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## Young Children Repeatedly Exposed to Anesthesia Are at Increased Risk for ADHD

Results from a recent study support the hypothesis that children repeatedly exposed to procedures requiring general anesthesia before age 2 years are at increased risk for the later development of attention-deficit/hyperactivity disorder (ADHD). Single exposures were not associated with increased risk. These results extend similar findings from a previous study that indicated the same correlation to learning disabilities (LDs).

In 2011, a multidisciplinary research team from the departments of Anesthesiology, Bioinformatics, Epidemiology, and Psychiatry and Psychology at Mayo Clinic in Rochester, Minnesota, used the existence of LDs to study the association between exposure to procedures performed under general anesthesia before age 2 years and development of LDs before age 19 years. They found that multiple exposures were associated with a 2-fold increase in the incidence of LDs in a population-based birth cohort.

### ADHD Study Extends LD Findings

Results of a 2012 study of the same cohort indicated that repeated exposure to procedures requiring general anesthesia before age 2 years was also associated with increased risk for later development of ADHD. That result extended similar findings of the same cohort from group-administered tests of cognition and achievement and pointed to defects in aspects of executive functioning as a potential phenotype of injury associated with procedures requiring anesthesia.

Many children with ADHD also have LDs. In this study's cohort, estimates of the propor-

tion of children with ADHD who also meet LD criteria ranged from 10% to more than 90%. Of the 5,357 children analyzed, the following results were found:

- 932 (17.4%) had a diagnosis of LD before age 19 years
- 341 (6.4%) had a diagnosis of ADHD
- 240 (4.5%) had a diagnosis of LD and ADHD

### Causative Mechanisms

Evidence suggests that health-altering insults before and after birth, including stress and inflammatory responses to surgery, may be associated with later adverse neurocognitive outcomes. In addition, anesthesia itself modulates these responses.

Family, twin, and adoption studies suggest that a genetic component and environmental factors are also associated with ADHD, indicating that gene-environment interactions are operative in this condition. Implicated environmental factors include maternal smoking, prenatal alcohol exposure, viral infections, nutritional deficiencies, low parental education level, and perinatal stress.



Robert C. Colligan, PhD, LP

### New Research

"These provocative findings stirred up interest in the anesthesiology literature," says Robert C. Colligan, PhD, LP, with the Department of Psychiatry and Psychology at Mayo Clinic in

Minnesota. "The results were also the impetus for developing a new National Institutes of Health proposal for a 5-year follow-up anesthesia study." The new project begins in November 2012. All participants will be children and adolescents with various exposures to anesthesia. They will be asked to complete a neuropsychological assessment battery measuring cognitive abilities, memory, executive functions, and academic achievement. They will also be described by their parents using behavior checklists.

The same multidisciplinary research team remains involved in this study, with the addition of Michael J. Zaccariello, PhD, LP, a pediatric neuropsychologist who helped to design and will supervise the follow-up assessments. "A truly novel part of the evaluation will employ a computer-administered set of tasks that has been

applied to primates and humans in studies at the Neurotoxicology Research Center in Arkansas, in conjunction with the Food and Drug Administration," says Dr Colligan.

#### For more information

"Attention-Deficit/Hyperactivity Disorder After Early Exposure to Procedures Requiring General Anesthesia" was published in *Mayo Clinic Proceedings*. 2012 Feb;87(2):120-9. Watch David O. Warner, MD, discuss this article on YouTube at [www.Youtube.com/watch?v=7dR50tx1MAg](http://www.Youtube.com/watch?v=7dR50tx1MAg).

"Cognitive and Behavioral Outcomes After Early Exposure to Anesthesia and Surgery" was published in *Pediatrics*. 2011 Nov;128(5):e1053-61. Epub 2011 Oct 3. Erratum in: *Pediatrics*. 2012 Mar;129(3):595.

## Chair's Corner: National Alzheimer's Plan Expands Investment in Translational Research

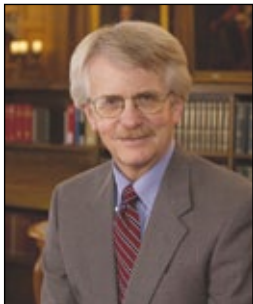


Mark A. Frye, MD

Alzheimer's disease (AD) is now the sixth leading cause of death in the United States. More than 5 million people in the United States have AD, a number certain to increase as baby boomers reach retirement age.

