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Psychopharmacological and Other Treatments in Preschool Children with Attention-Deficit/Hyperactivity Disorder: Current Evidence and Practice

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Abstract

Objective:

This article reviews rational approaches to treating attention-deficit/hyperactivity disorder (ADHD) in preschool children, including pharmacological and nonpharmacological treatments. Implications for clinical practice are discussed.

Data Sources:

We searched MEDLINE, PsychINFO, Cumulative Index to Nursing & Allied Health, Educational Resources Information Center, Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects for relevant literature published in English from 1967 to 2007 on preschool ADHD. We also reviewed the references cited in identified reports.

Study Selection:

Studies were reviewed if the sample included at least some children younger than 6 years of age or attending kindergarten, the study participants had a diagnosis of ADHD or equivalent symptoms, received intervention aimed at ADHD symptoms, and included a relevant outcome measure.

Data Extraction:

Studies were reviewed for type of intervention and outcome relevant to ADHD and were rated for the level of evidence for adequacy of the data to inform clinical practice.

Conclusions:

The current level of evidence for adequacy of empirical data to inform clinical practice for short-term treatment of ADHD in preschool children is Level A for methylphenidate and Level B for parent behavior training, child training, and additive-free elimination diet.

Introduction

Attention deficit/hyperactivity disorder (ADHD) frequently begins between 2 and 4 years of age (Connor 2002; Egger and Angold 2006). It is associated with significant impairment in terms of emotional distress for the preschool child and the caregivers (DuPaul et al. 2001), expulsion from daycare or early education settings (Blackman 1999), demands on the caregiver's time, exclusion from family events, and accident proneness and other safety concerns (Lahey et

al. 2004; Rappley et al. 1999). Children with ADHD have comorbid mental health and chronic health problems and are frequent users of the healthcare system (Rappley et al. 2002). As shown by several prospective longitudinal follow up studies, behavior problems in preschool children persist to school-age years and continue to be associated with significant impairment (Campbell and Ewing 1990; Campbell et al. 2000; Egeland et al. 1990; Fischer et al. 1984; Lahey et al. 2004; Lavigne et al. 1998; McGee et al. 1991; Richman et al. 1982). In a recent study, 79.2% of the preschool children who met full diagnostic criteria for ADHD and 34.5% of the preschool children who met criteria in one situation only at initial assessment continued to meet full ADHD diagnostic criteria and exhibited global academic and social impairment three years later (Lahey et al. 2004).

Impairment from ADHD and persistence of problems at later ages underscores the need for early intervention in preschool children with ADHD (Beckwith 2000; Bierman et al. 2007; Campbell 2002; Conduct Problems Prevention Research Group 1999; Elliot et al. 2002; Petras et al. 2008; Shure et al. 2001). Recently, the Preschool Psychopharmacology Working Group (PPWG) reviewed pharmacological treatment studies in preschool children and proposed treatment algorithms for preschool psychiatric disorders (Gleason et al. 2007), however the nonpharmacological treatments for ADHD were not reviewed in detail. The primary objective of this paper is to review rational approaches to pharmacological and nonpharmacological treatment of ADHD in preschoolers and the implications for clinical practice. For the purposes of this paper, we define preschool age as prior to starting formal schooling, i.e., first grade. Hence, we reviewed studies that included children in kindergarten and/or younger than 6 years of age. The Food and Drug Administration (FDA) provides additional demarcation for children younger than 6 years. Most of the pharmacological agents for treatment of ADHD are approved by the FDA only for children older than 6 years (with the exception of amphetamines), and the FDA considers their use in children younger than 6 years as "off-label."

Methods and Review

We searched MEDLINE, PsychINFO, Cumulative Index to Nursing & Allied Health, Educational Resources Information Center, Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects for relevant literature on treatment of preschool ADHD. We also reviewed the references cited in identified reports to locate other relevant studies. Due to limited literature in this area, we reviewed both controlled and non-controlled studies. The reviewed studies met the following inclusion criteria: Published in English in the past 40 years (between 1967 to 2007); included at least some children younger than 6 years of age and/or attending kindergarten who had a diagnosis of ADHD; or exhibited behavior problems that are part of the ADHD diagnostic criteria, involved intervention aimed at ADHD symptoms, and included an outcome measure to monitor ADHD symptoms. To determine the level of evidence to inform clinical practice, we adapted the International Psychopharmacology Algorithm Project criteria (Jobson and Potter 1995) previously used by Judice and Mayes (2003) to categorize psychopharmacology treatments in preschool children. Since most of the reviewed child training studies were single case design experiments (state of current evidence for child training studies), based on the Task Force on Promotion and Dissemination of Psychological Procedures guidelines (Task Force on Psychological Intervention Guidelines 1995) previously used by Chorpita et al. (2002) to assess efficacy of psychosocial treatment studies in children and adolescents, we modified the criteria to include single case design experiments in addition to randomized controlled trials.

A treatment was considered to have evidence at Level A, if it demonstrated a significant difference on an ADHD outcome variable in a sample of preschoolers with a Diagnostic and Statistical Manual (DSM) diagnosis of ADHD in at least two randomized controlled trials (RCT) or two series of single case design experiments comparing randomly assigned active treatment to a comparison treatment or placebo. A treatment was considered to have evidence at Level B, if it demonstrated a significant difference on an ADHD outcome variable in a sample of preschoolers with a DSM diagnosis of ADHD in one RCT, two or more RCTs with mixed results, or one series of single case design experiments comparing randomly assigned active treatment to a comparison treatment or placebo. Level C was assigned to a treatment to indicate that data were based on uncontrolled trials, case reports, retrospective chart reviews, or informed clinical opinion.

Treatment of Preschool Attention-Deficit/Hyperactivity Disorder

Here we review the current available evidence for psychopharmacological and nonpsychopharmacological interventions (psychosocial and alternative treatments) and clinical implications for preschool children with ADHD. Prior to starting any treatment, it is important to conduct a comprehensive assessment that is contextually relevant and takes into account the rapid developmental changes occurring during preschool years. Because a comprehensive discussion of the assessment process for diagnosing ADHD in preschool children is beyond the scope of this paper, the reader is referred to several excellent reviews addressing preschool nosology, diagnosis, and assessment (Angold et al. 2004; Campbell 2002; Carter et al. 2004; Egger and Angold 2006; Emde et al. 1993; Task Force on Research Diagnostic Criteria: Infancy and Preschool 2003). In general, a multi-method and multi-informant evaluation extending over multiple appointments to assess symptomatology and impairment in multiple environments and caregiving contexts is recommended (Carter et al. 2004; Gleason et al. 2007). A combination of diagnostic interviews and parent and teacher rating scales, with psychometric data in preschoolers, are commonly employed to aid in the diagnostic and assessment process. Examples of the parent and teacher rating scales include Conners' Rating Scales-Revised (CRS-R) (Conners 2001), Swanson, Nolan and Pelham (SNAP) rating scale (Swanson 1992), Child Behavior Checklist-1½(CBCL-1½) (Achenbach and Rescorla 2000), and ADHD Rating Scale (ADHD-RS) (DuPaul 1998; Gimpel and Kuhn 2000). The Preschool Age Psychiatric Assessment (PAPA) (Egger et al. 2006) is a reliable and valid semi-structured diagnostic parent-interview that is widely used in research studies of preschool pathology. However, clinical settings may find the cost and length of the PAPA training and administration to be a barrier for its use in routine clinical practice. Nonetheless, adequate history, mental status examination, and collateral information are important for developing an appropriate treatment plan that addresses the biopsychosocial issues specific to each family.

