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Predictors of ADHD Persistence in Girls at 5-Year Follow-Up

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Abstract

Objective—The main aim of this study was to examine the age-dependent remission from ADHD in girls transitioning through childhood into adolescence and early adulthood.

Method—We conducted a 5-year prospective follow-up study of 123 girls with ADHD and 106 non-ADHD control girls aged between 6 and 17 years at ascertainment. ADHD was considered persistent at follow-up if participants met full diagnostic criteria for *DSM-IV* ADHD or met residual criteria for *DSM-IV* ADHD with associated impairment (Global Age Forum [GAF] score < 60).

Results—By age 16 years, ADHD was persistent in 71% (95% CI = 61–79%) of girls with ADHD. Participants with persistent ADHD at follow-up had more psychiatric comorbidity, behavior problems, and functional impairment than girls with ADHD in remission. Remitted ADHD, however, continued to be associated with functional impairment relative to non-ADHD controls. Persistence at 5 years was predicted by increased behavioral impairment at baseline.

Conclusion—This 5-year follow-up suggests that many girls with ADHD experience persistent symptoms and/or functional impairment through late adolescence and into early adulthood.

Keywords

ADHD; female; follow-up; adolescence

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Introduction

In contrast to dozens of follow up studies of boys with ADHD, only three longitudinal studies of girls with ADHD have been conducted. The first was conducted more than 20 years ago and consisted of only 12 hyperactive girls (Mannuzza & Gittelman, 1984). Our group (Biederman, Monuteaux et al., 2006) conducted a larger case-control, blind, 5-year prospective longitudinal study of 140 girls with ADHD and 122 without ADHD. At the 5-year follow-up into late adolescence (average 16 years of age at follow-up), girls with ADHD were at significantly higher risk of disruptive behavior, mood, and anxiety disorders, and substance dependence than girls without ADHD. Hinshaw et al. (2006) conducted the other large controlled study of girls with ADHD (11–17 years at follow-up) and also documented that, compared to non-ADHD girls, ADHD girls at 5-year follow-up continued to display clinically significant deficits in multiple functional domains (Hinshaw et al., 2006).

Despite the contributions of these studies toward understanding of the morbidity associated with ADHD in girls, information on age-dependent symptom decline in girls with ADHD are lacking. As reviewed by Faraone et al. (2006) the available literature on the subject is almost entirely based on follow-up studies of ADHD boys. In our longitudinal study of boys with ADHD, results were highly dependent on the definition of persistence used, ranging from 40% for syndromatic persistence (full diagnostic criteria at follow-up) to 70% for symptomatic persistence (full or residual diagnostic criteria at follow-up; Biederman, Mick, & Faraone, 2000). In contrast, Hinshaw et al. (2006) reported a higher rate of syndromatic persistence (70%) in their follow-up of girls with ADHD suggesting that ADHD in girls may be more persistent than in boys. The aims of this study were to extend our previous work documenting the lifetime burden of psychiatric morbidity associated with ADHD (Biederman, Monuteaux et al., 2006) by estimating the ADHD persistence in girls, identifying functional sequela of ADHD persistence in girls, and examining possible predictors of ADHD persistence in girls.

Method

Participants

We originally ascertained female participants aged 6–17 years with (N = 140) and without (N = 122) *Diagnostic and Statistical Manual of Mental Disorders* (third edition, revised; *DSM-III-R*) ADHD from pediatric and psychiatric clinics (Biederman et al., 1999; Biederman, Monuteaux et al., 2006). Potential participants were excluded if they had been adopted, or if their nuclear family was not available for study. We also excluded potential participants if they had major sensorimotor handicaps (paralysis, deafness, blindness), psychosis, autism, inadequate command of the English language, or a Full Scale IQ (FSIQ) less than 80. The present study reports on the 5-year follow-up in which 123 ADHD and 112 control participants were successfully reascertained. Parents and adult offspring provided written informed consent to participate, and parents also provided consent for offspring under the age of 18. Children and adolescents provided written assent to participate.

