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

FEATURE

WINNERS OF NIAAA'S WEARABLE ALCOHOL BIOSENSOR CHALLENGE



We have a winner! In March 2015, NIAAA issued a challenge to the biotech community—create a wearable, non-invasive device capable of measuring blood alcohol levels in near real-time. Such a device would allow researchers to collect more accurate data on participants' drinking patterns and reduce reliance on self-report. More accurate data can enhance studies of alcohol use disorder (AUD) and other diseases affected by alcohol.

The goal of the NIAAA competition was to improve upon existing alcohol biosensor devices commonly used in the criminal justice system, which are effective but cumbersome and take readings only every 30 minutes. The new device had to be able to measure blood alcohol levels non-invasively and interpret and store the data (or transmit it to a smartphone or other device).

BACtrack, a company known nationally for designing and selling portable breath alcohol testers for consumer and professional use, received the \$200,000 first prize. Their winning prototype, the BACtrack Skyn, is worn on the wrist and offers continuous and non-invasive monitoring of a user's blood alcohol content (BAC). Alcohol is detected using a fuel-cell technology similar to that in devices used by law enforcement for roadside alcohol testing. The device connects via Bluetooth to a smartphone to store data.

"NIAAA issued this challenge to spark innovation in alcohol biosensor development. We were very pleased at the level of response and quality of prototypes that we received from the biotech community," said NIAAA Director George F. Koob, Ph.D.

The scientific community rose to the challenge, and NIAAA received eight submissions. The working prototypes were tested in the lab for accuracy compared to measured breath alcohol levels. Most of the designs took the form of fitness tracker-type watches and estimated BAC based on the amount of alcohol escaping through perspiration—a technique known as "transdermal monitoring." One notable exception was a color-changing temporary tattoo applied directly to the skin.

Second prize (\$100,000) was awarded to Milo, a Santa Barbara, California,

Continued on page 3

IN THIS ISSUE

FEATURES



- 1 Winners of NIAAA's Wearable Alcohol Biosensor Challenge



- 2 New NESARC Data Providing Key Information on Prevalence of Alcohol and Substance Abuse

NIAAA@WORK



- 3 Laboratory of Membrane Biochemistry and Biophysics, Section on Nuclear Magnetic Resonance

SPOTLIGHT



- 4 Review Articles by NIAAA Senior Staff: Sex Differences in Addiction Research; FASD History



- 4 Marlene Oscar Berman, Ph.D., Delivers Eighth Annual Mendelson Lecture

SIDEBAR



- 5 SALIS Makes NIAAA Monographs and Other References Widely Available



- 5 NIAAA Activities at the 2016 RSA Meeting

NEWS FROM THE FIELD



- 6 Translation in Stress Research—of Mice and Men



- 6 Anxiety and Depression Predict Relapse

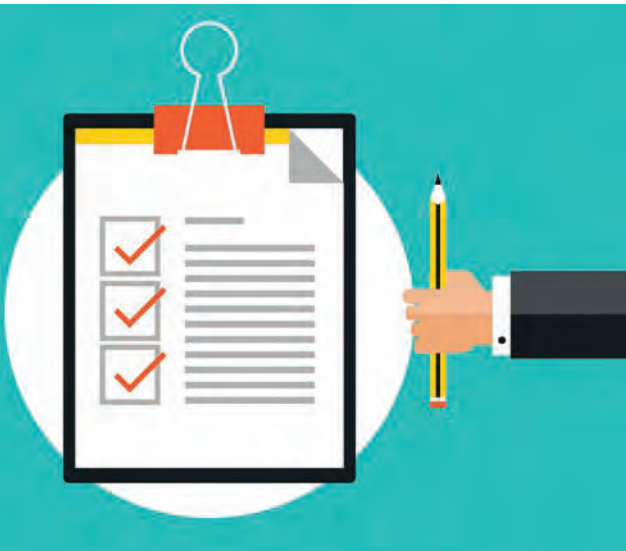
5 QUESTIONS WITH . . .



