Preschool ADHD: When Should We Diagnose it & How Should We Treat it?

Nathan J. Blum, M.D.
Professor of Pediatrics
The Children’s Hospital of Philadelphia

ADHD in Preschool Children
- Diagnosis of ADHD in Preschool Children: Impact of DSM-IV
- Is Preschool ADHD Associated with impairment
- Do subtypes differ?
- What do we know about the longitudinal course of ADHD symptoms in preschool children?
- Behavioral Treatment in Preschool Children
- Preschool ADHD Treatment Study (PATS)

Hyperactive-Impulsive Subtype in DSM-IV Increases Number of 3-7 y.o. Children Diagnosed with ADHD
- 4-7 y.o. children (Lahey et al., 1998)
  - 65% ADHD. Combined Type
  - 25% ADHD. Hyperactive Impulsive Type
  - 10% ADHD. Inattentive Type
- 3-5 year old children (DuPaul et al., 2001)
  - 65% ADHD. Combined Type
  - 28% ADHD. Hyperactive Impulsive Type
  - 7% ADHD. Inattentive Type

DSM: No Youngest Age For Diagnosis
- DSM-IV: Mixed Messages
  - “It is difficult to establish this diagnosis in children younger than 4-5 years of age…”
  - “Symptoms of inattention are often not readily observed because young children typically experience few demands for sustained attention.”
  - “Even the attention of toddlers can be held in a variety of situations”
  - “Substantial impairment has been demonstrated in preschool age children with ADHD”
- DSM 5
  - “Many parents first observe excessive motor activity when the child is a toddler, but symptoms are difficult to distinguish from highly variable normative behaviors before age 4 years…In preschool, the main manifestation is hyperactivity”

ADHD: AAP Practice Guideline
Pediatrics Vol. 128, November, 2011
- Evaluate children with symptoms from 4-18 yrs of age
- Previous guideline had only recommended evaluation in 6-12 year olds

Diagnosis and Pharmacologic Treatment of ADHD in US, 2003

MMWR, 2005;54:845.
Should We Diagnose ADHD in Preschool Children?

- Is preschool ADHD associated with impairment?
  - What about the HI presentation?
- Is the diagnosis of ADHD stable from preschool age to elementary school age children?
- Can we treat preschool ADHD?

ADHD in Preschool Children is Associated with Functional Impairment

<table>
<thead>
<tr>
<th></th>
<th>ADHD</th>
<th>Control</th>
<th>Effect Size</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% in Special Education</td>
<td>21</td>
<td>0</td>
<td>2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% with Unintentional Injury</td>
<td>30.1</td>
<td>11.6</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Teacher rating of being liked by other children (5 point scale)</td>
<td>5.17</td>
<td>4.26</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Teacher rating of disruptive behavior</td>
<td>12.91</td>
<td>8.16</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Child self report of friendship difficulties</td>
<td>9.14</td>
<td>6.60</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Is ADHD-HI a Valid Subtype?

- ADHD-HI is associated with Functional Impairment
- Impairments in Children with ADHD-HI do not differ greatly from those in ADHD-C
- Most Preschool Children with ADHD-HI will continue to meet criteria for ADHD at school age
- Most Preschool Children with ADHD-HI who continue to have ADHD will be diagnosed with ADHD-C at school age

ADHD-HI in Preschool Children is Associated with Functional Impairment

<table>
<thead>
<tr>
<th></th>
<th>ADHD-C</th>
<th>ADHD-HI</th>
<th>Control</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>% in Special Education</td>
<td>23.8</td>
<td>16.1</td>
<td>0</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>% with Unintentional Injury</td>
<td>32.5</td>
<td>35.7</td>
<td>11.6</td>
<td>0.06</td>
</tr>
<tr>
<td>Teacher rating of being liked by other children (5 point scale)</td>
<td>3.06</td>
<td>3.64</td>
<td>4.26</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Teacher rating of disruptive behavior</td>
<td>13.5</td>
<td>12.5</td>
<td>8.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Child self report of friendship difficulties</td>
<td>10.3</td>
<td>9.63</td>
<td>6.6</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Does Functional Impairment in ADHD-HI and ADHD-C Differ? Parent and Teacher Ratings

