

An Association Between Prenatal Acetaminophen Use and ADHD: The Benefits of Large Data Sets

Mark L. Wolraich, MD

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent disorder defined by a combination of symptoms that are likely due to malfunctions in those areas of the brain that are associated with executive functions, including the prefrontal cortex,¹ caudate nucleus,² and cerebellar vermis.³ Over the years, multiple factors have been identified that probably contribute to its possible etiology. The most prominent has been genetics; ADHD is often identified by a high familial pattern with a high concordance in twin studies.⁴ However, no specific gene, gene pattern, or marker gene has been able to explain all but a small amount of the variance. In addition, environmental factors both pre- and postnatally (including prenatal alcohol⁵ and smoking exposure⁶ and postnatal head injuries⁷) have been found to increase the risk of its presence. There is also a great deal of variation in the presentation of the disorder, with 3 subtypes, and even within the subtypes, there are 9 described behaviors in each of the behavioral dimensions that also vary greatly in how they are expressed in any person with the condition. Although both medications and behavioral interventions have demonstrated strong evidence of efficacy, they also have varying effects on patients.

With so many factors contributing to the condition, it becomes difficult to further identify any additional contributing factors with any certainty. The techniques employed by Ystrom

et al⁸ in their article “Prenatal exposure to acetaminophen and Risk of ADHD” demonstrate how it is possible to more specifically examine the possible association between prenatal exposure to acetaminophen and ADHD. They were able to use statistical techniques that required a large number of individuals with the condition. Obtaining such a large data set is expensive but easier to obtain through large health care systems in countries with central health care systems and in the United States in large academic centers or large health care organizations. The authors are careful to point out that their results from a relational study cannot establish a causal relationship between prenatal acetaminophen exposures and ADHD in the offspring, but they do suggest the possibility and raise the need for further study and more cautious consideration of acetaminophen use during pregnancy.

The possibility of a causal relationship brings to mind the association between aspirin and Reye syndrome. Establishing causal relationships ultimately led to a marked decrease in a syndrome that caused significant morbidity and mortality. Although the comparisons are far from perfect given the serious morbidity and risk of mortality associated with Reye syndrome, it does illustrate how finding associations between drug and disease can improve health outcomes. It is important to pursue further research on the possible drug associations with the development

FREE

Shaun Walters Professor of Pediatrics and Edith Kinney-Gaylord Presidential Professor, Child Study Center, University of Oklahoma, Oklahoma City, Oklahoma

Opinions expressed in these commentaries are those of the authors and not necessarily those of the American Academy of Pediatrics or its Committees.

DOI: <https://doi.org/10.1542/peds.2017-2703>

Accepted for publication Aug 10, 2017

Address correspondence to Mark L. Wolraich, MD, Pediatrics/CSC, University of Oklahoma Health Sciences Center, 1100 NE 13th St, Oklahoma City, OK 73117. E-mail: mark-wolraich@ouhsc.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2017 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to the article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2016-3840.

To cite: Wolraich ML. An Association Between Prenatal Acetaminophen Use and ADHD: The Benefits of Large Data Sets. *Pediatrics*. 2017;140(6):e20172703

of ADHD, and that research will require longitudinal follow-up of large numbers of children with and without ADHD.

ABBREVIATION

ADHD: attention-deficit/hyperactivity disorder

REFERENCES

1. Seidman LJ, Valera EM, Makris N. Structural brain imaging of attention-deficit/hyperactivity disorder. *Biol Psychiatry*. 2005;57(11):1263–1272
2. Hynd GW, Hern KL, Novey ES, et al. Attention deficit-hyperactivity disorder and asymmetry of the caudate nucleus. *J Child Neurol*. 1993;8(4):339–347
3. Berquin PC, Giedd JN, Jacobsen LK, et al. Cerebellum in attention-deficit hyperactivity disorder: a morphometric MRI study. *Neurology*. 1998;50(4):1087–1093
4. Larsson H, Chang Z, D’Onofrio BM, Lichtenstein P. The heritability of clinically diagnosed attention deficit hyperactivity disorder across the lifespan. *Psychol Med*. 2014;44(10):2223–2229
5. O’Malley KD, Nanson J. Clinical implications of a link between fetal alcohol spectrum disorder and attention-deficit hyperactivity disorder. *Can J Psychiatry*. 2002;47(4):349–354
6. Milberger S, Biederman J, Faraone SV, Chen L, Jones J. Is maternal smoking during pregnancy a risk factor for attention deficit hyperactivity disorder in children? *Am J Psychiatry*. 1996;153(9):1138–1142
7. Königs M, Heij HA, van der Sluijs JA, et al. Pediatric traumatic brain injury and attention deficit. *Pediatrics*. 2015;136(3):534–541
8. Ystrom E, Gustavson K, Knudsen PG, et al. Prenatal exposure to acetaminophen and risk of ADHD. *Pediatrics*. 140(5):20163840

An Association Between Prenatal Acetaminophen Use and ADHD: The Benefits of Large Data Sets

Mark L. Wolraich

Pediatrics 2017;140;

DOI: 10.1542/peds.2017-2703 originally published online October 30, 2017;

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/140/5/e20172703
References	This article cites 7 articles, 2 of which you can access for free at: http://pediatrics.aappublications.org/content/140/5/e20172703.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Current Policy http://classic.pediatrics.aappublications.org/cgi/collection/current_policy Developmental/Behavioral Pediatrics http://classic.pediatrics.aappublications.org/cgi/collection/development:behavioral_issues_sub Attention-Deficit/Hyperactivity Disorder (ADHD) http://classic.pediatrics.aappublications.org/cgi/collection/attention-deficit:hyperactivity_disorder_adhd_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: https://shop.aap.org/licensing-permissions/
Reprints	Information about ordering reprints can be found online: http://classic.pediatrics.aappublications.org/content/reprints

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

An Association Between Prenatal Acetaminophen Use and ADHD: The Benefits of Large Data Sets

Mark L. Wolraich

Pediatrics 2017;140;

DOI: 10.1542/peds.2017-2703 originally published online October 30, 2017;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/140/5/e20172703>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since . Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2017 by the American Academy of Pediatrics. All rights reserved. Print ISSN:

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

