NIAAA WELCOMES DR. GEORGE F. KOOB AS NEW DIRECTOR

Renowned addiction neuroscientist George F. Koob, Ph.D., became NIAAA’s new Director on January 27, 2014. Dr. Koob comes to NIAAA from The Scripps Research Institute, where he served as chairman of the committee on the neurobiology of addictive disorders, and director of the Alcohol Research Center, at Scripps’ campus in La Jolla, CA. He earned his Ph.D. in behavioral physiology at Johns Hopkins University.

“I look forward to applying evidence-based science to the challenges unique to alcohol, including understanding, preventing, and treating binge drinking, alcoholism, fetal alcohol syndrome, alcoholic liver disease; and the contribution of alcoholism to myriad other medical/psychiatric disorders,” said Dr. Koob. “I also look forward to promoting the science of addiction and applying it to our understanding of alcohol use disorders and co-abuse of other drugs such as tobacco.”

“We look forward to having Dr. Koob, a highly regarded leader in alcohol and addiction science, take the helm at NIAAA,” added Dr. Kenneth Warren, Ph.D., who has served as NIAAA’s acting director since 2008.

Dr. Koob’s early research interests were directed at the neurobiology of emotion, with a focus on the theoretical constructs of reward and stress. His contributions have led to the understanding of the anatomical connections of emotional systems and the neurochemistry of emotional function. Dr. Koob also is one of the world’s authorities on alcohol and drug addiction. He has contributed to the understanding of the neurocircuitry associated with the acute reinforcing effects of drugs of abuse and more recently on the neuroadaptations of these reward circuits associated with the transition to dependence.

In announcing Dr. Koob’s selection as NIAAA Director on October, 31, 2013, NIH Director Francis Collins, M.D., said, “With his distinguished reputation and vision, I am confident that George will encourage innovative ideas in the basic neurobiology of addiction and will be dedicated to bridging the gap between our understanding of alcohol abuse, alcoholism, and addiction and developing new, targeted treatments.”

Dr. Koob will oversee NIAAA’s $458 million budget, which supports a diverse program of alcohol-related research in a wide range of scientific areas, including genetics, neuroscience, epidemiology, organ damage, prevention, and treatment. The Institute also coordinates and collaborates with other research institutes and Federal programs on alcohol-related issues; and national, State, and local institutions, organizations, agencies, and programs engaged in alcohol-related work.
DR. KENNETH WARREN’S NIAAA LEGACY

The contributions of Kenneth Warren, Ph.D., are firmly woven into the fabric of NIAAA—and he continues to leave a bold mark. Over nearly four decades, Dr. Warren’s leadership has helped transform NIAAA from a newly created initiative to the Nation’s leading alcohol research institution. Dr. Warren served in a variety of leadership roles at NIAAA, and luckily, his career is far from over yet.

After serving for many years as the Director of the Office of Scientific Affairs, he was appointed Deputy Director of the Institute in early 2008. Dr. Warren became Acting Director with the retirement of Ting-Kai Li, M.D., later that year. Dr. Warren returned to his position as Deputy Director when George Koob, Ph.D., was appointed NIAAA’s Director in late January 2014.

Even in his relatively short time as Acting Director, Dr. Warren accomplished a tremendous amount, and he is especially gratified by the progress made in alcohol research.

“As I look back over the last five years, I’m proud of all we were able to achieve despite the extraordinary challenges posed by a very difficult economic climate and very limited resources,” Dr. Warren said.

Dr. Warren is particularly pleased about four research initiatives begun during his tenure. These programs will continue to provide important alcohol research findings in the years to come. The following are Dr. Warren’s four initiatives:

National Consortium on Alcohol and Neurodevelopment in Adolescence (N-CANDA)

The N-CANDA consortium, which started operations in late 2012, is a nationwide effort to determine the effects of alcohol exposure on the development of the human adolescent brain, and to identify brain- and behavior-related vulnerabilities that may place an adolescent at risk for later development of alcohol use disorders. The consortium brings together an administrative component from UC San Diego, a data analysis component at SRI International, and five research sites: UC San Diego, SRI International, Oregon Health & Science University, University of Pittsburgh, and Duke University. In addition to carrying out

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BY THE NUMBERS

ALCOHOL USE DISORDER OR ALCOHOL ABUSE AND DEPENDENCE? DSM–5 CHANGES EXPLAINED

In 2013, the American Psychiatric Association (APA) issued the fifth edition of its Diagnostic and Statistical Manual of Mental Disorders (DSM–5), which contains a number of important changes in the definition of alcohol use disorders—including changes in terminology, diagnostic criteria, and diagnostic thresholds—compared with DSM–IV.