ADHD cases were identified from either a major academic medical center, where we selected ADHD participants from consecutive referrals to its pediatric psychopharmacology clinic or from a major Health Maintenance Organization (HMO), in which ADHD participants were selected from consecutively ascertained pediatric clinic outpatients. Healthy controls were ascertained from outpatients referred for routine physical examinations to its pediatric medical clinics at each setting identified from their computerized records as not having ADHD. The ADHD sample comprised of 63 participants referred by psychiatric sources and 77 by pediatric sources. The control group

comprised of 55 hospital-based participants and 67 HMO-based participants. We previously demonstrated no clinically or statistically significant differences between ADHD participants ascertained from these two referral sources on baseline measures of psychopathology, cognitive performance, or psychosocial functioning (Busch et al., 2002).

A three-stage ascertainment procedure was used to select participants (Faraone & Tsuang, 1995). For ADHD participants, the first stage was their referral to a psychiatric or pediatric clinic resulting in a clinical diagnosis of ADHD by a child psychiatrist or pediatrician. The second stage confirmed the diagnosis by screening all children positive at the first stage by administering a telephone questionnaire to their mothers. Eligible case children meeting study entry criteria were recruited for the study and received the third stage, a diagnostic assessment with a structured interview. Only patients who received a positive diagnosis at all three stages were included in the final analysis.

We also screened potential non-ADHD controls in three stages. First, we ascertained them from consecutive referrals to medical clinics for routine physical examinations at both the psychiatric and pediatric sources. In stage two, the control mothers responded to the *DSM-III-R* ADHD telephone questionnaire about their daughters. Eligible controls meeting study entry criteria were recruited for the study and received the third stage, a diagnostic assessment with a structured interview. Only participants classified as not having ADHD at all three stages were included in the control group.

Follow-Up Assessment Procedures

Lifetime psychiatric assessments at the 5-year follow-up relied on the K-SADSE (Epidemiologic Version; Orvaschel, 1994) for participants younger than 18 years of age and the Structured Clinical Interview for *DSM-IV* (SCID; Spitzer, Williams, Gibbon, & First, 1990; supplemented with modules from the K-SADSE to assess childhood diagnoses) for participants 18 years of age and older. The onset, offset, number of symptoms at worst and current month, duration, and number of episodes (when applicable) were assessed in each interview model. We conducted direct interviews with participants and indirect interviews with their mothers (i.e., mothers complete the structured interview about their offspring). Of the 217 participants interviewed, the proportion that provided direct only, indirect only, and both types of reports were 22%, 17%, and 62% respectively. We combined data from direct and indirect interviews by considering a diagnostic criterion positive if it was endorsed in either interview. The interviewers were blind to the participant's baseline ascertainment group, the ascertainment site, and all previous assessments.

The interviewers had undergraduate degrees in psychology and were extensively trained. First, they underwent several weeks of classroom style training, learning interview mechanics, diagnostic criteria, and coding algorithms. Then, they observed interviews by experienced raters and clinicians. They subsequently conducted at least six practice (non-study) interviews and at least three study interviews while being observed by senior interviewers. Trainees were not permitted to conduct interviews independently until they executed at least three interviews that achieved perfect diagnostic agreement with an observing senior interviewer. We considered a disorder positive if *DSM-IV* diagnostic criteria were unequivocally met. Although standardized algorithms were used to determine each diagnosis, interviewers needed a mechanism to determine the clinical relevance of symptoms when participants were only able to provide unclear or imprecise information. Thus, a committee of board-certified child and adult psychiatrists and psychologists who were blind to the participant's ADHD status, referral source, and all other data resolved diagnostic uncertainties. Diagnoses presented for review were considered positive only when the committee determined that diagnostic criteria were met to a clinically meaningful degree.

We estimated the reliability of our diagnostic assessments for interviewer competency (interview-clinician reviewer reliability) and diagnostic consistency (inter clinician reviewer reliability). Rater competency was estimated from kappa coefficients of agreement between licensed psychiatrists or psychologists and interviewers assessments with clinicians assessing diagnostic criteria from audio taped interviews conducted with participants. Based on 500 assessments from interviews of children and adults, the median kappa coefficient was 0.98; kappa coefficients for individual diagnoses included: ADHD (0.88), conduct disorder (1.0), major depression (1.0), mania (0.95), separation anxiety (1.0), agoraphobia (1.0), panic (0.95), substance use disorder (SUD; 1.0), and tics or Tourette's (0.89). Computing kappa coefficients of agreement among clinician reviewers then assessed diagnostic consistency of the review process. For these diagnoses, the median reliability between individual clinicians and the review committee assigned diagnoses was.87. Kappa coefficients for individual diagnoses included: ADHD (1.0), conduct disorder (1.0), major depression (1.0), bipolar (0.78), separation anxiety (0.89), agoraphobia (0.80), panic (0.77), SUD (1.0), and tics or Tourette's (0.68).

