

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

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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 difficulty to distinguish from highly variable normative behaviors before age 4 years...In preschool, the main manifestation is hyperactivity”

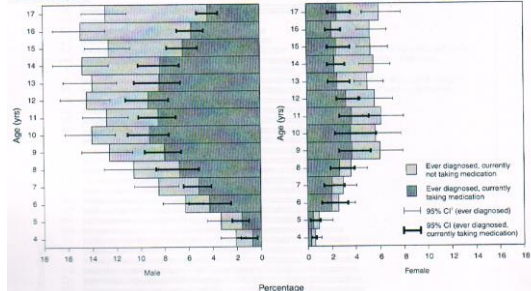
ADHD: AAP Practice Guideline

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

FIGURE 1. Percentage of children aged 4-17 years ever diagnosed with ADHD,¹ by age, sex, and medication treatment status — United States, 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

	ADHD	Control	P-value
% in Special Education	21	0	<0.05
% with Unintentional Injury	30.1	11.6	<0.05
Teacher rating of being liked by other children (5 point scale)	3.17	4.26	<0.05
Teacher rating of disruptive behavior	12.91	8.16	<0.05
Child self report of friendship difficulties	9.14	6.60	<0.05

Lahey et al., J Am Acad Child Adolesc Psychiatry 1998;695-702

ADHD in Preschool Children is Associated with Functional Impairment

	ADHD	Control	Effect Size	P-value
Parent Total Problem Behavior Standard Score	121 (12.5)	92.6 (10.4)	2.7	<0.001
Teacher Total Problem Behavior Standard Score	117.4 (16.1)	87.2 (12.2)	2.5	<0.001
Observation of non compliance in free play at home			1.8	0.01
Observation of inappropriate behavior during parent directed task			7.4	<0.01
Observation of negative social behavior in unstructured classroom settings			3.5	<0.01

DuPaul et al., J Am Acad Child Adolesc Psychiatry, 2001;508-515

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

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

*ADHD-HI vs Control

Lahey et al., J Am Acad Child Adolesc Psychiatry 1998;695-702

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

	ADHD-C (SD)	ADHD-HI (SD)	Effect Size	p value
Oppositional-P T score	66.7 (13.5)	65.7 (11.7)	0.07	0.73
Oppositional-T T score	70.9 (15.6)	75.5 (14.7)	-0.3	0.17
Anxious-P T-Score	53.5 (11.1)	53.2 (9.7)	0.03	0.90
Anxious-T T-Score	59.2 (11.6)	58.5 (12.2)	0.06	0.77
Social Skills-P Raw Score	37.5 (9.0)	41.5 (8.1)	-0.45	0.047
Social Skills-T Raw Score	25.8 (8.0)	22.7 (8.7)	0.37	0.08

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

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

	ADHD-C	ADHD-HI	Effect Size	p value *
	Mean % (SD)	Mean % (SD)		
Off-Task	6.33 (10.28)	8.62 (17.85)	-0.18	0.76
Disruptive	10.79 (11.03)	12.93 (11.31)	-0.19	0.34

*Mann-Whitney U test

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

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

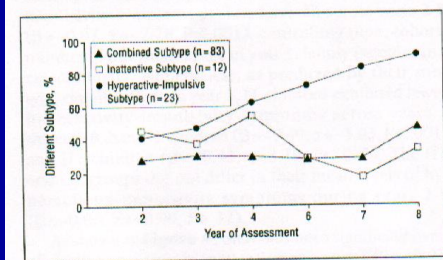


Figure 2. Percentage of children who met criteria for each subtype of attention-deficit/hyperactivity disorder in year 1 who met criteria for a different subtype in each of years 2 through 8.

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

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
 - 127 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

Rappley et al., JDBP 2002;23:30

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

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

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

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

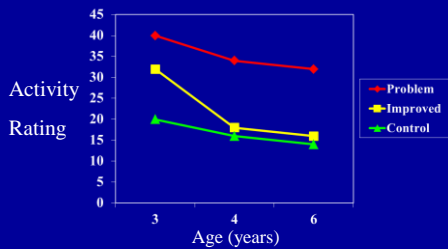
McGee et al., J Am Acad Child Adolesc Psychiatry
1991;30:224-232.

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

	Hyperactive N=18	Difficult N=21	Dev Cont N=20	Remainder N=724
% ADD	33.3%	9.5%	15%	5.8%
% Other	16.7%	9.5%	0%	11.0%
% No Disorder	50.0%	81.0%	85.0%	82.2%

McGee et al., J Am Acad Child Adolesc Psychiatry
1991;30:224-232.

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



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

Arnett et al. J Child Psychol Psychiatry 2013;54:1284-1294

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

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

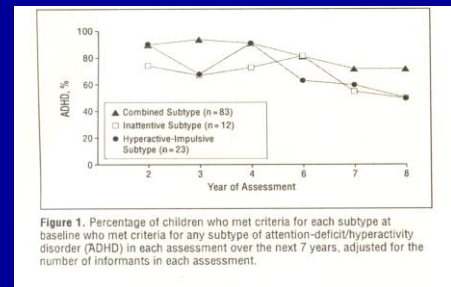


Figure 1. Percentage of children who met criteria for each subtype at baseline who met criteria for any subtype of attention-deficit/hyperactivity disorder (ADHD) in each assessment over the next 7 years, adjusted for the number of informants in each assessment.