- 7 Kathy Jung, Ph.D., Program Director, Division of Metabolism and Health Effects, NIAAA

FEATURE

NEW NESARC DATA PROVIDING KEY INFORMATION ON PREVALENCE OF ALCOHOL AND SUBSTANCE ABUSE



In April of this year, Dr. Grant's group reported results of a study in which they used NESARC-III data to examine the prevalence, correlates, psychiatric comorbidity, and treatment of *Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (DSM-5)* nicotine use disorder (NUD) and the public health burden of U.S. cigarette consumption among adults with

NUD and other psychiatric disorders. As Dr. Grant's group reported in the *Journal of Clinical Psychiatry*, the prevalences of 12-month and lifetime DSM-5 NUD were 20.0 percent and 27.9 percent, respectively. NUD was more common among men, non-Hispanic whites, younger individuals, previously married individuals, those with less education and lower incomes, and residents of rural areas. The 11.1 percent of U.S. adults who have current NUD and at least 1 psychiatric disorder were found to consume more than 50 percent of all cigarettes smoked in the United States. Only about 20 percent of individuals with 12-month NUD sought treatment, as did about 19 percent of those with lifetime NUD. Dr. Grant and her colleagues conclude that their findings underscore the need to address nicotine use in clinical settings and that recognizing psychiatrically vulnerable subpopulations may inform efforts to prevent and treat NUD.

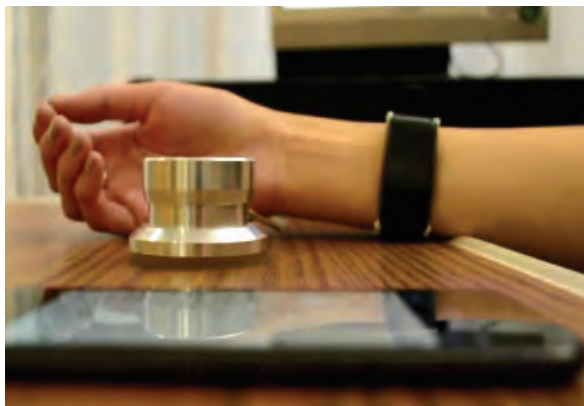
In March, Dr. Grant's group published findings of a study that analyzed marijuana use data from NESARC-III. Their analyses found that 2.5 percent of adults—nearly 6 million people—experienced marijuana use disorder in the past year, while 6.3 percent had met the diagnostic criteria for the disorder at some point in their lives. Consistent with previous findings, the new report showed that marijuana use disorder is about twice as common among men than women and that younger age groups are much more likely to experience the disorder than people ages 45 and older. The risk for onset of the disorder was found to peak during late

The NIAAA-sponsored National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III), conducted from 2012 to 2013, is the newest wave of the largest study ever conducted on alcohol, tobacco, and illicit drug use and disorders; related risk factors; and associated physical and mental disabilities. With data on more than 36,000 U.S. adults, NESARC-III promises to be a primary source of information for scientists throughout the United States, many of whom used earlier NESARC data in hundreds of studies across multiple disciplines and disease areas. Indeed, several important studies using NESARC-III data have recently been published by NIAAA scientists led by Bridget Grant, Ph.D., Ph.D., Chief of NIAAA's Laboratory of Epidemiology and Biometry. Dr. Grant has directed NIAAA's NESARC survey since its inception in 2001, and she and her colleagues routinely publish NESARC findings across broad areas of substance abuse and mental health.

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adolescence and among people in their early 20s, with remission occurring within 3 to 4 years. Also in keeping with previous findings, the new study found that past-year and lifetime marijuana use disorders were strongly and consistently associated with other substance use and mental health disorders.

FEATURE: Biosensor Challenge . . . Continued from page 1



technology startup, for their design for a wearable blood alcohol sensor. Milo's wrist-worn wearable pairs with a smartphone and uses disposable cartridges to continuously track BAC.

"The winning entries show important improvements in transdermal technology and performance, and certainly in wearability," said Kathy Jung, Ph.D.,

NIAAA program officer and co-organizer of the biosensor challenge.

