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Preschool Onset Attention-Deficit/Hyperactivity Disorder: Course and Predictors of Stability over 24 Months

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Abstract

Objective: The present study examined the course of ADHD over 24 months in a preschool population.
Method: n = 48 preschoolers with ADHD, aged 3.0-5.11 years, subjects included in a larger sample of preschoolers with depression and other disorders (n = 306) were comprehensively assessed at 3 annual time points over 24 months in a prospective longitudinal follow-up study.
Results: Baseline diagnoses of preschool MDD, ODD, and CD were risk factors for ADHD diagnosis over 24 months in this preschool population. Among older preschoolers and after controlling for key demographic variables, ADHD predicted later ADHD diagnosis, along with other significant risk factors - baseline diagnosis of ODD, and/or family history of disruptive disorders, and stressful life events.
Conclusions: ADHD showed greater homotypic continuity at later rather than earlier preschool ages. Other disruptive comorbidities also emerged as key predictors of stable ADHD course. Study findings may help to inform which preschool ADHD populations to target for early intervention. Larger sample sizes are needed to confirm these findings and to further explore the stability, course, and predictors of outcome of preschool onset ADHD.

Introduction

Validity of ADHD in preschoolers

Empirical studies in the area of preschool psychopathology have increased markedly over the last decade (Lavigne et al. 2009). The availability of age appropriate measures that accurately ascertain symptoms as they manifest at this early age has facilitated systematic investigations of preschool mental disorders (Egger et al. 2006). Data validating several Axis I psychiatric disorders arising during the preschool period have now become available (Egger and Angold 2006). These have included investigations of preschool depression (Kashani et al. 1997; Kashani and Carlson 1987; Kashani et al. 1986; Luby et al. 2002; Luby et al. 2003; Luby et al. 2009; Stalets and Luby 2006), posttraumatic stress disorder (PTSD) (Scheeringa et al. 2005), other anxiety disorders (Spence et al. 2001; Warren 2004), oppositional defiant disorder (ODD), conduct disorder (CD) (Keenan et al. 2007), and attention-deficit/hyperactivity disorder (ADHD) (Lahey et al. 2004).

Following the Robins and Guze (1970) criteria used to establish the validity of psychiatric disorders, the validity of preschool ADHD has been supported to date by *stability and specificity of symptoms*. Persistence of symptoms has been demonstrated in several longitudinal investigations from independent research groups (Campbell et al. 1986; Lahey et al. 2004; Lahey et al. 1998; McGee et al. 1991). Academic, social, and global *impairment* as reported by teacher and parent measures have been reported both cross-sectionally and longitudinally (Gadow et al. 2001; Kadesjo et al. 2001; Lahey et al. 2004; Tandon et al. 2009). The level of impairment of preschoolers with ADHD, has been reported to be similar to that of affected school age children (Wilens et al. 2002). More specifically, preschoolers with ADHD show poorer academic readiness for school entry, poorer fine motor skills, and are socially impaired relative to healthy controls (DuPaul 2001). Other related problems include preschool expulsion, difficulty maintaining babysitters and/or childcare and subsequently missed family work days and personal time (Barkley 2006). Finally, the validity of preschool ADHD is also supported by a ''greater family history of related disorder,'' and *genetics* is estimated to account for 80% of the variance in heritability of the disorder (Barkley 2006). While the diagnosis of ADHD in preschoolers has been reported at relatively high rates in clinical settings (Luby and Morgan 1997; Wilens et al. 2002), surprisingly, and in contrast to other preschool disorders noted above, there is a relative dearth of validity data for this preschool disorder.

Defining clinical level hyperactivity is more challenging during the preschool period as population-based studies indicate that this symptom alone is quite common among typically developing preschoolers (Smidts and Oosterlaan 2007). While high activity levels are also normative among preschoolers, clinical symptoms of ADHD have been observed in less than 10% of preschoolers (Egger and Angold 2006), which is noteworthy given recent concerns for overdiagnosis of ADHD at early ages (Evans et al. 2010). Further,

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other symptoms that are common and developmentally normative, such as ''often interrupts,'' occur at much higher rates in preschoolers with ADHD (Egger et al. 2006). For example, rates of ADHD symptom levels were reported as 4–8 times higher in clinic referred preschoolers with ADHD compared to age matched, non-ADHD preschoolers in a study of 3 to 7 year old children (Kadesjo et al. 2001).

Stability and Predictive Validity of ADHD in Preschoolers

Several longitudinal studies suggest symptoms of ADHD in preschoolers persist into elementary school (Beitchman et al. 1987; Campbell 1995; Lahey et al. 2004; Posner et al. 2007). These investigations informed *symptom* continuity (i.e., hyperactivity) or ''problem behavior'' rather than categorical *diagnostic* stability per se (Campbell 1995; Fischer et al. 1993). These studies suggested that problem behavior or hyperactivity as a symptom in preschoolers, predicted problematic behavior through adolescence. Other studies have suggested that while hyperactivity manifests as problematic behavior observed over several years, a myriad of other poor outcomes, including but not limited to ADHD are evident at increased rates by adolescence (McGee et al. 1991). This heterotypic continuity has also been shown in a more recent investigation by Lahey et al who reported not only homotypic continuity, but also that ADHD predicted higher severity of anxiety, depression and conduct symptoms, especially in females (i.e. heterotypic outcomes) (Lahey et al. 2007). In a prior report of a 3-year longitudinal investigation of preschoolers, ages 4 to 6 with ADHD, the majority of the sample ($n = 255$) continued to demonstrate impairing ADHD (Lahey et al. 2004). In addition to longitudinal studies of specific symptoms in preschool populations, several investigations have demonstrated the stability of preschool disruptive disorders such as ODD and CD. For example, Lavigne et al (1998; 1998; 2001) reported that the 2-year stability of any disruptive disorder (including ADHD) was 50% for 2–3 year olds and 65% for 4–5 year old preschoolers.