ADHD Persistence

Participants with at least six symptoms of hyperactivity, impulsivity or inattention met criteria for *DSM-IV* ADHD-Full and participants with at least three but less than six symptoms of hyperactivity-impulsivity or inattention but less than six symptoms on both scales met criteria for *DSM-IV* ADHD-Residual. Consistent with our previous studies in boys with ADHD (Biederman et al., 1996; Biederman et al., 2000), girls were considered to have persistent ADHD if they met full diagnostic criteria for *DSM-IV* ADHD-Full at 5-year follow-up or if they met criteria for *DSM-IV* ADHD-Residual with associated impairment (GAF score < 60). Using this definition, 44 of the 123 girls with ADHD were considered in remission and 99 were considered persistent. Three control participants met criteria for persistence (i.e., they endorsed ADHD-Residual criteria with impairment) and were removed from these analyses.

Functional Measures

Mothers also completed the Child Behavior Checklist (CBCL; Achenbach, Howell, Quay, & Conners, 1991) at baseline and follow-up for participants < 18 years of age. Socioeconomic status (SES) was measured using the 5-point Hollingshead scale (Hollingshead, 1975). Additionally, information about academic functioning, legal problems, sexual history, treatment history, and driving history was collected at the 5-year follow-up assessment.

Cognitive Assessment

We estimated FSIQ (Sattler, 1988) from the Vocabulary and Block Design subtests of the Wechsler Intelligence Scale for Children—Third Edition (WISC-III; D. Wechsler, 1991) for individuals < 17 years and the Wechsler Adult Intelligence Scale—Third Edition (WAIS-III; D Wechsler, 1997) for individuals ≥ 17. Tests of executive function (working memory, interference control, abstract problem solving/set shifting, and planning/visuospatial organization) included the Digit Span, Digit Symbol/Coding, and Symbol Search subtests from the WISC-III/WAIS-III (D. Wechsler, 1991, 1997); the color naming and interference scores from the Stroop Color Word Test (Golden, 1978); perseverative and non-perseverative errors on the Wisconsin Card Sorting Test (WCST)—computerized version (Heaton, Chelune, Talley, Kay, & Curtiss, 1993); the copy organization score from Bernstein and Waber's rating of the Rey-Osterrieth Complex Figure (ROCF; Bernstein & Waber, 1996; Osterrieth, 1944; Rey, 1944); the total (trials 1–5) score on the California Verbal Learning Test—Child Edition (Delis, Kramer, Kaplan, & Ober, 1994) and Second Edition (CVLT-II) for participants 17 years or older (Delis, Kramer, Kaplan, & Ober, 2000); and an auditory working memory Continuous Performance Test (CPT; Seidman et al.,

1998). As exhaustive analysis of the complete battery has been reported elsewhere, (Doyle, Biederman, Seidman, Reske-Nielsen, & Faraone, 2005; Seidman et al., 2005) we focus here on estimated FSIQ (as described earlier), Freedom from Distractibility (FFD; calculated from the Arithmetic and Digit Symbol Coding Wechsler subtests), and a binary indicator of "executive functioning deficit" created from the remaining battery, which we have validated in earlier publications. (Biederman et al., 2004; Biederman, Petty et al., 2006)

Statistical Analysis

Age-dependent estimates of persistence were calculated from the Kaplan-Meier cumulative survival function. Specifically, the Kaplan-Meier estimator weights the contribution of each participant by age at follow-up: participants with remitted ADHD are considered remitted at the reported age at offset and participants with persistent ADHD at follow-up are censored at their latest age of assessment. Psychiatric status at the 5-year follow-up assessment was based on the 12-month prevalence of each disorder. To make statistical comparisons between groups and to correct for potential confounders (including age at follow-up), logistic regression was used with binary data and ordinary least-squares linear regression was with continuous data. All analyses were two-tailed and statistical significance was defined at the 5%.