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

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

Law et al. Pediatrics 2014;133:659-667

ADHD Diagnosis in Preschool Children

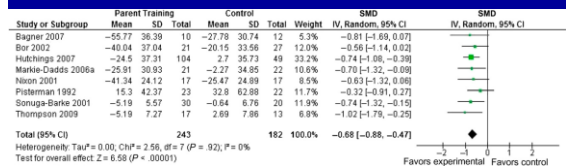
- Three Year Old Children
 - Rarely diagnose: up to 50% of hyperactive 3 year olds may improve
- 4-5 Year Old Children
 - Can be diagnosed
 - Particularly if symptoms have shown minimal improvement over a period of 12 months or more
 - Occur in the context of high internalizing or externalizing symptoms
 - Symptoms clearly occur in more than one setting
 - Other developmental disorders excluded

AAP Guidelines: Preschool Children

Pediatrics Vol. 128, November, 2011

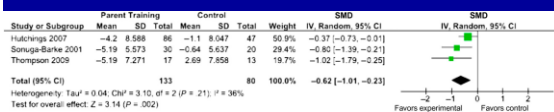
- Treatment
 - Evidence-based behavioral therapy is 1st line treatment
 - Methylphenidate if behavior therapy not sufficient
 - If behavior therapy not available, weigh risks of starting medicine early vs. risks of delaying treatment

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



Charach et al. Pediatrics 2013;131:e1584-e1604

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



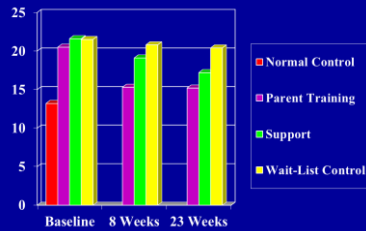
Charach et al. Pediatrics 2013;131:e1584-e1604

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
 - At end of 8 weeks and 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

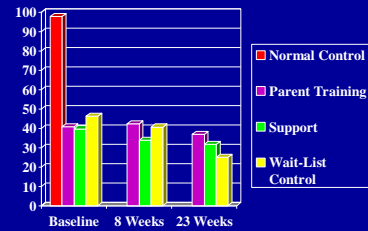
Sonuga-Barke et al., J Am Acad Child Adolesc Psychiatry 2001;40:402-408

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



Sonuga-Barke et al., J Am Acad Child Adolesc Psychiatry 2001;40:402-408

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

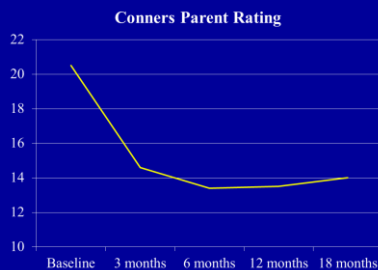
Hutching et al., BMJ 2007;334:678

Does Incredible Years Parenting Program Improve Outcome of Preschool ADHD?

	Effect Size: Intent to Treat	95% CI for Effect Size
Eyberg CBI-Intensity Scale	0.89	0.54-1.24
Eyberg CBI-Problem Scale	0.63	0.28-0.98
SDQ-Hyperactivity	0.41	0.06-0.76
Positive Parenting Observation	0.57	0.22-0.91
Child Problem Behavior-Observation	0.21	-0.13-0.55

Hutching et al., BMJ 2007;334:678

Are Improvements From Parent Training Sustained Over Time



Jones et al., Child: Care Health Dev 2008;34:380-390

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

Sonuga-Barke et al. British J Clin Psychol 2004;43:449-457.

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

Shelton et al. J Abnl Psychology 2000;28:253-266

Kindergarten-based Intervention for at-Risk Children

- At end of intervention children had greater improvements in aggression, social skills, and self-control than control group or parent training group
- “None of the initial post-treatment gains for the special classroom treated DB group resulted in any lasting differences from the untreated DB group at two years post-treatment follow-up”

Shelton et al. J Abnl Psychology 2000;28:253-266

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

Greenhill et al. J Am Acad Child Adol Psychiatry, 2006;45:1284-1293

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.

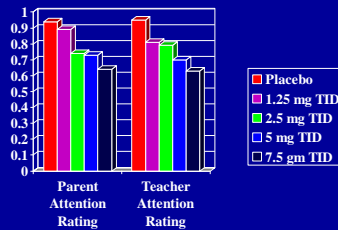
PATS Enrollment

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 (7days)	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

Non responders	5.5%
Placebo responders	9.6%
1.25 TID	16.5%
2.5 TID	17.9%
5 mg TID	20.7%
7.5 mg TID	25%

4.8 % were treated with 10 mg TID

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

Dose	Titration Phase	Clinical Trial Phase
1.25 mg	0.16	0.22
2.5 mg	0.34	0.48
5.0 mg	0.43	0.52
7.5 mg	0.72	0.87

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**