Comorbidities and Preschool Attention-Deficit/Hyperactivity Disorder

Disruptive disorders in general have been found to be highly co-morbid with ADHD in several investigations (Gadow and Nolan 2002; Keenan 2000; Schwebel et al. 2002; Wakschlag et al. 2007). For example, oppositional defiant disorder (ODD) has been found to be co-morbid with ADHD in 60% of referred preschoolers (Wilens et al. 2002; Wilens et al. 2002). The diagnosis of ODD has shown to be both reliable and valid in preschool populations (Keenan et al. 2007; Lavigne et al. 1998; Lavigne et al. 2001). In addition to the high co-morbidity rates with ADHD, co-morbid ODD has also been associated with other poor outcomes such as a higher rate of injuries when compared to those with ADHD alone (Schwebel et al. 2002). Further studies are now needed to elucidate the longitudinal stability of preschool onset ADHD and to inform the key factors that contribute to course.

Current Investigation

The current investigation examined the diagnostic stability of DSM-IV ADHD in preschoolers ages 3.0 to 5.11 over a 2-year period. The following analysis was conducted using data from a sample of children ascertained for a study of preschool MDD for which a disruptive comparison group was also sought using the same ascertainment methods. It was hypothesized that ADHD diagnosed in preschoolers would show diagnostic stability at school age. Potential contributors to stability of preschool ADHD were examined accounting for demographic variables, medication use, comorbidities, parental psychopathology and stressful life events. Preschoolers were included in a no disorder group if they did not meet criteria for any DSM-IV psychiatric disorder based on parent report on the Preschool Age Psychiatric Assessment (PAPA) (Egger et al. 1999), an age-appropriate, interviewer-based comprehensive diagnostic interview for the assessment of preschoolers.

Methods

Subjects

A sample of $n = 306$ preschoolers, aged 3–5.11 years, was ascertained from multiple community sites in the St. Louis metropolitan area. To obtain an ethnically and socioeconomically diverse sample, primary care, pediatric clinics, and preschools/daycares were selected at random using a geographically stratified method (Luby et al. 2009). The group was oversampled for depressive disorders on the basis of parent responses on a previously validated screening checklist, the Preschool Feelings Checklist (PFC) (Luby et al. 2004); however, children with disruptive symptoms were also sought and included as a psychiatric comparison group. A score of greater than 3 on the PFC, while highly sensitive to capturing depressive disorders is less specific and also useful to capture those at high risk for disruptive disorders (Luby et al. 2004). Therefore the disruptive group was ascertained using the same methodology as the depressed group. All diagnostic group designations were based on parent report on the PAPA. This disruptive group was of primary interest for the current investigation. Preschoolers with chronic medical or neurological problems, mental retardation, or autistic spectrum disorders were excluded. Concerns that age of presentation at follow-up could bias likelihood of diagnosis was addressed by controlling for age at baseline (91% of the children attended both follow-up periods). Approval for the study was obtained from the Washington University School of Medicine Institutional Review Board. Consent was obtained for parent and child's participation from legal guardians, and assent was obtained for children six years of age or older.

Measures

The DSM-IV diagnoses were based on parent report on the PAPA (Egger et al. 1999), an age-appropriate, interviewer-based comprehensive diagnostic interview for the assessment of preschoolers with established test-retest reliability (Egger et al. 2006). As is standard for this measure, final diagnoses were derived using computerized DSM-IV based algorithms. The PAPA was administered by bachelor or masters-level clinicians who have undergone a 4-day formal training and subsequent calibration process. Interviewers were blind to diagnoses of the subject from prior study waves. Information about the use of psychotropic medication in the study sample was obtained from the PAPA as well as from parent reports on the Health and Behavior Questionnaire (HBQ) (Armstrong et al. 2003). Both stressful (eg parental divorce, change in daycare/school, death of a pet) and traumatic life events (eg death of a parent, a natural disaster, attacked by an animal) were assessed using the PAPA. Family history was ascertained from primary caregivers using the Family Interview for Genetic Studies (Maxwell 1992), a widely-used and validated measure of family psychiatric history. For the current study, family history of psychiatric

disorders represented the proportion of all first- and second-degree biological relatives reported to have disorders [major depressive disorder (MDD), anxiety (anxiety disorders included separation anxiety disorder, generalized anxiety disorder, and PTSD), bipolar disorder (BP), CD, and ADHD]. Family history of disruptive disorders was ascertained but distinctions between ODD and CD were not made. Subjects were assessed at 3 annual study waves conducted over 24 months.

Data analysis

Demographic Characteristics of Diagnostic Groups at Baseline. Cross tabulation (χ^2) tests and analyses of variance (ANOVA) were used to examine demographic and risk factor differences between diagnostic groups at baseline. In addition, cross tabulation (χ^2) tests and Mann-Whitney *U* tests were conducted as appropriate to examine differences in the same factors between preschoolers who attended later study waves and those who dropped out.

