EDITORIAL

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[1] and the United Kingdom[2] 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[3] 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[4] 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.[3]

Related articles

In each study, the prevalence of adult-onset ADHD (Brazil, 10.3%[1]; United Kingdom, 5.5%[2]; and New Zealand, 2.7%[4]) was much larger than the prevalence of childhood-onset adult ADHD (United Kingdom, 2.6%; Brazil, 1.5%; and New Zealand, 0.3%). These estimates should be viewed with caution. The adults in the Brazil and UK studies were aged 18 to 19 years. That is too small a slice of adulthood to draw firm conclusions. Moreover, the rates of childhood-onset adult ADHD seem too low.[1] All rates are below 3.1%, which is the lower end of the 95% CI from a 10-country population study of adults.[5]

Why do the prospective studies of youth and population studies of adults disagree? One answer is the potential for recall biases in the latter studies.[6] Another reason for disagreement is noted in the Brazilian study[1]: the "false-positive paradox." This maxim states that, even when false-positive rates are low, many, or even most, diagnoses in a population study can be false. For example, if the prevalence of ADHD is 5% and the false-positive rate is 5%, then half the diagnoses in a population study will be false. The false-positive rate is sensitive to the method of diagnosis. The child diagnoses in the studies from Brazil,[1] the United Kingdom,[2] and New Zealand[4] used reports from parents and/or teachers, but the adult diagnoses were based on self-report. Self-reports of ADHD in adults are less reliable than informant reports, which is why the heritability of adult ADHD is low using self-reports but high using informant reports. In fact, the UK study found a very low heritability for adult ADHD (35%), which could be a sign of substantial measurement error and false-positive diagnoses. Of further concern, another longitudinal study[6] 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.[7] Based on clinical features and familial transmission, that study concluded that onset of ADHD in late adolescence and early adulthood is valid.[7]

The new articles proffer provocative conclusions: from Brazil,[1] that child and adult ADHD are "distinct syndromes," from the United Kingdom,[2] "that adult ADHD is more complex than a straightforward continuation of the childhood disorder," and from New Zealand,[4] that adult ADHD is "not a neurodevelopmental disorder." These conclusions seem premature. In each study, adult-onset ADHD was de novo only in the sense that full-threshold ADHD had not been diagnosed by the investigators at prior assessments. In the New Zealand study, compared with controls, the adult-onset ADHD group had more teacher-rated symptoms of ADHD, more conduct disorder in childhood and were more likely to have had a combined parent-teacher report of ADHD symptom onset prior to age 12 years. Likewise, the individuals in the adult-onset ADHD group in the UK study had significantly elevated rates of ADHD symptoms, conduct disorder, and oppositional defiant disorder in childhood. In the Brazilian study,[1] only 38% of participants with adult-onset ADHD were "neurotypical" as defined by ADHD and conduct disorder symptoms. Likewise, in a study of referred cases, one-third of late-adolescent and adult-onset cases had childhood histories of oppositional defiant disorder, conduct disorder, and school failure.[7] Thus, many of the "adult onsets" of ADHD appear to have had neurodevelopmental roots.

These neurodevelopmental roots point to another paradigm changer which, although not discussed by these investigators, can be deduced from their data: the existence of subthreshold

childhood ADHD. We know from another prospective population study[8] that subthreshold ADHD in childhood is an indicator of subsequent onset of the full-threshold disorder in adolescence. In subthreshold cases, the onset of symptoms and impairment could be separated by many years, particularly among individuals with strong intellectual abilities and those living in supportive, well-structured childhood environments. Such intellectual and social scaffolding would help youth with ADHD to compensate in early life, only to decompensate into a full ADHD syndrome when the scaffolding is removed. If we are correct, than we will improve public health by developing methods to detect subthreshold child ADHD before it emerges as adolescent- or adult-onset ADHD.

Our hypotheses about subthreshold ADHD argue against the idea that youth-onset and adult-onset are distinct syndromes. A parsimonious interpretation is that the multifactorial source of ADHD leads to wide variability in age at onset of the initial symptoms, symptoms exceeding the diagnostic threshold, and impairment arising from those symptoms. Such variability is accepted for many medical disorders. It is also consistent with the idea that ADHD is an extreme form of a dimensional trait, which is supported by twin and molecular genetic studies.[9] This view posits that symptoms and impairment emerge when the accumulation of environmental and genetic risk factors exceeds a threshold. Those with lower levels of risk at birth will take longer to accumulate sufficient risk factors and longer to develop symptoms and impairment. This multifactorial perspective allows for different risk factors to exert effects at different ages, as has been demonstrated in twin studies.[10] Yet, because these effects are multifactorial, there is no clean separation of etiologic factors in people older and younger than 18 years.

How should practitioners incorporate these new ideas about adult-onset ADHD into clinical practice? If you treat adults, recognize that adult onset of ADHD exists. Patients should not be denied services because *DSM-5* requires an earlier onset. However, document that the ADHD symptoms are impairing and are not transient effects of another disorder. Be cautious about self-reports of adult-onset ADHD unless convinced that the patients can introspect and have insight into the nature of their problems. When available, informants may clarify uncertain diagnoses. If you treat children, monitor cases of subthreshold ADHD, especially during times of transition that dismantle environmental scaffolding. In addition, prepare your ADHD patients for the transition to adulthood.