<table>
<thead>
<tr>
<th></th>
<th>ADHD-C (SD)</th>
<th>ADHD-HI (SD)</th>
<th>Effect Size</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oppositional-P T score</td>
<td>66.7 (13.5)</td>
<td>65.7 (11.7)</td>
<td>0.07</td>
<td>0.73</td>
</tr>
<tr>
<td>Oppositional-T</td>
<td>70.9</td>
<td>75.5</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>T score</td>
<td>(15.8)</td>
<td>(11.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxious-P T score</td>
<td>53.3</td>
<td>53.2</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Anxious-T</td>
<td>(9.1)</td>
<td>(9.7)</td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td>T Score</td>
<td>59.2</td>
<td>58.5</td>
<td>0.06</td>
<td>0.77</td>
</tr>
<tr>
<td>Social Skills-P</td>
<td>37.5</td>
<td>41.5</td>
<td>-0.45</td>
<td>0.047</td>
</tr>
<tr>
<td>Raw Score</td>
<td>(9.0)</td>
<td>(8.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Skills-T</td>
<td>28.8</td>
<td>22.7</td>
<td>0.37</td>
<td>0.08</td>
</tr>
<tr>
<td>Raw Score</td>
<td>(8.0)</td>
<td>(8.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lahey et al., J Am Acad Child Adolesc Psychiatry, 1998;695-702
DuPaul et al., J Am Acad Child Adolesc Psychiatry, 2001;508-515
Attention-Deficit/Hyperactivity Disorder
Nathan J. Blum, M.D.

Does Functional Impairment in ADHD-HI and ADHD-C Differ?
Observation During a Structured Task

<table>
<thead>
<tr>
<th></th>
<th>ADHD-C Mean % (SD)</th>
<th>ADHD-HI Mean % (SD)</th>
<th>Effect Size</th>
<th>p value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Off Task</td>
<td>6.33 (10.28)</td>
<td>8.62 (17.85)</td>
<td>-0.18</td>
<td>0.76</td>
</tr>
<tr>
<td>Disruptive</td>
<td>10.79 (11.03)</td>
<td>12.93 (11.31)</td>
<td>-0.19</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Mann-Whitney U test

Riley et al, JDBP 2009:28:270-275

Is ADHD-HI a Valid Subtype?

- In the preschool period ADHD-HI is associated with Functional Impairment that is similar to children with ADHD-C
- Most preschool children with ADHD-HI continue to have ADHD at school age, but are most likely to have ADHD-C by the end of elementary school

Long-Term Outcome for Hyperactive 3 Year Olds: Dunedin Health and Development Study

- Followed 1,037 children every two years beginning at age 3 years.
- 21 of the 3 year old rated as very difficult to manage by mothers and as hyperactive by trained observers during a developmental assessment
- 31 of the 3 year olds rated as very difficult to manage by mothers, but not rated as hyperactive by trained observers

Most Children with ADHD-HI at 4-7 are Later Diagnosed with ADHD-C

What About Very Young Children?

- 1991-1995 for 2-4 year old children
  - 3 fold increase in stimulant prescriptions (0.5-1.2% prescribed stimulants by 1995)
  - 7-28 fold increase in clonidine prescriptions (0.2% prescribed clonidine by 1995)
- Michigan Medicaid Database 1995-96
  - 223 children under age 3 diagnosed with ADHD
  - 12% treated with medications
    - 22 different psychotropic medications were used
    - 33% received simultaneous prescription of more than one psychotropic medication in 44 different combinations

Zito et al., JAMA 2000:1025-1030

Rapley et al., JDBP 2002:23-30

Dunedin Health and Development Study

- Hyperactive group had lower scores on language measures that the remainder of the sample
- Developmental control group—matched for language ability, but mothers did not rate the 3 year olds as difficult to manage and they were not rated as hyperactive by observers
Attention-Deficit/Hyperactivity Disorder
Nathan J. Blum, M.D.

Dunedin Health and Development Study: Follow-up at Age 7 & 9

<table>
<thead>
<tr>
<th></th>
<th>Hyperactive N=21</th>
<th>Difficult N=31</th>
<th>Dev Cont N=21</th>
<th>Remainder N=880</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reading-7</td>
<td>20.5</td>
<td>27.5</td>
<td>21.6</td>
<td>29.9</td>
</tr>
<tr>
<td>Reading-9</td>
<td>41.3</td>
<td>51.6</td>
<td>45.5</td>
<td>54.4</td>
</tr>
<tr>
<td>Math-9</td>
<td>8.9</td>
<td>9.7</td>
<td>8.4</td>
<td>9.8</td>
</tr>
<tr>
<td>Parent ADD-9</td>
<td>11.2</td>
<td>9.1</td>
<td>7.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Teacher ADD-9</td>
<td>9.4</td>
<td>6.4</td>
<td>5.4</td>
<td>4.5</td>
</tr>
</tbody>
</table>


Dunedin Health and Development Study: Follow-up at Age 11 DSM-III Diagnoses

<table>
<thead>
<tr>
<th></th>
<th>Hyperactive N=18</th>
<th>Difficult N=21</th>
<th>Dev Cont N=20</th>
<th>Remainder N=724</th>
</tr>
</thead>
<tbody>
<tr>
<td>% ADD</td>
<td>33.3%</td>
<td>9.5%</td>
<td>15%</td>
<td>5.8%</td>
</tr>
<tr>
<td>% Other</td>
<td>16.7%</td>
<td>9.5%</td>
<td>0%</td>
<td>11.0%</td>
</tr>
<tr>
<td>% No Disorder</td>
<td>50.0%</td>
<td>81.0%</td>
<td>85.0%</td>
<td>82.2%</td>
</tr>
</tbody>
</table>


