



Genetic Clues Link Depression and Alcohol Dependence

For more than a century, clinicians have tried to understand the association between depression and alcohol dependence, which co-occur in a third of individuals with either condition. In a chicken-or-egg-type conundrum, some believe alcoholism causes depression, either through direct pharmacologic effects on the brain or indirectly through negative social consequences, while others contend that depression can lead to alcoholism in individuals who use alcohol to self-medicate. Yet a third hypothesis suggests that shared genetic factors predispose some people to both disorders.

Now, new research from geneticist **Shizhong Han**, who joined the psychiatry faculty in August, gives credence to the third theory. His study, published online in *JAMA Psychiatry*, analyzed the depression polygenic risk score (PRS)—a measure of depression risk that incorporates many genetic variations across the genome—of

3,871 patients with alcohol dependence and 3,347 healthy controls who participated in four large genome-wide association studies: the Collaborative Study on the Genetics of Alcoholism; the Study of Addiction, Genetics and Environment (SAGE); the Yale-Penn genetic study of substance dependence; and the National Health and Resilience in Veterans Study (NHRVS).

In the work, an elevated PRS for major depressive disorder was found to also convey a significant increase in risk for alcohol dependence, suggesting that a shared genetic susceptibility contributes to the co-occurrence of both conditions.

This marks the first time scientists have provided evidence of this theory at the molecular genetics level on a genome-wide scale, says Han. Adds Psychiatry Director **James “Jimmy” Potash**, a study co-author, “The thing that’s so interesting is that we now have this powerful molecular genetic toolset that can actually give us a definitive answer after decades of people speculating or looking at tangential, indirect evidence.”

For Potash, this line of investigation has come full circle. He first researched the link between alcohol and mood disorders as a psychiatry resident here in 1996, under former director **Ray DePaulo**, who had just received a philanthropic

donation to examine the association. Then, the first step was studying how mental health problems ran in families; Potash published a paper in the *American Journal of Psychiatry* demonstrating that a subset of families with bipolar disorder also tended to have high rates of alcoholism and attempted suicide.

“We now have this molecular genetic information from millions of places in the genome on many thousands of people that can help find specific areas in the genome contributing to disease or highlight a particular individual’s risk for alcoholism and depression,” Potash says. “It’s very much a molecular extension of the same thing I was interested in 20 years ago, and it very clearly demonstrates that, yes, there is a shared genetic risk for both alcohol dependence and depression.”

Next, Han says, they’d like to identify particular genes or biological pathways underlying both disorders as well as determine to what extent other substance use disorders might also share in this common susceptibility. ■

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—JAMES “JIMMY” POTASH, PSYCHIATRY DIRECTOR



Shizhong Han and Jimmy Potash co-authored the study.



Jimmy Potash, M.D., M.P.H.

A New Dawn

Greetings to all! It is a pleasure to say “Welcome to *Brain Wise*” for the first time. As someone who was born at The Johns Hopkins Hospital and raised professionally under the dome, I am delighted to be back home after six years of chairing the psychiatry department at the University of Iowa. I have reconnected with many delightful people, such as our longstanding experts in eating disorders and geriatric psychiatry: Dr. Angela Guarda and Dr. Susan Lehmann, respectively, about whom you will read herein. I have also been pleased to discover wonderful new additions to our faculty, including Child and Adolescent Psychiatry Director Dr. Bob Findling, who recently published a new edition of his textbook on child and adolescent psychopharmacology.

It is exciting to return to a department that has led American psychiatry for more than a century. We aim to continue to lead by building a next-generation psychiatry department, but we also intend to preserve the strong foundation that has been laid for us. We are creating the next generation in psychiatry through work based on molecules and microcircuits. It is the molecules of the mind—such as DNA, neurotransmitters, and ion channels—that will bring us to an understanding of the causes and mechanisms of illness, and from there to new treatments.

