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ADHD: A Neurodevelopmental Disorder Through the Ages
ADHD - Points to be addressed

How the diagnosis is made.
Controversies
Why diagnosis is important.
Historical aspects.
Age related manifestations.
What happens through life.
Treatment options.
ADHD
Historical Timeline

1930
Minimal Brain Damage

1937
Hyperkinetic Reaction of Childhood (DSM-II)

1950
Efficacy of Amphetamine

1968
Attention Deficit Hyperactivity Disorder (DSM-III-R)

1980
Attention Deficit Disorder + or - Hyperactivity (DSM-III)

1987
Attention Deficit Hyperactivity Disorder (DSM-IV)

1994
Attention Deficit/Hyperactivity Disorder (DSM-IV)
How do we diagnose ADHD?

• In children, ADHD is diagnosed based on reports of behavior by caretakers, and other adults, especially teachers.
• The behaviors are extremes of common, ordinary, behaviors.
• Controversies arise from such behavioral approaches.
Diagnoses do NOT Include Variations of Normal Development

**Some Examples:**

- Tantrums in a 2 year old
- Distress at separation in early childhood
- Fear of animals at age 4
- Sibling rivalry
- Feeling down after a loss
- Resenting authority
- Lying to avoid being punished
When a child has a *psychiatric disorder*

- Important functions are delayed or impaired
- The dysfunctions are not under easy willful control (inflexible)
- The dysfunction are not reversed by simple environmental change
- There is *suffering or Impairment*
Controversies about diagnosing children

- We are medicalizing variations in normal development.
- Being young means not going with the flow - being different is normal.
- Diagnosing children stigmatizes them (no evidence for this).

*There are legitimate concerns, BUT*
We can help children and their families.

There are treatments that work.

We know that child and adolescent psychiatric disorders are not innocuous. They incur risk for future dysfunction in a proportion (not all).
Important Benefits of Psychiatric Classification-2

**Communication**: enables a common language.

**Clinical Care**: guides *treatment* choices.

**Prognosis**: tells us what we may expect over time (recovery/other problems).

**Knowledge**: unless we classify conditions, we cannot study them. We remain ignorant about what is best for the child.
Important Benefits of Psychiatric Classification-3

• **Knowledge:**

• *Studies of brain development have led to new insights about ADHD.*

Systematic studies that would not have been possible without the diagnosis have shown that ADHD is a “brain disorder” or a “neurodevelopmental disorder.”
1) ADHD has a strong genetic component
   - up to 92% concordance in monozygotic twins
   - heritability of 0.75
   - molecular genetic studies have implicated specific genes

2) children and adults with ADHD have thinner cortical volumes than normal children.
Total Cerebral Vol. Growth Curves

Castellanos, JAMA October 9, 2002

Controls > ADHD
P<.003
ADHD - Anatomic MRI Studies

Frontal Lobes Percent decrease in size in Individuals with ADHD Compared to controls (dozens of additional studies)

- Hynd et al (1990)
- Filipek et al (1997)
- Castellanos et al (1996)
Is Cortical Thickness Clinically Relevant?

- **Longitudinal study at NIMH found that:**

  Children with ADHD who had thinner prefrontal cortex than normal children were more likely to retain ADHD at follow-up\(^+\) than children whose prefrontal cortex\(^*\) was no different from controls.

\(^+\) 5.7 year follow-up to age 13

\(^*\) No effect of total cortex volume.