Results

Of the 140 ADHD and 122 control girls recruited at baseline, 123 (88%) and 112 (92%) respectively, were successfully reassessed at the 5-year follow-up. The rate of successful follow-up did not differ between the groups (c2[1] = 1.1, $p = .30$). Among the ADHD and control participants, there were no significant differences between those successfully followed up and those lost to follow-up on SES, age, GAF score, familial intactness, ascertainment source, or psychiatric comorbidity (Biederman, Monuteaux et al., 2006). At follow-up, there was no difference ($F[11, 227] = 1.95$, $p = .2$) in age between the ADHD (16.4 ± 3.8 years) and control (16.9 ± 3.0) participants, but among the girls with ADHD, persistent cases ($N = 99$) were statistically younger than remitted cases significantly ($N = 44$; 17.6 ± 4.1 vs. 15.6 ± 3.4, $F[1, 121] = 8.5$, $p = .004$). Thus, all subsequent analyses are adjusted by age at follow-up.

The age-related persistence of ADHD is illustrated with Kaplan-Meier survival estimates in Figure 1. The rate of persistence at each time point is estimated from the girls with ADHD who were still at risk for remission at that point (i.e., were that age or older and had not yet previously remitted from ADHD). Thus, the precision of our estimate of persistence decreases with increasing age as the number of participants is reduced at older ages. This curve suggests that by age 12, 87% (95% CI = 79–92%) of ADHD girls had persistent ADHD. By age 20, 55% of participants were persistent but because the number of girls at risk was smaller ($N = 58$) the estimate of persistence was less precise (95% CI = 43–66%).

Although by definition symptom means were highest in the persistent ADHD cases, ADHD girls with remitted ADHD continued to report persistence of symptoms of inattention and hyperactivity impulsivity and 45% ($N = 20$) had received ADHD pharmacotherapy within the past year. ADHD status at follow-up was not related to estimated FSIQ, FFD, or the presence executive function deficits with both persistent and remitted ADHD participants exhibiting similarly reduced cognitive function relative to non-ADHD controls. Behavioral problems as measured by the CBCL total problems and the clinical subscales *T*-score followed a "dose-response" relationship in which persistent ADHD was associated with the most severe behavioral problems, followed by remitted ADHD, and then non-ADHD control girls (Table 1).

A similar pattern of functional impairment was observed between the persistent and remitted ADHD participants relative to non-ADHD controls (Table 1). Both the persistent and remitted ADHD participants were more likely to have ever repeated a grade or have been placed in a special class or received tutoring in the past year than control girls without ADHD. Girls with persistent ADHD were at increased risk of disciplinary school detentions or school suspensions relative to both the remitted ADHD participants and the non-ADHD controls, however. Although not statistically significant, persistent ADHD girls tended to be less likely to have been employed or drive a car. Girls with either persistent or remitted ADHD were no more likely to be sexually active compared with non-ADHD control girls, but of the girls with persistent ADHD who were sexually active, 35% reported that they had been pregnant (Table 1).

The prevalence of SUD did not differ between the ADHD and control groups. Girls with persistent ADHD had a greater risk of psychiatric comorbidity (any comorbidity, mood disorder, and additional disruptive behavior disorder) relative to both the participants with remitted ADHD and non-ADHD controls (Table 1) whereas participants with remitted ADHD continued to express greater rates of psychiatric comorbidity with mood, anxiety, and disruptive behavior disorders than non-ADHD control participants. These rates of comorbidity at follow-up are a mixture of ongoing psychiatric disorders present at baseline and incident disorders arising during the follow-up period.

In Table 2 possible participant-level predictors of persistence were contrasted between the persistent and remitted ADHD participants and non-ADHD controls. We found no evidence that pharmacotherapy at baseline, psychiatric comorbidity at baseline, SUD at baseline, or GAF score at baseline predicted persistence of ADHD over 5-years of follow-up. Participants considered persistent at follow-up exhibited significantly more HI ADHD symptoms at baseline but no difference in IA ADHD symptoms, FFD, estimated FSIQ, or executive function deficits (Table 2). At baseline, persistent ADHD participants reported significantly more behavioral problems as measured by the CBCL Total Problems *T*-Score. Specific CBCL clinical subscales discriminating Persistent from Remitted ADHD at follow-up were the Withdrawn, Anxious/Depressed, Thought Problems, Social Problems, Attention Problems, Delinquent, and Aggressive Behavior subscales.

The relative rate of familial or environmental risk factors for ADHD is presented in Table 3. Overall ADHD status was associated with a family history of ADHD, major depression, multiple anxiety disorders, substance dependence, and indicators of psychosocial adversity. We found no evidence suggesting that prenatal exposure to substance use (alcohol, cigarette's, or drug), family history of psychopathology, or indices of psychosocial adversity discriminated persistent from remitted ADHD at follow-up (Table 3), however.

