nonsubstance addictions (e.g., pornography, gambling). Ruling out these non-ADHD symptom causes is more relevant in adulthood than childhood. Most of these alternative sources of cognitive impairment are unlikely to occur in children.

DSM-5 does not provide explicit instructions about what sources of cognitive dysfunction represent valid cases of ADHD. However, we agree that diagnosticians should anchor themselves to the conceptualization of ADHD as a chronic neurodevelopmental disorder; when symptom chronicity cannot be traced to childhood, the emergent ADHD symptoms must be scrutinized carefully. Clinicians should conduct a functional analysis in search of discrete environmental or biological antecedents to symptom onset.

Margaret H. Sibley, Ph.D.
L. Eugene Arnold, M.D.
James M. Swanson, Ph.D.
Traci M. Kennedy, Ph.D.
Brooke S.G. Molina, Ph.D.
Lily T. Hechtman, M.D.
Arunima Roy, Ph.D.
John T. Mitchell, Ph.D.

From the Department of Psychiatry and Behavioral Health, Florida International University, Miami; the Child Development Center, School of Medicine, University of California, Irvine; the Division of Child Psychiatry, McGill University, Montreal Children's Hospital, Montreal, Quebec, Canada; the Departments of Psychiatry and Psychology, University of Pittsburgh School of Medicine, Pittsburgh; the Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, N.C.; the Department of Psychiatry, Ohio State University, Nisonger Center, Columbus, Ohio; and the Division of Molecular Psychiatry, University Hospital Wuerzberg, Germany.

Address correspondence to Dr. Sibley (msibley@fiu.edu).

The authors' disclosures accompany the original article.

This reply was accepted for publication in February 2018.

Am J Psychiatry 2018; 175:480–481; doi: 10.1176/appi.ajp.2018.17121308r

Late-Onset ADHD: Case Closed or Open Question?

TO THE EDITOR: The article by Sibley et al. (1), published in the February 2018 issue of the *Journal*, investigated the validity of late-onset attention deficit hyperactivity disorder (ADHD). The study examined whether control participants in the Multimodal Treatment Study of Children with ADHD (MTA) developed ADHD after childhood. Among those with elevated ADHD symptoms postchildhood, a large proportion did not meet diagnostic criteria after a stepped diagnostic procedure applied to data collected during frequent assessments across childhood, adolescence, and young adulthood.

Do these findings mean the case is closed on late-onset ADHD? How do we reconcile these results with three population-based studies (2–4) that found a majority of adult ADHD cases had onset after childhood?

The conclusions of Sibley et al. have been taken by many to refute the concept of late-onset ADHD. However, while the generalizability of the findings is somewhat limited—the study population had above-average family income and was 80% male (late-onset ADHD is more common among women [3, 4])—even after the multistep diagnostic procedure, 3.3% were found to have late-onset ADHD. Excluding those whose ADHD remitted before age 20, this proportion is 1.7%. Although we cannot directly extrapolate to the proportion of the general adult ADHD population (prevalence estimated at 4.4% [5]) who may have late-onset ADHD, these results point to some children without ADHD developing the disorder later in life.

The study concludes that many late-onset cases are attributable to other mental health disorders or substance use. However, it is well established that ADHD is often comorbid with other disorders (5). Untreated ADHD can increase risk for poor mental health, and individuals with ADHD may self-medicate with drugs or alcohol. It can be difficult to disentangle whether ADHD symptoms cause or result from substance use or other mental health problems, especially when they occur concurrently. Previous studies from population-based cohorts investigated this issue by excluding from the late-onset group anyone with other comorbidities, and the studies found 33%−55% of the late-onset group remained (2–4). Research is needed to clarify the nature of the associations between ADHD symptoms and other disorders.

The importance placed on the origins of ADHD symptoms points to broader considerations related to diagnostic boundaries and the role of etiology in psychiatric nosology. Expanding from the discussion of differential diagnosis, as outlined by Caye et al. (6), we can consider the more general question of what valid exclusions for an ADHD diagnosis are. For example, if ADHD symptoms are caused by prolonged substance abuse or other adversity resulting in long-term damage to the brain, should this be considered ADHD? Whether we understand ADHD as a "complex phenotype" encompassing a range of possible etiologies or a "restricted phenotype" in which only certain underlying causes produce a "valid" diagnosis remains an important theoretical question with many practical implications.

All studies that examined late-onset ADHD have identified cases, albeit representing different proportions of each study population. More work needs to be done to reconcile these findings. The MTA and epidemiologic studies concur that this late-onset group experiences distress, impairment, and poor functioning and may require clinical attention. Crucial questions remain about late-onset ADHD and ADHD over the life course.

REFERENCES

1. Sibley MH, Rohde LA, Swanson JM, et al: Late-onset ADHD reconsidered with comprehensive repeated assessments between ages 10 and 25. Am J Psychiatry 2018; 175:140–149
2. 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; 172:967–977
3. Agnew-Blais JC, Polanczyk GV, Danese A, et al: Evaluation of the persistence, remission, and emergence of attention-deficit/hyperactivity disorder in young adulthood. JAMA Psychiatry 2016; 73:713–720
4. Caye A, Rocha TB, Anselmi L, et al: Attention-deficit/hyperactivity disorder trajectories from childhood to young adulthood: evidence from a birth cohort supporting a late-onset syndrome. JAMA Psychiatry 2016; 73:705–712

5. Kessler RC, Adler LA, Barkley R, et al: Patterns and predictors of attention-deficit/hyperactivity disorder persistence into adulthood: results from the national comorbidity survey replication. Biol Psychiatry 2005; 57:1442–1451
6. Caye A, Sibley MH, Swanson JM, et al: Late-onset ADHD: understanding the evidence and building theoretical frameworks. Curr Psychiatry Rep 2017; 19:106

Jessica Agnew-Blais, Sc.D.
Louise Arseneault, Ph.D.