For researchers, these new data are a "call to arms" to study adult-onset ADHD, determine whether and how to incorporate age at onset into future diagnostic criteria, and clarify how it emerges from subthreshold ADHD and other neurodevelopmental anomalies in childhood. The current age-at-onset criterion for ADHD, although based on the best data available, may not be correct. We hope that future research will determine whether and how it should be modified.

ARTICLE INFORMATION

Author Affiliations: Department of Psychiatry and Behavioral Sciences, SUNY Upstate Medical University, Syracuse, New York (Faraone); K. G. Jebsen Centre for Neuropsychiatric Disorders, Department of Biomedicine, University of Bergen, Bergen, Norway (Faraone); Department of Psychiatry, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts (Biederman); Pediatric Psychopharmacology Unit, Massachusetts General Hospital, Boston, Massachusetts (Biederman).

Corresponding Author: Stephen V. Faraone, PhD, Department of Psychiatry and Behavioral Sciences, SUNY Upstate Medical University, 750 E Adams St, Syracuse, NY 13210 (sfaraone@childpsychresearch.org).

Published Online: May 18, 2016. doi:10.1001/jamapsychiatry.2016.0400.

Conflict of Interest Disclosures: In the past year, Dr Faraone received income, potential income, travel expenses, and/or research support from Rhodes, Arbor, Pfizer, Ironshore, Shire, Akili Interactive Labs, CogCubed, Alcobra, VAYA Pharma, and NeuroLifeSciences. With his institution, he has US patent US20130217707 A1 for the use of sodium-hydrogen exchange inhibitors in the treatment of attention-deficit/hyperactivity disorder (ADHD). In previous years, he received income or research support from Shire, Alcobra, Otsuka, McNeil, Janssen, Novartis, Pfizer, and Eli Lilly. Dr Faraone receives royalties from books. Dr Faraone is also supported by the K. G. Jebsen Centre for Research on Neuropsychiatric Disorders, University of Bergen, Bergen, Norway, the European Union's Seventh Framework Programme for research, technological development, and the National Institute of Mental Health. Dr Biederman reported receiving research support from the AACAP, Alcobra, APSARD, ElMindA, Forest Research Institute, Ironshore, Lundbeck, Magceutics Inc, McNeil, Merck, the National Institutes of Health, Neurocentria Inc, PamLab, Pfizer, Shire Pharmaceuticals Inc, SPRITES, Sunovion, the US Department of Defense, the US Food & Drug Administration, and Vaya Pharma/Enzymotec; honoraria from the Massachusetts General Hospital (MGH) Psychiatry Academy for tuition-funded continuing medical education (CME) courses and Alcobra and American Academy of Child and Adolescent Psychiatry; and departmental royalties from a copyrighted rating scale used for ADHD diagnoses, paid by Ingenix, Prophase, Shire, Bracket Global, Sunovion, and Theravance; these royalties were paid to the Department of Psychiatry at MGH. Dr Biederman also has a US patent application pending (provisional No. 61/233,686) through MGH corporate licensing on a method to prevent stimulant abuse. No other disclosures were reported.

REFERENCES

1. Caye A, Rocha TB-M, Anselmi L, et al. Attention-deficit/hyperactivity disorder trajectories from childhood to young adulthood: evidence from a birth cohort supporting a late-onset syndrome [published online May 18, 2016]. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2016.0383.

2. Agnew-Blais JC, Polanczyk GV, Danese A, Wertz J, Moffitt TE, Arseneault L. Evaluation of the persistence, remission, and emergence of attention-deficit/hyperactivity disorder in young adulthood [published online May 18, 2016]. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2016.0465.

3. Faraone SV, Biederman J, Mick E. The age-dependent decline of attention deficit hyperactivity disorder: a meta-analysis of follow-up studies. *Psychol Med*. 2006;36(2):159-165.

4. Moffitt TE, Houts R, Asherson P, et al. Is adult ADHD a childhood-onset neurodevelopmental disorder? evidence from a four-decade longitudinal cohort study. *Am J Psychiatry*. 2015;172(10):967-977.

5. Fayyad J, De Graaf R, Kessler R, et al. Cross-national prevalence and correlates of adult attention-deficit hyperactivity disorder. *Br J Psychiatry*. 2007;190:402-409.

6. Sibley MH, Pelham WE, Molina BS, et al. When diagnosing ADHD in young adults emphasize informant reports, *DSM* items, and impairment. *J Consult Clin Psychol*. 2012;80(6):1052-1061.

7. Chandra S, Biederman J, Faraone SV. Assessing the validity of the age at onset criterion for diagnosing ADHD in *DSM-5* [published online February 27, 2016]. *J Atten Disord*.

8. Lecendreux M, Konofal E, Cortese S, Faraone SV. A 4-year follow-up of attention-deficit/hyperactivity disorder in a population sample. *J Clin Psychiatry*. 2015;76(6):712-719.

9. Larsson H, Anckarsater H, Råstam M, Chang Z, Lichtenstein P. Childhood attention-deficit hyperactivity disorder as an extreme of a continuous trait: a quantitative genetic study of 8,500 twin pairs. *J Child Psychol Psychiatry*. 2012;53(1):73-80.

10. Chang Z, Lichtenstein P, Asherson PJ, Larsson H. Developmental twin study of attention problems: high heritabilities throughout development. *JAMA Psychiatry*. 2013;70(3):311-318.