Discussion

In this study we report the age related course of ADHD over 5 years in controlled sample of girls aged 6–17 years at ascertainment. We considered participants to be persistent if they met full diagnostic criteria at follow-up or if they met criteria for residual ADHD (i.e., fewer symptoms than required for full diagnostic criteria, but more than half the required symptoms) with impairment (GAF < 60). Thus, remitted ADHD included girls with fewer than half the required symptoms for ADHD and those girls with residual ADHD but minimal functional impairment (GAF ≥ 60). We chose this definition because is mimics clinical practice which focuses on functional impairment and does not necessarily consider a disorder to be in remission simply because full *DSM* diagnostic criteria are no longer met. The clinical relevance of this definition of persistence is partially supported by the range of functional impairment elevated in the persistent relative to the remitted ADHD girls such as

the CBCL clinical scales and the increased likelihood of being disciplined or suspended from school.

Using survival analyses to account for the variable age at ascertainment of our sample, we report a persistence rate of 71% by 16 years. This estimate is consistent with the 5-year follow-up study of girls with ADHD conducted by Hinshaw et al. (2006) that found 70% of girls 11–17 years of age with ADHD met diagnostic criteria for at least one subtype of ADHD at follow-up. Notably, we also found that cognitive performance at follow-up—mean estimated FSIQ, mean FFD, and the prevalence of comorbid "executive function deficit"—was similar in girls with both Persistent and Remitted ADHD but different from the non-ADHD control participants. Our data are generally consistent with that of Hinshaw et al. (2007) but suggests a disassociation of behavioral ADHD symptomatology from cognitive performance overtime. This is consistent with our previous cross-sectional analyses (Biederman et al., 2004; Biederman, Petty et al., 2006) but additional longitudinal studies are needed in both boys and girls to delineate the developmental relationship between cognition and ADHD symptoms across the life cycle.

In a parallel study of boys with ADHD we found that familiality with ADHD, psychosocial adversity, and psychiatric comorbidity were potential predictors of a persistent ADHD course. (Biederman et al., 1996) We did not replicate that association in this sample of girls but instead found symptoms of hyperactivity and CBCL behavioral problems at baseline predicted persistence of ADHD at follow-up. If confirmed with independent samples, these divergent results may suggest a sex-specific effect of clinical, familial, and environmental factors on the course of ADHD. Lee and Hinshaw (2006) examined predictors of ADHD sequelae (e.g., academic performance, conduct problems, substance abuse, and social peer status) rather than the persistence of ADHD itself, but identified a similar set of predictors (e.g., noncompliance, ADHD symptom severity, antisocial behavior, etc.) for those outcomes as we identified for persistence of ADHD in girls. Thus, girls with ADHD and additional behavior problems seem to be at the greatest risk of both persistent ADHD symptoms and associated functional impairments as they transition through adolescence and into early adulthood.

Our results must be interpreted in the context of some methodological limitations. Because our participants were clinically referred these findings may not generalize to community samples of girls with ADHD. Our sample was originally ascertained according to *DSM-III-R* criteria, and it is possible that our results may not generalize to samples ascertained by *DSM-IV* criteria. However, considering the very high degree of overlap between the two definitions (93% of *DSM-III-R* cases received a *DSM-IV* diagnosis [Biederman et al., 1999] and our use of *DSM-IV* criteria in our follow-up assessment, any effect on these results should be minimal. Although we did not exclude any ethnic group, the majority of our participants were White and the proportion of girls with different ethnicity was too small to present stratified results.

We did not manipulate treatment as an independent variable, and cannot use our study to determine treatment effectiveness (Faraone, Simpson, & Brown, 1992) nor to describe the untreated course of ADHD. A second independent reporter was not available for all participants assessed which could have led to an underestimate of ADHD persistence. The sample is also of limited size and we have not yet followed participants long enough to observe some age-dependent outcomes such as SUD or legal complications. Larger studies and additional follow-up of this sample will be needed to conduct adequately powered analyses of uncommon correlates of ADHD in girls.

