Many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.

“When we began our studies in the 1960’s no one believed such children existed; while now people find them under every rock.”

Dr. Leon Eisenberg, child psychiatrist and ADHD pioneer
Increase in U.S. lifetime prevalence

https://www.cdc.gov/ncbddd/adhd/timeline.html
Increase in U.S. lifetime prevalence rates

2003 2007 2011

ADHD Overlap with ASD Current Research
The gold-standard treatment for childhood ADHD...

Table 1. MTA Study Treatment Conditions

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Medication Management Strategy (MedMgt)</th>
<th>Behavioral Treatment Strategy (Beh)</th>
<th>Combined Strategy (Comb)</th>
<th>Community Comparison Group (CC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>1-month blind titration with methylphenidate for best dose; if unsatisfactory, open titration with cl.-amphetamine, pemoline, TCA. When effective drug regimen is found, maintain monthly visits; adjust dose as indicated by monthly monitors and by algorithm.</td>
<td>Integrated all treatment components in first 2 conditions (except bibliotherapy), with (a) less expensive data base available from behavioral therapist to assist medication adjustment decisions and (b) information from pharmacotherapist to assist in decision about escalation of behavioral interventions.</td>
<td>None by MTA Staff. Assessed only at same time points as active treatment groups. Families obtain treatment of their choosing in the community, if already has a treatment provider, referred back for treatment; if not, give list of referral agencies, including community MH Center, which can help find community treatment.</td>
<td>None.</td>
</tr>
<tr>
<td>Supplementary</td>
<td>Supplementary general advice and bibliotherapy without systematic behavioral intervention.</td>
<td>Supplementary general advice and bibliotherapy.</td>
<td>Supplementary general advice and bibliotherapy.</td>
<td>None.</td>
</tr>
<tr>
<td>Case Manager</td>
<td>Therapist/consultant (TC).</td>
<td>Therapist/consultant, with weekly advice from combined-treatment clinical team.</td>
<td>None.</td>
<td>None.</td>
</tr>
<tr>
<td>Emergency Services</td>
<td>ASAP emergency services as needed.</td>
<td>ASAP emergency services as needed.</td>
<td>ASAP emergency services as needed.</td>
<td>None.</td>
</tr>
</tbody>
</table>

MTA, Multimodal Treatment of Attention-Deficit Hyperactivity Disorder.

Subjects in all 4 arms received comprehensive assessments at baseline, 3 months, 9 months, and 14 months.

ASAP, Adjunct Services and Attention Prevention. Each treated subject has a bank of eight "ASAP sessions" that can be used in emergencies, monitored by a cross-site clinical panel.

- 5. Percent “normalized” at 14-month endpoint across the four MTA groups. The classroom controls were drawn from the same room cohorts as MTA children were originally, and were age- and gender-matched to assure comparability with MTA subjects. The “normal” indicator was based on a composite of parent and teacher ratings, with the overall symptom cutoff required to be indicative of or no” symptoms (Swanson et al, 2001).
Parent management training

• **PMT** – a behavioral intervention that focuses on teaching effective parenting practices and strategies for coping with a child with ADHD. Similar to some components of ABA.

• **Goal**: Through teaching skills to parents, children will increase adaptive behavior and decrease maladaptive problem behaviors.
Medications

• Stimulants (increases dopamine and norepinephrine in PFC):
  • amphetamines (Adderall)
  • methylphenidates (Ritalin)
  • dextroamphetamine (Vyvanse)

• Nonstimulants (increases norepinephrine in PFC)
  • Atomoxetine (Strattera)

• Released in the CNS over 12-24 hours (longer acting ones are called XR)
ADHD

Overlap with ASD

Current Research

### Current Practice for ADHD Treatment

**Medication Treatment**

- In 2009-10, 81% of children with ADHD in Wisconsin took medication for ADHD during the past week, according to parent report.
- Among all states and D.C., the national average was 74%.
- Wisconsin ranked 9th highest out of 51.

![81%](map.png)

**Behavioral Treatment**

- In 2009-10, 39% of children with ADHD in Wisconsin received behavioral treatment for ADHD during the past 12 months, according to parent report.
- Among all states and D.C., the national average was 41%.
- Wisconsin ranked 43rd highest out of 51.

![38%](map.png)

**Both Treatments**

- In 2009-10, 31% of children with ADHD in Wisconsin received both treatments for ADHD, according to parent report.
- Among all states and D.C., the national average was 31%.
- Wisconsin ranked 27th highest out of 51.

![31%](map.png)

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National Center on Birth Defects and Developmental Disabilities

Division of Human Development and Disability

Significance and impact

• National prevalence of 9.4% in the U.S. (2016 survey)
  • 388,000 children aged 2–5 years
  • 4 million children aged 6–11 years
  • 3 million children aged 12–17 years

• Academic and social functioning

• Economic impact
  • $31.6B annual cost for health care, lost productivity, and impact on other family members

https://www.cdc.gov/ncbddd/adhd/research.html#ref1
Overlap with ASD
Can a person have both ADHD and ASD?

• Does it add any value for the child and parents to also diagnose ADHD when ASD is present?

