Original Investigation

Evaluation of the Persistence, Remission, and Emergence of Attention-Deficit/Hyperactivity Disorder in Young Adulthood

Jessica C. Agnew-Blais, ScD; Guilherme V. Polanczyk, MD, PhD; Andrea Danese, MD, PhD; Jasmin Wertz, MSc; Terrie E. Moffitt, PhD; Louise Arseneault, PhD

IMPORTANCE Attention-deficit/hyperactivity disorder (ADHD) is now recognized to occur in adulthood and is associated with a range of negative outcomes. However, less is known about the prospective course of ADHD into adulthood, the risk factors for its persistence, and the possibility of its emergence in young adulthood in nonclinical populations.

OBJECTIVE To investigate childhood risk factors and young adult functioning of individuals with persistent, remitted, and late-onset young adult ADHD.

DESIGN, SETTING, AND PARTICIPANTS The study sample was the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally representative birth cohort of 2232 twins born in England and Wales from January 1, 1994, to December 4, 1995. Evaluation of childhood ADHD (ages 5, 7, 10, and 12 years) included prenatal and perinatal factors, clinical characteristics, and aspects of the family environment. Among participants aged 18 years, ADHD symptoms and associated impairment, overall functioning, and other mental health disorders were examined. Data analysis was conducted from February 19 to September 10, 2015.

MAIN OUTCOMES AND MEASURES Attention-deficit/hyperactivity disorder according to *DSM-IV* diagnostic criteria in childhood and *DSM-5* diagnostic criteria in young adulthood.

RESULTS Of 2232 participants in the E-Risk Study, 2040 were included in the present analysis. In total, 247 individuals met diagnostic criteria for childhood ADHD; of these, 54 (21.9%) also met diagnostic criteria for the disorder at age 18 years. Persistence was associated with more symptoms (odds ratio [OR], 1.11 [95% CI, 1.04-1.19]) and lower IQ (OR, 0.98 [95% CI, 0.95-1.00]). At age 18 years, individuals with persistent ADHD had more functional impairment (school/work: OR, 3.30 [95% CI, 2.18-5.00], home/with friends: OR, 6.26 [95% CI, 3.07-12.76]), generalized anxiety disorder (OR, 5.19 [95% CI, 2.01-13.38]), conduct disorder (OR, 2.03 [95% CI, 1.03-3.99]), and marijuana dependence (OR, 2.88 [95% CI, 1.07-7.71]) compared with those whose ADHD remitted. Among 166 individuals with adult ADHD, 112 (67.5%) did not meet criteria for ADHD at any assessment in childhood. Results from logistic regressions indicated that individuals with late-onset ADHD showed fewer externalizing problems (OR, 0.93 [95% CI, 0.91-0.96]) and higher IQ (OR, 1.04 [95% CI, 1.02-1.07]) in childhood compared with the persistent group. However, at age 18 years, those with late-onset ADHD demonstrated comparable ADHD symptoms and impairment as well as similarly elevated rates of mental health disorders.

CONCLUSIONS AND RELEVANCE We identified heterogeneity in the *DSM-5* young adult ADHD population such that this group consisted of a large, late-onset ADHD group with no childhood diagnosis, and a smaller group with persistent ADHD. The extent to which childhood-onset and late-onset adult ADHD may reflect different causes has implications for genetic studies and treatment of ADHD.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Louise Arseneault, PhD, Medical Research Council Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology and Neuroscience, Box No. P080, De Crespigny Park, London SE5 8AF, United Kingdom (louise.arseneault@kcl.ac.uk).

JAMA Psychiatry. 2016;73(7):713-720. doi:10.1001/jamapsychiatry.2016.0465
Published online May 18, 2016.

To date, adult attention-deficit/hyperactivity disorder (ADHD) has been conceptualized as a continuation of childhood ADHD. However, recent findings[1] have suggested that, for some individuals, ADHD may not arise until adolescence or adulthood and may be associated with different risk factors and outcomes than childhood ADHD. In the present study, we took a prospective, developmental approach to clarifying the origins and correlates of young adult ADHD in a general population cohort.

Although ADHD was originally described as limited to childhood,[2,3] prospective follow-up studies[4] of clinic-referred children with ADHD indicate that approximately 15% will continue to meet full diagnostic criteria and an additional 50% will continue to have impairing ADHD symptoms as young adults. These studies have identified childhood risk factors associated with a more persistent course, including higher levels of symptoms, comorbid oppositional-defiant disorder, lower IQ, and family socioeconomic disadvantage.[5-9] However, most follow-up studies[10] of children with ADHD have been conducted with clinical samples, which may not represent the overall ADHD population. In addition, individuals who do not meet diagnostic criteria for ADHD in childhood are generally not included in studies following children with ADHD, resulting in a limited understanding of the potential emergence of the disorder in later life.