Our work also involves taking advantage of the enormous power of electronic circuits in our computers, cell phones and Fitbits. We can use these to monitor activity levels and voice patterns, for example, to assess facets of depression, and to mine the electronic medical record for both clinical and research purposes. We can also use big data to sort out brain images and pinpoint where neural circuits have aberrant activity.

But everything we do rests on a strong foundation of caring. All our efforts start with the idea that we are committed to the relief of suffering in our patients and their families. Total devotion to them is part of the ancient art of healing, and it remains at the core of what we do. I hope you enjoy this issue and its window into the important work underway in our department.

A Seasoned Look at Anorexia Treatment

Anorexia has a higher risk of mortality than any other psychiatric disorder, says **Angela Guarda**, director of the Johns Hopkins Eating Disorders Program. Yet, in an era of increasing accountability within health care, outcomes research on intensive treatment of anorexia nervosa has been “surprisingly absent.”

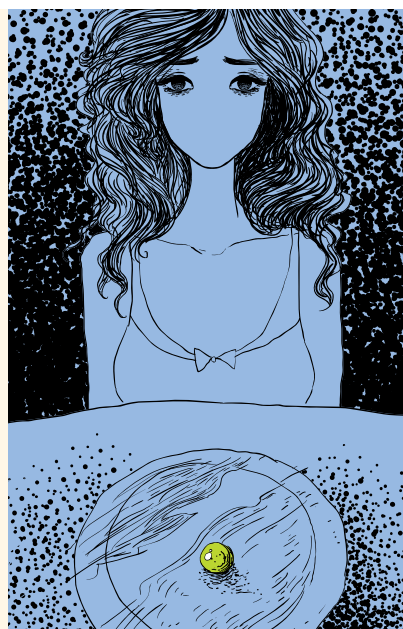
“Few programs publish outcomes and if they do, there’s often more marketing than evidence-based data, making it hard for families, patients or referral sources to judge a program’s effectiveness,” says Guarda. With many private, for-profit residential treatment programs marketing directly to consumers, “We feel that it’s very important for families and patients to know what questions to ask of programs, such as, *What is the rate of weight gain for anorexia?; What percentage of patients reach a normal weight prior to discharge?; and How do they do six months to a year after treatment?*”

In an article published in the *International Journal of Eating Disorders*, Guarda and colleagues

at Columbia University, the University of Pittsburgh and Weill Cornell Medical College called for more consistent, transparent outcomes data from eating disorder treatment programs. At a minimum, Guarda says, programs should freely share basic, de-identified information about their patients’ age and illness severity, diagnosis, and body mass index at admission—as well as weight restoration outcomes for patients with anorexia nervosa, so potential patients and their families can make informed decisions. Ideally, the programs should also include results from follow-up assessments three to six months after discharge.

“In a hospital setting, the cost per day is going to be higher than many freestanding residential programs. But in the Johns Hopkins program, with our emphasis on faster weight restoration and over 70 percent of our patients reaching a normal weight before leaving, the advantages are both clinical as well as economic.”

Guarda’s team found that among patients who argued that they did not need intensive treatment



Recasting Body Image and Food Choices

When Ashley Bilkie hit puberty, she got taller and lost her baby fat. What wasn’t as obvious to her parents was that she also began restricting her food intake, starting a nearly 14-year battle with anorexia nervosa.

Due to some other health issues and the fact that Ashley never appeared severely underweight, “We were not aware she had an eating disorder until she was in her early 20s,” says her father, Bob, president and CEO of a Michigan investment firm.

Over the next few years, Ashley moved in and out of four residential programs for eating disorders, never with any lasting benefit. Each time, she told her parents that as soon as she got out she would restrict her

eating again and lose weight.

In 2015, when Ashley was 28, Bob met a client whose daughter also suffered from anorexia. The client encouraged him to check out Johns Hopkins’ Eating Disorders Program.

Like Ashley, at least two-thirds of patients in the program have failed others, says Angela Guarda, director of the Hopkins Eating Disorders Program. “Treatment must focus on helping patients change their behavior around food,” she says. “Once this behavior changes, patients’ thoughts and feelings start to improve, which builds their confidence toward achieving recovery.”