Psychopharmacological treatment

There are several challenges to psychopharmacological treatment of preschool children with ADHD. Preschool age is a period of continued rapid neuronal maturation including synaptic remodeling and construction. Cortical synaptic density reaches its maximum at age 3 and is substantially modified by the pruning process from ages 3 to 7 years (Huttenlocher 1990). Cerebral metabolic rate peaks between 3 and 4 years of age (Chugani 1987). Aminergic systems play an important role in neurogenesis, neuronal migration, axonal outgrowth, and synaptogenesis (Coyle 1997) and are also the targets of action for many psychopharmacological agents as indicated by studies in preclinical models. Thus, clinicians are faced with a dilemma.

On one hand, whether it is prudent to recommend exposing the rapidly developing brain of a preschool child to psychopharmacological agents. On the other hand, clinicians also need to consider the consequences of an untreated disorder. Early exposure to adverse environmental circumstances and stress has been shown to result in long-lasting impact on the brain and emotional regulation of animals and humans (Graham et al. 1999; Matthews 2002; Nemeroff 2004).

Information about the use of psychopharmacological agents for treatment of ADHD is available mostly for school age children. In school age children, psychostimulants are the mainstay of treatment for ADHD; nonstimulant psychopharmacological agents are frequently recommended as a second-line treatment if a school age child's ADHD symptoms do not adequately respond to stimulants (Dulcan and Benson 1997). Recently, a nonstimulant psychopharmacological agent, atomoxetine, has been shown to be a safe and effective treatment of ADHD in school age children (Kratochvil et al. 2004; Michelson et al. 2001). Comparatively, there is limited information on the use of psychopharmacological agents for treatment of ADHD in preschool children. No pharmacokinetic and dose finding studies to identify dosage and frequency of drug administration in preschool children are available. Until recently, clinicians were left to extrapolate findings from older children to preschool children. However, medications used in older children may have specific toxicities in preschool children (Wigal et al. 2006), and there may be differences in efficacy in preschool children compared to school age children (Greenhill et al. 2006). Additionally, extrapolation to preschool children of data collected in older children is not always possible due to differences in development.

There are over 250 published studies of psychopharmacological agents in school age children with ADHD (Wilens et al. 2002). In contrast, there are a total of 24 published reports (blinded and open-label studies) on the use of psychopharmacological agents involving over 495 preschool children with ADHD. Of the 24 published reports (Tables 1 and 2), 20 published reports are on the use of stimulants, 2 published case reports on the use of $\alpha 2$ agonists, 1 published case report on the use of atomoxetine, and 1 published case report on the use of fluoxetine in preschool children with ADHD.

Psychostimulant studies.

Of the 20 published studies on the use of stimulants in preschool children, 12 double-blind group treatment studies (one parallel groups, 10 crossover and 1 ABA design) included 417 preschool children treated with methylphenidate (MPH). Two double-blind MPH/ placebo crossover studies included both preschool and older children, but did not specify the number of preschool participants (Barkley 1988; Fischer and Newby 1991); and one blinded time series treated one preschool child with dextroamphetamine (Speltz et al. 1988). The remaining five published reports are open-label studies or case reports involving a total of 61 preschool children treated with MPH or dextroamphetamine (Alessandri and Schramm 1991; Byrne et al. 1998; Cohen et al. 1981; Ghuman et al. 2001; Stiefel and Dossetor 1998).

Twelve of the fifteen blinded MPH studies treated typically developing preschool children with ADHD; seven studies included only preschool children (Barkley 1988; Conners 1975; Firestone et al. 1998; Greenhill et al. 2006; Musten et al. 1997; Schleifer et al. 1975; Short et al. 2004; Speltz et al. 1988), while the other six studies included both preschool and older children (Barkley et al. 1988; 1985; 1984; Chacko et al. 2005; Cunningham et al. 1985; Fischer and Newby 1991). Of the other two studies, one included a mixture of inpatient or outpatient preschool and school age children with ADHD who were either typically developing or had autism or other developmental disorders (Mayes et al. 1994), and the one remaining blinded

study treated preschool children with developmental disorders (Handen et al. 1999). The diagnostic procedure used most frequently included a combination of clinical interview and dimensional rating scales. With the exception of the recent PATS study, sample size was small ranging from 11–59, duration of the psychostimulant trials ranged from 3–9 weeks, and stimulant dose ranged from 0.15–0.6 mg/kg. Mixed outcomes were reported for efficacy. Based on direct observation of the preschool children's nursery school behavior, one study reported no improvement with MPH compared to placebo (Schleifer et al. 1975). Positive response to MPH was reported by other investigators in 80%–83% of typically developing preschool children (Conners 1975; Greenhill et al. 2006; Short et al. 2004) and 71%–73% of preschool children with developmental disorders (Handen et al. 1999). Data on side effect profile in preschool children was also divergent. Rates of side effects ranged from minimal or clinically negligible (Conners 1975) to 89% in typically developing preschool children (Schleifer et al. 1975) and 45%–50% in preschool children with developmental disorders (Handen et al. 1999; Mayes et al. 1994). Dysphoria, crying, whining, irritability, and solitary play were more frequently reported in preschool children than seen in older children.

The 6-site PATS study randomized 165 preschool children (3–5.5 years) diagnosed with ADHD in a placebo-controlled, double-blind crossover design, to one week each of 4 MPH doses (1.25 mg, 2.5 mg, 5 mg and 7.5 mg TID) and placebo. With the exception of the lowest MPH dose, improvements in parent- and teacher-rated ADHD symptoms were reported with MPH compared to placebo; the 7.5 mg TID dose was found to be the most effective. The effect sizes (Cohen's d) in the intent-to-treat sample ranged from 0.4–0.8 and were smaller than those reported for school age children treated with MPH (Greenhill et al. 2006). Interestingly, secondary analyses of the PATS efficacy data showed that preschoolers with ADHD with no or one comorbid disorder (primarily oppositional defiant disorder [ODD]) had treatment responses (Cohen's d = 0.89 and 1.00, respectively) at the same level as found in school age children (Ghuman et al. 2007). Preschoolers with 2 comorbid disorders had moderate treatment response (Cohen's d = 0.56) and preschoolers with 3 or more comorbid disorders did not respond to MPH (Ghuman et al. 2007). However, caution is needed in the generalization of the findings as there were only 15 preschoolers (9% of the sample) with 3 or more comorbid disorders compared to 150 preschoolers with two comorbid disorders (n = 34, 21% of the sample), one comorbid disorder (n = 69, 42% of the sample) or no comorbid disorders (n = 47, 28% of the sample). In addition to decreased appetite, stomach ache, and sleep difficulties usually seen in school age children, increased rates of social withdrawal and lethargy were reported especially at higher doses. A higher discontinuation rate (8.3%) due to MPH side effects was reported in the PATS study than the 0.5% discontinuation rate in the National Institute of Mental Health (NIMH) Multimodal Treatment of ADHD (MTA) study with school-age ADHD children (Wigal et al. 2006). Compared with the Center for Disease Control (CDC) norms, the preschool children with ADHD in the PATS were 2.0 cm taller and 1.8 kg heavier at baseline. A 20% less than expected annual height gain (-1.38 cm/year) and 55% less than expected annual weight gain (-1.32 kg/year) was reported for the children who continued MPH for a year in the open-label follow up phase (Swanson et al. 2006). Decrease in weight velocity was evident at the end of the 5-week double-blind crossover phase. Most preschoolers with ADHD were able to maintain improvement over 10 months of open-label follow up treatment (Vitiello et al. 2007).