Perhaps the most significant change from DSM–IV to DSM–5 is in the terminology used to describe alcohol problems. DSM–IV described two distinct disorders—alcohol abuse and alcohol dependence—with specific criteria for each, whereas the DSM–5 designates a single disorder called alcohol use disorder (AUD) with mild, moderate, and severe sub-classifications.

Under DSM–IV, the diagnostic criteria for abuse and dependence were distinct: anyone meeting 1 or more of 4 “abuse” criteria within a 12-month period would receive the “abuse” diagnosis. Anyone with 3 or more of 7 “dependence” criteria within a 12-month period would receive a “dependence” diagnosis. Under DSM–5, however, someone meeting any 2 of 11 “alcohol use disorder” criteria during the same 12-month period would receive a diagnosis of AUD.

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the consortium’s overall protocol, each research site is studying one additional issue. These include adolescent sleep patterns, recovery after abstinence, inhibitory control, and default mode network functioning.

**Neurobiology of Adolescent Drinking in Adulthood (NADIA)**

NADIA is a cooperative agreement that supports a multidisciplinary research effort to study persistent and complex brain changes that result from adolescent alcohol exposure. The ultimate goal of the NADIA project is to determine if underage drinking causes changes in brain function that remain even in adulthood. NADIA promotes interactions across scientific disciplines, methodologies, and levels of analysis.

**Severe Alcoholic Hepatitis Consortia**

Alcoholic hepatitis (AH) is one of the most serious forms of alcohol-induced liver disease. Its short-term mortality rate is extremely high—up to 60 percent of patients with severe AH die within 6 months. Patients who survive AH have a 70-percent chance of developing cirrhosis. There are few effective treatment options, so NIAAA established 4 consortia in 2012 to promote better understanding and treatment of the disease. The major goal of the AH consortia is to develop novel treatment approaches through groundbreaking research and new applications of previous discoveries. Members of the consortia include the University of Massachusetts, Indiana University, University of North Carolina, University of California at Los Angeles (UCLA), and University of Southern California.

For more information on funding opportunities, visit the NIAAA Web site: [http://www.niaaa.nih.gov/grant-funding/funding-opportunities](http://www.niaaa.nih.gov/grant-funding/funding-opportunities)

**Collaborative Research on Addiction at NIH (CRAN)**

CRAN provides a strong collaborative framework for NIAAA, the National Institute on Drug Abuse (NIDA), and the National Cancer Institute to integrate resources and expertise to advance substance use, abuse, and addiction research and improve public health outcomes. CRAN issues funding opportunity announcements (FOAs) for collaborative research on substance use, abuse, addiction, and related health consequences. It provides researchers and other stakeholders with Web-based information on CRAN and CRAN-related FOAs, news and events, and significant research accomplishments, and also promotes a close working relationship between the NIAAA and NIDA intramural research programs.

NIAAA fortunately will continue to benefit from Dr. Warren’s vast expertise, even following this latest transition.

**APIS ANNUAL UPDATE**

The NIAAA-sponsored Alcohol Policy Information System (APIS) recently released its latest update of State-by-State alcohol-related public policies. As of January 1, 2013, 26 substantive changes have been recorded.

Those changes include the following topic areas:

- Alcohol Control Systems
- Alcohol Taxes
- Underage Drinking Prevention
- Pregnancy and Alcohol
- Beverage Service Training and Related Practices
- Sunday Sales

Updates to current APIS policy topics are now posted online at [http://www.alcoholpolicy.niaaa.nih.gov/](http://www.alcoholpolicy.niaaa.nih.gov/).

Many of these changes are consistent with the goal of reducing underage drinking and its consequences, as well as the goal of reducing alcohol-related death and injury in the general population.
PROMISING RESULTS FOR SEIZURE MEDICATION IN CLINICAL TRIALS FOR ALCOHOL DEPENDENCE

The generic anticonvulsant medication gabapentin shows promise as an effective treatment for alcohol dependence, based on the results of a 150-patient clinical trial of the medication. Conducted by scientists supported by NIAAA, the study found that alcohol-dependent patients using gabapentin were more likely to stop drinking or refrain from heavy drinking than those taking placebo. Gabapentin already is widely prescribed to treat pain conditions and epilepsy.