Unlike other programs that focused on seeking an explanation for Ashley’s self-

GERIATRIC PSYCHIATRY

A New Push to Teach Doctors About Late-Life Depression

Looking defeated, the 80-year-old woman arrived at The Johns Hopkins Hospital from the Midwest. For two years, she’d seen doctors about her chronic shortness of breath and fatigue. But her heart turned out to be fine. Not sure what to do next, her husband found Johns Hopkins geriatric psychiatrist **Susan Lehmann** in an online search and scheduled an appointment.

Within minutes of meeting her new patient, Lehmann saw classic signs of depression: low self-esteem, poor sleep quality—and anxiety attacks, “the likely cause of her shortness of breath,” Lehmann says. “It’s not so mystical, but because she wasn’t tearful, her doctors never considered depression,” adds Lehmann, who directs the Johns Hopkins Geriatric Psychiatry Day Hospital Program and The Johns Hopkins University School of Medicine’s general psychiatry clerkship.

“Most doctors don’t recognize the threat geriatric mental health problems bring because they’re not trained to do so,” she says. Now, with the release of self-paced, online learning modules she’s crafted for medical students, Lehmann aims to heighten awareness

about late-life depression—and its nuances—for the next generation of doctors.

Depression affects as many as 15 percent of people age 65 and older. Other mood disorders, such as manic episodes, can also emerge later in life, says Lehmann, who recently published a book on bipolar disorder in older adults. And, she notes, suicide rates among the elderly are rising, especially among men.

Meanwhile, many Americans are living longer. About 15 percent of the U.S. population is 65 or older. By 2030, an estimated 20 percent of the population will be over 65. “We don’t have enough geriatric experts for the tens of millions affected by aging,” Lehmann says. “And a negative outlook on life can worsen comorbidities, like Parkinson’s disease, strokes and cardiac disease.”

But expertise in this field is woefully inadequate, says Lehmann. In a recently published paper in *MedEdPORTAL Publications*, Lehmann and colleagues found that some 21 percent of responding medical schools lacked specific instruction or clinical experience focused on geriatric psychiatry. Of those schools, 14 percent reported having no geriatric psychiatrist on the

A Biomarker for Emotional Impairment in Boys with ADHD?

Johns Hopkins psychologist **Karen Seymour** and neurologist **Stewart Mostofsky** research subcortical neuroanatomy in boys and girls with and without attention-deficit/hyperactivity disorder (ADHD). In a recent study published in *Psychiatric Research: Neuroimaging*, they analyzed volume and shape of subcortical structures that may serve as biomarkers for children with ADHD at risk for emotion dysregulation, an associated feature of ADHD. Their study is among the first to examine gender differences in subcortical structures using shape analysis. Results showed that for boys with ADHD, but not girls with ADHD, shape compressions in certain subcortical regions related to emotion regulation—when compared with those of typically developing (TD) boys—had anomalies associated with parent ratings of emotion dysregulation.