Our investigation aimed to characterize young adult ADHD by examining the persistence of the disorder from childhood to age 18 years and its possible emergence in young adulthood. First, we examined childhood predictors of persistence, including prenatal, perinatal, clinical, and family environmental factors. Second, we assessed whether some individuals who did not have an ADHD diagnosis in childhood developed the disorder by age 18 years and described childhood risk factors among these individuals. Third, we investigated the functioning of persistent, remitted, and late-onset ADHD groups at age 18 years to understand how these groups differ or resemble one another in young adulthood.

Key Points

Questions What are the childhood risk factors and what is the young adult functioning of individuals with persistent, remitted, and late-onset attention-deficit/hyperactivity disorder (ADHD) according to *DSM-5* criteria?

Findings In this population-based cohort, persistence of childhood ADHD was associated with more severe childhood ADHD. Among individuals with ADHD at age 18 years, more than two-thirds did not have ADHD diagnosed at any assessment in childhood.

Meaning The extent to which childhood and late-onset adult ADHD reflect different causes may have implications for research and treatment; further studies are needed to better understand the nature of the heterogeneity of the adult ADHD population.

Methods

Study Cohort

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, a birth cohort of 2232 British children. The sample was drawn from a larger birth register of twins born in England and Wales from January 1, 1994, to December 4, 1995.[11] Full details about the sample are reported elsewhere.[12] The E-Risk sample was constructed in 1999-2000, when 1116 families (93% of those eligible) with same-sex 5-year-old twins participated in home-visit assessments. This sample comprised 55% monozygotic and 45% dizygotic twin pairs; sex was evenly distributed within zygosity (49% male). Families were recruited to represent the UK population with newborns in the 1990s on the basis of residential location throughout England and Wales and mother's age. Teenaged women with twins were overselected to replace high-risk families who were selectively lost to the register through nonresponse. Older women having twins via assisted reproduction were underselected to avoid an excess of well-educated older women. At follow-up, the study sample represented the full range of socioeconomic conditions in the United Kingdom.[13,14]

The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave written informed consent and twins gave assent between ages 5 and 12 and then written informed consent at age 18. Participants received financial compensation.

Follow-up home visits were conducted when the children were aged 7 (98% participation), 10 (96%), 12 (96%), and 18 years (93%). Home visits at ages 5, 7, 10, and 12 included assessments with participants and their mothers; we conducted interviews only with participants at age 18 years (n = 2066). There were no significant differences between those who did and did not take part at age 18 years in socioeconomic status when the cohort was initially defined ($\chi^2 = 0.86$; $P = .65$), age 5 IQ ($t = 0.98$; $P = .33$), internalizing or externalizing problems ($t = 0.40$; $P = .69$ and $t = 0.41$; $P = .68$), or rates of childhood ADHD at ages 5, 7, 10, or 12 years ($\chi^2 = 2.08$; $P = .72$). With parents' permission, questionnaires were mailed to the children's teachers, who returned questionnaires for 94% of children at age 5 years, 93% of those followed up at age 7 years, 90% at age 10 years, and 83% at age 12 years. At age 18 years, participants were asked to identify individuals who know them well to act as coinformants; 99.3% of participants at age 18 years had coinformant data. Study interviewers completed postassessment questionnaires about their own impressions of the participants' mental health and personality, including 6 characteristics related to ADHD.

Childhood ADHD Diagnosis

We ascertained ADHD diagnosis on the basis of mother and teacher reports of 18 symptoms of inattention and hyperactivity-impulsivity derived from *DSM-IV* diagnostic criteria and the Rutter Child Scales.[15-17] Participants had to have 6 or more symptoms reported by mothers or teachers in the past 6 months, with the other informant endorsing at least 2 symptoms. We considered participants to have a diagnosis of childhood ADHD if they met criteria at age 5, 7,

10, or 12. In total, 247 participants (12.1%) met criteria for ADHD across childhood: 6.8% at age 5 (131/1921), 5.4% at age 7 (102/1880), 3.4% at age 10 (65/1912), and 3.4% at age 12 years (64/1884). Additional information is provided in the eTable in the Supplement.