Importance of symptom improvement at age 4 in predicting child improvement by 6

![Graph showing activity rating improvement from age 4 to age 6](image)

Campbell, 1987

Young Child Predictors of High ADHD Symptoms in 3rd Grade

- NICHD Study of Early Child Care and Youth Development
  - 15% of Sample with High ADHD Symptoms by parent and/or teacher report
    - More externalizing and sleep problems at 24 months and 36 months
    - More internalizing problems at 36 months
    - Lower receptive vocabulary at 36 months
  - No single factor or grouping of factors had high enough sensitivity and specificity to be clinically useful


Predictors of Persistent ADHD Symptoms at School Age

- Failure of Symptoms to Improve over 12 months
- Higher activity level and more child negative behaviors (even in infancy)
- Positive FH of ADHD
- Higher Family Stress Levels
- More Negative Parenting
- Lower Family SES

Lahey et al. Arch Gen Psych 2005;62:896-902

Percentage of 4-7 y.o. Children who Continue to Meet Criteria for ADHD

![Graph showing percentage of children (combined subtype, inattentive subtype, hyperactive-impulsive subtype) over 7 years](image)
Which Young Children Are Most Likely to Have Persistent ADHD

- Children 3 through 6 diagnosed with ADHD after interdisciplinary assessment
  - 70% continued to meet criteria for ADHD 7 years later
  - 11% diagnosed with ASD & 6% diagnosed with other learning or psychiatric disorders 7 years later
  - Factors Associated with persistent ADHD:
    - High externalizing symptoms (disruptive behaviors)
    - High internalizing symptoms (anxiety and mood symptoms)
    - Lower family income & parental educational level
    - Presence of parental psychopathology


ADHD Diagnosis in Preschool Children

- Three Year Old Children
  - Rarely diagnose: up to 50% of hyperactive 3 year olds may improve

- 4-5 Year Old Children
  - Can be diagnosed
    - Particularly if symptoms have shown minimal improvement over a period of 12 months or more
    - Occur in the context of high internalizing or externalizing symptoms
    - Symptoms clearly occur in more than one setting
    - Other developmental disorders excluded

AAP Guidelines: Preschool Children

- Treatment
  - Evidence-based behavioral therapy is 1st line treatment
  - Methylphenidate if behavior therapy not sufficient
  - If behavior therapy not available, weigh risks of starting medicine early vs. risks of delaying treatment

AAP Guidelines: Preschool Children

- Treatment
  - Evidence-based behavioral therapy is 1st line treatment
  - Methylphenidate if behavior therapy not sufficient
  - If behavior therapy not available, weigh risks of starting medicine early vs. risks of delaying treatment

Meta-Analysis: Effect of Parent Training on Disruptive Behavior in Preschool Children

- 83 three y.o. children diagnosed with ADHD
- Randomized to one of three groups
  - 8 session in home individual parent training
  - 8 session parent support—no behavioral strategies taught
  - Wait list control group
- Delivered by home visitors trained in mental health care
- Outcomes
  - 8 session with 23 weeks
  - Parent Interview of ADHD symptoms
  - Observation of attention/engagement and activity switches during play with a specified toy
  - Parental Sense of Competence Measure


Meta-Analysis: Effect of Parent Training on ADHD Symptoms in Preschool Children

- 78 three y.o. children diagnosed with ADHD
- Randomized to one of three groups
  - 8 session in home individual parent training
  - 8 session parent support—no behavioral strategies taught
  - Wait list control group
- Delivered by home visitors trained in mental health care
- Outcomes
  - 8 session with 23 weeks
  - Parent Interview of ADHD symptoms
  - Observation of attention/engagement and activity switches during play with a specified toy
  - Parental Sense of Competence Measure


Does New Forest Parenting Program Improve the Outcome of Preschool ADHD?

- 78 three y.o. children diagnosed with ADHD
- Randomized to one of three groups
  - 8 session in home individual parent training
  - 8 session parent support—no behavioral strategies taught
  - Wait list control group
- Delivered by home visitors trained in mental health care
- Outcomes
  - 8 session with 23 weeks
  - Parent Interview of ADHD symptoms
  - Observation of attention/engagement and activity switches during play with a specified toy
  - Parental Sense of Competence Measure

Attention-Deficit/Hyperactivity Disorder
Nathan J. Blum, M.D.

Parent Report of ADHD Symptoms

53% of the PT group, 38% of the support group, 25% of the wait-list control group had clinically significant improvement at 8 weeks.