TABLE 1. PUBLISHED BLINDED STUDIES OF STIMULANT TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PRESCHOOL CHILDREN

Authors	*Age Range (Mean ± SD)*	*N/ n < 6 years*	*Procedure for ADHD Diagnosis*	*Intervention Medication/ Dose*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behaviors)*	*Study Outcome*	*Side Effects/Safety*
Conners, 1975	<6 years (57.7 ± 13.2 months)	59/59	Clinical interview, parent questionnaire	(MPH 11.8 mg/day (1.5 mg/kg/day)	Double-blind, 2 parallel groups (MPH, placebo)/ 6 weeks	Parent Behavior Rating Scale, Global Clinical Improvement Rating, measures of vigilance, seat activity & impulsivity	Significant clinical improvement (93% improved on MPH, 11.5% improved on placebo) as rated by the physician on the Global Clinical Improvement Rating, significant reduction in restlessness and disruptive behavior as rated by the parents on the Parent Behavior Rating Scale. Measures of vigilance, seat activity & impulsivity did not show significant difference between MPH and placebo	Minimal side effects, trend towards elevated blood pressure in the MPH group
Schleifer et al., 1975	40–58 months (49 ± months[1])	26/26	Clinical interview	MPH 2.5–30 mg/day on a qd or bid schedule	Double-blind, crossover (placebo & MPH "optimal dose")/ 4–6 weeks	Nursery school observation, Hyperactivity Rating Scale measures of reflectivity-impulsivity, field independence and motor impulsivity	Improvement based on caregiver report, no improvement on nursery school observation or psychological measures	Dysphoria, social withdrawal, poor appetite, difficulty getting to sleep
Barkely et al., 1984	48–119 months (60.8 ± 7.6 months)	54/18	Clinical interview, Conners' Rating Scale-Parent (CRS-P), WWPARS	MPH 0.15 mg/kg bid, 1.5 mg/kg bid	Double-blind, crossover (placebo & 2 MPH doses)/ 3 weeks	Mother-child interaction	Significant improvement in child compliance and off-task behavior with MPH, "normalizing" effect of MPH on mother-child interactions	More frequent side effects on high MPH dose than low dose or placebo
Barkley et al., 1985	5–9 years (89 months[1])	60/12	Psychiatric assessment, CRS-P, Werry Weiss Peters Activity Rating Scale (WWPARS), Home Situations Questionnaire (HSQ)	MPH 0.3 mg/kg bid. 0.7 mg/kg bid	Double-blind, crossover (placebo & 2 MPH doses)/ 4 weeks	Mother-child interaction during free play and task periods	Child compliance and length of sustained compliance improved with the higher dose during the task period, drug effects did not differ during free play or across age levels	Greater number of side effects on MPH compared to placebo

Cunningham et al., 1985	4–6 years (68 months[1])	42/**12**	Clinical diagnosis CRS-P	Single dose of MPH 0.15 mg/kg, 0.50 mg/kg	Double-blind, crossover (placebo & 2 MPH doses)/ 4 sessions	Videotaped observations during freeplay, co-operative task, and simulated school setting	↓ actometer readings & ↑ on-task behavior during the simulated school setting, linear dose response, optimal ↓ in controlling and domineering interactions observed at 0.15 mg/kg dose with no incremental benefit on 0.50 mg/kg dose	Side effects were not monitored
Barkley, 1988	31–59 months (46.8 ± 6.7 months)	27/**27**	Clinical interview, CRS-P, WWPARS, HSQ	MPH 0.15 mg/kg bid, 1.5 mg/kg bid	Triple-blind, crossover (placebo & 2 MPH doses)/ 3 weeks	Mother-child interaction	↑ rates of compliance and length of sustained compliance with maternal commands, and on task behavior on higher dose during the task period	Trend for more frequent side effects on MPH compared to placebo
Barkley, at al., 1988	5–12 years (8.5 ± 2.3 years)	23/**not specified**	Semistructured parent interview, CRS-P or CRS-Teacher (CRS-T)	MPH 0.3 mg/kg bid, 0.5 mg/kg bid	Double-blind, crossover (placebo & 2 MPH doses)/ 3 weeks	Gordon Diagnostic System (GDS) for vigilance and impulse control, playroom observation during a restricted academic situation, CRS-P, CRS-T, HSQ, School Situations Questionnaire (SSQ)	80% of the children responded positivly to MPH on parent and teacher ratings of hyperactivity and disruptive behaviors, and ↓ off-task and hyperactivity ratings during playroom observation (restricted academic situation). Significant main drug effects for 16 of the 31 outcome measures, mostly on teacher ratings and observations during the restricted academic situation, both doses were equally effective	No difference in the number or severity of side effects. Two children discontinued the study due to development of tics in response to the medication and were excluded from the study analysis
Speltz et al., 1988[2]	51 months	1/**1**	Clinical interview, CRS-T	Dextroamphet-amine (DEX) 2.5 mg bid DEX 5 mg bid and Day Program	Double-blind time series (placebo & 2 DEX doses in counter-balanced order)/ 11 weeks	Daily observations of 15-minute work periods and 20-minute free play for frequency of on-task behavior, and teacher ratings of aggressive and disruptive behaviors and reports of side effects	↓ off-task and aggressive behavior on DEX compared to placebo Behavior gains maintained at follow up 2 years later	↑ whining, listlessness, solitary play, stomachache ↓ appetite, more frequent during 5 mg bid dose

(*continued*)

TABLE 1. PUBLISHED BLINDED STUDIES OF STIMULANT TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PRESCHOOL CHILDREN (CONT'D)