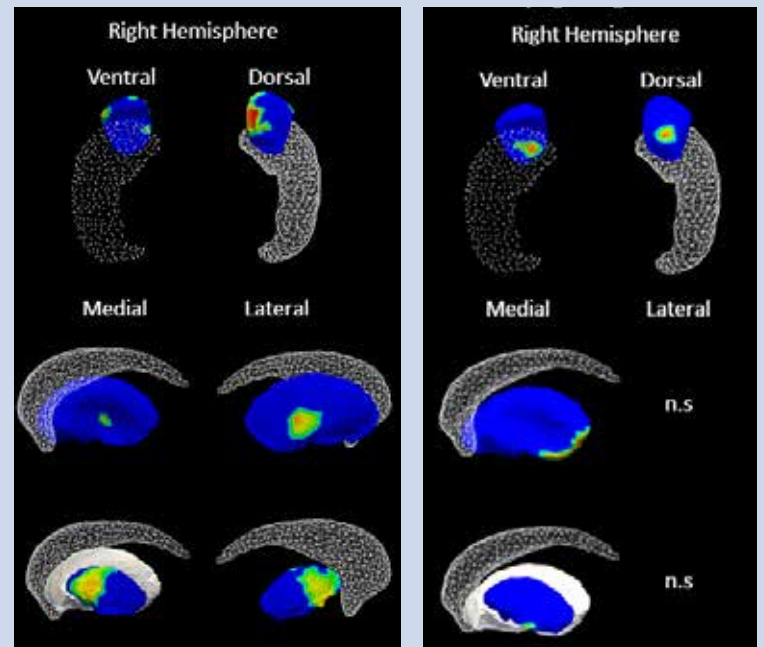


Figure 1

Figure 2

Figure 1 shows the shape compression of various structures in the brain related to emotion regulation in ADHD compared with typically developing (TD) boys. Figure 2 shows the brain-behavior correlations for ADHD boys between emotion dysregulation and regions of expansion on the amygdala, putamen and globus pallidus.

and were admitted under pressure from family or friends, more than 40 percent reported that within two weeks, they had changed their minds and felt treatment was helpful.

The Johns Hopkins program uses peer support from patients further along in treatment to help those newly admitted to change their eating habits. While many programs negotiate individual diet plans and calorie levels with patients, Johns Hopkins has patients follow a food plan with choices but also uniform calorie increases. This approach has been shown to safely achieve weight gain of at least 4 pounds each week—about twice the national average—while helping patients diversify their food choices and learn to eat balanced meals. “A standardized meal protocol like ours helps patients change



their behavior, complete meals and practice healthy eating skills,” Guarda says.

Guarda is upfront about Johns Hopkins’ treatment protocol. Treatment for anorexia nervosa is uncomfortable, she says—patients are ambivalent about changing driven and habitual eating and weight control behaviors. “Yet changing behavior and gaining weight are the

(continued on back cover)

starvation, Guarda and colleagues explained anorexia nervosa to Ashley and her parents as a driven behavioral problem best treated with a behavioral approach. Soon after entering the Hopkins program, Ashley called her parents—she was upset and asked to be released from the program, arguing that it wouldn’t help her. “But we knew she really had no other options,” says Bob. “This was our only chance to save her life.” With group therapy and the encouragement of other patients who had benefitted from the program, Ashley gradually engaged in treatment. Her anxiety decreased, and she learned to stop dieting. She gradually restored her weight and was encouraged to use her parents as a support to maintain her recovery.

When Bob and his wife, Shari, came to visit Ashley toward the end of her three-month stay,

they noticed a big difference when they dined together at the hospital cafeteria and a local restaurant: She had a hearty appetite, says Bob. Before admission, “She would pick at her food or avoid eating altogether,” he says. Now she’s able to choose, portion and consume a wide range of foods of different calorie densities with much less anxiety, and she can socialize at meals rather than avoid eating with others, adds Guarda.

Ashley is now studying to become a nurse and is engaged to be married. While things turned out well for her, Bob says he frequently shares a valuable lesson with other parents and caregivers of those with eating disorders: “We went along with (previous) therapy teams, assuming they knew what they were doing. I think that’s a mistake—you should be questioning everything, every step of the way.”

faculty. Yet at some point, says Lehmann, “Every doctor in almost every specialty will interact with geriatric patients. Students need to know what’s considered normal aging, from heart problems to memory to mental health.”



“Most doctors don’t recognize the threat geriatric mental health problems bring because they’re not trained to do so.”

—SUSAN LEHMANN

The new modules, says Lehmann, can bridge this gap with “easily digestible” clinical vignettes and videos showing how to engage with older patients and recognize and manage depression. Fourth-year Johns Hopkins medical students who piloted the modules found them easy to navigate and successful in increasing understanding of geriatric depression. She hopes more medical schools will adopt the modules, which are free of charge.





Lehmann draws from nearly 30 years of experience practicing and teaching geriatric psychiatry. In 2011, she was awarded the Berkheimer Faculty Education Scholar Grant, offering resources and time outside her regular duties to create the modules. After reviewing them, says Lehmann, students should be familiar with

the signs and symptoms of geriatric depression and screening tools to help establish the diagnosis.

