Is ADHD Always a Childhood Onset Disorder? Towards Understanding Adult Onset ADHD

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Adult Onset ADHD

- Recent *population based studies* raise the intriguing question as to whether adult ADHD is always preceded by childhood onset of symptoms or can develop anew in adult life.

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Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study

Results: As expected, childhood ADHD had a prevalence of 6% (predominantly male) and was associated with childhood comorbid disorders, neurocognitive deficits, polygenic risk, and polygenic risk factors.

Conclusions: The findings raise the possibility that adults presenting with the ADHD symptom picture may not have a childhood-onset neurodevelopmental disorder. If this finding is replicated, then the disorder’s place in the classification system must be reconsidered, and research must investigate the etiology of adult ADHD.

ADHD group did not show tested neuropsychological deficits in childhood or adulthood, nor did they show polygenic risk for childhood ADHD.
Childhood ADHD and Adult ADHD Groups in the Dunedin Cohort

A. Follow-Forward: Did Those With Childhood ADHD (N=61) Continue to Have Adult ADHD?

B. Follow-Back: Did Those With Adult ADHD (N=31) Have Childhood ADHD?

The figure shows that most of the participants who had childhood ADHD did not have adult ADHD, and most of those with adult ADHD did not have childhood ADHD. The childhood and adult ADHD groups comprised virtually nonoverlapping sets.

Problems with the Interpretation of The Dunedin Study Findings

- Childhood diagnosis based on informants (parents and teachers)
- Adult diagnosis by self report
- Subjects assessed in childhood and at the age of 38 making it difficult to assess age of onset of adult ADHD cases
- There were only 31 adult onset cases!!
THE BRAZILIAN STUDY
RESULTS At 11 years of age, childhood ADHD (C-ADHD) was present in 393 individuals (8.9%). At 18 to 19 years of age, 492 individuals (12.2%) fulfilled all DSM-5 criteria for young adult ADHD (YA-ADHD), except age at onset. After comorbidities were excluded, the prevalence of

CONCLUSIONS AND RELEVANCE The findings of this study do not support the assumption that adulthood ADHD is necessarily a continuation of childhood ADHD. Rather, they suggest the existence of 2 syndromes that have distinct developmental trajectories. adulthood, as measured by traffic incidents, criminal behavior, incarceration, suicide attempts, and comorbidities. However, only 60 children (17.2%) with ADHD continued to have ADHD as young adults, and only 60 young adults (12.6%) with ADHD had the disorder in childhood.

MAIN OUTCOMES AND MEASURES The ADHD status was first ascertained at 11 years of age using a screening instrument (hyperactivity subscale of the Strength and Difficulties Questionnaire) calibrated for a DSM-IV ADHD diagnosis based on clinical interviews with parents using the Development and Well-Being Assessment. At 18 to 19 years of age, ADHD diagnosis was derived using DSM-5 criteria, except age at onset. We estimated the overlap between these groups assessed at 11 and 18 to 19 years of age and the rates of markers of impairment in these 2 groups compared with those without ADHD.
C-ADHD indicates childhood attention-deficit/hyperactivity disorder; YA-ADHD, young adult attention-deficit/hyperactivity disorder; YA-ADHD-WC, young adult attention-deficit/hyperactivity disorder without comorbidities.

Caye et al. *JAMA Psychiatry.* 2016;73(7):705-712
Brazilian Study Results

• Only 15% of children with ADHD continued to have ADHD at ages 18-19, and only 12% of 18-19 year olds with ADHD had the disorder in childhood
Problems with the Interpretation of the Brazilian Study Findings

- ADHD status was first ascertained at age 11 based on clinical interviews with parents.
- At age 18 years, ADHD diagnosis was established by self report using DSM-5 criteria, except age-of-onset.
- Age 18-19 can hardly be considered “adults”.
- In most countries they will be in high school.
Problems with the Brazilian Study

Conclusions

• Both ADHD groups had similarly increased levels of impairment at 18-19, as measured by traffic accidents, criminal records, incarceration, suicide attempt, and comorbidities
THE UK STUDY
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.