Young Adult ADHD Diagnosis

We ascertained ADHD at age 18 years based on private structured interviews with participants regarding 18 symptoms of inattention and hyperactivity-impulsivity according to *DSM-5* criteria.[1] Participants had to endorse 5 or more inattentive and/or 5 or more hyperactivity-impulsivity symptoms to receive an ADHD diagnosis; we also required that symptoms interfered with individual's "life at home or with family and friends" and "life at school or work" were rated 3 or higher on a scale (1, mild interference; 5, severe interference), thereby meeting criteria for impairment and pervasiveness. The *DSM-5* requirement of symptom onset prior to age 12 was met if parents or teachers reported more than 2 ADHD symptoms at ages 5, 7, 10, or 12 years. Analyses were restricted to 2040 individuals with ADHD information in childhood and adulthood. A total of 166 participants (8.1%) met criteria for ADHD at age 18 years. We fitted a twin model and identified a heritability estimate of ADHD symptoms of 35% (95% CI, 25%-41%). Coinformants rated participants on 8 ADHD symptoms at age 18 years. Heritability estimates were virtually identical using coinformant reports, indicating that these estimates were not artifacts of twins' self-reports. Additional information is provided in the eTable in the Supplement.

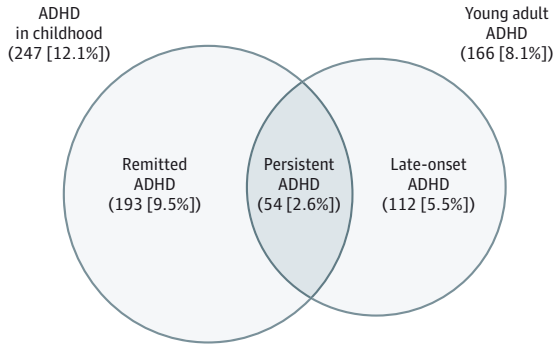
Persistent, Remitted, and Late-Onset ADHD Groups

Among individuals who met diagnostic criteria for ADHD in childhood or adulthood, we identified 3 mutually exclusive groups (**Figure**): individuals with persistent ADHD who met full diagnostic criteria both in childhood and at age 18 years (54 [2.6% of the total sample]); individuals with remitted ADHD who met diagnostic criteria in childhood but did not meet full diagnostic criteria at age 18 years (193 [9.5%]); and individuals with late-onset ADHD who did not meet criteria in childhood but had elevated symptoms and impairment at age 18 years (112 [5.5%]). A total of 1681 participants (82.4%) did not meet criteria for ADHD in childhood or adulthood. eFigures 1 and 2 in the Supplement show the distribution of inattentive and hyperactive/impulsive symptoms in childhood and at age 18 among different ADHD groups.

Statistical Analysis

We compared individuals with persistent, remitted, and late-onset ADHD with non-ADHD controls on a priori–selected factors using logistic regression. We contrasted individuals whose ADHD persisted with those who experienced remission to identify risk factors for persistence. We compared late-onset individuals with those whose ADHD persisted to characterize childhood features of the adult ADHD groups that differ on their childhood ADHD status. We examined functional outcomes at age 18 years by comparing each ADHD group with controls. We compared ADHD-persistent with ADHD-remitted individuals to examine the effect of remission on functioning, and persistent to late-onset groups to capture the extent to which these groups differed on characteristics at age 18 years. We used linear regression to assess whether characteristics associated with persistence were similar when ADHD symptoms at age 18 years were assessed with coinformant reports. Analyses were corrected for the nonindependence of twin observations with tests using the sandwich variance estimator in Stata, version 11.[18] Data analysis was conducted from February 19 to September 10, 2015.

Figure. Groups of Individuals With Childhood, Adult, and Subgroups of Attention-Deficit/Hyperactivity Disorder (ADHD)



Proportion and number of study participants who met diagnostic criteria for childhood ADHD only, adult ADHD only, and both childhood and adult ADHD.

Results

We compared participants who met diagnostic criteria for ADHD in childhood or adulthood with those who were never diagnosed with ADHD. Participants who met diagnostic criteria for ADHD in childhood or adulthood both differed from controls on prenatal and perinatal factors, clinical features, and family environment (**Table 1**).

Childhood Characteristics of Persistent vs Remitted ADHD

Among individuals who met diagnostic criteria for ADHD in childhood, 54 (21.9%) still met full criteria at age 18 years. Few childhood characteristics distinguished individuals with persistent and remitted ADHD (Table 1). Individuals with persistent ADHD had more symptoms across childhood (odds ratio [OR], 1.11 [95% CI, 1.04-1.19]) and lower IQ (OR, 0.98 [95% CI, 0.95-1.00]) compared with those whose ADHD remitted. Overall, characteristics of the family environment did not distinguish individuals with persistent ADHD from those with remitted ADHD except that families of individuals with persistent ADHD had comparatively higher maternal warmth (OR, 1.38 [95% CI, 0.99-1.93]) and less maternal depression (OR, 0.45 [95% CI, 0.22-0.89]).