Honorable Mentions went to BioInk, a color-changing tattoo design by a company of the same name, and TAMS (transdermal alcohol-monitoring system), from a team affiliated with Florida International University.

With wearable technology becoming increasingly popular, NIAAA hopes that the Wearable Alcohol Biosensor Challenge will stimulate public and private investment in alcohol-monitoring devices. Well-calibrated alcohol biosensors will provide an objective measure of alcohol consumption for research studies, with participants being able to avoid the inconvenience and discomfort

of having blood drawn at regular intervals. The data collected will also be more accurate than self-report. Alcohol biosensors have commercial appeal as well; members of the public concerned with their personal drinking, or in the counsel of a therapist, would be able to use the discreet device without stigma.

Challenge competitions are a creative way for the federal government to seek innovative solutions from the public. The Wearable Alcohol Biosensor Challenge marks the first time NIAAA has awarded a prize through Challenge.gov.

Challenge.gov:
A Wearable
Alcohol Biosensor
<https://www.challenge.gov/challenge/a-wearable-alcohol-biosensor/>

NIAAA@WORK

LABORATORY OF MEMBRANE BIOCHEMISTRY AND BIOPHYSICS, SECTION ON NUCLEAR MAGNETIC RESONANCE



You may be familiar with how doctors use pictures from magnetic resonance imaging machines, better known as MRIs, to diagnose injuries and other health problems. But did you know that NIAAA scientists have another technology that harnesses the power of strong magnets to study receptors in the brain that could be targets for alcohol therapies? NIAAA's Intramural Section on Nuclear Magnetic Resonance (NMR) uses an NMR spectrometer, which utilizes a strong magnetic field and radio waves to delineate the structure of brain proteins and of the membranes they are embedded in, allowing scientists to design selective new drug molecules that bind to these receptors. Unlike an MRI machine, an NMR spectrometer is not used directly on patients, but rather on very small samples, which are usually reconstituted highly purified protein-coupled membrane receptors, but could also be a preparation of natural cell membranes. These samples model the highly variable composition of a human cell membrane, allowing scientists to study its properties, including the function of certain receptors. The NMR spectrometer provides detailed information about the shape, dynamics, and interactions of molecules, and has been used in NIAAA studies to deepen our understanding of how substances such as docosahexaenoic acid—an omega-3 fatty acid—interact with membrane receptors. Findings from NIAAA's NMR studies have important implications for improving our understanding of human nutrition, including the influence of alcohol on the composition and function of membranes.

Above, NIAAA scientists Drs. Olivier Soubias, Klaus Gawrisch, and Walter Teague (L-R) are pictured in the room that was specially constructed to house the "big magnet." This device is powerful enough to resolve protein structures but is also so sensitive that it needs to be protected from temperature changes and vibrations in order to produce accurate data.

SPOTLIGHT

REVIEW ARTICLES BY NIAAA SENIOR STAFF: SEX DIFFERENCES IN ADDICTION RESEARCH; FASD HISTORY



In addition to publishing new research findings, NIAAA scientists often write review articles that summarize current knowledge and outline new research opportunities in a specific area of investigation. For example, recent review articles by NIAAA senior staff include one about sex differences in addiction research and another about the history of drinking during pregnancy and the identification of fetal alcohol spectrum disorder (FASD).

Sex Differences

Recent NIH-wide efforts to address sex differences in preclinical research

underscore the importance of such issues to scientists who study alcohol addiction.

“In fact, animal models of alcohol addiction reveal significant differences between males and females,” says NIAAA Director George F. Koob, Ph.D., “but we have little data thus far to help us understand the neurobiological mechanisms for those differences.”

NIAAA’s increased emphasis on research in this area will be informed by a timely new review article, co-authored by Dr. Koob and Dr. Jill Becker of the University of Michigan, titled, “Sex Differences in Animal Models: Focus on Addiction.” Published in the April 2016 issue of the journal *Pharmacological Reviews*, the article discusses ways to think about and study sex differences in preclinical animal models.