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.

ADHD; 112 (67.9%) 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.

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.
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.
Interpretation of the UK Study Findings

• **Twin Study**
• Age at follow up: **18 years**
• 22% of individuals with childhood ADHD, also met diagnostic criteria for the disorder at 18 years
• Persistence was associated with **more symptoms, lower IQ, more functional impairment (school/work, home/with friends), GAD, CD and marijuana dependence**
Interpretation of the UK Study Findings

• 68% of individuals with ADHD at age 18 did not meet criteria for (full) ADHD in childhood
• These “late-onset” ADHD cases showed fewer externalizing problems and higher IQ in childhood
At age 18, early and late-onset ADHD showed comparable ADHD symptoms and impairment as well as similarly elevated rates of mental health disorders.
HOW TO UNDERSTAND THESE “ADULT ONSET” ADHD CASES?
How to Understand Adult Onset ADHD?

• The three population based studies propose a paradigmatic shift in our understanding of ADHD

• They suggest that:
  – ADHD can onset in adulthood
  – Childhood onset and adult onset ADHD are distinct syndromes

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The Brazilian Study argues that child and adult ADHD are “distinct syndromes”

The UK Study argues “that adult ADHD is more complex than a straightforward continuation of the childhood disorder”

The NZ study argues that adult ADHD is not a neurodevelopmental disorder

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PROBLEMS WITH SELF REPORTS OF ADHD SYMPTOMS IN POPULATION STUDIES
Problem with Self Reports in Population Studies

- Population studies use non-referred samples
- Participants may not always be self-aware of their symptoms increasing the risk of false negatives

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Self awareness is not an issue for subjects referring themselves to clinical care since, by definition, it is their self awareness that brings them to the clinic.
WERE THE CHILDHOOD-ONSET CASES WITHOUT ADULT ADHD DIAGNOSIS TRULY REMITTERS? IT ALL DEPENDS ON HOW REMISSION IS DEFINED
The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies

Conclusions. Our results show that estimates of ADHD’s persistence rely heavily on how one defines persistence. Yet, regardless of definition, our analyses show that evidence for ADHD lessens with age. More work is needed to determine if this reflects true remission of ADHD symptoms or is due to the developmental insensitivity of diagnostic criteria for the disorder.

Method. We analyzed data from published follow-up studies of ADHD. To be included in the analysis, these additional studies had to meet the following criteria: the study included a control group and it was clear from the methods if the diagnosis of ADHD included subjects who did not meet full criteria but showed residual and impairing signs of the disorder. We used a meta-analysis regression model to separately assess the syndromatic and symptomatic persistence of ADHD.
Figure 2 | The age-dependent decline and persistence of attention-deficit/hyperactivity disorder throughout the lifetime. Follow-up studies have assessed children with attention-deficit/hyperactivity disorder (ADHD) at multiple time points after their initial diagnosis. Although they document an age-dependent decline in ADHD symptoms, ADHD is also a highly persistent disorder when defined by the persistence of functional impairment\(^7\) or the persistence of subthreshold (three or fewer) impairing symptoms\(^8\). By contrast, many patients remit full diagnostic criteria\(^7\).
Adult Onset ADHD

• This meta-analysis of longitudinal studies document an age dependent decline in the expression of ADHD symptoms such that two-thirds of ADHD youth continued to have impairing symptoms of ADHD in young adulthood despite only 15% meeting full diagnostic criteria for the disorder

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ARE THE RATES OF PERSISTENCE OF CHILDHOOD ADHD ATYPICAL?
Adult Onset ADHD

- The persistence of the **full** ADHD disorder of 17%-22% by ages 18-19 years in the Brazilian and UK studies are consistent with the expected rate of persistence of the full disorder in the literature

- **Subsyndromal and functional persistence was not assessed**

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Low Persistence of Childhood ADHD in the NZ Study