Finally this study, and any other study of persistence, is limited by the definition of persistence used. To reflect common clinical practice we chose a definition of persistence that considered both continued symptoms of ADHD and a general measure of impairment but did not incorporate additional secondary functional measures (such as comorbidity, school problems, treatment status, etc.) into this definition. Broadening the definition of persistence too widely would have prohibited us from examining these correlates at follow-up (e.g., there would be no comorbidity in remitted ADHD cases if girls with comorbidity were considered persistent) and would have reduced the remitted ADHD group ($N = 10$) prohibiting meaningful statistical analyses. We should also view these data as a snapshot in time and appreciate that persistence/remission status may not be static. Just as many of the girls with persistent ADHD may remit from the disorder over the next 5 years, some of the girls currently considered in remission may reevaluate the presence and effect of ADHD symptoms as they progress through their 20s and into their 30s and become persistent again. More work is needed in older individuals of both genders as they transition through adolescence and into early adulthood to characterize the optimal functional and diagnostic criteria for ADHD persistence.

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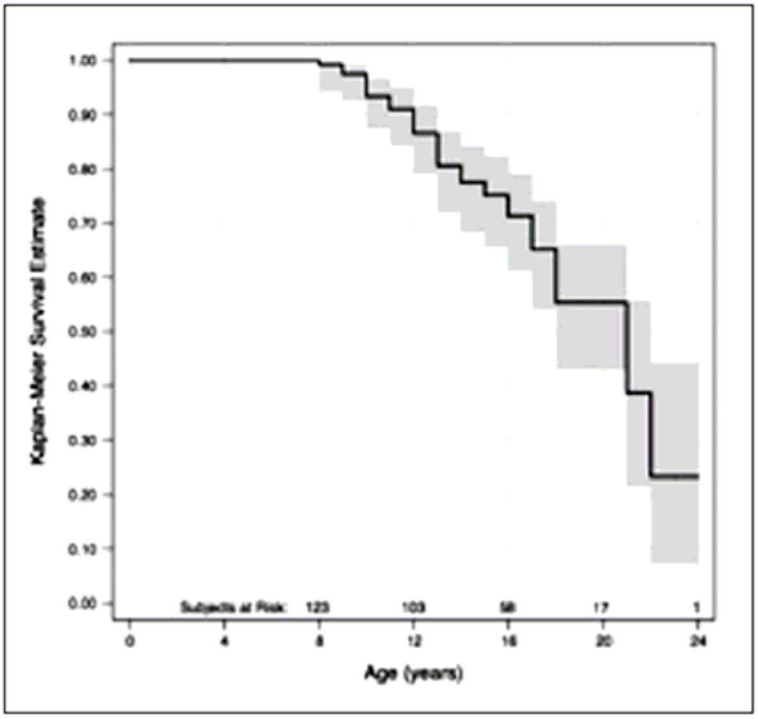

Figure 1. ADHD persistence during 5-year follow-up

The Kaplan-Meier estimate of ADHD persistence as a function of age at follow-up is depicted in black with the 95% confidence intervals shaded in gray. This estimate of persistence is calculated on the number of participant still at risk at each time point: the number at risk is indicated at regular time points.