Authors	*Age Range (Mean ± SD)*	*N/ n < 6 years*	*Procedure for ADHD Diagnosis*	*Intervention Medication/ Dose*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behaviors)*	*Study Outcome*	*Side Effects/Safety*
Fischer & Newby, 1991	2–17 years (8.9 ± 2.9 years)	161/**not specified**	Semistructured parent interview, CRS-P, CRS-T, Child Behavior Checklist (CBCL), Teacher Rating Form (TRF)	MPH 0.2 mg/kg & 0.4 mg/kg BID	Double-blind crossover (placebo & 2 MPH doses)/ 3 weeks	CRS-P, CRS-T, HSQ SSQ, reaction time, GDS viligance task	Significant positive medication response on parent and teacher ratings of hyperactivity and laboratory measures of viligance and off-task behaviors, higher dose was most effective	No side effects reported
Mayes et al., 1994[3]	2–13 years (7.1 years[1])	69/**14**	Clinical interview	MPH 7.5–30 mg/day on a tid schedule	Double-blind, ABA (placebo & MPH "optimal dose")/3 weeks	Conners' 10-item ADHD Parent Rating Scale	79.4% improved on MPH based parent ratings on the Conners' scale	50.7% experienced side effects irritability, ↓ appetite, lethargy
Musten et al., 1997; Firestone et al., 1998	48–70 months (58.1 ± 8.2 months)	31/**31**	Diagnostic Interview for Children and Adults-Parents (DICA-P), Swanson, Nolan and Pelham checklist (SNAP), CRS-P, attention task	MPH 0.3 mg/kg bid, 0.5 mg/kg bid	Double-blind, crossover (placebo & 2 MPH doses)/ 3 weeks	Parent-child interaction tasks, CRS-P, GDS Delay and Vigilance Tasks	↑ attention and on-task during laboratory observation, ↓ impulsivitiy and hyperactivity as rated by parents on the CRS-P, no improved in compliance to parent requests	10% experienced severe side effects: social withdrawal, sadness. ↑ number & ↑ severity of side effects with the higher dose
Handen et al., 1999[4]	48–71 months (58.9 ± 8.2 months)	11/**11**	Clinical interview, Preschool Behavior Questionaire (PBQ), CRS-P	MPH 0.3 mg/kg/dose & 0.6 mg/kg/dose qd to tid	Double-blind, crossover (placebo & 2 MPH doses)/ 3 weeks	CRS-T, PBQ, direct behavior observation	72.7% improved on MPH based on at-least 40% reduction in teacher ratings of hyperactivity and inattention, significant improvement on clinic-based observations of activity level and compliance, more improvement on the higher dose	45% experienced side effects (social withdrawal and irritability); side effects more frequent at the higher dose

Short et al., 2004	<6 years (63 months[1])	28/**28**	Diagnostic Interview Schedule for Children-Parent (DISC-P) or clinical interview, Conners' Abbreviated Symptoms Questionnaire (CASQ), ADHD Rating Scale (ADHD-RS)	MPH 5 mg, 10 mg, 15 mg bid or mixed amphetamine salts (MAS; Adderall) 5 mg, 10 mg & 15 mg qd	Double-blind, crossover (placebo & 2 or 3 MPH or MAS doses)/ 3–4 weeks	ASQ, ADHD-RS, HSQ	Improved parent and teacher ratings of ADHD on either stimulant by at least 1 SD in 82% of the children and by 2 SD in 50% of the children. Clinical ratings of normalized behavior on best dose in 82% of the children	↓ appetite, crying & rebound effects
Chacko et al., 2005	5–6 years (6.1 ± 0.57 months)	36/**14**	Structured parent interview, parent and teacher Disruptive Behavior Disorder rating scales	MPH 0.3 mg/kg & 0.6 mg/kg bid and Behavior Modification System in a Summer Treatment Program	Double-blind, crossover (placebo & 2 MPH doses)/ 8 weeks	Point system, classroom rules, productivity and accuracy of class work	Improved classroom behavior for following rules and non-compliance and class work completion on both MPH doses compared to placebo, little incremental improvement in classroom measures on the higher MPH dose compared to the lower MPH dose. 28% children improved with classroom behavioral intervention & showed no incremental benefit of MPH	↓ appetite
Greenhill et al., 2006	3–5.5 years (53 ± 8 months)	165/**165**	Clinical assessment for DSM-IV diagnosis of ADHD, unanimous consensus by the panel of investigators, CRS-P, CRS-T	MPH 1.25 mg, 2.5 mg, 5.0 mg, 7.5 mg tid	Double-blind, crossover (placebo & 4 MPH doses) after 10 weeks of parent training/ 5 weeks	Swanson, Kotkin, Atkins, M-Flynn, and Pelham (SKAMP), Conners, Loney and Milch (CLAM) rating scales	Significant ↓ in parent- and teacher-rated ADHD symptoms on the 3 higher doses	↓ appetite stomachache, and sleep difficulties, ↑ rates of social withdrawal and lethargy, ↓ growth velocity, 8.3% discontinued due to MPH side effects

[1]SD not provided.
[2]Individualized weekly parent training sessions, classroom behavior management program and social skills training group were also administered concurrently.
[3]Included inpatient or outpatient preschool and school age children with autism, other developmental disorders or no developmental disorders.
[4]Included preschool children with mental retardation.
ADHD = attention-deficity/hyperactivity disorder; MPH = methylphenidate.

TABLE 2. PUBLISHED OPEN-LABEL STUDIES OF STIMULANT TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PRECHOOL CHILDREN

Authors	*Age Range (Mean ± SD)*	*N/n < 6 years*	*Diagnostic Procedure for Eligibility*	*Medication/ Dose*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behaviors)*	*Study Outcome*	*Side Effects/Safety*
Cohen et al., 1981	Kindergarten aged[1]	24/24	Clinical interview, Connors' Rating Scale-Teacher (CRS-T)	MPH 10–30 mg/day	Three randomized parallel groups (MPH, Cognitive Behavior Management [CBM], and CBM + MPH), open-label treatment/ 10 weeks	Cognitive and motor impulsivity tasks, parent and teacher behavior rating scales, classroom observation	No treatment effect in any of the groups	4 of the 14 (29%) children on MPH stopped medication due to side effects and were reassigned to either CBT or no treatment
Alessandri & Scharmm, 1991	50 months	1/1	Clinical interview, Connors' Rating Scale-Parent (CRS-P)	DEX 2.5 mg bid	Open-label A-B-A-B reversal design/ 16 weeks	Blinded ratings of off-task behavior, level of cognitive play and social participation during structured activity and unstructured play; teacher rated PBQ, CRS-T	↓ off-task behavior, ↑ attention, ↑ developmentally appropriate goal-directed, organized and symbolic play, & improved social functioning on direct observation ratings of behavior during structured activity and unstructured play	↑ solitary & parallel play
Byrne et al., 1998	62 months[1]	8/8	Clinical interview, Continuous Performance Test for Preschoolers—Visual (CPTP-V), CPT-Auditory (A), CRS-P, CBCL	MPH 15–20 mg/day or DEX 7.5–15 mg/day on qd-tid schedule	Open-label/ 5 months	CPTP-V, CPT-A, CRS-P, Child Behavior Checklist (CBCL)	↑ attention & social relations, ↓ problem behaviors	No information
Stiefel & Dossetor, 1998	5 years	1/1	Clinical interview	DEX 5 mg bid	Open-label/ 4 years	Clinical assessment	Improved behavior	Initial problem with reduced appetite and getting to sleep ameliorated with time
Ghuman et al., 2001	40–70 months (56.4 ± (9.6 months)	27/27	Clinical interview	MPH 0.55 mg/kg/day or DEX 0.43 mg/kg qd-qid	Chart review/ 24 months	Clinical Global Impressions-Severity (CGI-S) and CGI-Improvement	74% experienced improvement at 3 months and 70% at 12 and 24 months	63% experienced side effects; poor appetite, stomachache, irritability, dysphoria, sleep disturbance, headache, dull/tired; 11% stopped stimulants due to side effects

[1]Mean age not provided.
MPH = methylphenidate; DEX = dextroamphetamine.