• Persistence of childhood ADHD in the NZ study was defined as those meeting full diagnostic criteria ignoring the much higher persistence rate of impairing and subsyndromal ADHD symptoms

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ARE THESE ADULT ONSET CASES REALLY ADULTS?
Adult Onset ADHD

- The “adults” in the Brazilian and UK studies were 18 or 19 years old
- This is too small a slice of adulthood to draw firm conclusions about Adult onset ADHD
- The NZ studies assessed subjects in childhood and then at the age of 38 and do not report the age of onset of their adult-onset cases

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ISSUE OF REPORTER BIAS
In the three studies while the child diagnosis of ADHD informant based (parents and teachers), the adult diagnosis was based exclusively on self-report.
DOES REPORTING SOURCE MATTER?
The Persistence of Attention-Deficit/Hyperactivity Disorder Into Young Adulthood as a Function of Reporting Source and Definition of Disorder

Russell A. Barkley, Mariellen Fischer, and Lori Smallish

This study examined the persistence of attention-deficit/hyperactivity disorder (ADHD) into young adulthood using hyperactive ($N = 147$) and community control ($N = 71$) children evaluated at ages 19–25 years. ADHD was rare in both groups (5% vs. 0%) based on self-report but was substantially higher using parent reports (46% vs. 1.4%). Using a developmentally referenced criterion (+2 $SD$), prevalence remained low for self-reports (12% vs. 10%) but rose further for parent reports (66% vs. 8%). Parent reports were more strongly associated with major life activities than were self-reports. Recollections of childhood ADHD showed moderate correlations with actual parent ratings collected in childhood, which suggests some validity for such recollections. The authors conclude that previous follow-up studies that relied on self-reports might have substantially underestimated the persistence of ADHD into adulthood.

When Diagnosing ADHD in Young Adults Emphasize Informant Reports,

**Results:** Results indicated that although a majority of young adults with a childhood diagnosis of ADHD continued to experience elevated ADHD symptoms (75%) and clinically significant impairment (60%), only 9.6%–19.7% of the childhood ADHD group continued to meet DSM-IV-TR (DSM, 4th ed., text rev.) criteria for ADHD in young adulthood. Parent report was more diagnostically sensitive than self-report. Young adults with ADHD tended to underreport current symptoms, while young adults without ADHD tended to overreport symptoms. There was no significant incremental benefit beyond parent report alone to combining self-report with parent report. Non-DSM-based, adult-specific symptoms of ADHD were significantly correlated with functional impairment and endorsed at slightly higher rates than the DSM-IV-TR symptoms. However, DSM-IV-TR items tended to be more predictive of diagnostic group membership than the non-DSM adult-specific items due to elevated control group item endorsement.

**Conclusions:** Implications for the assessment and treatment of ADHD in young adults are discussed (i.e., collecting informant reports, lowering the diagnostic threshold, emphasizing impairment, and cautiously interpreting retrospective reports).
• Thus, the UK, Brazilian and NZ studies may have underestimated the persistence of ADHD and overestimated the prevalence of adult onsets
IS LATER ONSET ADHD DIFFERENT FROM EARLIER ONSET ADHD?
IN THE THREE POPULATION STUDIES, EARLY AND LATE-ONSET ADHD SHOWED COMPARABLE ADHD SYMPTOMS AND IMPAIRMENT AS WELL AS SIMILARLY ELEVATED RATES OF MENTAL HEALTH DISORDERS
Diagnosing Adult Attention Deficit Hyperactivity Disorder: Are Late Onset and Hyperactive-impulsive Patterns a Common Comorbid Presentation?