Table 1

Clinical and Functional Correlates of ADHD Persistence at 5-Year Follow-Up

	Persistent ADHD *N* = 79	Remitted ADHD *N* = 44	Non-ADHD Controls *N*=106	
	M ± *SD*	*M* ± *SD*	*M* ± *SD*	*p* Value
ADHD pharmacotherapy	49 (62)[g]	20 (45)[g]	1 (1)	<.0001
IA symptoms	6.6 ± 2.1[gh]	2.4 ± 3.0[g]	0.6 ± 1.3	<.0001
HI symptoms	4.9 ± 2.5[gh]	2.4 ± 1.8[g]	0.6 ± 1.0	<.0001
GAF	54.1 ± 7.2[gh]	62.8 ± 4.3[g]	66.5 ± 5.2	<.0001
Estimated FSIQ	103.4 ± 15.1[g]	107.2 ± 15.3[g]	113.2 ± 13.7	.0004
FFD IQ	95.7 ± 12.7[g]	99.3 ± 16.2[g]	109.0 ± 12.7	<.0001
Executive function deficit	39 (53)[g]	16 (42)[g]	13 (13)	<.0001
CBCL total problems	66.6 ± 9.0[gh]	54.4 ± 9.6[g]	41.2 ± 10.8	<.0001
Withdrawn	58.2 ± 7.1[gh]	52.8 ± 4.5	52.1 ± 5.22	<.0001
Anxious/depressed	61.4 ± 9.6[gh]	55.5 ± 5.8	52.2 ± 4.6	<.0001
Somatic complaints	61.8 ± 9.7[gh]	57.1 ± 8.9[g]	52.9 ± 5.1	<.0001
Thought problems	59.9 ± 7.2[gh]	52.9 ± 4.6	50.9 ± 2.4	<.0001
Social problems	66.8 ± 11.8[gh]	56.2 ± 6.7[g]	50.9 ± 2.6	<.0001
Attention problems	71.2 ± 5.6[gh]	57.4 ± 5.6[g]	51.3 ± 2.9	<.0001
Delinquent	62.2 ± 9.6[gh]	55.2 ± 7.1	52.6 ± 4.9	<.0001
Aggressive behavior	66.0 ± 11.6[gh]	56.8 ± 7.8[g]	51.2 ± 2.3	<.0001
	N(%)	*N*(%)	*N*(%)	
Comorbidity (Past year)	54 (68)[gh]	21 (48)[g]	14 (13)	<.0001
Mood disorder[a]	29 (37)[gh]	7 (16)[g]	2 (2)	<.0001
Multiple (>2) anxiety disorder[b]	30 (38)[g]	14 (32)[g]	12 (11)	.0002
Disruptive behavior disorder[c]	36 (46)[gh]	7 (16)[g]	3 (3)	<.0001
SUD	11 (14)	3 (7)	11 (10)	.1
Repeated grade[d]	26 (33)[g]	8 (18)[g]	3 (3)	<.0001
Special class	16 (20)[g]	5 (11)[g]	0 (0)	<.0001
Tutoring	43 (54)[g]	17 (39)[g]	16 (15)	<.0001
School detention	30 (71)[gh]	11 (39)	39 (45)	.01
School suspension	18 (45)[gh]	3 (12)	6 (7)	<.0001
Arrested	5 (11)	1 (3)	4 (5)	.2
Been employed	27 (59)	21 (72)	68 (77)	.4
Drives a car	18 (37)	15 (48)	46 (51)	.5
Citing for violations[e]	8 (44)	5 (33)	11 (24)	.3
Car accident[e]	8 (44)	8 (53)	23 (50)	.9
Sexually active	20 (44)	11 (39)	34 (40)	.3

	Persistent ADHD *N* = 79	Remitted ADHD *N* = 44	Non-ADHD Controls *N*=106	
	M* ± *SD	***M* ± *SD***	***M* ± *SD***	***p* Value**
Condom use[f]	16 (80)	10 (90)	33 (97)	.3
Pregnancy[f]	7 (35)[g]	2 (18)	5 (14)	.1

Note: All between group comparisons were made with logistic or linear regression adjusting for age at follow-up. FSIQ = full scale IQ; CBCL = child behavior checklist; FFD IQ = froadom from discractibilky IQ; GAF = global age forum; SUD = substance use disorder.

[a] mania or depression in past year.

[b] two or more anxiety disorders in the past year.

[c] conduct disorder, oppositional defiant disorder, or antisocial personality disorder in the past year.

[d] lifetime rate of repeated grade.

[e] among girls who can drive only.

[f] among sexually active girls only.

[g] indicates $p < .05$ versus control participants.

[h] indicates $p < .05$ versus remitted ADHD participants.