Two of the open-label stimulant studies were prospective open-label treatment trials, two were case reports, and one was a retrospective chart review. Positive response to stimulants (MPH or dextroamphetamine) was reported in four of the open-label studies; one prospective treatment trial reported no treatment effect and reported a 30% discontinuation rate due to MPH adverse effects (Cohen et al. 1981).

Non-stimulant studies.

The two published case reports of open-label treatment with $\alpha 2$ agonists in 5 preschool children with ADHD reported improvement in hyperactive and impulsive behavior (Cesena et al. 1995; Lee 1997), one published case report of open-label treatment with atomoxetine in 10 preschool children reported improvement in hyperactive, impulsive and inattentive symptoms (Kratochvil et al. 2007), and one published case report of open-label treatment with fluoxetine in one preschool child with ADHD reported improvement in attention span (Campbell et al. 1995) (Table 3).

Prescribing patterns.

Despite controversy and scarcity of empirical information regarding dose guidelines, safety, and efficacy, psychopharmacological agents are being prescribed to preschool children.

This is a serious public health concern and was identified as a research priority by the Surgeon General (National Institutes of Health 2000; US Public Health Service 2000) and the White House (Pear 2000).

In 1994, 226,000 MPH prescriptions were written for children under 6 years of age (US Food and Drug Administration 1997). A three-fold increase in MPH use in 2–4 year old children was reported from 1991–1995 (Zito et al. 2000); Marshall (2000) reported that 150,000 to 200,000 children between the ages of 2 and 4 years were estimated to be taking MPH. Outpatient prescription data from 7 state Medicaid programs revealed 67.3% stimulant and 26% α-agonist use in 2001 in 2–4 year old children treated with psychotropic agents (Zito et al. 2007).

Pre-school children with ADHD symptoms are more often treated with stimulants in the community than with any other drug. Those not treated with stimulants, are often given other psychotropic medications, including those that have not been shown to have any efficacy in ADHD, such as selective serotonin reuptake inhibitors (SSRIs) (Rappley et al. 2002) and those with some efficacy for ADHD but leading to severe long-term adverse events (e.g., tardive dyskinesia), such as neuroleptics (Minde 1998; Rappley et al. 2002). Health Maintenance Organization (HMO) and Medicaid database surveys in 1995 showed frequent use of psychotropic medications in preschool children diagnosed with ADHD. Frequency of psychotropic drug prescription in 1–3 year old children diagnosed with ADHD (N = 223) in the Michigan Medicaid system was 57% (n = 127) compared to 26% (n = 47) for psychosocial intervention (Rappley et al. 1999). Psychotropic medications alone as a sole intervention strategy were utilized in 40% children (n = 89); comparatively psychosocial intervention as a sole treatment was utilized in only 9% (n = 21). Stimulants were prescribed for 93.7%, α2 agonists for 44.9%, tricyclic antidepressants for 33.1%, neuroleptics for 15.7%, and SSRIs for 11% of the preschool children receiving psychotropic medications. More than half of the children received treatment for longer than 6 months. Medication monitoring was inadequate—for 75 children (59%) follow-up visits occurred every 3 months and for 25 children (19%) at intervals greater than 6 months (Rappley et al. 2002).

Summary of psychopharmacological treatments.

There is evidence for short-term efficacy and long-term effectiveness and tolerability of psychostimulants, especially MPH, in preschool children with ADHD. Response is reported to be less robust and response rate is reported to be lower in preschool children with ADHD compared to older children. Preschool children with ADHD are sensitive to developing more side effects especially at higher doses and have unique adverse effect profile including more irritability and mood changes. This sensitivity to stimulant adverse effects may be a limiting factor in achieving an adequate and/or robust response in preschool children with ADHD. Only open-label information is available regarding effectiveness and tolerability of one non-stimulant, atomoxetine, in preschool children with ADHD. Additionally, pharmacological interventions may be effective in reducing core ADHD symptoms such as impulsivity, overactivity, and inattention among preschool children with ADHD (Greenhill et al. 2006); however, there is little evidence to suggest that psychostimulants improve long-term interpersonal relationships known to be important in predicting outcomes for children displaying disruptive behaviors (Coie and Dodge 1998; Pelham et al. 1998; Rubin et al. 2006). Moreover, no information is available about long-term safety and effects of psychopharmacological agents on brain development in preschool children.

Psychosocial treatments

Concerns about the short- and long-term safety of psychopharmacological agents especially on the developing brain of preschool children, coupled with ethical, societal, and political beliefs about manipulating behavior through medication and perceived overprescription (Jensen et al. 1999) often lead families and providers to favor other interventions for preschoolers (Dulcan and Benson 1997). In this section, we will review current evidence for success of psychosocial treatments in preschool children with ADHD.

TABLE 3. PUBLISHED REPORTS OF NON-STIMULANT TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PRESCHOOL CHILDREN

Authors	*Age Range (Mean ± SD)*	*N/n < 6 years*	*Procedure for Eligibility*	*Diagnostic Medication/ Dose*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behavior)*	*Study Outcome*	*Side Effects/Safety*
Campbell et al., 1995	3 years	1/1	Clinical interview	Fluoxetine 10 mg qd	Open-label/ 6 weeks	Clinical assessment	Improved attention even-tempered, ↓ aggression	No significant side effects
Cesena et al., 1995[1]	56 months (4.8 years)	1/1	Clinical interview	Clonidine 0.025 mg tid	Open-label/ 5 months	ASQ, Clinical Global Impressions (CGI) ADHD	Normalization of hyperactivity & attention on teacher ASQ, improved sleep	Sedation early in treatment, was resolved later in the course of treatment
Lee, 1997	31–42 months	4/4	Clinical interview, Child Behavior Checklist (CBCL)/2/3, Connors' Rating Scale-Parent (CRS-P)	Guanfacine 0.25 mg bid-1.25 mg/day	Open-label/ 2–6 months	Clinical assessment	↓ impulsive hyperactive and aggressive behavior, ↓ tantrums, improved mother-child relations	Sedation and transient benign chest pain
Kratchovil et al., 2007	5–6 years (6.1 ± 0.58 years)	22/10	Diagnostic Interview Schedule for Children-4 (DISC-4), clinical interview, ADHD Rating Scale (ADHD-RS)	Atomoxetine 10–45 mg/day qd or bid	Open-label/ 8 weeks	ADHD-RS, CGI	Improved ADHD-RS scores and CGI	Mood lability, reduced appetite, weight loss (mean = 1.04 ± 0.8 kg)

[1]Child's ADHD symptoms were seen as manifestation of HIV encephalopathy.
ADHD = attention-deficit/hyperactivity disorder.