Childhood Characteristics of Late-Onset vs Persistent ADHD

Among 166 individuals with adult ADHD), 112 (67.5%) had late-onset ADHD. Late-onset individuals were more likely to be female (OR, 2.48 [95% CI, 1.19-5.16]) and, controlling for sex, had fewer childhood externalizing problems (OR, 0.93 [95% CI,

Table 1. Characteristics Among Individuals With and Without ADHD

Characteristic[a]	No ADHD (n = 1681)[b]	Childhood ADHD				Young Adult ADHD		*P* Value	
		Remitted (n = 193)[c]	*P* Value	Persistent (n = 54)[c]	*P* Value	Late-Onset (n = 112)	*P* Value	Persistent vs Remitted	Persistent vs Late-Onset[c]
Prenatal and Perinatal Factors									
Male sex, No. (%)	743 (44.2)	140 (72.5)	<.001	36 (66.7)	.004	49 (44.6)	.93	.44	.02
Birth weight, mean (SD), g	2449.0 (540)	2372.2 (503)	.01	2364.4 (538)	.19	2467.8 (529)	.74	.97	.15
Stress during pregnancy, No. (%)	329 (20.6)	45 (26.0)	.21	17 (32.1)	.09	29 (26.4)	.17	.43	.83
Smoking during pregnancy, No. (%)	372 (23.3)	65 (39.4)	<.001	23 (43.4)	.003	34 (31.5)	.06	.63	.09
Child Clinical Characteristics									
Age 5-12 y ADHD symptoms, mean (SD)[d]									
Inattentive	0.83 (1.2)	4.96 (2.6)	<.001	6.32 (3.2)	<.001	1.72 (1.3)	<.001	.004	<.001
Hyperactive/ impulsive	1.33 (1.5)	5.53 (2.5)	<.001	6.63 (3.0)	<.001	2.41 (1.6)	<.001	.02	<.001
Total	2.15 (2.4)	10.49 (4.2)	<.001	12.93 (5.5)	<.001	4.14 (2.5)	<.001	.002	<.001
Age 5-12 y comorbid problems									
ODD, No. (%)	167 (9.9)	83 (43.0)	<.001	25 (46.3)	<.001	26 (23.2)	<.001	.68	.01
CD, No. (%)	168 (10.0)	90 (46.6)	<.001	28 (51.9)	<.001	33 (29.5)	<.001	.51	.02
Internalizing score, mean (SD)	10.72 (6.2)	15.81 (8.4)	<.001	17.45 (9.2)	<.001	12.71 (6.7)	<.001	.26	.002
Externalizing score, mean (SD)	14.20 (9.8)	31.87 (14.9)	<.001	36.85 (17.9)	<.001	22.24 (11.2)	<.001	.07	<.001
Age 5 y IQ and executive functioning									
IQ, mean (SD)	101.38 (14.6)	93.04 (14.6)	<.001	87.96 (14.7)	<.001	96.91 (15.7)	.004	.03	.001
Performance IQ, mean (SD)	9.98 (2.8)	8.53 (2.7)	<.001	7.43 (2.9)	<.001	9.23 (2.9)	.009	.03	.001
Verbal IQ, mean (SD)	9.12 (3.0)	7.81 (3.1)	<.001	7.35 (2.8)	<.001	8.44 (3.2)	.03	.30	.02
Executive functioning, mean (SD)	11.84 (3.0)	10.54 (3.3)	<.001	10.64 (3.4)	.02	10.97 (2.8)	.001	.85	.69
Family Environment									
Parental factors									
Antisocial behavior, No. (%)	422 (25.2)	82 (42.7)	<.001	23 (42.6)	.01	37 (33.0)	.08	.99	.19
Substance use, No. (%)	381 (22.8)	66 (34.4)	.004	25 (46.3)	.001	42 (37.5)	.001	.13	.38
Maternal factors									
Depression, No. (%)	438 (26.2)	90 (46.9)	<.001	15 (28.3)	.81	34 (30.4)	.36	.02	.57
Warmth, mean (SD)	3.33 (1.0)	2.83 (1.1)	<.001	3.17 (1.0)	.36	3.17 (0.9)	.08	.055	.99
Negativity, mean (SD)	1.45 (0.9)	2.01 (1.1)	<.001	1.96 (1.1)	.001	1.71 (1.0)	.007	.79	.20
Low social class, No. (%)	513 (30.5)	94 (48.7)	<.001	24 (44.4)	.045	47 (42.0)	.01	.61	.74
Domestic violence exposure, No. (%)	670 (40.2)	102 (53.1)	.004	26 (48.2)	.31	59 (52.7)	.01	.55	.69
Child maltreatment, No. (%)	198 (11.8)	44 (22.8)	<.001	9 (16.7)	.39	24 (21.4)	.005	.38	.40

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CD, conduct disorder; ODD, oppositional-defiant disorder.

[a] Data were missing on some variables; all available data were used in analysis.