Table 2

Baseline Predictors of ADHD Persistence

	Persistent ADHD *N* = 79	Remitted ADHD *N* = 44	Non-ADHD Controls *N* =106	
	M ± *SD*	*M* ± *SD*	*M* ± *SD*	*p* Value
ADHD pharmacotherapy	55 (69)	30 (68)	—	.6
IA symptoms	7.3 ± 2.1[d]	6.8 ± 2.3[d]	0.7 ± 1.4	<.0001
HI symptoms	5.8 ± 2.5[d,e]	4.5 ± 2.0[d]	0.5 ± 1.0	<.0001
GAF	58.1 ± 6.3[d]	59.8 ± 5.9[d]	69.5 ± 4.6	<.0001
Estimated FSIQ	103.3 ± 12.8[d]	105.4 ± 12.1[d]	110.5 ± 11.2	.0005
FFD IQ	97.5 ± 12.9[d]	101.8 ± 15.5[d]	110.3 ± 13.6	<.0001
Executive function deficit	27 (35)[d]	12 (27)[d]	13 (12)	.004
CBCL total problems	62.8 ± 11.3[d,e]	54.3 ± 11.5[d]	38.7 ± 9.3	<.0001
Withdrawn	57.6 ± 8.7[d,e]	53.0 ± 6.3	51.1 ± 3.1	<.0001
Anxious/depressed	61.9 ± 10.9[d,e]	55.6 ± 7.2[d]	51.1 ± 3.1	<.0001
Somatic complaints	59.5 ± 9.8[d]	56.5 ± 8.3[d]	52.1 ± 4.4	<.0001
Thought problems	58.1 ± 8.7[d,e]	53.9 ± 6.1[d]	50.7 ± 2.4	<.0001
Social problems	63.9 ± 11.7[d,e]	55.6 ± 7.6[d]	51.0 ± 3.6	<.0001
Attention problems	69.0 ± 10.2[d,e]	61.5 ± 8.1[d]	50.6 ± 2.2	<.0001
Delinquent	57.7 ± 8.8[d,e]	54.6 ± 6.6[d]	51.0 ± 2.9	<.0001
Aggressive behavior	62.3 ± 10.4[d,e]	56.6 ± 7.5[d]	50.7 ± 2.6	<.0001
	N(%)	*N*(%)	*N*(%)	
Comorbidity (Past year)	39 (49)[d]	23 (52)[d]	7 (7)	<.0001
Mood disorder[a]	18 (23)[d]	7 (16)[d]	1 (1)	.0008
Multiple (>2) anxiery disorder[b]	18 (23)[d]	12 (27)[d]	2 (2)	.0006
Disruptive behavior disorder[c]	25 (32)[d]	12 (27)[d]	4 (4)	.0001
SUD	2 (3)[d]	3 (7)[d]	0 (0)	<.0001

Note: All between group comparisons were made with logistic or linear regression adjusting for age at follow-up. FSIQ = full scale IQ; CBCL = child behavior checklist; FFD IQ = freedom from distractibility IQ; GAF = global age forum.

[a] mania or depression in past year; SUD = substance use disorder.

[b] two or more anxiety disorders in the past year.

[c] conduct disorder, oppositional defiant disorder. or antisocial personality disorder in the past year.

[d] indicates $p < .05$ versus control participants.

[e] indicates $p < .05$ versus remitted ADHD participants.

Table 3

Familial and Environmental Predictors of ADHD Persistence

	Persistent ADHD *N* = 79	Remitted ADHD *N* = 44	Non-ADHD Controls *N* = 106	
	***N* (%)**	***N* (%)**	***N* (%)**	***p* Value**
Prenatal SUD exposure				
Smoking	8 (11)	3 (8)	5 (5)	1
Alcohol	7 (9)	3 (7)	3 (3)	.3
Drugs	4 (5)	1 (2)	3 (3)	.6
Family history				
ADHD[a]	56 (58)[e]	23 (52)[e]	29 (27)	<.0001
CD/ASPD	27 (34)[e]	12 (27)	20 (19)	.08
Substance dependence	47 (60)[e]	22 (50)	41 (39)	.006
Blpolar-I disorder	4 (17)	2 (17)	4 (12)	8
Major depression[b]	35 (44)[e]	12 (27)	18 (17)	.0004
Multiple (>2) anxiety disorder[c]	30 (38)	23 (52)[e]	27 (25)	.007
Psychosocial adversity[d]	41 (52)[e]	22 (50)[e]	31 (29)	.005
Large family size	16 (20)	15 (34)	27 (25)	.3
Low SES	14 (18)	8 (18)	12 (11)	.4
Paternal antisocial	12 (15)	2 (5)	8 (8)	.3
Maternal psychiatric	28 (36)[e]	16 (36)[e]	13 (12)	.0004
Family conflict	54 (69)[e]	33 (75)[e]	53 (50)	.005

Note: All between group comparisons were made with logistic or linear regression adjusting for age at follow-up. CD/ASPD = Conduct Disorder/ Antisocial Personality Disorder, SES = socioeconomic status; SUD = substance use disorder.

[a] ADHD wich moderate or severe impairment.

[b] major depression with severe impairment

[c] two or more anxiety disorders.

[d] two or more Rutter's indicators of psychosocial advenicy.

[e] indicates $p < .05$ versus control participants.