

**Team ADHD Faculty  
Featured this Issue:**



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Dr. Mattingly has been a principal investigator in over 200 clinical trials focusing on ADHD, anxiety disorders, major depression, bipolar disorder, and schizophrenia, and has received numerous awards and distinctions for clinical leadership and neuroscience research. Dr. Mattingly currently serves on the board of directors for the American Professional Society of ADHD and Related Disorders.

**HIGHLIGHTS FROM A RECENT ADHD PRESENTATION BY DR. GREG MATTINGLY**

*Sponsored by Supernus*

The prevalence of ADHD in children and adolescents in the United States and around the world is around **9% to 11%** and we know that about **4% to 5%** of adults will continue to have ADHD. So, it starts in childhood and tends to persist into adulthood for the majority of our patients. We used to think of ADHD being a disorder of boys. We now know that in children and adolescents, it's about twice as common in boys as girls. In adults, it is equally common in men and women.

**ADHD and Activity of Daily Living**

ADHD isn't just a set of symptoms, but symptoms that dramatically impair the lives of our patients across numerous domains of normal daily living. For the child, impairment is not only seen at school, but also in forming peer relationships and getting along with their family. Adolescents will continue to have academic challenges in their college years and begin to experience substance diversion and misuse. As they move away from home for college or independent living, inability to cope with routine tasks may become evident. Our ADHD patients have higher rates of car and occupational accidents, legal problems, unwanted pregnancies, comorbid psychiatric conditions, substance abuse, and financial and marital issues.

**ADHD and Comorbidity**

The majority of our patients with ADHD don't just have ADHD and nothing else, but frequently have ADHD comorbid with other psychiatric conditions—**anxiety, tics, behavior disorders, mood disorders, and substance use disorders.** In fact, comorbidity in ADHD is the rule rather than the exception.

**ADHD and Mortality**

ADHD also imparts a higher mortality rate. Studies show up to a 3-times higher risk for premature death and up to a 4-times greater risk for death from all causes in those with ADHD compared to individuals without ADHD, often due to accidents and trauma, comorbid psychiatric disorders, and suicide. Of note, the risk for death significantly increased when ADHD was diagnosed at or after age 18. Also, among individuals with ADHD who died, 82% were a result of unintentional injury or suicide.

**The New Approach to ADHD**

There is a new approach to the treatment of ADHD that is comorbid with select psychiatric disorders. The old approach was to treat the most serious disorder first. ADHD was often considered a secondary condition and maybe not as impairing. Now, the new approach is to treat ADHD aggressively and appropriately—**treat ADHD and other select psychiatric conditions at the same time, leading to a customized holistic model for treatment.**

**Hot Topics  
in ADHD**

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**To learn more about complex ADHD  
please visit [TEAM-ADHD.com/Updates](http://TEAM-ADHD.com/Updates)**

# Hot Topics in ADHD

This issue's Hot Topics are provided by Greg Mattingly, MD, Associate Clinical Professor, Department of Psychiatry, Washington University School of Medicine.

## #1: New Findings In ADHD Neural Connectivity

- f-MRI scans of adults with ADHD show increased functional connectivity in sensory regions but decreased connectivity in higher order cognitive connections
- Increased sensory connectivity may explain sensory overload and distractibility in adults with ADHD
- Greater ADHD severity was associated with lower connectivity in cognitive regions

### Stepwise Functional Connectivity Reveals Altered Sensory Multimodal Integration In Medication-Naïve Adults With Attention Deficit Hyperactivity Disorder

Pretus C, Marco-Vidal L, Martínez-García M, et al.

**ABSTRACT:** – To access article in full go to: <https://onlinelibrary.wiley.com/doi/abs/10.1002/hbm.24727>

Neuroimaging studies indicate that children with attention-deficit/hyperactivity disorder (ADHD) present alterations in several functional networks of the sensation-to-cognition spectrum. These alterations include functional overconnectivity within sensory regions and underconnectivity between sensory regions and neural hubs supporting higher order cognitive functions. Today, it is unknown whether this same pattern of alterations persists in adult patients with ADHD who had never been medicated for their condition. The aim of the present study was to assess whether medication-naïve adults with ADHD presented alterations in functional networks of the sensation-to-cognition spectrum. Thirty-one medication-naïve adults with ADHD and 22 healthy adults underwent resting-state functional magnetic resonance imaging (rs-fMRI). Stepwise functional connectivity (SFC) was used to characterize the pattern of functional connectivity between sensory seed regions and the rest of the brain at direct, short, intermediate, and long functional connectivity distances, thus covering the continuum from the sensory input to the neural hubs supporting higher order cognitive functions. Compared to controls, adults with ADHD presented increased SFC degree within primary sensory regions and decreased SFC degree between sensory seeds and higher order integration nodes. In addition, they exhibited decreased connectivity degree between sensory seeds and regions of the default-mode network. Consistently, the higher the score in clinical severity scales the lower connectivity degree between seed regions and the default mode network.

## #2: Mortality Rates Dramatically Increase With ADHD Comorbidity

- A nationwide study published in *JAMA* found significantly higher mortality rates in children and adults with ADHD
- Mortality rates increased with each additional psychiatric comorbidity: Hazard Ratio (HR) =1.56 for no comorbidities, HR=4.21 for 1 comorbidity, HR=8.57 for 2 comorbidities and HR=29.29 for 4 or more comorbidities
- Increased causes of mortality included accidental injury, suicide, and natural causes

### Association of Psychiatric Comorbidity With the Risk of Premature Death Among Children And Adults With Attention-Deficit/Hyperactivity Disorder

Sun S, Kuja-Halkola R, Faraone SV, et al.

