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

FEATURE

BRAIN RESEARCH: A FOCUS ON CHILDHOOD TRAUMA AND ALCOHOL MISUSE



News reports of college drinking tragedies, and concerns about increased access to alcohol in the home during the pandemic, make clear that COVID-19 has provided no reprieve from the problems of underage drinking. A perennial public health priority, alcohol misuse by young people

increases the likelihood of myriad serious consequences, including altered brain development, academic problems, unsafe sexual behavior, physical and sexual assault, traffic crashes, injuries, overdoses, and alcohol use disorder (AUD).

To be sure, efforts to reduce underage drinking have seen success in recent decades. Epidemiological data from the annual [Monitoring the Future survey](#), funded by the National Institute on Drug Abuse, show that by 2020, proportional declines in the prevalence of binge drinking, following recent peaks reached in the 1990s, were 66 percent, 60 percent, and 47 percent for grades 8, 10, and 12, respectively.

George F. Koob, Ph.D., Director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), notes “We are indeed making progress at reducing alcohol misuse among adolescents and young adults; however, the declines have been larger among males than females, and trends in serious alcohol-related harms have not matched the trends in drinking prevalence. Also, drinking to cope with stress is a growing concern.”

Recent and ongoing studies supported by NIAAA indicate that investigations of the relationship between childhood trauma and alcohol misuse, and the neural substrates through which that relationship is mediated, will provide important avenues for continued progress against underage drinking, its subsequent problems, and their potential treatment. Many of these studies include examination of emotional stress and mental health problems, such as [post-traumatic stress disorder \(PTSD\)](#), that frequently co-occur with AUD.

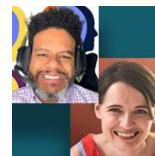
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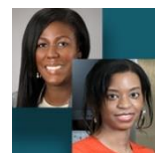


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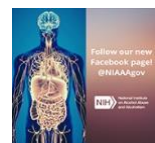


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For example, in a [2020 study led by scientists at Arizona State University](#), researchers found that recollections of childhood trauma (such as sexual and emotional abuse) may contribute to [PTSD symptoms](#) and impaired control over drinking among college students. The researchers found that reducing PTSD symptoms may help individuals regain control over their drinking. Also last year, [researchers at Virginia Commonwealth University reported](#) that young adults with a history of childhood maltreatment may use alcohol to cope with trauma-related negative emotions. The study's findings suggest that targeting emotional distress in people exposed to trauma in childhood may be helpful in preventing and treating alcohol-related problems in this vulnerable population. In a [recent analysis](#) conducted by the NIAAA-supported Collaborative Study on the Genetics of Alcoholism, researchers showed that having a family history of AUD and exposure to trauma during adolescence may be associated with increased PTSD and AUD symptoms and poor problem-solving abilities in adulthood.

NIAAA supports the [National Consortium on Alcohol and Neurodevelopment in Adolescence \(NCANDA\)](#), a major research initiative established to determine the effects of alcohol misuse on the developing adolescent brain and to examine brain characteristics that predict AUD. In a recent study, researchers used NCANDA data to investigate the relationships among childhood trauma, functional brain connectivity, impaired executive function, and future binge drinking during adolescence. Led by scientists at the University of California San Diego, [the study found](#) that functional brain networks, particularly from regions important for cognitive and sensorimotor control, explain the relationship between childhood trauma and impaired executive function and are important for predicting binge drinking. Age, severity of childhood trauma, extent of executive function deficits, and functional brain connectivity together were useful in accurately predicting binge drinking 1–4 years after research participants were initially assessed for alcohol misuse.

Another [NCANDA study](#) recently demonstrated that adolescent alcohol misuse and early-life trauma led to increased hippocampus growth and decreased amygdala growth with age. The hippocampus and amygdala are brain regions that regulate goal-directed behaviors, inhibition, memory, anxiety, and fear responses. [NCANDA investigators have also demonstrated](#) that non-drinking or low-drinking adolescents who reported experiencing trauma and symptoms of post-traumatic stress escalated their alcohol intake during a 4-year followup period more quickly than adolescents who did not experience trauma. Taken together, these NCANDA findings demonstrate a relationship between early adverse experiences, brain development, and alcohol misuse, and suggest that interventions that target trauma may be beneficial in preventing future alcohol misuse and AUD.