“We use the framework of addiction to illustrate the importance of considering sex differences,” says Dr. Koob, “and we have outlined major quantitative,



population, and mechanistic sex differences in the addiction domain. We also emphasize the need for new studies to help us understand those differences.”

Reference:

Becker, J.B., and Koob, G.F. Sex differences in animal models: Focus on addiction. *Pharmacological Reviews* 68(2):242–263, 2016. PMID: 26772794

History of Attitudes About Drinking During Pregnancy

Although it is now well-accepted that prenatal alcohol exposure is the primary

Continued on page 8

SPOTLIGHT

MARLENE OSCAR BERMAN, PH.D., DELIVERS EIGHTH ANNUAL MENDELSON LECTURE

Marlene Oscar Berman, Ph.D., delivered the eighth annual Jack Mendelson Honorary Lecture on May 25 in the Lipsett Amphitheater at the NIH Clinical Center. This lecture series is a tribute to Dr. Jack Mendelson, who made remarkable contributions to the field of clinical alcohol research. Each spring, the series features a lecture by an outstanding alcohol investigator whose clinical research has made a substantial contribution to our understanding of alcohol susceptibility, alcohol’s effects on the brain and other organs, and the prevention and treatment of alcohol use disorder (AUD).

Dr. Berman presented a talk titled, “Brain Mechanisms Underlying the Perceptual, Emotional, and Cognitive Impairments Associated with Chronic

Alcohol Use Disorder.” Dr. Berman is Professor of Neurology, Psychiatry, and Anatomy & Neurobiology, and Director of the Laboratory of Neuropsychology at the Boston University School of Medicine. She is also a career research scientist in the Department of Veterans Affairs Healthcare System in Boston.

Through her more than 40 years as a researcher and educator, Dr. Berman has advanced our understanding of the brain mechanisms underlying the perceptual, emotional, and cognitive impairments associated with chronic AUD. Her research program uses neuropsychological tests and imaging measures of brain structure and function to assess the effects of chronic AUD in men and women. During her talk, Dr. Berman discussed her decades

of research in its historical context, starting with the pioneering studies characterizing the severe memory impairments in Korsakoff’s syndrome that are the result of brain damage caused by chronic AUD. Her research on memory in individuals with AUD also showed that certain functions (such as encoding a memory) may be spared from the negative effects of alcohol abuse, suggesting that these functions could be used to help compensate for impaired performance. Some of Dr. Berman’s most recent work comparing men and women with chronic AUD found differential effects of alcohol on brain structure and on cognitive and emotional functioning.



SALIS “DIGS” PROJECT MAKES NIAAA MONOGRAPHS AND OTHER REFERENCES WIDELY AVAILABLE



The Substance Abuse Librarians and Information Specialists (SALIS), in partnership with NIAAA and a non-profit digital library called the Internet Archive (IA), are working to digitize the literature of the alcohol-and-other-drugs field that is not already available online—specifically, books and government documents. To date, this digitization (or “Digs”) project has posted 758 items, ranging from the basic to social sciences and including academic, popular press, and historical and biographical documents. All 37 NIAAA monographs that were published

between 1982 and 2002 will be available in this library. Currently, it is possible to search for items by title, author, subject, or date. Eventually, the content of all materials will be fully searchable as well. These digitized books and documents can be “checked out” for 2 weeks at no cost and are automatically returned to the system at the end of the borrowing period. To access this valuable repository of information, please visit the SALIS Collection at <https://archive.org/details/salis>, and if you have questions, please contact salis@salis.org.

NIAAA ACTIVITIES AT THE 2016 SCIENTIFIC MEETING OF THE RESEARCH SOCIETY ON ALCOHOLISM (RSA)



On Sunday, June 26, at 8:10 a.m., NIAAA Director Dr. George F. Koob will present the *NIAAA Update* at the Annual Scientific Meeting of the Research Society on Alcoholism (RSA) in New Orleans, Louisiana. Below is a selection of other NIAAA activities at RSA. For the full program and latest schedule updates, please consult the RSA Web site at <http://www.rsoa.org/>.

