

NIAAA SPECTRUM

Volume 9, Issue 1 | February 2017 | <https://www.spectrum.niaaa.nih.gov>

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Institute on Alcohol Abuse and Alcoholism

FEATURE

NIAAA PLAYS INTEGRAL ROLE IN FIRST SURGEON GENERAL'S REPORT ON ADDICTION



On November 17, 2016, NIAAA Director George F. Koob, Ph.D., joined other leading scientific and health experts in a national summit at the historic Paramount Theater in Los Angeles, California, as Surgeon General Vivek H. Murthy, M.D., released the first-ever Surgeon General's report dedicated to substance misuse and substance use disorders. Titled *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*, the report provides the state of the science of alcohol, illicit drug, and prescription drug misuse and addiction; calls for a cultural shift in the way Americans talk about these issues; and recommends actions to promote prevention, expand treatment,

and ensure that recovery is possible for everyone.

Dr. Koob and other NIAAA staff played an integral role in the development of the report from its inception, working closely with colleagues at the National Institute on Drug Abuse (NIDA) and other federal agencies. For example, Dr. Koob and NIDA Director Nora Volkow, M.D., co-authored the report's chapter on the neurobiology of substance use, misuse, and addiction. NIAAA staff were central to the iterative, collaborative process involved in bringing together other chapters, which are dedicated to prevention, treatment, recovery, health systems integration, and recommendations for the future.

"Alcohol and drug addiction take an enormous toll on individuals, families, and communities," says Dr. Murthy. "Most Americans know someone who has lost a family member as a consequence of alcohol or drugs. Yet 90 percent of people with a substance use disorder are not getting treatment. That has to change."

Although substance misuse and substance use disorders may occur at any age, adolescence and young adulthood are particularly critical at-risk periods, especially for misuse. Preventing or even just delaying young people from trying substances

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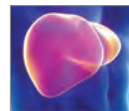
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FEATURE

A SECOND CHALLENGE COMPETITION FOR THE WEARABLE ALCOHOL BIOSENSOR



Many alcohol studies rely on participants to self-report how much and how often they drink, which can, at times, result in unreliable data. Biomarkers (biological markers) based on indicators in blood or other bodily fluids can be objective measures of alcohol use. Some biomarkers directly measure whether an individual has recently been drinking by measuring components of alcohol in blood or urine after it is metabolized. Other biomarkers work by detecting the toxic effects that alcohol misuse may be having over time on organ systems or body chemistry, indirectly signaling an alcohol problem. Biomarkers have a variety of uses, including screening for possible alcohol problems in people who are unwilling or unable to provide accurate self-reports of their drinking, and objectively showing that someone with alcohol use disorder has abstained from drinking.

However, there are limitations to using currently recognized biomarkers. Some biomarkers are less accurate in certain groups, such as women and younger individuals, and it is often difficult to interpret the type of drinking (quantity/duration) measured by the biomarker. For these reasons, it is recommended that biomarkers be used in conjunction with self-report.

But what if researchers had access to a tool that could give perfectly accurate

data about a person's drinking? To this end, NIAAA is once again challenging the biotech community to design a wearable device capable of measuring blood alcohol in near real-time. This time, however, developers are being tasked with creating a device that measures alcohol concentration in the blood or in the interstitial fluid that surrounds the body's cells, as opposed to using technology that detects alcohol released through the skin in sweat or vapor. As in the first competition, the ideal biosensor would be capable of measuring alcohol levels noninvasively as a sleek and unobtrusive device. The creators of the winning prototype will be awarded \$200,000 through Challenge.gov, which lists federal incentive prizes and competitions. The second place developers will receive \$100,000.

"Our first Challenge was a huge success. The winning devices made important strides in improving transdermal alcohol sensing," says NIAAA Director George F. Koob, Ph.D.

In May 2016, NIAAA announced that BACtrack had won the first Wearable Alcohol Biosensor Challenge with its Skyn prototype. The wrist-worn device detects blood alcohol concentration (BAC) using a fuel-cell technology similar to that in devices used by law enforcement for roadside alcohol

testing. MILO, Inc., won second prize for its design using disposable cartridges to continuously track BAC.

"We have learned that there is real interest in the private sector around wearable alcohol biosensors, and that innovation using distinct means of alcohol detection is on the horizon," says M. Katherine Jung, Ph.D., Director of NIAAA's Division of Metabolism and Health Effects, and co-leader of the competition.

Innovation is encouraged, and creative solutions could include, but are not limited to, the adaptation and miniaturization of technologies such as spectroscopy or wave technology.