“Gabapentin showed similar or greater positive outcomes when compared to existing FDA [U.S. Food and Drug Administration]-approved treatments for alcohol dependence,” said first author Barbara J. Mason, Ph.D., of The Scripps Research Institute (TSRI) in La Jolla, CA.

“Plus, it’s the only medication shown to improve sleep and mood in people who are quitting or reducing their drinking, and it’s already widely used in primary care—that’s an appealing combination.”

Dr. Mason and her colleagues randomly assigned alcohol-dependent patients to receive a moderate or high dose of gabapentin (900 milligrams or 1,800 milligrams) or a placebo. Over the 12-week treatment, patients receiving the 1,800-milligram dose were twice as likely to refrain from heavy drinking (45 percent vs. 23 percent) and four times as likely to stop drinking altogether (17 percent vs. 4 percent), compared with placebo. Participants receiving gabapentin also reported improved sleep and mood and fewer alcohol cravings. The medication appeared to be well tolerated with few side effects.

Source:

RESEARCH-BASED STRATEGIES HELP REDUCE UNDERAGE DRINKING: A REVIEW

Strategies recommended by the Surgeon General to reduce underage drinking have shown promise when put into practice, according to scientists at NIAAA. These approaches include nighttime restrictions on young drivers and strict license suspension policies, interventions focused on partnerships between college campuses and the community, and routine screening by physicians to identify and counsel underage drinkers.

NIAAA researchers Ralph Hingson, Sc.D., and Aaron White, Ph.D., evaluated studies conducted since the 2007 Call to Action To Prevent and Reduce Underage Drinking. A report of their findings appears in the January issue of the Journal of Studies on Alcohol and Drugs.

The researchers’ analysis of recent studies on driving policies found that certain driving laws affecting underage drivers deter drunk driving and reduce fatal crashes. Graduated driver licensing laws, which include nighttime restrictions, and use/lose laws that lead to license suspension for an alcohol violation, have been effective, the review revealed. Individuals under the age of 21 are half as likely to drive after drinking in States with the strongest use/lose and graduated licensing laws, based on a national study.

“While progress has been made in addressing underage drinking, the consequences still remain unacceptably high,” said Dr. Hingson, director of NIAAA’s Division of Epidemiology and Prevention Research. “We must continue research to develop new interventions and implement existing strategies that have been shown to be effective.”

Source:
MODERATE ALCOHOL USE MAY ENHANCE VACCINE RESPONSE

Research published recently in the journal *Vaccine* suggests that while heavy drinking impairs immune response, moderate alcohol intake can improve vaccine response.

Researchers conducted a small study in 12 rhesus macaques of response to the modified vaccinia ankara (MVA) vaccine. The study included eight monkeys that were provided open access to alcohol after receiving the vaccine and four control monkeys who did not have access to alcohol. The monkeys in the experimental arm were allowed to choose between drinking water and drinking alcohol for 22 hours per day; these animals’ blood ethanol concentrations (BECs) were measured regularly. There were differences in the monkeys’ individual drinking patterns, with some falling into a “heavy-drinking” group (mean BEC level of 90 to 126% mg) and others into a “moderate-drinking” group (mean BEC level of 22.3 to 48.8% mg.)

All 12 monkeys showed a similar response to the initial vaccination. However, when the vaccine booster was administered after several months of drinking, researchers found that the monkeys in the moderate-drinking group (four monkeys) had a more robust response to the vaccine, and the monkeys in the heavy-drinking group (four monkeys) a lower response to the vaccine, in comparison with the control group that received the vaccination and booster but was not exposed to alcohol.

The researchers cite previous studies in both animals and humans showing that chronic heavy alcohol use can impair vaccine immune response. They note that their study not only confirms that “chronic alcohol intoxication suppresses this response,” but also that “moderate alcohol consumption enhances recall vaccine responses,” suggesting a need for further investigation.


SIBLING STUDY HELPS CLARIFY ADOLESCENT ALCOHOL RISK FACTORS

A recent study of more than 600 adoptive and biological sibling pairs supports earlier research that showed environmental factors outweigh genetics as an influence on adolescent alcohol use. What sets this study apart is that it investigated specific sources of environmental influence. The research focused on two major risk factors for adolescent drinking: having friends who drink and otherwise get into trouble; and having positive expectations about drinking, such as hoping to feel more outgoing.