[b] Comparisons are between remitted, persistent, and late-onset ADHD groups, with the no-ADHD diagnosis group serving as controls.

[c] Statistical comparisons adjusted for sex using logistic regression.

[d] Childhood ADHD symptoms from ages 5 to 12 years are computed as the mean of the sum of mother-reported and teacher-reported ADHD symptoms across ages 5, 7, 10, and 12 years. The range of total inattentive symptoms in childhood was 0 to 18 (range, 0-9 for mother and teacher reports separately); the range of total hyperactive/impulsive symptoms in childhood was 0 to 18; and the range of total ADHD symptoms in childhood was 0 to 36.

Table 2. Functioning Among No-ADHD and ADHD Groups at Age 18 Years

Characteristic[a]	No ADHD (n = 1681)[b]	Childhood ADHD				Young Adult ADHD		*P* Value	
		Remitted (n = 193)[c]	*P* Value	Persistent (n = 54)[c]	*P* Value	Late-Onset (n = 112)	*P* Value	Persistent vs Remitted	Persistent vs Late-onset[c]
Age 18 y ADHD Symptoms and Impairment									
Self-report, mean (SD)									
Inattentive	2.63 (2.2)	3.51 (2.4)	<.001	5.72 (2.2)	<.001	6.13 (1.8)	<.001	<.001	.29
Hyperactive/impulsive	2.44 (2.2)	3.33 (2.4)	<.001	5.63 (2.2)	<.001	5.27 (2.4)	<.001	<.001	.34
Total	5.08 (3.9)	6.89 (4.3)	<.001	11.37 (3.5)	<.001	11.42 (3.2)	<.001	<.001	.99
ADHD interference									
School or work	1.93 (1.0)	2.03 (1.1)	.14	3.73 (1.1)	<.001	3.91 (0.8)	<.001	<.001	.39
Home or with friends	1.55 (0.8)	1.65 (0.8)	.05	3.59 (1.0)	<.001	3.45 (0.7)	<.001	<.001	.31
Coinformant report of ADHD symptoms, mean (SD)	0.42 (1.1)	1.25 (1.9)	<.001	2.31 (2.6)	<.001	1.37 (2.2)	<.001	.003	.04
Interviewer personality impressions, No. (%)									
Not conscientious	151 (9.0)	38 (19.9)	<.001	21 (38.9)	<.001	21 (18.9)	.001	.006	.01
Not diligent	240 (14.4)	56 (29.2)	<.001	28 (54.9)	<.001	30 (27.3)	<.001	.001	.001
Not planful	290 (17.3)	66 (34.6)	<.001	16 (30.2)	.02	37 (33.0)	<.001	.56	.60
Disorderly	49 (2.9)	15 (7.8)	.002	7 (13.2)	<.001	13 (11.6)	<.001	.24	.97
Not focused	219 (13.1)	49 (25.7)	<.001	20 (37.0)	<.001	25 (22.3)	.007	.13	.05
Not persevering	133 (8.1)	35 (18.5)	<.001	20 (37.0)	<.001	19 (17.0)	.002	.005	.005
Functioning[d]									
IQ, mean (SD)	102.49 (14.5)	93.33 (15.9)	<.001	89.78 (14.8)	<.001	96.12 (14.3)	<.001	.13	.006
Life satisfaction, mean (SD)	3.92 (0.7)	3.75 (0.7)	.002	3.48 (0.9)	<.001	3.44 (0.8)	<.001	.06	.93
Job preparedness, mean (SD)	17.23 (2.4)	16.45 (2.9)	<.001	14.64 (4.2)	<.001	15.42 (3.0)	<.001	.001	.07
Currently studying, No. (%)	1231 (73.2)	113 (58.6)	<.001	33 (61.1)	.08	71 (63.4)	.03	.75	.78
Comorbid Diagnoses, No. (%)									
Generalized anxiety disorder	108 (6.4)	11 (5.8)	.67	13 (24.1)	<.001	18 (16.1)	<.001	.001	.22
Major depressive episode	300 (17.9)	41 (21.4)	.06	19 (35.2)	.001	48 (42.9)	<.001	.049	.50
Conduct disorder	200 (11.9)	45 (23.6)	.006	20 (38.5)	<.001	39 (35.1)	<.001	.04	.95
Marijuana dependence	54 (3.2)	11 (5.7)	.35	8 (14.8)	.002	13 (11.6)	<.001	.04	.68
Alcohol dependence	182 (10.8)	32 (16.6)	.08	7 (13.0)	.81	35 (31.5)	<.001	.55	.01

Abbreviation: ADHD, attention-deficit/hyperactivity disorder.

[a] Data were missing on some variables; all available data were used in analysis.

[b] Comparisons were between remitted, persistent, and late-onset ADHD groups, with the no-ADHD diagnosis group serving as controls.