Risk Factors Contributing to Stability of Preschool ADHD. Because repeated observations of an individual may be correlated, a Generalized Estimating Equations (GEE) model, which accounts for correlations, was used in this longitudinal study to examine risk factors such as family history of psychiatric diagnoses, life events, baseline diagnosis of MDD, anxiety, ODD, and CD, contributing to the stability of preschool ADHD. Demographic factors were controlled in the model.

Likelihood of Chronicity of Preschool ADHD. Multinomial logistic regression analyses were conducted to test the likelihood that preschoolers in the ADHD group vs those in the no-disorder or psychiatric comparison groups would have ADHD, no disorders, or another psychiatric disorder at follow up {baseline (T1, ages 3–5.11) vs. 1 year follow up (T3, ages 4–6.11); T1 vs. 2 year follow up (T5, ages 5–7.11); and T3 vs. T5. Logistic regression models were conducted to test whether an ADHD diagnosis at an earlier wave predicted an ADHD diagnosis at follow-up (e.g. T1 to T3, T1 to T5, and T3 to T5) while statistically controlling for demographic variables, co-morbid diagnoses (split into separate MDD, anxiety, CD, and ODD categories), stressful life events, and family history of MDD/anxiety, bipolar and disruptive disorders at baseline. The severity scores of ADHD were examined as well.

Differences between Preschoolers with ADHD who Recovered vs. had Stable Course at School Age. Cross tabulation (χ^2) and nonparametric (Mann Whitney) tests were used to examine the differences between preschoolers who had a diagnosis of ADHD at preschool age (younger than 71 months) and also had data for school age ADHD status (yes vs. no); a further multivariate logistic regression model was conducted to examine factors that were associated with the differences. (*SPSS software, version 17.0 (SPSS Inc, Chicago, Illinois), was used to conduct all statistical analyses)*

Results

Diagnostic groups and sample characteristics

Using baseline diagnoses, preschoolers were categorized into 1 of 3 hierarchical diagnostic groups: (1) the ADHD group was composed of those who met criteria for ADHD with or without any other co-morbidity ($n = 48$); (2) the psychiatric group was composed of those who met criteria for other disorders except ADHD ($n = 106$), including MDD, any anxiety (anxiety disorders included SAD, GAD, and PTSD) and/or disruptive disorders (disruptive disorders included ODD and CD); (3) preschoolers were included in a no disorder group ($n = 146$) if they did not meet criteria for any DSM-IV psychiatric disorder based on parent report on the PAPA. Two preschoolers met symptom criteria only for bipolar disorder type I at baseline and were excluded due to the current lack of clarity on this diagnosis in preschool children, and 4 preschoolers had excessive missing data; therefore, these 6 subjects were excluded from the analyses that follow.

Results from a 1-way ANOVA with post hoc pair-wise comparisons indicated that the number of life events the preschoolers experienced prior to baseline (for stressful life events, $F_{2, 296} = 4.24$, $p = .015$, for traumatic life events, $F_{2, 296} = 4.89$, $p = .008$) and the proportion of family members with a history of bipolar disorder (collected at baseline, $F_{2, 287} = 3.17$, $p = .043$) were significantly different among diagnostic comparison groups. Specifically, preschoolers in the ADHD group had experienced significantly more life events (both stressful and traumatic) at baseline than preschoolers in the no disorder group ($p = .012$ for both) (Table 1). Cross tabulation χ^2 test results indicated that caregivers of preschoolers in the ADHD group had a lower education level than caregivers in both the psychiatric ($\chi^2_3 = 9.80$, $p = .020$) and the no disorder ($\chi^2_3 = 17.29$, $p = .001$) groups. Total family income was significantly lower in the ADHD group compared with the psychiatric ($\chi^2_3 = 10.05$, $p = .018$) and the no disorder ($\chi^2_3 = 15.61$, $p = .001$) groups. Preschoolers in the ADHD group were less likely to come from married parents compared with the no disorder group ($\chi^2_4 = 12.70$, $p = .013$). Of the caregivers of preschoolers with baseline ADHD, 38% reported married, and 36% reported cohabitation over 6 months, which was included in the never married category. No other significant demographic or risk factor differences were found between diagnostic groups at baseline. Preschoolers in the ADHD group had a marginally higher proportion of family members with a history of bipolar disorder than preschoolers in the no-disorder group (non significant, $p = .091$).

Two hundred seventy-three subjects (38 with ADHD, 100 with psychiatric disorders, and 135 with no disorders) were retained during the longitudinal study (subjects who returned for at least one of the two annual follow-up waves). The Mann-Whitney *U* test and cross tabulations (χ^2 tests) results indicated that within the no-disorder group, preschoolers who had parents with higher education levels were less likely to drop out ($p = .011$). Within the ADHD group, preschoolers who had no baseline diagnosis of CD ($p = .003$) and who had less family history of bipolar disorder at baseline ($p = .028$) were more likely to be retained in the study. No other statistically significant differences were found. The use of medications was examined and found to be non-significant.