At the University of Minnesota, NIAAA grantees working on the Sibling Interaction and Behavior Study (SIBS) worked with adoption agencies to recruit 407 families with two mid-to-late adolescents who were not biologically related and whose ages were within 5 years of one another. For comparison, they recruited 206 families with two biological children who satisfied the same age criterion.

The researchers analyzed a series of assessments taken by sibling pairs and found that overall, environmental factors, particularly shared experiences while being raised, had a greater effect than genetics on the associations between adolescents’ choice of peers, their expectations about alcohol, and their alcohol use. This adds important information to our understanding of environmental influences on alcohol-related behaviors in childhood and adolescence.

HUNGRY FOR MORE TREATMENT OPTIONS FOR ALCOHOL DEPENDENCE

Researchers are hoping to “cook up” a novel medication for alcohol dependence that’s based on the actions of an appetite-stimulating hormone, ghrelin. The medications currently available to treat alcohol dependence don’t work for everyone, so more options are needed. Studies in animals and people suggest that blocking ghrelin’s activity in the brain could be the basis of a new medication.

When you go a long time without eating, cells in the lining of the stomach increase production of ghrelin, a 28-amino acid hormone. Ghrelin travels through the bloodstream to the brain, where it signals hunger and influences the desire to eat. When food is consumed, ghrelin levels drop. Similarly, when alcohol-dependent people abstain from drinking, their ghrelin levels increase along with their craving for alcohol. Drinking, in turn, causes ghrelin levels to drop.

Research has shown that ghrelin is an essential part of the brain circuitry that reinforces alcohol use. Drinking stimulates the release of dopamine—a “feel good” chemical messenger—that is associated with alcohol’s “rewarding” effects in the brain, and receptors for ghrelin are present in brain regions that release dopamine. Mice that were either bred to lack ghrelin receptors or treated with drugs that block the receptors did not exhibit an alcohol-induced dopamine response, suggesting that ghrelin was required. A separate study showed that blocking the ghrelin signal to the brain in rodents reduced the rewarding properties of alcohol following gastric bypass surgery, a procedure previously shown to increase alcohol use. Building on these and other animal studies, clinical studies are now focusing on whether interfering with the ghrelin “gut-brain” signaling pathway could be effective in treating alcohol dependence.

In a clinical research laboratory supported jointly by NIAAA and the National Institute on Drug Abuse (NIDA), investigators led by Dr. Lorenzo Leggio are exploring ghrelin’s role in alcohol craving and consumption among patients who drink heavily. Recently, they showed that alcohol affects ghrelin levels not only in the stomach but also more globally in the bloodstream. They observed that giving alcohol intravenously to people who were fasting blunted the expected rise in ghrelin. “Altogether, a growing body of clinical and animal research is highlighting the role of the gut-brain axis and ghrelin signaling in alcohol reward,” said Dr. Leggio.

Dr. Leggio’s team also is collaborating with other investigators in the NIAAA Intramural Program, as well as with Dr. Fatemeh Akhlaghi of the University of Rhode Island and Pfizer Pharmaceuticals, to test an oral diabetes medication that interferes with the ghrelin pathway to see if this drug can be used to treat alcohol dependent individuals. Through a pilot initiative of the National Center for Advancing Translational Sciences (NCATS), the group will first conduct safety studies to determine how the drug interacts with alcohol in humans. Then they will look for evidence of the drug’s effectiveness in treating alcohol dependence, including the use of functional brain imaging to see if the drug dampens the brain’s craving signals for alcohol.

The ghrelin-based oral medication study is in its early stages; it will be several years before safety and effectiveness are fully evaluated. Nonetheless, “the hope is that this research may eventually lead to the development of a novel and effective pharmacological treatment for patients who suffer from alcohol use disorders,” said Dr. Leggio.

Resources:


TOM DONALDSON

Tom Donaldson has served as the Chief Executive Officer of the National Organization on Fetal Alcohol Syndrome (NOFAS) since 1998 and as its President since 2002. He recently received the NIAAA Senator Harold Hughes Memorial Award for his significant contributions to the field. Specifically, he has helped expand outreach and prevention services nationwide for those affected by Fetal Alcohol Spectrum Disorders (FASD) and successfully advocated for increased Federal and State FASD-related research.