"We want to continue to harness the power of the private sector, because if alcohol biosensors become a part of the 'wearable toolbox,' then tangible new opportunities will become available that can profoundly affect the field of alcohol research," says Dr. Jung.

In addition to its potential for researchers, alcohol biosensors could also be a tool for consumers who wish to track their personal drinking patterns.

Competition submissions (a working prototype, data proving functionality/reliability, and photos/videos) will be accepted until May 15, 2017, with winners announced on or after August 1, 2017.

Details about the competition are posted at <https://www.niaaa.nih.gov/research/challenge-prize> and <https://www.challenge.gov/challenge/wearable-alcohol-biosensor/>. For more information, please email NIAAACHallengePrize@mail.nih.gov.

FEATURE: First Surgeon General's Report . . . Continued from page 1



Shown left to right, attendees of the launch of Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health included: Dr. Jinhee J. Lee, Substance Abuse and Mental Health Services Administration (SAMHSA); Dr. A. Thomas McClellan, Treatment Research Institute; Dr. George F. Koob, NIAAA; Dr. Keith Humphreys, Stanford University; Dr. Nora Volkow, NIDA; Dr. Vivek H. Murthy, U.S. Surgeon General; Kana Enomoto, SAMHSA; Dr. Constance Weisner, Kaiser Permanente; Dr. H. Westley Clark, Santa Clara University; and Dr. Jorielle Brown Houston, SAMHSA.

is important for reducing the likelihood of a disorder later in life. The report notes, for example, NIAAA research that found that people who use alcohol before the age of 15 are 4 times more likely to develop alcohol use disorder later in life compared to those who have their first drink at age 21 or older.

One in seven people in the United States is expected to develop a substance use disorder at some point in their lives. Among other things, the Surgeon General's report shows that disorders typically develop over time, following repeated episodes of misuse that result in changes to the brain circuitry that underlies addiction.

"Decades of research have demonstrated that addiction is a brain disease with the potential for both recovery and recurrence—not a moral failing," says Dr. Koob. "One of the important findings of this report is that effective preventive and treatment interventions are available. We have evidence-based interventions that can be implemented at the individual, family, school, and community levels and prevent substance misuse and related problems

before they occur. Ensuring access to evidence-based treatment is essential for reducing substance misuse and its consequences, and for promoting recovery."

The new report, which has been likened in importance to 1964's landmark *Smoking and Health: Report of the Advisory Committee of the Surgeon General of the Public Health Service*, notes that nearly 21 million Americans—more than 1.5 times the number of people who have all cancers combined—suffer from substance use disorders. Yet only 1 in 10 receives treatment. This treatment gap can be attributed to many factors, including lack of screening for substance use disorder, fear of shame and discrimination associated with addiction, costs of care, and fragmentation of services in our health care system. Additionally, many people seek or are referred to substance use disorder treatment only after a crisis, such as an overdose, or through involvement with the criminal justice system. But there are proven interventions for treating substance use disorders and

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promoting recovery, often involving a combination of medication, behavioral counseling, and social support.

"As with other chronic, relapsing medical conditions, treatment can manage the symptoms of substance use disorders and prevent relapse," says Dr. Koob. "Rates of relapse following treatment for substance use disorders are comparable to those of other chronic illnesses such as diabetes, asthma, and hypertension. Evidence-based treatments—both medications and behavioral therapies—can save lives and restore people's health, well-being, and functioning."

(See <https://addiction.surgeongeneral.gov>)

SPOTLIGHT

NIAAA FEATURED IN HBO DOCUMENTARY *RISKY DRINKING*

On December 19, 2016, HBO Documentary Films premiered *Risky Drinking*, which follows the stories of four people whose drinking dramatically affects their relationships and their lives. This 85-minute film features commentary by experts including NIAAA Director George F. Koob, Ph.D., and NIAAA Medical Project Officer Deidra Roach, M.D. By offering a new perspective on alcohol use as it falls along a broad spectrum of risk and including life-saving information about what can help people dial back or stop their drinking, the film aims to provoke a much-needed conversation about how to identify “risky drinking” and to suggest alternatives to a one-size-fits-all approach that prevents many people from seeking help.



SPOTLIGHT

NIH CLINICAL CENTER CHANGES WILL ENHANCE PATIENT CARE AND QUALITY ASSURANCE WHILE CONTINUING TO FACILITATE GROUNDBREAKING RESEARCH



In recent months, the National Institutes of Health (NIH) announced several steps emphasizing a renewed focus on patient safety at the Clinical Center, its award-winning research hospital. In addition to a number of organizational changes, NIH established a series of new, centralized approaches to ensure delivery of the highest-quality clinical care, and to maintain ongoing monitoring of all operations and facilities related to patient care and quality assurance.