**ABSTRACT:** – To access article in full go to: <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2739304>

In this nationwide cohort of 2,675,615 individuals: 1,374,790 (51.4%) were male (57,919 with an ADHD diagnosis) and 1,300,825 (48.6%) were female (28,751 with an ADHD diagnosis). Mean (SD) age at study entry was 6.4 (5.6) years. During follow-up, 424 individuals with ADHD and 6,231 without ADHD died, resulting in mortality rates of 11.57 and 2.16 per 10,000 person-years, respectively. The association was stronger in adulthood (HR, 4.64; 95% CI, 4.11-5.25) compared with childhood (HR, 1.41; 95% CI, 0.97-2.04) and increased substantially with the number of psychiatric comorbidities with ADHD (HR for individuals with only ADHD, 1.41 [95% CI, 1.01-1.97]; HR for those with  $\geq 4$  comorbidities, 25.22 [95% CI, 19.60-32.46]).

# Hot Topics in ADHD

## #3: How Many ADHD Patients Do You Have To Treat To Prevent A Negative Life Event?


- Dr Biederman et al. used data from several prospective trials to evaluate if ADHD treatment prevented negative life outcomes
- Number needed to treat (NNT) evaluates how many patients would need to be treated “N” to prevent “X”
- NNT was:
  - 3 to prevent an anxiety disorder, 3 to prevent a case of ODD, and 3 to prevent a child from repeating a grade
  - 4 to prevent a major depressive disorder or to prevent a motor vehicle collision
  - 5 to prevent a case of bipolar disorders
  - 10 to prevent a case of substance abuse

### Quantifying the Protective Effects of Stimulants on Functional Outcomes in Attention-Deficit/Hyperactivity Disorder: A Focus on Number Needed to Treat Statistic And Sex Effects

*Joseph Biederman, Maura DiSalvo, et al.*

**ABSTRACT:** — To access article in full go to: [https://www.jahonline.org/article/S1054-139X\(19\)30305-2/fulltext](https://www.jahonline.org/article/S1054-139X(19)30305-2/fulltext)

Aim of the study was to help quantify the protective effects of stimulant treatment on important functional outcomes in ADHD using the NNT statistic and examine whether these effects are moderated by sex. Subjects were derived from 3 independent samples, 2 similarly designed case control, 10-year prospective follow-up studies of boys and girls with and without ADHD grown up and a cross-sectional randomized clinical trial of lisdexamfetamine on driving performance and behavior. For all studies, subjects were evaluated with structured diagnostic interviews. To measure psychopharmacologic treatment in the follow-up studies, information about each subject’s stimulant medication use, age at onset, and age at termination of treatment was collected. Subjects in the driving study underwent 2 driving simulation assessments (premedication and after 6 weeks of treatment on lisdexamfetamine or placebo). For each outcome, the authors ran a logistic regression model that included an interaction between sex and treatment status. Lifetime rates were used to calculate the NNT statistic. The authors also calculated adjusted NNT statistics that accounted for sex, age, socioeconomic status, and family intactness.



# ADHD Patient Resource Corner

To download these resources or provide support for your patients interested in learning more about ADHD, go to: [MoreToADHD.com](http://MoreToADHD.com)



**Talking to Teachers**  
Tips for a successful school year, and questions to help guide discussions with a child's teacher.



**IEPs and Section 504 Plans**  
This chart compares the main points of each plan side by side, to help parents understand the differences.



To learn more about complex ADHD please visit [TEAM-ADHD.com/Updates](http://TEAM-ADHD.com/Updates)

## References

Fayyad J, et al. *Atten Defic Hyperact Disord.* 2017;9(1):47-65.  
 Visser SN, et al. *J Am Acad Child Adolesc Psychiatry.* 2014;53(1):34-46.  
 Merikangas KR, et al. *J Am Acad Child Adolesc Psychiatry.* 2010;49(10):980-989.  
 Kessler RC, et al. *Am J Psychiatry.* 2006;163(4):716-723.  
 Faraone SV, et al. *Nat Rev Dis Primers.* 2015;1:15020.  
 Banaschewski T, et al. *Dtsch Arztebl Int.* 2017;114(9):149-159.  
 MTA Cooperative Group. *Arch Gen Psychiatry.* 1999;56(12):1073-1086.  
 Jensen CM, Steinhausen HC. *Atten Defic Hyperact Disord.* 2015;7(1):27-38.  
 Caye A, et al. *JAMA Psych.* 2016;73(7):705-712.  
 Clemow DB, et al. *Neuropsychiatr Dis Treat.* 2017;13:357-371.  
 Dalsgaard S, et al. *Lancet Psychiatry.* 2015;2(8):702-709.  
 Chien WC, et al. *Res Dev Disabil.* 2017;65:57-73.  
 Mattingly GW, *CNS Spectr.* 2016;21(S1):45-59.  
 Mattingly GW, et al. *Postgrad Med.* 2017;129(7):657-666.  
 Dalsgaard S, et al. *Lancet.* 2015;385(9983):2190-2196.  
 London AS, Landes SD. *Prev Med.* 2016;90:8-10.  
 Sun S et al. *JAMA Psychiatry.* 2019 Aug 7. doi: 10.1001.



**October is ADHD Awareness Month**