[c] Statistical comparisons adjusted for sex using logistic regression.

[d] A full description of these variables is provided in the eTable in the Supplement.

0.91-0.96]) and higher IQ (OR, 1.04 [95% CI, 1.02-1.07]) compared with those who had persistent ADHD (Table 1). Prenatal and perinatal factors and characteristics of the family environment did not differ between these groups.

Young Adult Functioning of Persistent vs Remitted ADHD

Coinformants (ie, parents and co-twins) rated individuals with persistent ADHD as having more symptoms at age 18 years than individuals with remitted ADHD (OR, 1.23 [95% CI, 1.07-1.41]), and interviewers rated them as less conscientious (OR, 0.39 [0.20-0.76]), diligent (OR, 0.34 [0.17-0.66]), and persevering (OR, 0.39 [95% CI, 0.20-0.75]); further data are reported in **Table 2**. At age 18 years, individuals with persistent ADHD had more functional impairment (school/work: OR, 3.30 [95% CI, 2.18-5.00]; home/with friends: OR, 6.26 [95% CI, 3.07-12.76]) compared with those with remitted ADHD. Persons with persistent ADHD had higher rates of generalized anxiety disorder (OR, 5.19 [95% CI, 2.01-13.38]), conduct disorder (OR, 2.03 [95% CI, 1.03-3.99]), and marijuana dependence (OR, 2.88 [95% CI, 1.07-7.71]) compared with those whose ADHD had remitted. However, the remitted group still showed impairment: compared with controls, individuals with remitted ADHD had more self-rated (OR, 1.12 [95% CI, 1.07-1.16]) and coinformant-rated ADHD symptoms (OR, 1.38 [95% CI, 1.27-1.51]), lower life satisfaction (OR, 0.73 [95% CI, 0.60-0.89]) and job preparedness (OR, 0.88 [95% CI, 0.83-0.94]), and higher rates of major depression (OR, 1.46 [95% CI, 0.98-2.16]), alcohol dependence (OR, 1.45 [95% CI, 0.96-2.19), and conduct disorder (OR, 1.71 [95% CI, 1.17-2.52]).

Young Adult Functioning of Late-Onset vs Persistent ADHD

Individuals with late-onset ADHD differed from the persistent ADHD group on few variables at age 18 years (Table 2). Late-onset ADHD individuals had higher age-18 IQ compared with the persistent ADHD group (OR, 1.04 [95% CI, 1.01-1.06]), but the 2 groups did not differ significantly on life satisfaction, job preparedness, and rates of being engaged in formal education. Individuals with late-onset and persistent ADHD did not differ on age-18 psychiatric comorbidity: both had elevated rates of generalized anxiety disorder, conduct disorder, and marijuana dependence. Late-onset ADHD individuals had significantly higher rates of alcohol dependence compared with those with persistent ADHD (OR, 3.40 [95% CI, 1.31-8.84]).

We examined whether having a co-twin with childhood ADHD conferred increased risk for late-onset ADHD and found no significant difference in the proportion of individuals who developed late-onset ADHD among those who had a co-twin with childhood ADHD (7.9%) and those who did not (6.0%) (P = .39).

Childhood Characteristics of Coinformant-Rated ADHD at Age 18 Years

As when predicting age-18 ADHD using self-report, the number of childhood ADHD symptoms was the most significant predictor of coinformant-reported symptoms of ADHD at age 18 years (β = 0.43; P < .001). Maternal stress during pregnancy (β = 0.19; P = .02), comorbid conduct disorder (β = 0.19; P = .006), oppositional-defiant disorder (β = 0.15; P = .04), and higher externalizing score (β = 0.30; P < .001) in childhood were also associated with more coinformant-rated symptoms.

Discussion

Our study was particularly well suited to investigate the persistence and emergence of *DSM-5* adult ADHD given its prospective follow-up of a general population sample of children with and without ADHD from early childhood to young adulthood. We found that ADHD persistence was associated with more ADHD symptoms and lower IQ in childhood. In addition, we identified heterogeneity in the young adult ADHD population, such that this group consisted of a minority of individuals for whom ADHD persisted from childhood and a larger proportion who did not meet criteria for the disorder until young adulthood. Our results suggest that adult ADHD is more complex than a straightforward continuation of the childhood disorder.

Persistence and Remission of ADHD From Childhood to Age 18 Years

Although we examined a wide range of risk factors, we found persistence to be most strongly associated with the severity of childhood ADHD symptoms, consistent with some,[5,19] but not all,[6,20] prospective studies in clinical samples. We also found that lower IQ was associated with persistence. Although most prenatal, perinatal, and family environment factors were associated with the incidence of ADHD in childhood, overall they were not associated with its persistence into adulthood. It may be possible that remission of ADHD at age 18 years is associated with the increased opportunities for young adults to select environments more suited to their ADHD symptoms; in this way, concurrent lifestyle factors rather than childhood environment may be more important for determining remission of ADHD at age 18 years.