Risk factors contributing to stability of preschool ADHD

Results from the GEE model indicated that preschoolers' ADHD diagnoses were relatively stable across 24 months. There was no significant difference among rates of ADHD diagnosis at different waves (Wald $\chi^2 = 2.457$, df = 2, $p = .293$). There were four risk factors contributing to preschoolers' ADHD diagnoses: baseline ODD (Wald $\chi^2 = 27.433$, OR: 6.196, 95% CI 3.131 –12.261, $p < .001$), baseline CD (Wald $\chi^2 = 11.270$, OR: 3.537, 95% CI 1.692 – 7.396, $p = .001$), baseline MDD (Wald $\chi^2 = 5.852$, OR: 2.287, 95% CI 1.170 – 4.470, $p = .016$), and family history of bipolar

Table 1. Characteristics of the Sample at Baseline

Characteristic	Patients, No. (%)				
	ADHD (n = *48*)	*Other Psychiatric Disorder* (n = *106*)	*No Disorder* (n = *146*)	χ^2	p-*value*
Age, y				9.41	0.052
3	21 (44)	25 (24)	47 (32)		
4	13 (27)	48 (45)	66 (45)		
5	14 (29)	33 (31)	33 (23)		
Ethnicity				5.53	0.237
White	21 (44)	51 (53)	87 (60)		
African American	18 (37)	35 (33)	45 (31)		
Other	9 (19)	15 (14)	13 (9)		
Sex				2.34	0.311
M	29 (60)	56 (53)	70 (48)		
F	19 (40)	50 (47)	76 (52)		
Total family income, $				16.26	0.012
≤20,000	18 (37)	20 (21)	25 (18)		
20,001–40,000	13 (27)	18 (19)	20 (15)		
40,001–60,000	8 (17)	16 (26)	27 (20)		
≥60,001	9 (19)	42 (44)	63 (47)		
Parent education				19.92	0.003
High school diploma	14 (29)	16 (15)	27 (18)		
Some college	25 (52)	45 (42)	42 (29)		
4 year college degree	3 (6)	22 (21)	35 (24)		
≥Graduate education	6 (13)	23 (22)	42 (29)		
Parent marital status				15.99	0.043
Married	18 (38)	57 (55)	94 (66)		
Widowed	0	0	1 (1)		
Separated	1 (2)	4 (4)	2 (1)		
Divorced	5 (10)	10 (9)	7 (5)		
Never married	24 (50)	33 (32)	39 (27)		
No. of life events, mean (SD)					
Stressful life events	4.13 (2.20)	3.45 (1.85)	3.19 (1.91)	$F = 4.24$	0.015
Traumatic life events	1.83 (1.39)	1.56 (1.24)	1.24 (1.14)	$F = 4.89$	0.008
Total	5.96 (3.11)	5.01 (2.46)	4.43 (2.49)	$F = 6.51$	0.002
Age, mean (SD), mo	52.04 (10.55)	54.36 (9.70)	52.12 (9.15)	$F = 1.90$	0.151
Proportion of family history disruptive disorder, mean (SD)	5.92 (9.00)	6.11 (10.50)	5.31 (12.62)	$F = 0.16$	0.853
Proportion of family history MDD/ANX, mean (SD)	13.50 (13.71)	15.48 (15.33)	12.95 (13.90)	$F = 0.93$	0.394
Proportion of family history BP, mean (SD)	3.70 (5.43)	3.10 (5.48)	1.83 (4.69)	$F = 3.17$	0.043

SD = standard deviation; MDD = major depressive disorder; ANX = anxiety; BP = bipolar disorder.

disorder at baseline (Wald $\chi^2 = 4.765$, OR: 1.051, 95% CI 1.005 – 1.099, $p = .029$) (see Table 2).

Likelihood of stability of preschool ADHD: Homotypic vs. heterotypic ADHD outcomes

In this study sample, there were $n = 32$ preschoolers diagnosed with ADHD at baseline who attended both subsequent waves. $N = 13$ out of these (40.6%) preschoolers were diagnosed with ADHD at T3. $N = 10$ ($n = 8$ from T3 ADHD group, $n = 1$ from T3 other psychiatric disorder group, and $n = 1$ from T3 no disorder group) were diagnosed with ADHD at T5 (10/32 = 31.3%). Together there were $n = 15$ (46.9%) preschoolers diagnosed with ADHD at follow-up waves. There were $n = 12$ (12/32 = 37.5%) preschoolers diagnosed with other psychiatric disorders (no ADHD) at follow-up waves ($n = 9 - 1 = 8$ from T3 other psych group, and 4 more at wave T5 from the T3 no disorder group). Only $n = 5$ (5/32 = 15.6%) preschoolers who had an ADHD diagnosis at baseline recovered at later waves (no disorder at both follow-up waves).

Baseline (T1) vs. 12 month follow-up (T3) diagnostic groups. Compared to preschool children with no disorder at baseline, preschool children with baseline ADHD were 18.2 times as likely to have a diagnosis of ADHD at T3 and 5.3 times as likely to have a diagnosis of ADHD rather than another psychiatric disorder at T3. Further, preschool children with baseline ADHD were 6 times as likely to have a diagnosis of ADHD at T3 compared to preschool children with other psychiatric diagnoses at baseline (see Table 3 for Odds Ratios along with their 95% confidence intervals for all comparisons).

Baseline vs. 24 month follow-up (T5) diagnostic groups. Compared to preschool children with no disorder at baseline, preschool children with baseline ADHD were 22.3 times as likely to have a diagnosis of ADHD at T5 and 4.4 times as likely to have a diagnosis of ADHD rather than another psychiatric disorder at T5. Further, preschool children with baseline ADHD were 4.5 times as likely to have a diagnosis of ADHD at T5 compared to preschool children with other psychiatric diagnoses at baseline (see Table 3).