They are both part of the same cluster in the DSM-5

• **Neurodevelopmental disorders** – impairment of the growth and development of the brain and/or CNS; affect emotion, learning, self-control, and memory.
  • ADHD
  • ASD
  • Learning disorder
  • Communication disorder
  • Motor disorder
  • Intellectual disability
Red flags in identifying ADHD in a child with ASD

1. ‘Often fails to give close attention to details or makes careless errors in schoolwork, at work or during other activities’
2. ‘Often has difficulty sustaining attention in tasks or activities’, and ‘often unable to play or engage in leisure activities quietly’
3. ‘Often avoids, dislikes or is reluctant to engage in tasks that require sustained mental effort’
4. ‘Often loses things necessary for tasks or activities’
5. ‘Often forgetful in daily activities’

Rommelse, Visser & Hartman, 2018 in European Child and Adolescent Psychiatry
Identifying ASD in a child with ADHD

• ‘Deficits in nonverbal communicative behaviors used for social interaction’
• ‘Stereotyped or repetitive motor movements, use of objects, or speech’
• ‘Insistence on sameness, inflexible adherence to routines or ritualized patterns or verbal or nonverbal behavior’
• ‘Highly restricted, fixated interests that are abnormal in intensity or focus’
• ‘Hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment’

Rommelse, Visser & Hartman, 2018 in European Child and Adolescent Psychiatry
How common is the overlap?

• As many as 50% of individuals with ASD present with signs of ADHD; nearly two-thirds of individuals with ADHD similarly present with features of ASD. Davis NO, Kollins SH. Treatment for Co-Occurring Attention Deficit/Hyperactivity Disorder and Autism Spectrum Disorder. *Neurotherapeutics* 2012;9:518–30.

Treatments?

• Compared to youths with ADHD or ASD alone, youths with both ASD and ADHD are the most likely group to be prescribed psychotropic medications. Frazier TW, Shattuck PT, Narendorf SC, Cooper BP, Wagner M, Spitznagel EL. Prevalence and Correlates of Psychotropic Medication Use in Adolescents with an Autism Spectrum Disorder with and without Caregiver-Reported Attention-Deficit/Hyperactivity Disorder. *Journal of Child and Adolescent Psychopharmacology* 2011;21:571-9. [https://doi.org/10.1089/cap.2011.0057](https://doi.org/10.1089/cap.2011.0057).

• No compelling evidence (i.e., RCTs) that indicate children with ASD and ADHD respond well to these treatments.

Research

What causes the overlap?
Many disorders have a strong genetic basis

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia</th>
<th>Bipolar disorder</th>
<th>MDD</th>
<th>Autism Spectrum</th>
<th>ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>$h^2$</td>
<td>0.81</td>
<td>0.75</td>
<td>0.37</td>
<td>0.80</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Cross disorder group of Psychiatric Genomics Consortium, 2013 in *Nature Genetics*
Genome-wide association study of ASD

Fig. 1 | Manhattan plots. The x axis shows genomic position (chromosomes 1-22), and the y axis shows statistical significance as \(-\log_{10}(P)\) of \(z\) statistics. a. The main ASD scan (18,381 cases and 27,969 controls), with the results of the combined analysis with the follow-up sample (2,319 cases and 342,379 controls) in yellow in the foreground. Genome-wide-significant clamps are green, and index SNPs are shown as diamonds. b-d: Manhattan plots for three MTAG scans of ASD together with schizophrenia\(^a\) (34,129 cases and 45,512 controls), b. educational attainment\(^b\) (n=328,917), and c. major depression\(^c\) (n=31,962 cases and 312,313 controls). d. Full-size plots are shown in Supplementary Figs. 45-48. In all panels, the results of the composite of the five analyses (consisting of the minimal \(P\) value of the five for each marker) is shown in gray in the background.
Using genomics to predict complex outcomes
Using genetic information to help diagnose ADHD?

Li, 2019 in Psychological Medicine
But...what if some ADHD genes = ASD genes?

Grove et al., 2019 in Nature Genetics
ASD and ADHD genes are enriched in similar brain regions

Demontis et al., 2018

Grove et al., 2019 in Nature Genetics
Combining genetics and brain imaging to improve diagnostic precision

- ASD?
- ADHD?
- ASD + ADHD?
- Typical Development?
Our guiding research questions

• Can genetic information be used to diagnose ASD, ADHD, and their co-occurrence in early life?

• Can genetic information for ASD, ADHD, and their co-occurrence be traced to brain regions so that we know which areas of the brain to target in the development of new therapeutics?
Preliminary results

Genes for ASD only predict ASD

Genes for ADHD only predict ADHD

Wang, Li, Travers, and Lu, in prep.
Genetic information used for early diagnosis → early intervention → better outcomes

Genes for ASD only predict ASD

Genes for ADHD only predict ADHD

Wang, Li, Travers, and Lu, in prep.
Infant Later Diagnosed with Autism is going to go on to develop autism.
Thank you!

• Email: james.li@wisc.edu
• Social and Behavioral Development Lab
• The Motor and Brain Development Lab
• UW Social Genomics group
• All the families and children that participated in our studies