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Article

Method: The authors addressed the validity of DSM-IV’s age-at-onset and symptom threshold criteria by comparing four groups of adults: 127 subjects with full ADHD who met all DSM-IV criteria for childhood-onset ADHD, 79 subjects with late-onset ADHD who met all criteria except the age-at-onset criterion, 41 subjects with subthreshold ADHD who did not meet full symptom criteria for ADHD, and 123 subjects without ADHD who did not meet any criteria. The authors hypothesized that subjects with late-onset and subthreshold ADHD would show patterns of psychiatric comorbidity, functioning similar to those seen in subjects with full ADHD.
FIGURE 1. Functional Impairment of Probands

- Ever arrested (N=75)
- Ever convicted (N=14)
- Ever imprisoned (N=8)

Legal Incidents

No ADHD
Subthreshold ADHD
Late-onset ADHD
Full ADHD

FIGURE 2. Treatment for Attention Deficit Hyperactivity Disorder

- None
- Pharmacotherapy
- Counseling and pharmacotherapy
- Counseling

Lifetime Treatment for ADHD

Subthreshold ADHD (N=41)

Late-Onset ADHD (N=79)

Full ADHD (N=127)

Objective: Research about Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) age of onset criterion for ADHD led to increasing that criterion to 12 in Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5). Although an improvement from the previous age at onset of 7, whether this new criterion is adequate to capture all cases with ADHD remains uncertain.

Method: We compared three groups of adults: (a) ADHD participants who met all DSM-5 criteria for ADHD (n = 182), (b) late-onset ADHD participants who met all criteria except for later age at onset (n = 17), and (c) non-ADHD participants who did not meet criteria for ADHD (n = 117). We assessed patterns of symptoms, psychiatric comorbidity, functional impairment, familial transmission, quality of life, social adjustment, and intelligence.

Results: Compared with non-ADHD participants, all ADHD groups had poorer quality of life and had more impaired social adjustment. Compared with each other, the ADHD groups had similar patterns of psychiatric comorbidity, functional impairment, familial transmission, and intelligence. Conclusion: When assessing adult ADHD, self-reported onsets of ADHD after 12 years of age may be warranted.

DID THE ADULT ONSET CASES TRULY LACKED NEURODEVELOPMENTAL FEATURES?
Did the adult onset cases truly lacked neurodevelopmental features?

• In the three population studies, adult onset ADHD was *de novo* only in the sense that full-threshold ADHD had not been diagnosed by the investigators at prior assessments

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Did the adult onset cases truly lacked neurodevelopmental features?

• In the NZ study, the adult onset ADHD group had more teacher-rated symptoms of ADHD, more conduct disorder (CD) in childhood and were more likely to have had a combined parent/teacher report of ADHD symptom onset prior to age 12 than Controls

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Adult Onset ADHD: What Does It Mean?

• Likewise, the adult onset cases in the UK study had significantly elevated rates of ADHD symptoms, CD and oppositional defiant disorder (ODD) in childhood

• In the Brazilian study, only 38% of adult onsets were “neurotypical” as defined by levels of ADHD and CD symptoms

• Thus, many “adult onsets” of ADHD appear to have neurodevelopmental roots

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Adult Onset ADHD

• These neurodevelopmental roots point to the existence of subthreshold childhood ADHD, which is impairing in its own right and may also predict subsequent onset of the full-threshold disorder

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Adult ADHD

• This view of ADHD posits that symptoms and impairment may emerge due to the accumulation of environmental and genetic risk factors
Adult ADHD

• Those with lower levels of risk at birth will take longer to accumulate sufficient risk factors and longer to onset with symptoms and impairment.

• This multifactorial perspective allows for different risk factors to exert effects at different ages thereby influencing age of onset.
Adult Onset ADHD

Because these effects are multifactorial, there is no clean separation of etiologic factors in people above and below the ages of 12 years set forth in DSM-V or 18 years.
Interpretation of Adult Onset ADHD Findings

• Thus, results from these population based reports do very little to help clarify whether these “adults” do not recall childhood symptoms, are unable to report on them, or are unable to distinguish onset of symptoms from onset of symptoms-associated impairments that may account for the different ages of onset.