The majority of individuals with ADHD in childhood no longer met full criteria at age 18 years. However, this remitted group reported interference with functioning due to their ADHD symptoms. In addition to showing more ADHD symptoms, the remitted group continued to have lower IQ and higher rates of depression, alcohol dependence, and conduct disorder, which could also negatively affect functioning at age 18 years. Although this group no longer meets full diagnostic criteria for ADHD, residual ADHD symptoms, comorbidity, and functional impairment suggest that they may require clinical attention.

ADHD Among Women and Girls

Although an ADHD diagnosis is more common in boys than girls in childhood, epidemiologic surveys[21] of adult ADHD identify a sex ratio closer to 1:1. The larger proportion of women in the E-Risk adult ADHD group is due to a higher number of women with late-onset ADHD joining the population in adulthood rather than childhood symptoms being especially persistent in women. In girls, ADHD symptoms may be less likely to come to the attention of parents and teachers owing to lower rates of externalizing-type behaviors,[22] resulting in fewer girls with ADHD diagnosed in childhood.

What Is Late-Onset ADHD?

A few studies[23,24] point to the possibility of ADHD emergence after childhood and offer suggestive evidence that, for some individuals, ADHD symptoms may increase into adolescence and adulthood. Findings from the Dunedin Study[1] demonstrated that 90% of the individuals with adult ADHD at age 38 years had not met criteria for the disorder in childhood. We found that already by age 18 years, individuals with late onset constituted a large proportion of the adult ADHD population. However, many questions remain as to the nature of late-onset ADHD. We considered 3 possibilities. First, individuals with late onset may have the same underlying liability for ADHD as those with childhood ADHD, but the disorder may be masked in childhood owing to protective factors, such as particularly supportive family environments or highly developed cognitive skills. In such cases, symptoms may not become impairing until the increasing challenges of later, more demanding schooling.[25]

Second, individuals with late onset may not have ADHD at age 18 years but rather have another disorder with similar symptoms. We found that those with late-onset ADHD exhibit elevated rates of anxiety, depression, and marijuana and alcohol dependence. To investigate whether the late-onset group is entirely accounted for by ADHD-like symptoms caused by other disorders, we excluded individuals with diagnoses of anxiety, depression, and marijuana and alcohol dependence. Approximately one-third of the late-onset group remained

after excluding individuals with these comorbidities and presented similar levels of ADHD impairment and coinformant-rated ADHD symptoms. However, persons with late-onset ADHD may have other disorders (eg, obsessive-compulsive disorder or social anxiety) or subthreshold comorbidity that account for ADHD symptoms.

Third, late-onset adult ADHD could be a distinct disorder. The late-onset ADHD group showed several characteristics that differ from childhood-onset ADHD, including a dissimilar sex composition (the late-onset group included more women) and lower heritability. Indeed, these differences are consistent with the extant research[21,26] on the characteristics of childhood and adult ADHD populations. We found that the risk of developing late-onset ADHD was similar regardless of whether the participant's twin had childhood ADHD. The extent to which the etiology differs between childhood-onset and late-onset ADHD has broad implications for our understanding of the adult ADHD population. Studies of adult ADHD that examine the genetic origins of the disorder or the effectiveness of different treatments may benefit from considering this heterogeneity of the adult ADHD population.

Limitations

Our findings should be considered in light of potential limitations. First, diagnostic information on ADHD at age 18 years was based only on self-reports. However, a strength of our study is the availability of reports from coinformants at age 18 years. Coinformants rated individuals with persistent ADHD as having more symptoms than those in the remitted group, corroborating self-reports, and childhood risk factors for persistence were similar using age-18 coinformant reports (**Table 3**).

Second, we defined young adult ADHD using an age-of-onset criterion; therefore, the late-onset ADHD group had young adult onset of the full ADHD syndrome rather than ADHD symptoms. This definition could be considered a limitation since we did not focus on individuals with ADHD at age 18 who had no apparent ADHD symptoms in childhood. However, those with no reported childhood ADHD symptoms are a somewhat distinctive group because it is normative to display some ADHD behavior in childhood (>85% of our sample had some mother- or teacher-reported ADHD symptoms in childhood). Including the age-of-onset criterion is also a strength because our adult ADHD group met *DSM-5* criteria, which stipulate symptom onset before age 12 years. Third, as an epidemiologic cohort, our study did not have practitioner interviews and may include false positives. However, we provide evidence of construct validity since our ADHD groups were associated with known correlates and were rated as having more ADHD symptoms by coinformants. Taken together, this network of information lends validity to our diagnostic procedures. Fourth, results regarding childhood characteristics and age-18 functioning did not differ significantly when we removed the age-of-onset criterion for the young adult ADHD diagnosis. Fifth, the sample was composed of twins, so the results may not generalize to singletons. However, our prevalence of childhood ADHD at each age is well within the range of 3.4% to 11% estimated previously.[27,28] In addition, our rate of ADHD persistence is similar to that found in a meta-analysis.[4]