For Institutes and Centers (ICs) with a clinical research program in the Clinical Center, clinical directors will now report directly to their IC director rather than other leadership in their IC. At NIAAA, the Office of the Clinical Director, headed by David Goldman, M.D., will now work more closely with NIAAA Director George F. Koob, Ph.D. In addition, all clinical staff performance plans will now include language about strengthening patient safety measures and providing the highest quality of care.

Other new measures include:

- A new Office of Research Support and Compliance (ORSC), which will implement an extensive effort to improve the facilities and operations for producing drug products for use in patients and research participants and to reduce risk and promote patient safety at the Clinical Center.
- A toll-free hotline (1-866-444-8811) for staff, patients, and visitors to report

anonymously any concerns related to patient safety or patient care at the Clinical Center.

Dr. Goldman says, “Clinical care and patient safety are the foundation of clinical research to advance our understanding of alcohol’s impact on health and well-being. The NIH Clinical Center in Bethesda has been called ‘the nation’s hospital.’ Our dedicated staff will continue to live up to that vision by safeguarding safety and providing the highest standard of care.”

Anyone interested in joining a research study at NIAAA’s inpatient treatment program or participating in a study as an outpatient, whether as a patient or a healthy volunteer, can learn more by accessing “Join a Study” on NIAAA’s homepage: <https://www.niaaa.nih.gov/research/division-intramural-clinical-and-biological-research/clinical-trials-niaaanih>.

SPOTLIGHT

NIAAA LAB CHIEF DR. ANDREW HOLMES WINS AWARD FOR OUTSTANDING RESEARCH

Andrew Holmes, Ph.D., has won the prestigious Daniel H. Efron Research Award from the American College of Neuropsychopharmacology (ACNP). This award is presented to an individual for outstanding basic research contributions to neuropsychopharmacology. Dr. Holmes received the award on December 5, 2016, at the ACNP's 55th Annual Meeting.

"I am especially gratified by this honor because the ultimate goal of our work is to help identify new directions for new drug treatments, and ACNP has led the psychiatric community in promoting this goal," says Dr. Holmes.

Dr. Holmes is Chief of the NIAAA Laboratory of Behavioral and Genomic

Neuroscience. "My research is focused on using the latest neuroscience and genetic tools to study and hopefully deepen our understanding of the causes of alcohol use disorder and highly comorbid neuropsychiatric conditions such as post-traumatic stress disorder," explains Dr. Holmes.

To this end, Dr. Holmes's lab examines how alcohol exposure, stress, and trauma reshape brain circuits to modify behavior, and why they do so in a manner that varies greatly from individual to individual as a function of genetics, sex, and age. A current focus of his lab is delineating the structure and function of circuits connecting the prefrontal cortex with

limbic and dorsal striatal regions that are critical for the regulation of fear, cognition, and executive control over drug-seeking.

Dr. Holmes received his Ph.D. from the University of Leeds. He joined NIAAA in 2004, after completing a postdoctoral fellowship at the National Institute of Mental Health. He is the recipient of other awards for his research, including the 2012 Jacob P. Waletzky Award from the Society for Neuroscience.



NOTEWORTHY

NEW DIVISION DIRECTOR AND CLINICAL DIRECTOR SELECTED



M. Katherine Jung, Ph.D., has been selected as Director of the Division of Metabolism and Health Effects (DMHE). Dr. Jung earned her Ph.D. in biochemistry from Ohio State University. She has worked and published in the areas of cell biology, alcohol-induced organ damage, cancer biology, and drug discovery. Dr. Jung



led the NIAAA Biosensor Challenge, served as NIAAA's SBIR/STTR coordinator, and has been a program officer in DMHE for many years. Dr. Jung has an enduring interest in the effect of alcohol consumption on the propensity to organ damage and on impairment of host defense. In her new role, she will lead DMHE in promoting

the highest-quality research that seeks to understand the mechanisms of alcohol's pathological effects on organ function, with the goal of improving patient care.

In addition, David Goldman, M.D., has been selected as Clinical Director of NIAAA, a position in which he will be responsible for patient safety and oversee clinical staff in the intramural program sections and in laboratories conducting clinical research. Dr. Goldman has served as Chief of the Laboratory of Neurogenetics since 1991. He graduated cum laude from Yale University and magna cum laude from the University of Texas Medical Branch, Galveston, where he was also a Resident in Psychiatry. Throughout his career, Dr. Goldman has focused on identifying genes that influence vulnerability to alcohol use disorder and other psychiatric diseases.