From the Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, London.

Address correspondence to Dr. Agnew-Blais (jessica.agnew-blais@kcl.ac.uk).

Dr. Agnew-Blais has received fellowship funding from the Medical Research Council (MR/P014100/1). Dr. Arseneault is the ESRC Mental Health Leadership Fellow.

The authors report no financial relationships with commercial interests.

This letter was accepted for publication in February 2018.

Am J Psychiatry 2018; 175:481–482; doi: 10.1176/appi.ajp.2018.17111240

Addressing Incomplete Psychiatric Histories in Adult ADHD: Response to Agnew-Blais and Arseneault

TO THE EDITOR: We thank Drs. Agnew-Blais and Arseneault for raising points that seem to require clarification in the results of our article reconsidering adult-onset attention deficit hyperactivity disorder (ADHD), based on longitudinal data from the Multimodal Treatment Study of Children with ADHD (MTA). Based on our findings, as well as the findings of recent epidemiological studies, we agree that late-onset ADHD-like symptoms may first emerge after age 12, the age of onset specified in DSM-5. However, our data suggest the need for caution when drawing conclusions about the scope, timing, and cause of this phenomenon.

First, as Drs. Agnew-Blais and Arseneault indicate, the MTA local normative comparison group should not be used to firmly estimate the proportion of adult ADHD cases with a late-onset presentation. The sampling of the local normative comparison group was designed to demographically match the MTA childhood ADHD sample rather than create a representation of the general population. However, the original MTA sample had been deliberately recruited from multiple sources (schools, advertising, self-help organizations, as well as clinics) to promote generalizability, and the full socioeconomic spectrum was spanned. The purpose of our study was to understand what type of correction might be placed on the epidemiological prevalence rates to account for incomplete psychiatric histories in those studies (i.e., long periods of time with unmeasured symptom levels, incomplete childhood ADHD, and adult mental health and substance use histories). Our conclusion was that 53%−83% of cases that initially met symptom, impairment, pervasiveness, and chronicity criteria for late-onset ADHD were eventually excluded from diagnosis when fuller psychiatric histories were considered. Fewer than 1% met the actual criteria for adult-onset ADHD.

Second, it is important to note that the most common "late-onset" presentation in our MTA article was adolescent-onset symptoms that remitted by adulthood. The 3.3% MTA late-onset prevalence rate cited by Agnew-Blais and Arseneault is largely carried by these four cases. Two other adolescent-onset cases were determined to be late-identified, rather than late-onset. We detected only two adult-onset ADHD cases, and both had complex psychiatric histories. These cases represented less than 1% of the local normative comparison group.

Agnew-Blais and Arseneault express concern that the MTA was quick to dismiss cases with comorbidity from late-onset consideration. However, the comorbidity and substance use rule-outs in the MTA were applied very conservatively. As outlined in the data supplement that accompanies the online edition of our article, we conducted detailed case reviews by licensed psychiatrists and psychologists and required evidence that comorbidity or substance abuse was the most likely cause of ADHD symptoms (that symptoms were present only during the comorbidity or substance abuse), as specified by the fifth DSM-5 criterion. In the data supplement, readers can view each individual case's symptom profile and history to form their own conclusions in this debate.

Our suggested methodological correction would rule out approximately 80% of presumed adult-onset cases in the epidemiological studies. Agnew-Blais and Arseneault refer to Caye et al.'s comparison between the complex and the restricted phenotype paradigm for ADHD. In line with this paradigm (note that the authorship overlaps with our article), we agree that an important next step for the field is determining what symptom etiologies are deserving of an ADHD diagnosis. We must also anticipate the consequences of these decisions, which could include a different label for the symptom and impairment clusters. These questions are particularly relevant to adult ADHD because adults have had longer life histories to acquire biological and environmental experiences (i.e., illness, injury, deprivation, trauma, chemical side effects, stress response) that impair cognitive domains traditionally associated with ADHD (i.e., executive functions, attention, memory). As research progresses in this field, revisiting the adult ADHD diagnostic criteria may be necessary.

Margaret H. Sibley, Ph.D.
L. Eugene Arnold, M.D.
James M. Swanson, Ph.D.
Traci M. Kennedy, Ph.D.
Brooke S.G. Molina, Ph.D.
Lily T. Hechtman, M.D.
Arunima Roy, Ph.D.
John T. Mitchell, Ph.D.

From the Department of Psychiatry and Behavioral Health, Florida International University, Miami; the Child Development Center, School of Medicine, University of California, Irvine; the Division of Child Psychiatry, McGill University, Montreal Children's Hospital, Montreal, Quebec, Canada; the Departments of Psychiatry and Psychology, University of Pittsburgh School of Medicine, Pittsburgh; the Department of Psychiatry and Behavioral Sciences, Duke