In January 2011, President Barack Obama signed the National Alzheimer's Project Act into law. It set a goal of finding new treatments, prevention programs, and training for physicians by 2025. The plan requires the following outcomes:

- Creation of an integrated national plan to overcome AD
- Coordination of AD research and services across federal agencies
- Development of treatments to prevent, halt, or reverse the course of AD
- Improved early diagnosis and coordination of care and treatment for people with AD
- Improved outcomes for ethnic and racial minority groups that are at higher risk for AD
- Coordination with international organizations to fight AD



Ronald C. Petersen, MD, PhD

Ronald C. Petersen, MD, PhD, with the Department of Psychiatry and Psychology at Mayo Clinic in Rochester, Minnesota, was chair of the Advisory Council on Alzheimer's Research, Care, and Services, which was charged with developing the plan.

The Obama Administration announced a \$156 million investment in support of the plan in February 2012. It provided \$26 million for improved data funding and analysis immediately and will also sustain and grow investment in AD research over time. The funding also supports geriatric education centers around the

country whose purpose is to develop curricula and free training on AD and dementia for health professionals.

"The National Alzheimer's Plan provides both direction and funding to expand research into prevention and treatment," says Mark A. Frye, MD, chair of the Department of Psychiatry and Psychology. "It helps us accelerate the movement of promising drugs into clinical trials and the translation of best practices from research to patient care."

#### New Diagnosis Guidelines

Mayo Clinic researchers worked with the National Institute on Aging and the Alzheimer's Association in April 2012 to develop and publish new guidelines for the diagnosis of Alzheimer's disease (AD). These guidelines separate the progression of AD into 3 stages: preclinical (or presymptomatic) AD, mild cognitive impairment (MCI) due to AD, and AD dementia.

Glenn E. Smith, PhD, LP, a consultant in the Department of Psychiatry and Psychology at Mayo Clinic in Minnesota, discussed the positive impact of the new guidelines in a June 2012 interview with the American Psychological Association (APA).

"Outcomes of clinical trials with medications for treating AD have been disappointing. Historically, they've involved patients with dementia, because the presence of dementia was required for the diagnosis of AD. There is a growing concern that by the time dementia is present, the brain may be so ravaged that medications cannot be effective," says Dr Smith.

## Secondary Prevention Strategies

Because substantial progress has been made in the ability to detect AD before dementia is present, “we can now reliably diagnose MCI and so can introduce secondary prevention strategies that seek to prevent or delay progression to full dementia,” says Dr Smith.

Various behavioral treatments show promise as secondary prevention strategies. Physical and mental inactivity, smoking, obesity, diabetes mellitus, hypertension, and depression—each modifiable with behavioral intervention—have been shown to be risk factors for the development of AD. Barnes and Yaffee (*Lancet Neurology*, 2011 Sep;10[9]:818-28) suggest that a 10% to 25% improvement in these 7 conditions among the general population would prevent as many as 16.5% of AD cases in the United States.

“At Mayo Clinic, we have launched an intensive multicomponent intervention that combines daily physical activity, cognitive exercise, a memory compensation strategy, wellness education, and support groups. This

intervention produces short-term improvement and longer-term stabilization of a patient’s ability to function,” says Dr Smith.

## The Role of Psychologists

“Psychologists, especially those who specialize in aging or cognition science, are particularly well positioned to recognize, formally assess, and explain the implications of cognitive changes associated with the diagnosis of MCI,” says Dr Frye. “And as more people find themselves in the role of caregiver for a family member with Alzheimer’s, psychologists are responding by developing state-of-the-art interventions to enhance caregiver resilience.”

## For more information

Alzheimer’s Disease Clinical Trials at Mayo Clinic. National Plan to Address Alzheimer’s Disease Expert Offers Insight on Alzheimer’s Causes, Prevention, Diagnosis, and Treatment. APA Newswise, June 20, 2012.



Glenn E. Smith, PhD, LP

## Prazosin Can be Effective in the Treatment of PTSD-Related Nightmares

A systematic literature review of the use of prazosin in the treatment of nightmares related to posttraumatic stress disorder (PTSD) indicates that the drug is well tolerated and can take effect within days or weeks.

For people who have PTSD, one of the most distressing effects is the experience of nightmares, the kinds of dreams that ruin sleep with extremely frightening images of physical or emotional threats. Nightmares can be so profoundly disturbing that they contribute to alcoholism, substance abuse, and suicidal thinking.

“Nightmares are difficult to treat. There are few pharmacologic options,” says Simon Kung, MD, with the Department of Psychiatry and Psychology at Mayo Clinic in Rochester, Minnesota, and principal investigator of the study. “They are also increasingly clinically relevant. Physicians can expect to see more patients with symptoms of PTSD, including nightmares and reduced sleep quality, as more veterans of military deployments are reintegrated into civilian life.”