T3 vs. T5 diagnostic groups. Compared to preschool children with no disorder at T3, preschool children with T3 ADHD were 315 times as likely to have T5 ADHD and 6.5 times as likely

Table 2. Generalized Estimating Equations (GEE) Examining Risk Factors for ADHD Diagnosis over 24 Months

Variables entered into the model[a]	*Wald* χ^2	*df*	*OR (95% CI)*	p-*value*
Child's age, mo	0.036	1	1.003 (0.971-1.036)	.849
Sex (M = 1/ F = 0), Male	0.501	1	0.800 (0.432-1.483)	.479
Ethnicity	3.933	2		.140
White			1 [Reference]	
Black	0.363	1	0.781 (0.350-1.743)	.547
Other	1.867	1	2.006 (0.739-5.442)	.172
Family income, $	2.209	3		.530
≤ 20,000			1 [Reference]	
20,001–40,000	1.513	1	0.582 (0.245-1.379)	.219
40,001–60,000	0.52	1	0.693 (0.239-2.012)	.500
≥ 60,001	2.22	1	0.535 (0.209-1.373)	.194
Maternal education	5.378	3		.146
High school			1 [Reference]	
Some college education	2.173	1	1.788 (0.826-3.870)	.140
4-year college degree	0.741	1	0.595 (0.182-1.941)	.389
≥ Graduate education	0.494	1	1.447 (0.516-4.054)	.482
Major depressive disorder	5.852	1	2.287 (1.170-4.470)	.016
Anxiety disorder	0.681	1	0.750 (0.378-1.486)	.409
Conduct disorder	11.270	1	3.537 (1.692-7.396)	.001
Oppositional defiant disorder	27.433	1	6.196 (3.131-12.261)	< .001
No. of stressful life events	0.024	1	0.993 (0.910-1.084)	.877
Family history of disruptive disorder	0.280	1	1.006 (0.983-1.030)	.597
Family history of MDD/anxiety disorder	1.005	1	1.010 (0.991-1.030)	.316
Family history of bipolar disorder	4.765	1	1.051 (1.005-1.099)	.029
Wave	2.457	2		.293
Wave = 3 vs. Wave = 1	1.959	1	0.735 (0.263-1.249)	.162
Wave = 3 vs. Wave = 2	0.234	1	0.864 (0.480-1.558)	.628
Wave = 2 vs. Wave = 1	2.108	1	0.663 (0.381-1.155)	.147

CI = confidence interval; OR = odds ratio; MDD = major depressive disorder.
[a]The model included a total of 270 subjects, all variables were recorded at baseline, except for stressful life events, which were the total events the child had encountered prior to each study period.

to have a diagnosis of ADHD rather than other psychiatric disorder at T5. (see Table 3).

Examining ADHD Stability Accounting for Demographics, Comorbidities and other Risk/Protective Factors. All 3 logistic regression models were significant, Cox & Snell $R^2 = .26$, $\chi^2 = 65.82$, $df = 17$, $p < .001$ for the model T3 ADHD with T1 ADHD as the predictor, Cox & Snell $R^2 = .23$, $\chi^2 = 55.73$, $df = 17$, $p < .001$ for the model T5 ADHD with T1 ADHD as the predictor, and Cox & Snell $R^2 = .30$, $\chi^2 = 75.64$, $df = 17$, $p < .001$ for the model T5ADHD with T3 ADHD as the predictor. Table 4 displays the results of these analyses with variables grouped into logical categories. Demographic variables, co-morbid disorders, other risk factors, and ADHD diagnosis were entered simultaneously. Five variables were significant using the model T3 ADHD with T1 ADHD as the predictor. The diagnosis of preschool ADHD at T1 (baseline) (OR: 10.06, $p = .001$) was the strongest predictor of T3 ADHD, followed by ODD at baseline (OR: 4.18, $p = .03$), family history of bipolar disorder at baseline (OR: 1.12, $p = .01$), age in months at baseline (OR: 1.07, $p = .04$), and family history of disruptive disorder (CD and/or ADHD) at baseline (OR: 1.05, $p = .01$) (see Table 4a). Three variables were significant when predicting T5 ADHD with baseline ADHD. The diagnosis of preschool ODD at baseline (OR: 15.4, $p < .001$), ADHD at baseline (OR: 8.05, $p = .01$) and family history of bipolar disorder at baseline (OR: 1.12, $p = .03$), were significant predictors of T5 ADHD even when controlling for all other risk factors (see Table 4a). When examining the model T5 ADHD with T3 ADHD, the diagnosis of T3ADHD (OR: 85.57, $p < .001$) was the strongest predictor of T5 ADHD, followed by ODD at baseline (OR: 16.85, $p = .001$) (see Table 4b).

Severity of ADHD was measured using number of symptoms met per DSMIV and was found to predict later wave ADHD; however, there were no significant clinical differences in use of summed symptoms vs. categorical diagnosis to predict later ADHD diagnosis. The same logistic regression models were conducted using baseline ADHD severity scores to predict T3 and T5 ADHD, using T3 ADHD severity scores to predict T5 ADHD. Baseline ADHD severity score (Wald $\chi^2 = 12.89$, OR: 1.33, 95% CI 1.14 – 1.56, $p < .001$), family history of disruptive disorders (Wald $\chi^2 = 4.81$, OR: 1.04, 95% CI 1.00 – 1.08, $p = .028$) and family history of bipolar disorder (Wald $\chi^2 = 4.71$, OR: 1.11, 95% CI 1.01 – 1.21, $p = .030$) were 3 significant factors for predicting T3 ADHD; baseline ADHD severity score (Wald $\chi^2 = 12.04$, OR: 1.31, 95% CI 1.13 – 1.53, $p = .001$) and baseline ODD (Wald $\chi^2 = 11.89$, OR: 14.07, 95% CI 3.13 – 63.22, $p = .001$) were significant factors for predicting T5 ADHD; T3 ADHD severity score (Wald $\chi^2 = 16.36$, OR: 1.69, 95% CI 1.31 – 2.17, $p < .001$) and baseline ODD (Wald $\chi^2 = 9.84$, OR: 20.83, 95% CI 3.12 – 138.8, $p = .002$) were significant factors for predicting T5 ADHD.