There is evidence from studies in school-age children that long-term behavioral improvements may require psychosocial interventions (Ialongo et al. 1993). Inhibitory processes play a critical role in impaired functioning in children with ADHD (Barkley 1997; Barkley 1998; Barkley 2003; Nigg 2001; Nigg 2003; Quay 1997) and these, although rudimentary, are developing rapidly during the preschool period (Davidson et al. 2006; Diamond and Taylor 1996; Espy et al. 1999; Garon et al. 2008; Jones et al. 2003; Rueda et al. 2005). Psychosocial interventions targeting key executive functions, especially inhibitory processes, may be particularly helpful (Diamond et al. 2007; Dowsett and Livesey 2000).

Limited psychosocial intervention research has been conducted with preschool samples of children formally diagnosed with ADHD (Bryant et al. 1999; McGoey et al. 2002); however, there is considerable evidence that parent, child, and parent-child interventions can reduce problem behaviors in young children displaying a range of disruptive behaviors, including excessive hyperactivity and inattention as reviewed in the following section. We have grouped the psychosocial intervention studies into those that train parents in behavioral techniques and use the parents as the primary agent of change, and those that train children in a classroom setting to reduce problematic behaviors.

Parent training.

Among psychosocial interventions, parent training to help parents learn and implement behavioral treatment has the strongest evidence base showing positive effects for school age children with ADHD (Chorpita and Daleiden 2002). For preschool children with ADHD, parent training in behavior management is an especially helpful and the most appropriate psychosocial intervention (Stanley and Stanley 2005; Webster-Stratton et al. 2001). When children are young, parents have an enormous impact on their child's behavior (Capage et al. 1998; Eyberg et al. 1995; Funderburk et al. 1998; Hembree-Kigin and McNeil 1995) creating a window of opportunity to teach parents how to be positive and consistent in their parenting responses, help reduce noncompliant and aggressive behaviors, and help their child persist at a difficult task and provide successful experiences for their child, thus reducing risk for continued problems in later years. Parent behavior training programs for preschool children have been modeled after efficacious programs developed with older children (Anastopoulos et al. 1993; Dishion and McMahon 1998), and draw upon both social-learning and attachment theories to varying extent. Parent training programs may include sessions with parents, parent-child dyad, or a combination of parent sessions and work with the parent-child dyad to improve parent-child relationship, and increase the child's prosocial behaviors and decrease negative behaviors.

There are 15 published reports of parent behavior training treatment trials (either controlled, case series or case reports) that monitored outcomes in ADHD symptoms in preschool children with a DSM diagnosis of ADHD or preschool children displaying ADHD symptoms (Tables 4 and 5). However, there was a wide variation in the study design, type of control groups, inclusion criteria, diagnostic measures, type of psychosocial intervention, method of intervention delivery, and outcome measures employed in the studies. Nine studies used a randomized parallel groups design with control groups ranging from wait-list, community treatment, combination treatment to minimal treatment (Barkley et al. 2000; Bor et al. 2002; Corrin 2004; Jones et al. 2007; McGoey et al. 2005; Pisterman et al. 1992; 1989; Sonuga- Barke et al. 2001; Strayhorn and Weidman 1989; Strayhorn and Weidman 1991) and six studies did not employ any control group (Chang et al. 2004; Danforth 1999; Drash et al. 1976; Erhardt and Baker 1990; Henry 1987; Huang et al. 2003). Eight of the nine controlled studies included only preschool children and four of these eight studies selected the preschoolers based on a DSM

diagnosis of ADHD through clinical or structured parent interview (Bor et al. 2002; Pisterman et al. 1992; 1989; Sonuga-Barke et al. 2001), and the other four selected preschoolers based on a rating scale cutoff. The ninth controlled study included both preschool-age and school-age children with a DSM diagnosis of ADHD. Sample sizes ranged from 20-50 per group. Most studies employed group-training sessions except for three studies that employed individual training sessions with the parents (Bor et al. 2002; Henry 1987; Sonuga-Barke et al. 2001). Training was conducted over 8–12 sessions, each parent training session lasting 1–3 hours. Most studies included both teaching/ modeling sessions with the parents and work with the parent-child dyad with the exception of one study that included parent training sessions only (Jones et al. 2007), one study that included parent and/or child training sessions separately (Corrin 2004) and two studies that included only didactic teaching sessions with the parents (Barkley et al. 2000; Huang et al. 2003). Outcome assessments varied among the studies and included parent ratings of ADHD and disruptive behaviors, and direct behavior observation by independent raters for on-task behavior, child compliance with maternal commands, and parent-child interaction quality during structured play.

Improvements in ADHD symptoms were reported in three of the eight controlled studies that included only preschool children (Jones et al. 2007; Sonuga-Barke et al. 2001; Strayhorn and Weidman 1989) and only one of these studies (Sonuga-Barke et al. 2001) was in preschoolers formally diagnosed with ADHD. Preschoolers diagnosed with ADHD (N = 78) were randomized to 8 weeks of parent training, parent counseling and support, or a wait-list group (Sonuga-Barke et al. 2001). Improvements in ADHD symptoms were reported with parent training compared to the other two conditions; positive effects were maintained at 6 month follow-up. No improvement in hyperactive, impulsive and/or inattentive symptoms on parent ratings or direct observation was reported in the remaining 5 controlled studies that included only preschool children. Improvements in ADHD symptoms were also reported in most of the non-randomized non-controlled case series (Drash et al. 1976; Erhardt and Baker 1990; Huang et al. 2003).

With the exception of Barkley et al (2000), most investigators reported improvements in parenting skills, parenting style of interaction, and child compliance. Barkley et al. (2000) reported poor treatment response with parent behavior training in kindergarteners (N = 158) who met dimensional rating scale cutoff criteria for hyperactive, impulsive, inattentive, and aggressive behavior. The kindergarteners were assigned to one of four treatment groups: parent training only, classroom day treatment only, a combined condition, or a no treatment control group. The parent training intervention produced no effects.

There may be several reasons for the poor treatment response in this study. Inclusion criteria for the study were based on a rating scale cutoff and no clinical or structured diagnostic interviews were conducted for a diagnosis of ADHD. Most important, neither the children's caregivers nor their teachers had indicated impaired functioning in the kindergartners included in the study. There is evidence that psychosocial treatment approaches have greater impact on those children rated with higher levels of problems (Kellam et al. 1998; Wilson and Lipsey 2007). Furthermore, only 25% of the parents attended more than four parent behavior training sessions, and, finally, the parent behavior training was delivered in a didactic format.