## Prazosin Blocks Norepinephrine Receptors

One possible cause of nightmare symptoms such as disrupted sleep is the development of overstimulated chemical messenger norepinephrine receptors in the central nervous system. Increased norepinephrine cerebrospinal fluid concentrations

have been found in patients with PTSD and are associated with greater severity of PTSD symptoms. This increased central nervous system noradrenergic state contributes to the disruption of normal rapid eye movement sleep, in turn contributing to nightmares.

Prazosin is a lipid-soluble  $\alpha_1$ -adrenergic receptor antagonist that crosses the blood-brain barrier and decreases the sympathetic outflow in the brain. Following research that began a decade ago, some Veterans Affairs hospitals have used prazosin to treat PTSD-related nightmares.

Dr Kung, in collaboration with Zelde Espinel, MD, MPH (Department of Psychiatry, Universidad El Bosque, Bogota, Colombia, and Department of Epidemiology and Public Health, University of Miami School of Medicine, Miami, Florida), and Maria I. Lapid, MD, formed the research team that reviewed 21 studies—4 randomized controlled trials, 4 open-label studies, 4 retrospective chart reviews, and 9 single case reports—in which the prazosin dose ranged from 1 to 16 mg/d. Articles met criteria for inclusion if prazosin was used to treat nightmares and outcome measures included nightmares or



Maria I. Lapid, MD, and Simon Kung, MD



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## Contact Us

Mayo Clinic welcomes inquiries and referrals, and a request to a specific physician is not required to refer a patient.

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866-629-6362

### Florida

800-634-1417

### Minnesota

800-533-1564

## Resources

[mayoclinic.org/medicalprofs](http://mayoclinic.org/medicalprofs)

Clinical trials, CME, Grand Rounds, scientific videos, and online referrals



related symptoms of sleep disorders. Reduced nightmare severity with use of prazosin was consistently reported in these studies. Some patients reported a return of nightmares when the course of prazosin was stopped.

“Pharmacologic agents like prazosin that block norepinephrine receptors may be ideal in treating nightmares,” says Dr Lapid. “The low level of side effects of prazosin,

as reported in these studies, also extends the possibilities for trying prazosin in non-PTSD nightmares.”

#### For more information

“Treatment of Nightmares With Prazosin: A Systematic Review” was published in the September 2012 issue of *Mayo Clinic Proceedings* (87[9]:890-900).

## News

**Patient Education Videos and Pamphlets Receive Awards** — The Mayo Clinic Section of Patient Education collaborates with the Department of Psychiatry and Psychology and 42 other Mayo clinical areas, as well as Media Support Services, to provide educational print and video materials for Mayo patients and their families, free of charge. Several psych-related reference materials have received awards for excellence:

**2012** — Finalist Award for the International Television and Film Awards. Golden Reel Award from Media Associations International. Bronze Telly Award for “Living in the Moment” (video)

**2011** — Bronze National Health Information Award for “Pharmacogenetics: Finding the Right Medications for You” (video). Merit National Health Information Award for “Teens and School: Coping With Chronic Pain and Fatigue” (pamphlet)

## Upcoming Courses

For more information or to register for courses, visit [www.mayo.edu/cme/psychiatry-and-psychology](http://www.mayo.edu/cme/psychiatry-and-psychology), call 800-323-2688 (toll free), or e-mail [cme@mayo.edu](mailto:cme@mayo.edu).

#### Psychiatry in Medical Settings:

January 17-19, 2013, in Phoenix, Arizona

#### Windows into Hope: Stories of Addiction

and Recovery: January 26, 2013, in Minneapolis, Minnesota

#### Biological Frontiers of Addiction:

April 25-26, 2013, in Rochester, Minnesota

#### Aeschi West: Basic Principles in Working with

Suicidal Patients: May 29-June 1, 2013, in Vail, Colorado

#### Approaches to Pediatric Depression and

Related Disorders: September 20, 2013, in Minneapolis, Minnesota

#### Acute Care Psychiatry Clinical Review:

October 31-November 2, 2013, in Lake Buena Vista, Florida

## Positions Available

To learn more, visit [www.mayoclinic.org/physician-jobs](http://www.mayoclinic.org/physician-jobs).

**Adult Psychiatrist** to participate in an innovative program delivering care to a large population in southeastern Minnesota. Job posting number 15593BR

**BC/BE Adult Psychiatrist** for a primarily outpatient position at Mayo Clinic Health System in Eau Claire, Wisconsin. Job posting number 16570BR

**Clinical or Counseling Psychologist** with expertise in the care of women with sexual concerns. Job posting number 14554BR

**Psychologist** with experience in the delivery of behavioral health services for position in integrated primary care. Job posting number 15160BR

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