Differences between Preschoolers with ADHD who Recovered vs. had Stable Course at School Age

A subsample of $n = 27$ subjects ($n = 17$ from T1 and $n = 10$ from T3) had a diagnosis of ADHD at preschool age (younger than 71

Table 3. Odds Ratios for Homotypic Versus Heterotypic Continuity of Preschool ADHD and Other Psychiatric Disorders

T1 group	*T3 group*	*OR*	*95% CI*
ADHD vs No disorder	ADHD vs No disorder	18.20***	5.61-59.09
	ADHD vs Other Psychiatric disorder	5.25*	1.47-18.77
	Other Psychiatric disorder vs No disorder	3.47***	1.22-9.85
ADHD vs Other Psychiatric disorder	ADHD vs No disorder	6.00**	1.99-18.08
	ADHD vs Other Psychiatric disorder	6.00**	1.89-19.04
	Other Psychiatric disorder vs No disorder	NS	
Other Psychiatric disorder vs No disorder	ADHD vs No disorder	3.03*	1.02-9.05
	ADHD vs Other Psychiatric disorder	NS	
	Other Psychiatric disorder vs No disorder	3.47***	1.82-6.61
T1 group	*T5 group*	*OR*	*95% CI*
ADHD vs No disorder	ADHD vs No disorder	22.27***	5.97-83.08
	ADHD vs Other Psychiatric disorder	4.44*	1.08-18.36
	Other Psychiatric disorder vs No disorder	5.01**	1.79-14.00
ADHD vs Other Psychiatric disorder	ADHD vs No disorder	4.46**	1.49-13.30
	ADHD vs Other Psychiatric disorder	3.44*	1.09-10.86
	Other Psychiatric disorder vs No disorder	NS	
Other Psychiatric disorder vs No disorder	ADHD vs No disorder	5.00**	1.49-16.75
	ADHD vs Other Psychiatric disorder	NS	
	Other Psychiatric disorder vs No disorder	3.88***	1.94-7.76
T3 group	*T5 group*	*OR*	*95% CI*
ADHD vs No disorder	ADHD vs No disorder	314.7***	35.55-2785
	ADHD vs Other Psychiatric disorder	6.52**	1.93-22.02
	Other Psychiatric disorder vs No disorder	48.27***	5.82-400.4
ADHD vs Other Psychiatric disorder	ADHD vs No disorder	304.0***	25.70-3596
	ADHD vs Other Psychiatric disorder	22.22***	4.24-116.4
	Other Psychiatric disorder vs No disorder	13.68*	1.63-114.7
Other Psychiatric disorder vs No disorder	ADHD vs No disorder	NS	
	ADHD vs Other Psychiatric disorder	NS	
	Other Psychiatric disorder vs No disorder	3.47***	1.79-6.96

T1 = baseline, T3 = 12 month follow-up, T5 = 24 month follow-up.
*$p < .05$ **$p < .01$ ***$p < .001$.
ADHD = attention-deficit/hyperactivity disorder; OR = odds ratios; CI = confidence interval.

months) and who also had data available for school age ADHD status ($n = 16$ had school age ADHD, $n = 11$ did not). Cross tabulation (χ^2 tests) and nonparametric methods (Mann Whitney *U* tests) were used to examine the differences between these two groups; factors examined included demographic variables, family history, preschool age life events, ADHD, ODD, and CD. Results indicated that compared with preschoolers with ADHD who had recovered from ADHD by school age, those who continued to have ADHD at school age had more maternal history of affective disorder, more preschool traumatic life stressors, and were more likely to have an ODD diagnosis at preschool age. Further multivariate analysis were used with all three factors entered in a logistic regression model; using stepwise selection, results indicated that preschool age ODD was significant (Wald $\chi^2 = 4.90$, OR: 17.62, 95% CI 1.39 – 223.81, $p = .027$), and preschool traumatic life stressors showed trend-level significance (Wald $\chi^2 = 3.30$, OR: 3.43, 95% CI 0.91 – 12.99, $p = .069$); mother's affective disorder was no longer significant.

Discussion

The present study utilized a sample of preschoolers with ADHD (ascertained as a comparison group for a longitudinal investigation of preschool depression) to investigate the longitudinal course of preschool ADHD. The current investigation examined the course of ADHD at three time points over two years, including at baseline (T1, ages 3–5.11), 12 months later (T3, ages 4–6.11), and 24 months later (T5, ages 5–7.11). The odds of retaining a diagnosis of ADHD were 9 times greater between T3 and T5 than between T1 and T3, providing strongest support for homotypic continuity of ADHD at later waves. These findings converge with Tandon et al (2009) in which performance based attentional deficits were more highly correlated with ADHD diagnoses made at later rather than earlier preschool waves. The findings also call into question the stability of early diagnoses in younger preschoolers using DSM-IV criteria as they stand and calls for caution in diagnosis of very young children supporting recent evidence for such caution in independent studies (Evans et al. 2010). Overall, study findings support the stability of diagnosis of ADHD from the preschool period into school age. In the current study, any interpretation of age itself as predictor of stability of ADHD must be made cautiously given that each study subject may present at a different age within the same wave of the study. For example one subject presented to the study for the first time at age 3.0, while another may have presented for the first time at age 5.0. However, greater stability was evident between later rather than earlier waves which