NIAAA-supported research continues to build a solid foundation for the development of unique strategies for treating alcohol problems that arise during the developmentally risky period of adolescence. Recently, NIAAA issued a [Notice of Special Interest](#) to expand research on how treatment strategies can be tailored for adolescents. These strategies include behavioral treatments that take into account the developmental, biological, neurocognitive, psychological, emotional, and social needs of youth, as well as intervention approaches that account for comorbidity, cultural, and other factors.

“Prevention and treatment strategies grounded in a developmental framework that takes into account early life stress will help us maximize the odds that individuals make it into young adulthood cognitively and emotionally prepared for the rigors of adult life,” says Dr. Koob.

He adds that the unprecedented stressors experienced by young people during the COVID-19 pandemic will linger to some degree, even as society begins to contemplate the potential end of the pandemic. “Current public health measures, and the uncertainties and anxieties they engender about the future, lost income, and social isolation, will be with us for a while longer. And the transition to a post-pandemic reality will itself be a likely source of new stressors and anxieties as society adjusts to a new ‘normal,’ underscoring the importance of ongoing NIAAA investigations into the relationship between stress and alcohol misuse.”

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NEWS FROM THE FIELD

EMOTIONAL RESPONSES TO ALCOHOL MAY PREDICT ALCOHOL-RELATED PROBLEMS



Catharine Fairbairn, Ph.D., and Walter James Venerable, III, M.S., led the University of Illinois at Urbana-Champaign project assessing emotional responses to alcohol.

Alcohol can induce temporary positive feelings such as elation and happiness and reduce negative feelings like distress. These emotional responses to alcohol are believed to contribute to drinking behaviors that lead to alcohol use disorder or that make abstaining from drinking more difficult for some people. A new study funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) now sheds more light on the link between emotional responses to alcohol and drinking behaviors. It also reveals that emotional responses may be a predictor of alcohol-related problems.

To examine alcohol’s effects on emotions and drinking behaviors over time, Catharine Fairbairn, Ph.D., and Walter James Venerable, III, M.S., at the University of Illinois at Urbana-Champaign, combined laboratory

and real-world assessments that measured emotional responses to alcohol with long-term followup surveys of alcohol consumption. In the study, 60 young adults who engaged in heavy drinking attended two beverage-administration sessions in a laboratory, in which they consumed their beverages in social groups, designed to mirror real-world drinking conditions. They also completed surveys that measured their anxiety and positive and negative moods, such as cheerful and upbeat or annoyed and sad, respectively. In one session, participants received an alcoholic beverage, and in the other session they received a nonalcoholic beverage. A subset of participants also participated in a real-world, or ambulatory, assessment for 7 days to evaluate their alcohol consumption and mood in everyday contexts. This group wore transdermal alcohol monitors and responded to

random survey prompts about their mood six times per day. They also provided daily reports of their alcohol consumption. The researchers followed up with participants 18 months later.

The researchers found that participants who experienced a greater degree of positive mood after alcohol administration in the laboratory study were more likely to binge drink regularly and experience drinking problems at the 18-month followup. Similarly, participants who experienced greater reductions in negative mood were more likely to have drinking problems 18 months later. In the ambulatory study, alcohol-related reductions in negative mood measured in everyday contexts significantly predicted drinking problems at followup.

The results of the study support prior research demonstrating that emotional responses contribute to problematic drinking and that alcohol's ability to enhance positive mood and reduce negative mood may predict problematic drinking patterns later on.

Note:

NIAAA defines heavy drinking as follows:

- *For men, consuming more than 4 drinks on any day or more than 14 drinks per week*
- *For women, consuming more than 3 drinks on any day or more than 7 drinks per week*

Reference:

Venerable, W.J.; and Fairbairn, C.E. A multimodal, longitudinal investigation of alcohol's emotional rewards and drinking over time in young adults. *Psychology of Addictive Behaviors* 34(5):601–612, 2020. [PMID: 32118462](https://pubmed.ncbi.nlm.nih.gov/32118462/)

NEWS FROM THE FIELD

INSIGHTS ON ALCOHOL-RELATED BRAIN INFLAMMATION, AND HINTS ABOUT HOW TO REDUCE IT



Research suggests that long-term alcohol exposure leads to inflammation and damage to tissue in the brain and other organs—and inflammation could also potentially be involved in alcohol use disorder (AUD). A [recently published mouse study](#) supported by the National Institute on Alcohol Abuse and Alcoholism suggests a mechanism that contributes to this process: the migration and recruitment of blood-circulating immune cells to the brain. The study also shows that blocking one step along this pathway reduces this immune cell recruitment—opening a door to a potential therapeutic target for reducing inflammation-related damage in the brain.