NEWS FROM THE FIELD

DUAL-TARGETING STRATEGY SHOWS PROMISE AGAINST LIVER FIBROSIS



Liver fibrosis is a consequence of chronic liver injury associated with alcoholic or nonalcoholic fatty liver disease, viral hepatitis, or metabolic diseases, and can lead to cirrhosis and even cancer. While there are no

effective treatments for liver fibrosis, previous research has shown that compounds that block receptors for molecules similar to those found in the marijuana plant (endocannabinoids) can interfere with the development of liver fibrosis. However, the development of therapies based on these cannabinoid-1 receptor (CB1R)-blocking compounds was halted, because they have unwanted neuropsychiatric side effects of CB1R-blocking agents acting in the brain.

In a new study, NIAAA-supported researchers have developed a CB1R-blocking compound that could avoid those side effects, because it accumulates in the liver without penetrating the brain. An added benefit of the new compound is that it also targets an enzyme called inducible nitric oxide

synthase (iNOS), which also promotes the development of liver fibrosis. In studies that used mouse models of liver fibrosis, the researchers found that the new compound surpassed the antifibrotic ability of other CB1R blockers or iNOS inhibitors without inducing anxiety-like behaviors or CB1R blockade in the central nervous system.

The researchers note that the dual targeting of peripheral CB1R and iNOS exemplifies the therapeutic advantage of simultaneously hitting more than one molecule involved in a pathogenic process, particularly in light of emerging experience with recently developed antifibrotic medications, which indicates that targeting a single pathway has limited effect on fibrotic diseases.

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NEWS FROM THE FIELD

ANIMAL STUDY SUGGESTS ALCOHOL USE BEFORE PREGNANCY MAY INCREASE VULNERABILITY OF OFFSPRING TO STRESS IN ADULTHOOD



The effects of alcohol use during pregnancy on an unborn child are well known. However, a recent NIAAA-funded study in rats has shown that a mother's alcohol use before conception also could have negative effects on her

child's health and response to stress during adulthood.

To study the effects of preconception alcohol use, the research team, led by Dipak Sarkar, Ph.D., at Rutgers University, gave female rats 4 weeks of access to a diet containing 6.7 percent alcohol,

which raised their blood alcohol levels similar to that of binge drinking in humans. Alcohol was then removed from the rats' diet, and they were bred 3 weeks later. After the rats' offspring reached adulthood, the researchers

used standard laboratory techniques to evaluate their response to stress, anxiety-like behaviors, changes in levels of stress regulatory genes and protein hormones, as well as epigenetic changes—chemical modifications to DNA that occur in the absence of changes in sequence and can alter gene function.

The team found that offspring of rats that were exposed to alcohol before conception had increased levels of stress hormones in their blood in response to an immune challenge and changes in the expression and epigenetic profiles of genes that play a role

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5 QUESTIONS WITH . . .

DEIDRA ROACH, M.D.

Medical Project Officer, Division of Treatment and Recovery Research



1 Much of your current work focuses on women’s health. Historically, how have women’s drinking patterns differed from men’s, and why?

Men have historically consumed more alcohol and experienced more alcohol-related problems than women, who have tended to drink less because of cultural norms and being more sensitive to alcohol’s effects. For example, women have less body water than men pound for pound, so the same amount of alcohol will be more concentrated in a woman’s body than in a man’s. The effect of this difference is that, generally speaking, when a man and woman consume the same amount of alcohol, the woman’s blood alcohol concentration will rise more quickly and stay elevated longer.

2 Recent reports suggest that women’s drinking patterns are beginning to resemble those we have traditionally seen in men. Is that true, and why?

While men continue to drink more than women, the differences in alcohol consumption and related outcomes have been narrowing over recent decades. In the United States, for example, there has been a steady increase in current drinking and binge drinking among women that started in the late 1970s and appears to be continuing. One reason

that binge drinking is on the rise among young women is that the culture around women’s drinking has changed dramatically over the past 50 years. These days, women often go out for a night on the town with the intention of getting drunk for the enjoyment of it, and we see the evidence for this all over social media. Stress is another factor. Women experience higher rates of anxiety and depression than men do, and more often drink in response to negative mood states. But while alcohol may “take the edge off” anxiety or elevate a depressed mood in the moment, over the long term, alcohol misuse only makes these problems worse.

3 Can you tell us about some recent scientific advances in the area of women and alcohol, and are there any promising developments on the horizon?