TABLE 4. PUBLISHED CONTROLLED STUDIES OF PSYCHOSOCIAL TREATMENTS IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: PARENT TRAINING

Authors	*Age range in years (Mean age ± SD)*	*N/n < 6 years*	*Procedure for ADHD Diagnosis; Inclusion Criteria*	*Psychosocial intervention*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behaviors)*	*Study Outcome*
Strayhorn & Weidman, 1989; 1991	2–5 (3.9[1])	96/**96**	No clinical assessment, parent questionnaire based on DSM III-R diagnostic criteria; At-risk for behavior problems (complaints of ADHD, disruptive behaviors or emotional difficulties, low socioeconomic status), 40% parents endorsed ≥ 8 of 14 ADHD symptoms	Group parent training and individual sessions work with the parent-child dyad	Two randomized parallel groups: parent behavior training (PBT) or minimal treatment control group, open-label treatment/ 12 sessions	Parent and teacher ratings on ADHD, compliance, and internalizing symptoms on the Behar Preschool Behavior Questionnaire; direct observation of parent and child behaviors, parenting practices	Improvement in the PBT group in parent-rated ADHD and internalizing symptoms, and child and parent behaviors on direct observation. No improvement in teacher ratings, or verbal ability measures. Improved parent behavior correlated positively with improved child behavior Improvement in teacher-rated classroom behavior at 1 year follow-up
Pisterman et al., 1989	3–6 (4.15 ±0.78)	50/**50**	Structured screening interview, >1 SD on the Conners' Hyperactivity Index; DSM-III criteria for ADDH	Group parent training and 2 individual sessions with the parent-child dyad	Two randomized parallel groups: immediate treatment or delayed treatment group, open-label treatment/ 12 weeks	Parent ratings on the Conners' Hyperactivity Index, direct behavioral assessment of child attention, child compliance and parental style of interaction	No treatment effect on child attention or parent-rated Conners' Hyperactivity Index. Improvement in the immediate treatment group in child compliance; improved parental style of interaction. Outcome reported only for 46 of the 50 randomized children; four children (8%) dropped out after group assignment. Five children received methylphenidate during the study. Improvement maintained at 3 month follow up

Pisterman et al., 1992	3–6 (3.9 ± 0.62)	57/57	Semi-structured screening interview, cutoff threshold for parent or teacher Swanson, Nolan and Pelham (SNAP) rating scale and Conners' Hyperactivity Index; DSM-III criteria for ADDH	Group parent training and 2 individual sessions with the parent-child dyad	Two randomized parallel groups: immediate treatment or delayed treatment group, open-label treatment/ 12 weeks	Direct behavioral assessment of child attention, child compliance and parental style of interaction	No treatment effect on child attention on direct observation Improvement in child compliance and parental style of interaction in the immediate treatment group. Outcome reported only for 45 of the 57 randomized children; 12 children (21%) dropped out after group assignment with a higher drop-out rate for less educated parents. Four children received stimulants during the study. Improvement maintained at 3 month follow up
Barkley et al., 2000; Shelton et al., 2000	4.5–6 (4.8 ± 0.5)	158/158	Diagnostic Interview Schedule for Children-Parent (DISC-P), Conners' rating Scale-Parent (CRS-P); Cutoff dimensional threshold for Hyperactive, Oppositional &/or Conduct Problem factors on CRS-P, no clinical diagnosis of ADHD required for inclusion, 66% children met ADHD criteria on the DISC-P	10 weekly group parent training sessions followed by 6 monthly booster sessions, special treatment classroom	Four randomized parallel groups; Parent Training (PT) Special Treatment Classroom (STC), combined (PT and STC) or no treatment control groups, open-label treatment/ 9 months (school year)	DISC-P, parent and teacher ratings of child behavior on Child Behavior Checklist (CBCL), Home Situations Questionnaire (HSQ), School Situations Questionnaire (SSQ), Self-Control Rating Scale (SCRS); Continuous Performance Test (CPT); parent self-report on parenting practices and competence; clinic observation for disruptive behavior and parent-child interaction; and classroom observation	No improvement and poor attendance in the PT group. STC produced improvement in parent ratings of adaptive behavior, teacher ratings of social skills, attention and aggression; and classroom observation ratings of externalizing behavior. No improvement in academic achievement or parent ratings of home behavior; and no improvement in laboratory measures of attention, impulse control or parent-child interaction in any of the treatment groups. No difference in the groups at 2 year follow-up

(*continued*)

TABLE 4. PUBLISHED CONTROLLED STUDIES OF PSYCHOSOCIAL TREATMENTS IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: PARENT TRAINING (CONT'D.)

Authors	*Age range in years (Mean age ± SD)*	*N/n < 6 years*	*Procedure for ADHD Diagnosis; Inclusion Criteria*	*Psychosocial intervention*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behaviors)*	*Study Outcome*
Sruga-Barke et al., 2001	3[2]	78/78	Structured clinical interview (Parental Account of Childhood Symptoms (PACS), Werry-Weiss-Peters Activity Scale (WWPAS); Cuttoff threshold for the ADHD Hyperkinesis scale of the PACS and cutoff threshold on the WWPAS	Eight 1-hour weekly in-home individual parent training sessions and work control with the mother-child dyad	Three randomized parallel groups: parent training (PT), parent counseling and support (PC&S) or waiting-list (WLC) groups, open-label treatment/ 8 weeks	Clinician ratings of ADHD based on parent interview using the PACS; play observation for attention/parent self-engagement: Parenting report on the Satisfaction and Parenting Efficacy scales of the Parental Sense of Competence (PSOC) scale	PT more effective than PC&S and WLC in improving ADHD symptoms both on parent interview and play observation, and improvement in mothers' sense of well-being Improvement maintained at 23 weeks
Bor et al., 2002	3–4 (3.42 ± 0.31)	87/87	Structured diagnostic interview, Eyberg Child Behavior Inventory (ECBI); DSM IV diagnosis of ADHD, >90th percentile on the Inattentive Behavior subscale of the ECBI and at least 1 family adversity factor	Ten 60–90-minute individual sessions (7 parent training sessions and 3 parent-child sessions) for the Standard and 12 for the Enhanced Behavior Family Intervention (SBFI and EBFI)	Three randomized parallel groups: SBFI, EBFI, waitlist (WL) control group. open-label treatment/ 15–17 weeks	Parent ratings on the ECBI, Parent Daily Report (PDR), Parenting Sense of Competency (PSOC) scale, Parenting Scale (PS), Parent Problem Checklist (PPC), observation of mother-child behavior	No treatment effect on parent-rated inattentive behavior. Improvement in parent-reported child behavior problems, dysfunctional parenting, and parental competence with both SBFI and EBFI; significantly less observed child negative behavior with EBFI; no difference in SBFI and EBFI conditions. Outcome reported only for 63 of the 87 randomized children; 24 children did not complete intervention and post-assessment. Gains maintained at 1-year follow-up
Corrin, 2004	4.5–8.5 (6.6 ± 1.25)	55/9	Structured parent interview, CRS-P; DSM diagnosis of ADHD	Ten weekly group child and parent training sessions	Two randomized parallel groups: child group training or combined parent and child training, open-label label treatment/ 10 weekly sessions	CBCL, CRS-P, HSQ	Improvement in CRS-P Hyperactivity scale in both treatment groups, 17 children were on stimulant medication