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Adult Onset ADHD

• In many cases, the **onset of ADHD symptoms** and **onset of associated impairment** could be separated by many years, particularly among those with strong intellectual abilities and those living in supportive, well-structured childhood environments.

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Adult Onset ADHD

- Such intellectual and social scaffolding would help some ADHD youth to compensate in early life, only to decompensate into a full ADHD syndrome when the scaffolding is removed

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Adult Onset ADHD

- If this hypothesis is correct, developing methods to detect subthreshold child ADHD before it emerges as adult onset ADHD will improve public health

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Adult Onset ADHD

• These hypotheses about subthreshold ADHD argue against the idea that youth onset and adult onset are distinct syndromes.
Adult Onset ADHD

• Such an interpretation would suggest that the etiology of ADHD leads to a wide variability in age at onset of initial symptoms, symptoms exceeding diagnostic threshold and impairment arising from those symptoms.

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In this context it is important to remember that the age of onset of ADHD of 12 years proposed in DSM-V, while an improvement from the previous age of onset of 7 years, is still completely arbitrary creating the immediate dilemma on how to diagnose patients who have an onset of symptoms after 12 years of age.

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Adult Onset ADHD

• Such a scenario may suggest that ADHD may be a disorder with a continuum of ages of onsets, with some subjects starting their symptoms earlier while others later

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Adult Onset ADHD

• These concerns do not argue against the existence of adult onset ADHD or the idea that it is a clinically relevant syndrome

• In fact, as a group, the adult onset cases in the population studies showed significant functional impairments

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Adult Onset ADHD: Clinical Implications

- These new data are a ‘call to arms’ to study adult onset ADHD and to clarify how it emerges from subthreshold ADHD and other neurodevelopmental anomalies in childhood

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Can Attention-Deficit/Hyperactivity Disorder Onset Occur in Adulthood?

Stephen V. Faraone, PhD; Joseph Biederman, MD

In this issue of JAMA Psychiatry, 2 large, longitudinal, population studies from Brazil and the United Kingdom propose a paradigmatic shift in our understanding of attention-deficit/hyperactivity disorder (ADHD). They conclude, not only that the onset of ADHD can occur in adulthood, but that childhood-onset and adult-onset ADHD may be distinct syndromes.

Prior to these publications, the diagnosis of ADHD in adults had evolved in 2 directions. A meta-analysis of longitudinal studies documented an age-dependent decline in the expression of ADHD symptoms. Two-thirds of youth with ADHD continued to have impairing symptoms of ADHD in young adulthood, despite only 15% meeting full diagnostic criteria for the disorder. The Brazilian and UK studies found the expected rate of persistence to ages 18 to 19 years: 17.2% and 21.9%, respectively. A longitudinal population study from New Zealand observed a 4.9% persistence rate of ADHD to age 38 years. Practitioners take heed: these low rates of cases meeting full diagnostic criteria ignore the much higher persistence rate of impairing ADHD symptoms, which are relevant in clinical practice.

Stability for adult ADHD (35%), which could be a sign of substantial measurement error and false-positive diagnoses. Of further concern, another longitudinal study found that current symptoms of ADHD were underreported by adults who had had ADHD in childhood and overreported by adults who did not have ADHD in childhood. Because these concerns suggest that the UK, Brazilian, and New Zealand studies may have underestimated the persistence of ADHD and overestimated the prevalence of adult-onset ADHD, it would be a mistake for practitioners to assume that most adults referred to them with ADHD symptoms will not have a history of ADHD in youth.

These concerns do not argue against the existence of adult-onset ADHD or the idea that it is a clinically relevant syndrome. In fact, as a group, the adult-onset cases showed significant functional impairment. Moreover, one of the studies ruled out the idea that adult-onset ADHD is a misdiagnosis of another disorder. Further support for the validity of adult-onset ADHD comes from a study of referred adults who retrospectively reported childhood symptoms. Based on clinical features and familial transmission, that study concluded that onset of ADHD in late adolescence and early adulthood is valid.