Previous research suggests that immune cells from the body can infiltrate the brain following long-term alcohol exposure. The immune cells in question—monocytes—can wreak havoc if they are recruited to an organ such as the brain or liver. In the brain, monocytes transform into a type of immune cell called macrophages, which can play a role in kicking off a chain reaction of inflammation and tissue damage.

In the current study, the researchers found that feeding mice alcohol over the course of 6 weeks increased the number of macrophages in the brain. Once in the brain, macrophages contribute to signs of brain injury, such as the activation of brain-specific immune cells known as microglia, and the release of cytokines (a cell-signaling

molecule). This increase in macrophages was particularly noticeable in the hippocampus (compared to the cerebellum or cortex).

The researchers then tested whether they could reduce neuroinflammation after chronic alcohol use by blocking the CCR2/CCR5 pathway via administration of a drug called cenicriviroc (CVC). Previous research suggested that the CCR2/CCR5 pathway is involved in monocyte recruitment to tissues like the brain following long-term alcohol exposure. For example, there is evidence that alcohol exposure ramps up the amount of the protein—CCL2—that binds to the CCR2 receptor protein and promotes the recruitment of monocytes. The researchers showed that CVC is effective in reducing the recruitment of monocytes to the brain after long-term alcohol exposure. CVC also decreased certain signs of alcohol-induced brain inflammation. This finding complements results of ongoing research with CVC aimed at reducing inflammation in the liver, suggesting CVC could reduce inflammatory damage in multiple organ systems.

Taken together, this research reveals a potential molecular target to curb brain and liver inflammation due to long-term alcohol consumption, such as in individuals with AUD and alcohol-associated liver disease.

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NOTEWORTHY

NIAAA ANNOUNCES NEW EXTRAMURAL RESEARCH DIVISION



The National Institute on Alcohol Abuse and Alcoholism (NIAAA) recently introduced the Division of Treatment and Recovery (DTR), formed from the merger of the Institute's Division of Medications Development and Division of Treatment and Recovery Research. The new division focuses on identifying and improving pharmacological and behavioral treatments for alcohol use disorder (AUD), enhancing methods for sustaining recovery, and increasing the use of evidence-based treatments in real-world practice. DTR is led by Raye Litten, Ph.D., Acting Director, and Joanne Fertig, Ph.D., Acting Deputy Director, and is composed of a Medications Development Branch and a Treatment, Services, and Recovery Branch.

The Medications Development Branch oversees the development of medications for AUD by translating neuroscience discoveries into promising compounds and advancing them through the medications development pipeline. This includes funding studies to enable investigators to obtain Investigational New Drug status from the U.S. Food and Drug Administration for compounds that show promise, and conducting and supporting alcohol interaction, human laboratory, and Phase II clinical trials. The Medications Development Branch also seeks to:

- Identify new targets for AUD medications in collaboration with the Division of Neuroscience and Behavior and Division of Metabolism and Health at NIAAA,
- Develop screening models that predict a high probability of clinical efficacy and safety,
- Engage pharmaceutical and biotechnical companies in medications development for AUD, and
- Facilitate the use of alcohol treatment medications in clinical practice.

The Treatment, Services, and Recovery Branch supports a broad portfolio of behavioral treatment and recovery research. This includes:

- Developing and improving behavioral interventions for AUD,
- Increasing the use of evidence-based behavioral treatments in a wide range of practice settings,
- Improving treatments for individuals with AUD and co-occurring psychiatric and substance use disorders,
- Gaining a better understanding of the dynamics of recovery, and
- Developing innovative methods and technologies for AUD treatment and recovery.

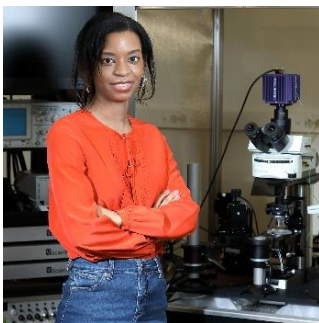
The Treatment, Services, and Recovery Branch is also interested in advancing research on topics focusing on special-emphasis and underserved populations, including minority populations, adolescents and young adults, older adults, individuals with fetal alcohol spectrum disorders, and persons living with HIV/AIDS. Together both branches will facilitate the overall goals of the Division of Treatment and Recovery to advance precision medicine in the treatment of AUD and promote and facilitate treatment of AUD across all groups in our diverse society.