TABLE 4A. LOGISTIC REGRESSION OF PRESCHOOL ADHD AND SUBSEQUENT ADHD CONTROLLING FOR KEY RISK FACTORS[a]

Variables entered into model[b]	%	*Model 1: T3ADHD as response variable*			*Model 2: T5ADHD as response variable*		
		Wald χ^2	*OR (95% CI)*	p-*value*	*Wald* χ^2	*OR (95% CI)*	p-*value*
Child's age, mean (SD) mo	53.09 (9.52)	4.31	1.07 (1.00-1.15)	.04	3.45	1.07 (1.00-1.14)	.06
Sex (M = 1/ F = 0), Male	49.1	0.29	1.41 (0.41-4.84)	.59	0.01	0.95 (0.27-3.36)	.94
Family income, $							
≤ 20,000	19.4	1.89	1 [Reference]	.60	2.38	1 [Reference]	.50
20,001–40,000	16.2	0.90	0.39 (0.06-2.71)	.34	1.27	0.25 (0.02-2.83)	.26
40,001–60,000	21.3	1.80	0.26 (0.04-1.85)	.18	0.00	1.07 (0.12-9.41)	.95
≥ 60,001	43.1	0.75	0.42 (0.06-2.95)	.39	0.08	1.38 (0.14-13.33)	.78
Maternal education							
High school	15.3	3.28	1 [Reference]	.35	3.12	1 [Reference]	.37
Some college education	35.6	2.80	7.05 (0.72-69.29)	.09	0.08	1.39 (0.13-14.77)	.78
4-year college degree	22.2	2.53	8.92 (0.60-132.3)	.11	0.20	0.52 (0.03-9.07)	.65
≥ Graduate education	26.9	2.92	9.92 (0.71-138.0)	.09	0.67	2.87 (0.23-35.56)	.41
Major depressive disorder	21.3	1.42	2.19 (0.60-7.94)	.23	0.09	1.23 (0.32-4.65)	.76
Anxiety disorder	21.3	0.07	0.82 (0.19-3.61)	.79	2.04	0.25 (0.04-1.68)	.15
Conduct disorder	11.6	3.81	5.24 (0.99-22.67)	.05	1.05	2.99 (0.37-24.34)	.31
Oppositional defiant disorder	22.7	4.57	4.18 (1.13-15.51)	.03	13.90	15.40 (3.66-64.79)	< .001
No. of stressful life events, mean (SD)	8.95 (4.51)	0.01	1.01 (0.88-1.16)	.92	0.19	0.97 (0.85-1.11)	.66
Family history of disruptive disorder, mean (SD), %	5.41 (11.32)	7.51	1.05 (1.02-1.09)	.01	0.02	0.99 (0.92-1.07)	.89
Family history of MDD/anxiety disorder, mean (SD), %	14.18 (14.63)	0.04	1.01 (0.96-1.05)	.84	1.82	1.03 (0.99-1.07)	.18
Family history of bipolar disorder, mean (SD), %	2.57 (5.12)	6.89	1.12 (1.03-1.22)	.01	4.97	1.12 (1.01-1.23)	.03
Preschool ADHD	13.4	10.45	10.06 (2.48-40.80)	.001	8.00	8.05 (1.90-34.19)	.01

TABLE 4B. LOGISTIC REGRESSION OF 12 AND 24 MONTH FOLLOW-UP ADHD CONTROLLING FOR RISK FACTORS[a]

Variables entered into model[b]	*T5ADHD as response variable*		
	Wald χ^2	*OR (95% CI)*	p-*value*
Child's age, mean (SD) mo	1.15	1.05 (0.96-1.14)	.28
Sex (M = 1/ F = 0), Male	0.89	0.49 (0.11-2.18)	.35
Family income, $			
≤ 20,000	2.53	1 [Reference]	.47
20,001–40,000	0.17	0.55 (0.03-9.50)	.68
40,001–60,000	0.86	3.37 (0.26-43.57)	.35
≥ 60,001	0.82	3.76 (0.21-65.98)	.37
Maternal education			
High school	2.63	1 [Reference]	.45
Some college education	0.44	0.39 (0.03-6.20)	.51
4-year college degree	1.33	0.13 (0.00-4.18)	.25
≥ Graduate education	0.03	0.75 (0.04-14.71)	.85
Major depressive disorder	0.08	0.80 (0.16-3.94)	.78
Anxiety disorder	1.75	0.18 (0.01-2.32)	.19
Conduct disorder	0.08	1.53 (0.08-29.82)	.78
Oppositional defiant disorder	11.42	16.85 (3.27-86.72)	.001
No. of stressful life events, mean (SD)	0.92	0.92 (0.78-1.09)	.34
Family history of disruptive disorder, mean (SD), %	0.31	0.98 (0.92-1.05)	.58
Family history of MDD/anxiety disorder, mean (SD), %	1.61	1.03 (0.98-1.08)	.20
Family history of bipolar disorder, mean (SD), %	0.93	1.06 (0.94-1.19)	.33
T3 ADHD	19.80	85.57 (12.06-607.4)	< .001

CI = confidence interval; OR = odds ratio.