Importance of the Disorder

- Elevated prevalence in the population (abt 5%)
- Most common disorder in child psychiatric clinics
- Incurs impairment in multiple domains of function - at ALL AGES
- Can have deleterious long-term consequences
Functional impairment with ADHD at all Ages

✓ Interferes with learning
✓ Problematic relationships with adults and peers
✓ Rejected by peers
✓ Stress on the environment
  ➢ School or Work Place
  ➢ Family
ADHD

• Inattention, hyperactivity, impulsivity that are inconsistent with developmental level and lead to significant problems for the person.
• The overt manifestations of ADHD vary with developmental level
  – Preschool
  – School age (6 – 12)
  – Adolescence
  – Adulthood
Inattention

- Careless mistakes
- Difficulty sustaining attention
- Seems not to listen
- Fails to finish tasks
- Difficulty organizing
- Avoids tasks requiring sustained attention
- Loses things
- Easily Distracted
- Forgetful
Hyperactivity

- Unable to stay seated
- Moving excessively (restlessness)
- Difficulty engaging in leisure activities quietly
- “On the go”
- Talking excessively
Impulsivity

✓ Blurting out answers
✓ Difficulty awaiting turn
✓ Interrupting/intruding upon others
✓ Impatient
Well-Documented Domains of Impairment in Individuals with ADHD (at all ages)

- Social Relationships
- Family Function
- School or Work Performance, and/or Adjustment
Impairment – All Ages (Social Relationships)

✓ Significantly impaired relationships
✓ Often loud and intrusive
✓ Others quickly form negative impressions, leading to rejection.
✓ Negative social relationships affect all important functions (work, marriage, parenting)
Impairment (Family Function)

 ✓ Families have high levels of conflict
 ✓ Family members are stressed
 ✓ Parents are often overwhelmed and demoralized
Impairment in Children (Academic Performance)

✓ Significantly more school failure
✓ Many require special tutoring
✓ Placement in special classes or having to repeat a grade is common
✓ Rates of learning disorders range from 10% to 20%
Impairment with ADHD in Children (School Adjustment)

- Teachers see as working less hard, learning less, behaving less appropriately
- Disrupts the class; parents often have to visit the school about child’s behavior
- Difficulty completing homework
Teacher reports of ADHD-like behavior have been controversial

• Are teachers intolerant? It’s the teacher’s problem, not the child’s.

• Understandable, but not likely…..
“Blind” Observers’ Classroom Ratings of Hyperactive Children and Classmates

% of Interference, Off-Task, Gross Motor, Non-Compliance, Out of Chair behaviors among Hyperactive and Non-Hyperactive (NonHyp) children (n=120).
A very legitimate concern has been the long-term adjustment of young children diagnosed as having ADHD.
Longitudinal Study of Boys with ADHD from Age 8 to 41 Years

• We diagnosed Combined ADHD in 207 Caucasian boys, 6 to 12 years (mean, 8).

• They have been followed up 3 times:
  – At age 18 – 10 years after the original diagnosis
  – At Age 25 – 17 years after the original diagnosis
  – At age 41 – 33 years after the original diagnosis (the longest prospective study).
Not All Children Referred Had Cross-Situational ADHD

- A number of children were reported to have ADHD only by their parents, and others only by their teachers.

- Did this matter? Yes:
  - Outcome was a function of the disorder’s pervasiveness.
ADHD at Follow-Up - 10 Years Later

- Pervasive Probands (n=94): 22%
- School Only (n=24): 12%
- Home Only (n=14): 0%
- Normal Controls (n=78): 3%
Conduct Disorder at Follow-Up – 10 Years Later

- Pervasive Probands (n=94) 32%
- School Only (n=24) 29%
- Home Only (n=14) 0%
- Normal Controls (n=78) 8%
• Two brief descriptions for a flavor of the children we diagnosed and followed up.
Rob, 6, First Grade

**History:** There have been complaints about Rob’s behavior since nursery school (where he fell, “had a concussion because he would not stay still”). The teacher could not control him.

**At Referral**

**In School:** Rob is “uncontrollable”, “will not sit still for a minute”, and is “disruptive”. Teachers have him in isolation and don’t allow him into the lunch area.

**At Home:** Rob is “very active”, “constantly moving and talking”. “He tries to behave but he says he can’t help it.”

**During testing:** Rob was in constant motion and had difficulty sustaining attention.
Francis, 8, Third Grade

**History:** F. “has always been a hyperactive kid, even as an infant”. Parents, school, and pediatrician complained about it. In nursery school, he was inattentive and overactive.