Monday, June 27

9:15 a.m.–10:45 a.m.

- *Heavy and Extreme Binge Drinking in Youth: Prevalence, Correlates, and Consequences* (symposium)

Co-chaired by Dr. Kasey Creswell, Carnegie Mellon University, and Dr. Aaron White, Senior Scientific Advisor to the Director, NIAAA. Dr. Ralph Hingson, Director, Division of Epidemiology and Prevention Research, NIAAA, will

present a lecture titled, “Beyond the Binge Threshold: Predictors, Consequences, and Changes in the Prevalence of High Peak Levels of Alcohol Consumption in the United States, 2001/2002 to 2013/2014.”

9:15 a.m.–10:45 a.m.

- *Epigenetic Interventions in Alcoholism—Recent Advances and Future Challenges* (symposium)

Co-chaired by Dr. Antonio Noronha, Director, Division of Neuroscience and Behavior, NIAAA, and Dr. Subhash Pandey, University of Illinois at Chicago

1:20 p.m.–2:50 p.m.

- *Bad Behavior in Clinical Trials—Research Subject Dishonesty/Deception, Intentional Nonadherence, and “Professional Subjects”* (roundtable)

Co-chaired by Dr. Raye Litten, Acting Director, Division of Medications Development, NIAAA, and Dr. David McCann, Associate Director, Division of Therapeutics and Medical Consequences, National Institute on Drug Abuse

Tuesday, June 28

9:15 a.m.–10:45 a.m.

- *From Rodents to Primates—The Effects of Chronic Ethanol Exposure on Neural Circuitry Involved in Development of Alcohol Use Disorders*, which will feature a talk titled, *Dorsal Striatum*

Neuroadaptations in Dopamine Signaling Associated with Long-Term Ethanol Exposure and Withdrawal (symposium)

Chaired by Dr. David Lovinger, Deputy Scientific Director, Division of Intramural and Clinical Biological Research, NIAAA

Wednesday, June 29

9:15 a.m.–10:45 a.m.

- *Current Trends and Future Directions in Recovery-Based Research for Alcohol Use Disorders—Moving Beyond Formal Treatment* (symposium)

Co-chaired by Dr. Brett Hagman, Division of Treatment and Recovery Research, NIAAA, and Dr. Sarah Zemore, Alcohol Research Group, Public Health Institute, Emeryville, California

9:15 a.m.–10:45 a.m.

- *Developmental Origins of Adult Health and Disease—A New Take On Prenatal Alcohol Exposure* (symposium)

Co-chaired by Dr. Bill Dunty, Division of Metabolism and Health Effects, NIAAA, and Dr. Joanne Weinberg, University of British Columbia

NEWS FROM THE FIELD

TRANSLATION IN STRESS RESEARCH—OF MICE AND MEN



Both humans and animals experience stress. Ideally, stress serves as a survival tool, allowing organisms to adapt and overcome adversity in an unpredictable environment. As a result, higher-order animals have developed complex systems to perceive, react to, and adapt to psychological stress, ensuring that they can respond to

environmental dangers that might harm or kill them. But for some, the response to stress can go awry, and what started as a natural response to a changing environment can ultimately become a chronic disease such as depression, anxiety disorder, or posttraumatic stress disorder (PTSD). A recent review in *Nature Neuroscience* explores how innovative findings in animals can advance our understanding of stress-related mental disorders in humans.

The review, written by Dr. Ahmad Hariri, Duke University, and Dr. Andrew Holmes, NIAAA Laboratory of Behavioral and Genomic Neuroscience, notes that the neural circuits and underlying genes that control the stress response are similar across species. Hence, studies in animals (known as preclinical studies) have revealed much

about the systems that play a central role in psychological stress, such as the hypothalamic–pituitary–adrenal axis, a complex interaction between three endocrine glands. Based on preclinical work, scientists also have an important understanding of how the brain perceives and processes stressful experiences. Across species, the amygdala, hippocampus, and prefrontal cortex work together to play a critical role in both short-term and long-term response to stress. Using animal models, scientists have also been able to identify genetic variants that contribute to stress-related disorders. These candidate genes could help identify people at risk for such disorders and provide possible targets for developing treatments.