NOTEWORTHY

NIAAA INTRAMURAL SCIENTISTS NAMED TO CELL MENTOR'S LIST OF INSPIRING BLACK SCIENTISTS IN AMERICA

The Cell Mentor website (<http://crosstalk.cell.com/en/cell-mentor>) is a dedicated resource provided by Cell Press to help individuals build the skills necessary for a successful career in science. Cell Mentor collects blog posts, video interviews, experimental tutorials, handbooks, and Cell Press journal articles to empower and inspire early career researchers. On December 28, 2020, Cell Mentor posted a list of 1,000 inspiring Black scientists in America.

Included in the Cell Mentor list were two National Institute on Alcohol Abuse and Alcoholism (NIAAA) intramural scientists:



Michelle Antoine, Ph.D., Chief of the [Section on Neural Circuits](#). Dr. Antoine joined NIAAA in 2020 as an Earl Stadtman Tenure-Track Investigator and is currently an NIH Distinguished Scholar. Her laboratory focuses on genetic and environmental factors that impair neurocircuit activity, leading to neurodevelopmental disorders. Her recent work on neuron signal activity led to important new insights into autism spectrum disorder. At NIAAA, Dr. Antoine is applying her basic research experience in neurocircuit function to neurodevelopmental comorbidities commonly seen in fetal alcohol spectrum disorders.



Paule Valery Joseph, CRNP, Ph.D., Chief of the [Section of Sensory Science and Metabolism](#). A Lasker Clinical Research Scholar and an NIH Distinguished Scholar, Dr. Joseph leads a research group conducting preclinical, clinical, and translational studies that aims to improve the diagnosis, prevention, and management of chemosensory disorders and symptoms (taste and smell alterations). A focus of Dr. Joseph’s research at NIAAA is to explore, at the neurobiological level, how senses such as smell and taste are involved in cues that trigger craving for alcohol, a diagnostic feature of alcohol use disorder.

Congratulations to Dr. Joseph and Dr. Antoine!

SPOTLIGHT

NIAAA EXPANDS ITS SOCIAL MEDIA PRESENCE TO FACEBOOK

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) recently launched a new Facebook page. This expansion of the Institute’s social media footprint allows NIAAA to reach the rich diversity of Facebook users—particularly individuals, families, educators, and other adults who could benefit from NIAAA’s resources and health messages. Follow us on Facebook today at <https://www.facebook.com/NIAAAgov>.

Alcohol affects the lives of many Americans. According to the 2019 National Survey on Drug Use and Health, 54.9 percent of adults reported that they drank alcohol sometime in the past month and 25.8 percent reported binge drinking in the past month. Through Facebook, NIAAA will be able to provide users of this platform with valuable information about how alcohol misuse affects human health and development, and about the work of NIAAA.



Learn more about NIAAA’s [social media efforts](#) and other ways to stay connected.

SPOTLIGHT

RACIAL EQUITY AND INCLUSION IN BIOMEDICAL RESEARCH—
AND THE NIH UNITE PROGRAM



Ending
Structural
Racism



This past March, the National Institutes of Health (NIH) launched the [UNITE initiative](#) to address structural racism at NIH, NIH-supported institutions, and anywhere NIH research activities take place. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) Director George F. Koob, Ph.D., announced his enthusiastic support of UNITE and his commitment to equity, diversity, and inclusion at NIAAA and in the alcohol research enterprise.

The UNITE program aligns with the efforts that NIAAA has made—and continues to make—to promote equity, diversity, and inclusion. For example, NIAAA recently established an *Equity, Diversity, and*

Inclusion Steering Committee to inform its efforts. To make the foundational changes that are needed, NIAAA will focus on the following domains: improving the NIAAA intramural and extramural *workplace* and culture, increasing diversity and equity in the scientific and administrative *workforce*, and enhancing the NIAAA intramural and extramural scientific *research portfolio*.

Looking ahead, NIAAA is dedicated to expanding career opportunities for researchers, clinicians, and administrators from diverse and underserved communities. “Because our alcohol research community is so focused and we know that diversity enriches our efforts in every way, we can dedicate ourselves to engaging diversity to sustain our field. As such, I believe we have a unique opportunity to expand opportunities for future alcohol researchers and administrators. Let’s remember, a focus on equity does not apply solely to those who work on our purely scientific endeavors, but to all of us who support this critical biomedical enterprise dedicated to the diagnosis, prevention, and treatment of alcohol misuse,” says Dr. Koob.

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.

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