[a]All three models included a total of 216 subjects with valid data for all 13 variables. Model 1 $\chi^2\square_{17} = 65.82$, $p < .001$, Model 2 $\chi^2\square_{17} = 55.73$, $p < .001$, Model 3 $\chi^2\square_{17} = 75.64$, $p < .001$.

[b]All variables were recorded at baseline, except for stressful life events, which were the total events the child had encountered both prior to and during study periods, and T3ADHD is the diagnosis at 12 month follow-up.

suggests age may be a factor. Overall findings inform important risk factors and demonstrate stability of the ADHD diagnosis between the preschool and school age period.

A baseline diagnosis of ODD also emerged as an important risk factor for persistence of ADHD in our study. These findings are similar to those previously reported by Lavigne et al (2001), who showed a significant relationship between baseline ODD and subsequent diagnosis of ADHD. Furthermore, family history findings were noteworthy in the current investigation. The odds of a later diagnosis of ADHD increased in children with a family history of disruptive disorder (includes CD and/or ADHD; data for family history of ODD was not obtained). Interestingly, those preschoolers with family history of BP at baseline also had higher odds of T3 and T5 ADHD; however, when examining risk factors between T3 and T5 ADHD, family history of BP at baseline was no longer significant. The mechanism by which a family history of bipolar disorder confers risk for ADHD to preschoolers or school age children remains unclear (Birmaher et al. 2009; Chang et al. 2003). However, given the high rates of co-morbidity of these disorders in childhood reported by multiple research groups (DuPaul and Stoner 2003; Geller et al. 2000; Wilens et al. 2002), this risk relationship is an area worthy of future investigation.

Conversely, there were no significant associations between family history of MDD or Anxiety to later ADHD. Of note, older age at baseline was associated with an increased likelihood of a later diagnosis of ADHD at T3. This stands in contrast to longitudinal findings investigating ODD in which younger age at baseline was associated with later ADHD (Lavigne et al. 2001). Also in contrast to the importance of gender in the longitudinal course of ODD reported by Lavigne et al (Lavigne et al. 2001), no gender differences were associated with later diagnosis of ADHD in the present study.

There are several noteworthy limitations to the study. First, given the limited sample size of children with a diagnosis of ADHD in this study, the potential for a Type I error cannot be ruled out. ADHD diagnosis was made using parent informant only and did not include teacher reports. It is possible that the use of only parent informant in this study may have either inflated or deflated the number of children diagnosed with ADHD; however, parents were queried as to symptom presence in at least two settings. Next, the study sample was oversampled for depressive disorders, which limits the overall generalizability to the general population. Another limitation was the small sample size due to the low rate of retention of preschoolers with ADHD. However, when analyses were run with imputed data, no significant differences in the results were found. Another limitation of the study is that while the use of medications was examined and found to be non-significant, the study was not a controlled treatment study; therefore, any conclusion about the impact of treatment should be taken as speculative. Further, the impact of non-pharmacological interventions on diagnoses was not examined. Future investigations examining interventions such as parent management training and course of ADHD are certainly warranted.

In conclusion, while limited by a small sample size of preschoolers with ADHD (due to the main focus of the study being on mood disorders) the current study findings provide relatively greater support for homotypic 46.9% (15/32) rather than heterotypic 37.5% (12/32) continuity of baseline ADHD. This finding is supported by Lahey et al (2004); however, the positive predictive value of ADHD predicting later ADHD was lower in the current study than in that reported by Lahey. Several reasons for this discrepancy are possible. Unlike the study by Lahey et al. (2004), in which study subjects were ascertained for ADHD symptoms at baseline from psychiatric clinics, the current study utilized a community sample. Therefore the Lahey sample was likely to have had more severe baseline symptomotology than those in the current study, accounting for the higher stability rates and homotypic continuity than found in this study. Of note, current study findings also inform the likelihood of no disorder 15.6% (5/32) at follow-up (both T3 and T5) after diagnosis of baseline ADHD.

Clinical Implications

This investigation of continuity suggests that an early diagnosis of ADHD is clinically important from a general mental health risk standpoint. Findings also add to the literature that the subgroup of preschoolers with ADHD and one or more additional risk factors as outlined (co-morbid ODD, family history of disruptive disorders) would be the most important group to target for early intervention given the much greater likelihood for stable symptoms. This is underscored by the notion that earlier intervention in mental disorders may be more effective, although ADHD intervention should be specifically addressed (Greenhill et al. 2008; Jones et al. 2007; McGoey et al. 2002; Rappaport et al. 1998).

The study findings of relatively greater homotypic continuity of ADHD specifically in those older preschoolers with co-morbid diagnosis of ODD, may help elucidate a particular subset of preschoolers at increased risk for stable course into school age, and hence a group to target for early intervention. Study findings suggesting lesser stability of ADHD diagnoses made at earlier preschool ages are noteworthy and call for caution in diagnosis, as well as need for further investigations to inform clinicians and caregivers, particularly prior to any pharmacologic or other treatment interventions. Finally, a detailed family history of disruptive disorders and bipolar disorder may further inform likelihood of persistence of preschool ADHD. The recruitment of a larger sample of preschoolers with ADHD is now needed to better inform the longitudinal trajectory of this disorder. Further studies that elucidate the longitudinal course of preschool ADHD are also warranted to determine clinical course and outcomes into school age and early adolescence (Posner et al. 2007).

Disclosures

Drs. Tandon and Luby and Ms. Si have no conflicts of interest or financial ties to disclose.

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