Continued on page 8

NEWS FROM THE FIELD

ANXIETY AND DEPRESSION PREDICT RELAPSE IN AUD PATIENTS WITH CHRONIC PAIN



Interventions to reduce anxiety and depression may help prevent relapse in individuals with chronic pain who are recovering from alcohol use disorder (AUD). This conclusion comes from a recent study in which investigators reanalyzed data collected from people with chronic pain who participated in one of two major clinical trials on alcohol treatment, one in the United States and one in the United Kingdom. Both trials included the collection of data that allowed the authors of the present study

to look at the links between pain, negative affect, and relapse. In the present study, the researchers conducted a separate reanalysis for each of the two original studies.

People in recovery from AUD commonly have relapses to heavy drinking following a stretch of abstinence or cutting back. Previous research has shown that risk factors for relapse include stress, craving, and the “negative affect” states of anxiety and depression. Pain has not been widely studied as a risk factor, even though chronic pain is common and often self-managed with alcohol.

Based on their new analyses, the authors report that people with higher pain levels in both studies tended to have higher levels of negative affect and increased rates of relapse. The key finding, however, was that the participants’ levels of anxiety or depression in

both studies predicted relapse better than their particular pain levels.

It is important to note that in the U.K. clinical trial, a high-intensity behavioral intervention called social behavior network therapy (SBNT) appeared to reduce the effects of pain on negative affect and relapse. Participants in that trial were randomly assigned to receive either SBNT, which helped build social networks that supported abstinence or reduced drinking, or a lower-intensity motivational enhancement therapy (MET). In the MET group, participants with greater pain scores at the end of treatment tended to have more heavy-drinking days 12 months later. In contrast, those in the SBNT group with greater pain scores at the end of treatment did not drink significantly

Continued on page 8

5 QUESTIONS WITH . . .

KATHY JUNG, PH.D.

Program Director, Division of Metabolism and Health Effects, NIAAA



1 You recently co-organized the Alcohol Biosensor Challenge Prize. How does a mechanism like this compare to a typical NIAAA grant program?

The Challenge Prize is a relatively new federal-funding mechanism that so far has been used by only a few NIH Institutes and Centers. The Wearable Alcohol Biosensor Challenge is NIAAA's first project of this type. Using this mechanism, agencies hoping to make an advance in a particular area issue a challenge in the form of a competition. The goal is to enlist innovators and talented people who wouldn't typically apply for a grant, and encourage them to present a solution—a sort of crowd-sourcing approach. The cash prize—which is one way to do it—stimulates involvement, while the competitive nature of the challenge creates some buzz about areas of interest to the sponsor. For NIAAA, expanding intellectual efforts beyond the alcohol research community is especially beneficial in a case like the biosensor challenge, where engineering expertise is needed more than, or as well as, biological or medical expertise. Another advantage of this approach is financial: while grants and contracts pay to support an attempt, which may or may not succeed, challenges only pay for a result.

2 In general, why is transdermal biosensor research so important?

Wearable alcohol biosensors have many potential uses. Circumventing the need for self-report, better real-time alcohol biosensors will be useful in research, and in the management of alcohol use disorder and alcohol-induced organ damage, as well as the management of other diseases that may be negatively affected by alcohol consumption, such as HIV. The ability to accurately monitor blood alcohol in real time will also be useful to individuals, for example those who monitor their health carefully or who may seek to control their drinking.

While until now, wearable sensors have used transdermal technology, which detects alcohol that has passed through the skin in perspiration, there may be even greater promise in newer technologies that can detect alcohol in the blood, which would reflect real-time physiology better than measuring alcohol in perspiration.