Table 3. Associations Between Childhood Characteristics and Age 18 Coinformant-Rated Symptoms Among Individuals With Childhood ADHD

Characteristic	Standardized β Value	*P* Value
Prenatal and perinatal factors		
Male sex	0.14	.055
Birth weight, g	0.13	.15
Stress during pregnancy	0.19	.02
Smoking during pregnancy	0.15	.06
Child ADHD characteristics		
Childhood ADHD symptoms at age 5-12 y		
Total inattentive	0.37	<.001
Total hyperactive and impulsive	0.37	<.001
Total symptoms	0.43	<.001
Comorbidity at age 5-12 y		
ODD	0.15	.04
CD	0.19	.006
Internalizing score	0.13	.08
Externalizing score	0.30	<.001
IQ and executive functioning at age 5 y		
IQ	−0.12	.11
Performance IQ	−0.13	.12
Verbal IQ	−0.06	.35
Executive functioning	−0.07	.42
Family environment		
Parental factors		
Antisocial behavior	−0.08	.28
Substance use	−0.04	.62
Maternal factors		
Depression	0	.98
Warmth	0.02	.79
Negativity	0.08	.37
Low social class	0.02	.79
Domestic violence exposure	−0.11	.14
Child maltreatment	0.02	.77

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CD, conduct disorder; ODD, oppositional-defiant disorder.

Conclusions

Owing to the prospective longitudinal design of the E-Risk study, we were able to identify heterogeneity in the adult ADHD population. Our findings highlight the importance of taking a developmental approach to understanding ADHD. Although many questions remain regarding the nature of late-onset ADHD, this group showed significant levels of ADHD symptoms and impairment, as well as poor functioning and high rates of psychiatric comorbidity. Therefore, the absence of a childhood diagnosis of ADHD should not preclude adults with ADHD from receiving clinical attention. Whether individuals with late-onset vs childhood-onset ADHD respond differently to treatment is an open question, and further research is required to better understand the causes, course, and optimal treatment of late-onset ADHD.

ARTICLE INFORMATION

Submitted for Publication: September 9, 2015; accepted February 15, 2016.

Published Online: May 18, 2016. doi:10.1001/jamapsychiatry.2016.0465.

Author Affiliations: Medical Research Council Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom (Agnew-Blais, Danese, Wertz, Moffitt, Arseneault); Department of Psychiatry, University of São Paulo Medical School, São Paulo, Brazil (Polanczyk); Department of Child and Adolescent Psychiatry, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, United Kingdom (Danese); National and Specialist Child Traumatic Stress and Anxiety Clinic, South London and Maudsley National Health Service Foundation Trust, London, United Kingdom (Danese); Department of Psychology and Neuroscience, Duke University, Durham, North Carolina (Moffitt); Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, North Carolina (Moffitt).

Author Contributions: Drs Agnew-Blais and Arseneault had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Agnew-Blais, Danese, Wertz, Moffitt, Arseneault.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Agnew-Blais, Wertz.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Agnew-Blais, Wertz, Arseneault.
Obtained funding: Danese, Moffitt, Arseneault.
Administrative, technical, or material support: Agnew-Blais, Danese, Wertz.
Study supervision: Polanczyk, Danese, Moffitt, Arseneault.

Conflict of Interest Disclosures: None reported.

Funding/Support: The Environmental Risk (E-Risk) Longitudinal Twin Study is funded by grant G1002190 from the United Kingdom Medical Research Council UKMRC. Additional support was provided by grant HD077482 from the National Institute of Child Health and Human Development and the Jacobs Foundation. Ms Wertz is supported by the National Institute for Health Research Mental Health Biomedical Research Centre at South London and Maudsley National Health Service Foundation Trust and King's College London.

Role of the Funder/Sponsor: The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: Avshalom Caspi, PhD (Duke University and King's College London), and Michael Rutter, MD, PhD (King's College London), participated in the establishment of the E-Risk cohort, and Thomas Achenbach, PhD (University of Vermont), provided permission to adapt the Child Behavior Checklist. No financial compensation was provided for this involvement. We thank the members of the E-Risk team for their dedication, hard work, and insights and are grateful to the study mothers and fathers, the twins, and the twins' teachers for their participation.

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