**At Referral**

**In School:** “He lacks self-control, has a short attention span, is disorganized, forgetful, impulsive and constantly moving; other children are annoyed by his impulsivity”.

**At home:** “He can’t seem to sit still, is extremely active, and constantly running and jumping.” Doesn’t follow directions, must be told several times to do the same thing, he’s difficult to discipline.

**During testing:** Restless and somewhat hyperactive.
Major Findings 10 and 17 Years Later (at ages 18 and 25)
Compared to Non-ADHD Controls, ADHD Probands

- Had *poorer academic performance and completed less schooling* (by age 41, 32% had not completed HS, vs. 5% of controls).
- Had *poorer social functioning*.
- Had *lower occupational rankings*.
Only *Three disorders* were significantly more prevalent in the ADHD group:

- ADHD
- Antisocial Personality Disorder
- Substance Use Disorders

Are these related?  YES
10 Year later: Antisocial Disorder depended on the Persistence of ADD

P < .01: ADD > No ADD, Controls
Substance disorders depended on the development of antisocial disorders.
Is elevated SUD due to greater drug exposure in children with ADHD?

NO

77% of ADHD individuals and 75% of Controls had tried drugs.
Relationship between Antisocial Personality Disorder (APD) and Multiple Arrests

% with Multiple Arrests

- Probands with APD
- Probands w/o APD
- All Controls
Developmental Cascade of Psychiatric Disorders

1. *Childhood ADHD*, on to
2. *Adolescent Antisocial Disorder*, on to
3. *Substance Use Disorder*, on to
4. Criminality into *adulthood*
How About At Age 41, 33 Years Later?

✓ 198 of the 207 boys with ADHD were located and contacted. Of these, 15 (8%) were identified as *Deceased*.

✓ 173 of the 178 Male Controls were located and contacted. Of these, 5 (3%) were identified as *Deceased*.

8% vs. 3%, Chi-Square = 3.97, p = .05
## Rates (%) of Ongoing Diagnoses -

<table>
<thead>
<tr>
<th>DSM-IV Diagnosis</th>
<th>ADHD (n = 135)</th>
<th>Controls (n = 136)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD**</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>Antisocial Personality Disorder***</td>
<td>16%</td>
<td>0</td>
</tr>
<tr>
<td>Substance Use Disorder</td>
<td>22%</td>
<td>17%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>10%</td>
<td>15%</td>
</tr>
<tr>
<td>Drugs (Cannabis, Cocaine, etc.)**</td>
<td>14%</td>
<td>5%</td>
</tr>
<tr>
<td>Nicotine Dependence***</td>
<td>30%</td>
<td>9%</td>
</tr>
</tbody>
</table>

*p < .05  **p < .01  ***p < .001
|                     | ever hospitalized (n=135) | controls (n=136) | p ≤  
|---------------------|---------------------------|------------------|-------
| probands            | 20 (15%)                  | 7 (5%)           | .01   

N (%) Psychiatrically Hospitalized
## Mean Number of Psychiatric Hospitalizations (among those hospitalized)

<table>
<thead>
<tr>
<th>ADHD Group</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Range</td>
<td>Range</td>
</tr>
<tr>
<td>3.4 (4.3)</td>
<td>1.6 (.9)</td>
</tr>
<tr>
<td>1-24</td>
<td>1-3</td>
</tr>
</tbody>
</table>
Substance Use Disorders Had Very Negative Consequences.

They were strong predictors of 1) psychiatric hospitalizations, and 2) major depression.
We know that children with ADHD are at risk for other disorders during adolescence.