Observation of Engagement and Activity

Does Incredible Years Parenting Program Improve Outcome of Preschool ADHD?

- 153 3-4 y.o. children with disruptive behavior-disadvantaged families in Wales
- Randomized (2:1) to intervention (104) or wait-list control group (49)
  - Intervention: 12 weekly 2-2.5 hour group sessions
- Outcome
  - Eyberg Child Behavior Inventory
  - Conners Parent Rating Scale
  - Dyadic parent child interaction coding system in a 30 minute home observation

Hutching et al., BMJ 2007:334:678

Are Improvements From Parent Training Sustained Over Time

Conners Parent Rating

Can Less Specialized Providers Provide the Parent Training

- Deliver of New Forest Parenting Program by Trained Primary Care Home Visitors (2.5 days of training with weekly support)
- No significant improvement in ADHD symptoms in the intervention or control group at 23 weeks

**Kindergarten-based Intervention for at-Risk Children**
- Entering kindergarten in the Worcester, MA public schools
- Score 1.5 SD above the mean on a parent rating of ADHD symptoms and ODD symptoms
- 59% agreed to participate
- Special Education Classrooms
  - 14-16 children
  - 1 teacher and an aide
  - Teacher expert in behavioral treatment ½-day


**Can Parent Training Improve the Outcome of Preschool ADHD?**
- Most studies show improvements in disruptive behavior and ADHD symptoms when interventions are provided with high fidelity
- Some evidence of long-term benefits at 6-12 months post intervention in most, but not all studies.

**Preschool ADHD Treatment Study (PATS)**
- 6-Center Randomized Controlled Trial of Methylphenidate in Children 3-5.5 y.o.
- 10 weeks of parent training prior to medication
- Only those with persistent ADHD after parent training were offered Methylphenidate
- Doses 1.25 mg BID to 7.5 mg TID


**PATS Inclusion Criteria**
- 36-65 months of age
- In school at least 2 half-days per week
- Score >1.5 SD above the mean on Hyperactive/Impulsive subscale of parent and teachers Conners Rating Scale
- Met DSM-IV Criteria on DISC-IV
- CGAS Score <55
- IQ >70
- Excluded: Tics, Adjustment disorder, Autism, Psychosis, history of abuse, any other psychiatric disorder requiring medication

**PATS Parent Training**
- 10 weekly 2 hour group parent training sessions
- Significant Improvement
  - More than 30% reduction in parent and teacher rating
  - Rated as improved by at least 2 of the three raters: parents, teachers, clinicians.
Attention-Deficit/Hyperactivity Disorder
Nathan J. Blum, M.D.

PATS Enrollment
- 279 in Parent Training (PT)
- 261 Completed PT
- 19 (7.3%) Significant Improvement
- 18 (6.9%) Satisfied with Improvement
- 34 refused medication, 11 other
- 183 Open safety lead in (7 days)
- 4 enrolled without parent training
- 11 (6.0%) med side effects
- 2 refused meds, 2 lost to f/u
- 1 terminated by investigators, 2??
- 165 Placebo Controlled Trial

PATS Medication Trial
- Titration Phase (5 weeks)
  - Randomized to one of 5 medication orders
  - 1 week each of the following doses TID: Placebo, 1.25 mg, 2.5 mg, 5.0 mg, 7.5 mg
  - 10 mg dose option based on response to above doses
- Clinical Trial phase (4 weeks)
  - 50% placebo, 50% best MPH dose
- Open label maintenance (10 months)
  - All children in study
  - Started at best dose, but could be adjusted upper or down

Titration Phase MPH Dose Response

Titration Phase Optimal Dose

Clinical Trial Phase
- Best Dose Methylphenidate
  - 22% meet significant improvement criteria
  - 15% Discontinued
- Placebo
  - 13% meet significant improvement criteria
  - 45% Discontinued

Dose Related Effect Sizes
Attention-Deficit/Hyperactivity Disorder
Nathan J. Blum, M.D.

**PATS Significant Side Effects**
- 21 (11%) stopped medication because of side effects
  - 57% Irritability or emotionality
  - 19% Decreased appetite
  - 9% Tics
  - 9% Insomnia
  - <5% Social isolation, possible seizure, rash, depression, anxiety
  - Some had more than one reason for stopping the medication

Wigal et al. J Am Acad Child Adol Psych, 2006;45:1294-1303

**Stimulants and Growth**
- PATS Study 95 children treated an average of 401 days
  - Growth rate 1.38 cm/year less than expected
  - No untreated control group
- MTA Study
  - Growth rate 0.86 cm/year less than the untreated

**Summary**
- Preschool ADHD is associated with significant functional impairments
- Both behavioral Treatment and medication can result in improvements, but less than half are excellent responders
- Methylphenidate side effects, particularly irritability and growth suppression may be more significant than in school age children