McGoey et al., 2005	3–5 (4.04 ± 0.72)	57/57	Semi-structured parent interview for DSM-IV criteria for ADHD, and cutoff threshold for parent and teacher Hyperactivity or Inattention subscale of the CRS; at-risk for ADHD	Multi-component intervention including 12 weekly group parent training sessions & 9 monthly booster sessions, preschool consultation, and medication consultation as needed	Two randomized parallel groups: Early Intervention (EI) or a Community Treatment Control (CTC) group, open-label treatment/ 12 months	Preschool and Kindergarten Behavior Scales (PKBS), direct observation of classroom behavior and parent-child interaction, Medical Outcomes and Service Utilization, Consumer knowledge ratings	No treatment effect reported on parent- and teacher-rated Attention problems/Overactivity subscale of the PKBS, improvement in on-task performance, compliance, self-control, and social skills; increased positive parenting behaviors, reductions in negative parent behavior, and positive changes in family coping were seen in both groups. Outcome reported for completers (21 out of the 30 children (70%) randomized to EI) only. Four children were prescribed stimulants or clonidine.
Jones et al., 2007; 2008	3–4 (3.86 ± 0.51)	79/79	No clinical assessment, cutoff threshold for parent Hyperactivity subscale of the Strengths and Difficulties Questionnaire (SDQ); cutoff threshold for parent problem or intensity subscale of the ECBI and Hyperactivity subscale of the SDQ	Twelve 2.5 hour-weekly Incredible Years Basic Parent Training (IY-BPT) group sessions and weekly telephone calls	Two randomized parallel groups: IY-BPT or waitlist (WL) control group, open-label treatment/ 12 weeks	Parent ratings on the Conners' Abbreviated Parent Rating Scale (CAPRS), and Child Deviance (negative and destructive behavior and non-compliance) subscale score of the Dyadic Parent-Child Interaction Coding System (DPICS) based on observation of mother-child behavior	Parents reported greater reduction on the CAPRS scores in the IY-BPT group compared to the WL group, and improvement was significant even after controlling for co-occurring conduct problems as measured by the Child Deviance subscale scores of the DPICS Gains maintained at 6 months, 12 months and 18 months post-intervention.

[1]SD not provided.
[2]Mean age not provided.
ADHD = attention-deficity/hyperactivity disorder; ADDH = attention-deficit disorder with hyperactivity.

TABLE 5. PUBLISHED NON-CONTROLLED STUDIES OF PSYCHOSOCIAL TREATMENTS IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: PARENT TRAINING

Authors	*Age range in years Mean age ± SD)*	*N/n < 6 years*	*Procedure for ADHD Diagnosis & Inclusion Criteria*	*Psychosocial intervention*	*Study Design/ Duration*	*Outcome Assessment (for ADHD and disruptive behaviors)*	*Study Outcome*
Drash et al., 1976	2–4.8 (2.8[1])	5/5	Clinical diagnosis of ADHD	Weekly 3-hour parent classes (two mother-child pairs also received direct training), child group training in a classroom setting	Case series, prospective, no control group. open-label treatment/ 9 months	Parent-rated Behar Preschool Behavior Questionnaire (BPBQ), direct behavior observation during group classroom situation and a standardized task completion activity	Parent-rated BPBQ Hyperactivity and Distractibility subscale scores, decreased from 90th percentile to 52nd percentile, high rates of compliance rates across settings Two children received psychotropic medication
Henry, 1987	4.5–10.5 (7.3[1])	6/n < 6 years not specified	DSM- III diagnosis of ADHD by a psychiatrist and a psychologist, stabilized on psychostintulant medication	Four 20-minute symbolic modeling sessions with the child followed by six 60-minute combined symbolic modeling and parent training sessions administered	Case study, prospective, no control group, open-label treatment/ 10 weeks	Parent Conners' Symptom Questionnaire, observation of child compliance to parental task during a structured task	3/5 children improved on the parent ratings of the Conners' Symptom Questionnaire. A combination of medication, symbolic modeling and parent training was more effective than a combination of medication and symbolic modeling or medication alone in reducing noncompliance. Parent training for time-out procedure was most effective. Combined symbolic modeling and medication was not any more effective than medication alone. Gains maintained at 6 months
Erhardt and Baker, 1990	5.2–5.8	2/2	Diagnosed as being hyperactive by the pediatrician. parent score of >15 on the Abbreviated Symptom Questionnaire (CASQ)	Six 2-hour group parent training and four 1-hour individual consultation and parent-child interactive sessions	Case study, prospective, no control group, open-label treatment/ 10 sessions	Parent ratings on the CASQ, Iowa Conners' Rating Scale. Werry-Weiss-Peters Activity Scale (WWPAS), Child Behavior Checklist (CBCL)	Improved parental ratings of hyperactivity, tantrums, aggression, compliance and social functioning

Danforth, 1999	4.0 (Twins)	2/2	DSM IV diagnosis of ADHD and oppositional defiant disorder (ODD), clinical diagnosis by the referring pediatrician	Eight 1-hour weekly parent training sessions using the Behavior Management Flow Chart	Case study, prospective, no control group, open-label treatment/ 8 sessions	Conners' Rating Scale-Parent (CRS-P), CBCL, Parent Daily Report telephone checklist, direct observation of mother-child interaction	CRS-P Hyperactive Index T scores decreased from 80 to 50 for one twin and remained unchanged for the other twin; increased compliance and decreased aggressive behavior on direct observation of mother-child interaction
Huang et al., 2003	3–6 (5.42 1.1)	23/23	Diagnosis of ADHD on Barkley's semistructured interview questionnaire	Nine 1-hour weekly group parent training sessions and 1 booster session 4 weeks later	Prospective, no control treatment condition, open-label treatment/ 10 sessions	Disruptive Behavior Rating Scale-Parent Form, Child Attention Profile, and Home Situations Questionnaire	Improved parental ratings for ADHD and ODD symptoms, significant decline in the severity of symptoms and problem behaviors at home. Outcome reported for completers (n = 14, 61% of the recruited sample) only Four children were also taking stimulants during the trial
Chang et al., 2004	4–6 (6 ± 0.8)	8/8	DSM IV diagnosis of ADHD by 2 child psychiatrists	Eight 2-hour weekly group parent training and joint parent-child social skills training group sessions	No control group/ 8 sessions	No information provided regarding how outcome assessment was conducted	Parents reported improved ADHD behaviors in 3 (37.5%) children; improvement in emotional expression/regulation, less parental frustration and increased satisfaction regarding child's behavior at home.

[1]SD not provided.
ADHD = attention-deficit/hyperactivity disorder.