Respect for the elderly comes naturally to Lehmann. She grew up with four active grandparents, one of whom practiced medicine well into his 80s. “They were great teachers,” she says, “and I loved hearing their stories.” It pains Lehmann that poking fun at aging is socially acceptable. “I feel a sense of mission to our older patients,” she adds, noting that geriatric depression is highly treatable. “It’s so rewarding to help people find a better quality of life.”

As for the octogenarian from the Midwest, she benefited from antidepressants and psychotherapy—and became the inspiration for a video vignette in the modules. Lehmann hopes her case will serve as

4 Things That Might Surprise You About Depression in Older Adults:

-  1. It’s never a normal part of aging.
-  2. Clinicians may recognize depression but often undertreat it with low doses of drugs.
-  3. It’s sometimes confused with dementia.
-  4. Suicide rates among the elderly are growing, especially among 85-plus-year-old white men (47 per 100,000).

a touchstone for doctors as they see elderly patients. The online modules are available at no cost to medical educators on MedEdPortal. ■

bit.ly/recognizinggeriatricdepression
bit.ly/recognizinggeriatricdepression2

A Seasoned Look at Anorexia Treatment (continued from page 3)



“Although the process is challenging, patients tell us our program is more helpful than a slower meal progression because no change feels slow enough when you have anorexia.”

—ANGELA GUARDA

essential first steps needed for recovery,” Guarda says.

The multidisciplinary team in the Johns Hopkins Eating Disorders Program also treats concurrent medical and psychiatric illnesses and severe complications of eating disorders.

Most patients transition from inpatient to the partial hospitalization program, Guarda says, where focus shifts to relapse

prevention skills training. Patients practice eating meals independently across different social settings “and work with the clinical team to plan their transition home and return to a full life.” ■

▶ Watch a video with Angela Guarda about the Eating Disorders Program: bit.ly/anorexiaJHM

New Books by Faculty

Psychological and Cognitive Impact of Critical Illness

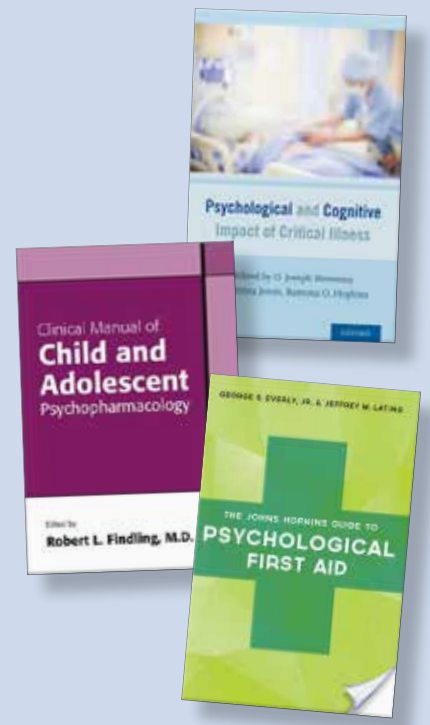
Edited by O. Joseph Bienvenu, M.D., Ramona O. Hopkins, M.D., and Christina Jones, M.D. Oxford University Press

Clinical Manual of Child and Adolescent Psychopharmacology

by Robert Findling, M.D. American Psychiatric Publishing, Incorporated

The Johns Hopkins Guide to Psychological First Aid

George Everly, Ph.D. and Jeffrey Lating Johns Hopkins University Press



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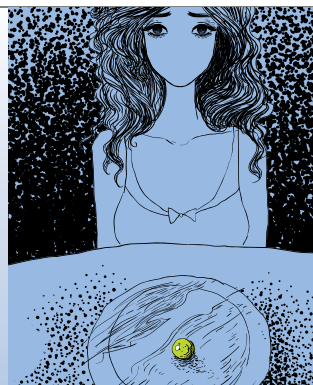
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