1 Do you believe that FASD issues get the attention they deserve?

Unfortunately, FASD largely remains a hidden disability despite that it was identified over 40 years ago and as many as 40,000 newborns are affected each year in the United States alone. Too often, service providers are not prepared to identify and treat children and adults with FASD, and too many disease classifications do not recognize FASD as a condition eligible for services. The good news is it does get the attention it deserves from a basic research standpoint. Now the challenge is to promptly translate new findings into practice to improve identification and clinical intervention and to prevent the disorders.

2 Advocacy organizations like NOFAS serve many functions. What do you believe is your greatest contribution to the national discussion on FASD?

As a national organization focused solely on FASD, our first obligation is to serve individuals and families in need. To do so effectively and to ensure that there are appropriate resources, NOFAS organizes FASD constituents to appeal for change to policymakers and systems of care at every level. I believe there is a growing interest in addressing FASD and the risk of alcohol consumption during pregnancy; the goal for NOFAS is to leverage this recognition into greater investment and expanded services.

3 Are there any exciting advances or promising developments on the horizon?

Yes, quite a few. For example, the recently published fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) provisionally recognizes neurodevelopmental disorders associated with prenatal alcohol exposure for the first time. Ninety-four percent of adults with the full Fetal Alcohol Syndrome have behavioral health problems, so its inclusion in DSM–5 as a diagnosable, treatable disorder will be critical for them and can help reduce the secondary disabilities linked to FASD. The Collaborative Initiative on FASD (CIFASD) also is making enormous strides in our understanding of how prenatal alcohol exposure interferes with brain development and behavior, possible protective factors, effective interventions, and other facets of the alcohol and pregnancy issue.

4 You’ve just been awarded the prestigious Hughes Award from NIAAA. What does that mean to NOFAS?

Any attention for NOFAS and FASD helps to advance the cause. Because of its significance, the Hughes Award goes far beyond acknowledgment of the NOFAS mission. It affirms that FASD is as important as any alcohol-related issue in society, and it provides another mandate for research, public health, intervention, and other initiatives. Over the years, NOFAS has benefited greatly from our partnership with NIAAA. With the Institute’s support and that of other agencies in the Department of Health and Human Services, we have been able to develop an FASD medical school curriculum, implement alcohol screening and brief intervention at Federally qualified community health centers in eight States, create a health promotion campaign targeting women of child-bearing age in Washington, D.C., and develop a Webinar series featuring FASD researchers discussing their published findings.

5 You are a lifelong Redskins fan. Any advice for the team?

Well, the team certainly doesn’t need advice from me or anyone else—even if they happen to be part of the organization—who doesn’t know how to put together and run a football operation. They’ll be on the right track with a healthy RG III, a new coach, and some new players.
The severity of an AUD—mild, moderate, or severe—is based on the number of criteria met.

The specific diagnostic criteria have changed somewhat as well. The DSM–5 eliminates “legal problems” as a criterion for AUD (legal problems was one of the alcohol abuse criteria in the DSM–IV), and adds “craving” as a criterion for an AUD diagnosis. Craving was not included in the DSM–IV.


Importantly, the DSM has long been the standard used by health care providers and health insurers alike in diagnosing these conditions and billing for their treatment.

The DSM initially developed out of a need to collect statistical information about mental disorders in the United States. The first attempt to collect information on mental health began in the 1840 census. By 1880, the Bureau of Census had developed seven categories of mental illness. In 1917, the Bureau of Census began collecting uniform statistics from mental hospitals across the country. Not long afterward, the APA and the New York Academy of Medicine collaborated to produce a “nationally acceptable psychiatric nomenclature” for diagnosing patients with severe psychiatric and neurological disorders.

In 1952, the APA Committee on Nomenclature and Statistics published the first edition of the Diagnostic and Statistical Manual: Mental Disorders (DSM–I). The DSM–I included a glossary describing diagnostic categories and included an emphasis on how to use the manual for making clinical diagnoses. Subsequent editions were published in 1968 (DSM–II), 1980 (DSM–III), 1987 (DSM–III–R), 1994 (DSM–IV), and 2000 (DSM–IV–TR). NIAAA’s fact sheet provides more details about these editions, each of which aimed to improve clinicians’ ability to understand and diagnose a wide range of psychiatric conditions.