3 What are some of the recent developments in this field?

Improvements in detection of alcohol in sweat vapor or sweat have been stalled for some time, so the responses to NIAAA's challenge have been encouraging. While the majority of the entries are early prototypes using sweat or sweat vapor, and still require further refinement, some are novel, and most of them overcome some of the disadvantages of the current technology.

Furthermore, as mentioned above, it is already possible to assess alcohol concentration using optical technology, but so far this is only possible in devices far too large to be wearable. Spectroscopic devices exhibited recently at the 2016 Consumer Electronics Show demonstrated tremendous advances in miniaturization, increasing the possibility that this

technology may soon translate to a wearable device.

4 Are there any particularly exciting breakthroughs on the horizon for the field? Should we be optimistic?

Now that NIAAA has stimulated the field, or restimulated it, there will be new designs, even new fundamental approaches to detecting alcohol in the blood. It is likely that an increasingly competitive market will spur the development and availability of reliable alcohol biosensors that are attractive to consumers.

5 What made you decide to become a scientist?

I've always been interested in how things work, particularly the cellular and molecular processes in the healthy body, and in what goes wrong in disease. I was attracted to biochemistry, and my dad advised me that a major in chemistry would provide a strong foundation. For me, the research process—asking a question, then designing a rigorous experimental approach so that the results don't fool us—is more fun than work. I've conducted research on mitosis and other aspects of cell biology, and also worked in cancer biology and in drug discovery. I am motivated to find answers that can be used to solve problems.

SPOTLIGHT: FASD History . . . Continued from page 4

cause of FASDs, that knowledge was either unknown or ignored for the majority of the 20th century.

“Indeed, the belief that there was no risk to the mother or the fetus from prenatal alcohol persisted well into the 1970s,” says Kenneth R. Warren, Ph.D., currently NIAAA Senior Advisor for Science and Operations.

Dr. Warren recently reviewed key events that changed physician and public understanding of the risks posed by

prenatal alcohol use during pregnancy. These events, he notes, were aided by the creation of NIAAA in 1971.

“Early research studies supported by NIAAA provided the foundation for the first government health advisory on alcohol and pregnancy, issued by NIAAA in 1977,” notes Dr. Warren.

Ultimately, the efforts of NIAAA and other federal agencies resulted in a new health advisory under the auspices of the U.S. Surgeon General, encouraging

avoidance of alcohol consumption in pregnancy. In subsequent years, congressional attention to FASD resulted in the Alcoholic Beverage Labeling Act, which requires a government warning that women should not drink alcoholic beverages during pregnancy.

Reference:

Warren, K.R. A review of the history of attitudes toward drinking in pregnancy. *Alcoholism: Clinical and Experimental Research* 39(7):1110–1117, 2015. PMID: 26137906

NEWS FROM THE FIELD: Translation in Stress . . . Continued from page 6

Preclinical models have been developed for a wide range of disorders. The authors note that “translational stress research is thus positioned to be a standard bearer for the charge toward

the recasting of mental illness as manifestations of disordered brain circuits and the behavioral processes they subserve.”

Reference:

Hariri, A., and Holmes, A. Finding translation in stress research. *Nature Neuroscience* 18(10):1347–1352, 2015. PMID: 26404709

NEWS FROM THE FIELD: Anxiety . . . Continued from page 6

more a year later, than those with lower pain scores. The authors suggest that the healthy social support system built by the SBNT group may have reduced the participants’ tendencies to drink heavily in response to pain or negative affect.

The analysis was designed to show associations among pain, negative

affect, and alcohol use, but not whether one factor came before or caused another. The authors concluded that the findings lend support for the SBNT intervention as well as future research into the potential benefits of negative-affect treatments for people with AUD and chronic pain.

Reference:

Witkiewitz, K.; McCallion, E.; Vowles, K.E.; Kirouac, M.; Frohe, T.; Maisto, S.A.; Hodgson, R.; Heather, N. Association between physical pain and alcohol treatment outcomes: The mediating role of negative affect. *Journal of Consulting and Clinical Psychology* 83(6):1044–1057, 2015. PMID: 26098375

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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