How about during adulthood (from age 21 on)?
Rates of New Disorders Since Age 21*  
(Mean Age 41)

<table>
<thead>
<tr>
<th>DSM-IV Diagnosis</th>
<th>Probands (n = 135)</th>
<th>Controls (n = 136)</th>
<th>p  &lt;</th>
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<tbody>
<tr>
<td>Adjustment Disorder</td>
<td>4%</td>
<td>6%</td>
<td>NS</td>
</tr>
<tr>
<td>Substance Use Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>6%</td>
<td>10%</td>
<td>NS</td>
</tr>
<tr>
<td>Non-alcohol</td>
<td>4%</td>
<td>6%</td>
<td>NS</td>
</tr>
<tr>
<td>Any Alcohol or Non-Alcohol</td>
<td>4%</td>
<td>10%</td>
<td>.03</td>
</tr>
<tr>
<td>Nicotine</td>
<td>8%</td>
<td>6%</td>
<td>NS</td>
</tr>
<tr>
<td>Mood Disorders</td>
<td>30%</td>
<td>22%</td>
<td>NS</td>
</tr>
<tr>
<td>Anxiety Disorders</td>
<td>11%</td>
<td>8%</td>
<td>NS</td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
<td>0%</td>
<td>NS</td>
</tr>
<tr>
<td>Any Disorder Excluding ADHD</td>
<td>7%</td>
<td>14%</td>
<td>.05</td>
</tr>
</tbody>
</table>

*Unpublished data
Contrary to expectation, during adulthood:

The subjects with a childhood history of ADHD did not develop new psychopathology more often than controls.
The persistence of childhood ADHD into late adolescence was the main cause of negative outcomes.
The period of increased risk for new psychopathology was limited to adolescence.

This does not mean that, in adulthood, ADHD children were not worse off than controls. They were.

But their elevated dysfunction in adulthood reflects persistence of malfunction that had its onset in adolescence.
Our findings stress the importance of continued monitoring and treatment of children with ADHD, even when conduct disorder is absent when they are first seen.
Chronology of ADHD, Antisocial Disorder, and SUD
(Original N = 207 with ongoing ADHD)

ADHD at Age 18
(n = 71)

NO ADHD at Age 18
(n = 124)

Antisocial Disorder at Age 25
43%

Antisocial Disorder at Age 25
17%

SUD at Age 41
37%

SUD at Age 41
19%
Treatments for ADHD

- **Psychostimulants**
  - **Amphetamines, levo- and dextro-amphetamine** *(Benzedrine, Dexedrine, Desoxin)*
  - **Methylphenidate**

**History of:**
- how they were discovered (1920’s)
- their further development
  - short and long-acting
  - oral and patch delivery
Non-stimulant Medications

- Atomoxetine (Strattera)
- Bupropion – (Wellbutrin)

They do not have nearly the same efficacy as stimulants and should not be first line treatments (possible exception – SUD).
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Studies of Psychosocial Treatments

- Two long-term controlled studies compared multimodal treatment to stimulant medication –
  1) MTA* with duration of 14 months
  2) New York/Montreal study of 24 months

* MTA, Multimodal Treatment of ADHD
MTA Study - 14 Month Outcomes on ADHD Symptoms

- In children with ADHD, age 7-10 years:
  
  Medication was superior to the intensive multimodal behavioral treatment

(14 months with parents, teachers and children)
Children, average 8 years, were ALL treated with a stimulant for 2 years:

- One third got nothing else.
- One third also received a very active multimodal treatment.
- One third also received a “control”, or mock, multimodal treatment.

All for 2 years
Conners Parent Scale: Impulsive-Hyperactive Factor

- Baseline
- Month 6
- Year 1
- Month 18
- Year 2
Observed Levels of Classroom Interference

NORMS
- Baseline = 8.08 (6.13)
- Month 6 = 6.24 (4.72)
- Year 1 = 6.39 (5.38)
- Month 18 = 5.56 (5.37)
- Year 2 = 4.62 (4.43)

F (Group X Time) = 1.12, p = ns
Treatment Considerations

Key Implications for Parents and Practitioners:

- Continued treatment, with adequate doses of medication is essential

- *Combined treatments* may be desired by parents, and may help them cope, but they do not affect the child’s ADHD symptoms