While research has shown that all the available treatments for alcohol use disorder (AUD) are equally effective in women and men, we are finding that tailoring treatment to address some of the special needs of women may make these treatments even more effective for them. One of the most promising developments in women’s treatment is the emergence of trauma-informed therapy. When we look just at the population of women in treatment for alcohol and other substance use disorders, we find that the prevalence of past physical and sexual abuse is generally upwards of 50 percent. That is why we strongly encourage practitioners to screen for trauma and mental health problems at the same time that they screen for misuse of alcohol and other substances.

Another very exciting development in treatment research is the movement toward personalized treatment. One day in the foreseeable future, it is going to be possible to predict which specific treatments will likely work best in a particular patient, based on her or his individual genetic and psychological

profile. In terms of future directions for research focused specifically on women and girls, we are particularly excited about our new partnership with the National Institute on Drug Abuse and the NIH Office of Research on Women’s Health, titled “Model Continuums of Care Initiative (MCCI) for Women and Girls at Risk and Living with HIV/AIDS and Harmful Alcohol and Associated Comorbidities.” Our vision is that MCCI will be a community-based participatory health systems/services research initiative that will accelerate the translation of effective women- and family-focused HIV, alcohol and other drug-related prevention, and treatment interventions to community practice.

4 What do you hope the average person understands about this issue a decade from now that we do not, as a society, understand now?

I sincerely hope that a decade from now the average person understands that AUD and addiction in general are brain diseases and not character flaws. Addiction is still too often seen as a moral issue rather than a medical issue, and this is particularly true when the affected person is a woman. While the norms around women’s drinking have shifted dramatically over the past 50 years, problem drinking among women is still heavily stigmatized, which poses a significant barrier to treatment.

5 With your medical degree, how did your career path lead you to the issue of women and alcohol?

I first became interested in understanding addiction as a child growing up in a family in which several loved ones struggled with addiction for many years, including some who died of complications of this disease. As I got older, I grew in my understanding of addiction as a community health issue,

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NEWS FROM THE FIELD: *Liver Fibrosis . . . Continued from page 6*

They therefore conclude that the approach illustrated by their study shows promise as an effective anti-fibrotic strategy.

Reference:

Cinar, R.; Iyer, M.R.; Liu, Z.; Cao, Z.; Jourdan, T.; Erdelyi, K.; Godlewski, G.; Szanda, G.; Liu, J.; Park, J.K.; Mukhopadhyay, B.; Rosenberg, A.Z.; Liow, J.S.; Lorenz, R.G.; Pacher, P.; Innis, R.B.; and Kunos, G. Hybrid inhibitor of peripheral cannabinoid-1 receptors and inducible nitric oxide synthase mitigates liver fibrosis. *JCI Insight* 1(11):e87336, 2016. PMID: 27525312

NEWS FROM THE FIELD: *Alcohol Use Before Pregnancy . . . Continued from page 6*

in regulating stress responses in their brains. However, the researchers observed changes in anxiety-like behaviors only in the male offspring.

Previous research has indicated that epigenetic mutations may be passed from parent to child and also that epigenetic mutations may play a role in the expression of anxiety-linked behaviors and response to stress. Alcohol problems are known to run

in families, and increased alcohol consumption in humans has been associated with increased anxiety.

Taken together, these findings suggest that epigenetic changes in the mother as a result of alcohol misuse before conception may be passed on to her offspring. These changes could have lifelong effects on a child's response to stress.

Reference:

Jabbar, S.; Chastain, L.G.; Gangisetty, O.; Cabrera, M.A.; Sochacki, K.; and Sarkar, D.K. Preconception alcohol increases offspring vulnerability to stress. *Neuropsychopharmacology* 41(11):2782–2793, 2016. PMID: 27296153

5 QUESTIONS WITH . . . Continued from page 7

with many points of intersection with broader social and economic issues affecting certain marginalized communities, including but not limited to unemployment and poverty, substandard education, and inadequate general health care. In retrospect, it seems only natural that I gravitated to addiction treatment after completing my medical

training, and pursued a career path that bridged multiple addiction-related disciplines, from treatment to policy-making to—most recently at NIH—research administration. I have complete confidence that the problem of epidemic alcohol and other substance misuse can be resolved, but only by building strong and viable partnerships among all key

stakeholders, including health care providers, researchers, policymakers, insurers, advocacy groups, and—first and foremost—the individuals, families, and communities most profoundly affected by harmful alcohol and other substance use.

ABOUT US

NIAAA Spectrum is NIAAA's Webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field for a wide range of audiences.

Each issue includes feature-length stories, new research findings from the field, image and data analyses, and an interview with an NIAAA staff member or alcohol researcher. *NIAAA Spectrum* is published three times a year.

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