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

FEATURE

GROWING UP IN A FAMILY WITH ALCOHOL PROBLEMS: CURRENT RESEARCH AND RESOURCES



For the estimated 10 percent of children who live in a home where a parent has an alcohol problem,¹ a parent's drinking can cause a great deal of suffering and have repercussions that can extend long into adulthood. Children of individuals with alcohol use disorder (AUD) are at greater risk for many problems, including their own issues with drugs and alcohol, as well as depression, anxiety, impulse control problems, and impaired cognitive and verbal skills. Research also indicates that these children are much more likely to be abused or neglected by their parents and have a greater likelihood of entering the foster care system.

The promising news is that much work has been done by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and others to understand the problems faced by children of people with AUD and the children's own susceptibility to alcohol problems, as well as to develop preventions,

interventions, and treatments that can help lessen their burden and bolster their resilience.

Although genetic factors inarguably contribute to the risk of developing alcohol problems—current studies show that genes are responsible for about 50 percent of overall risk for AUD—genes are not destiny, and many children of parents with AUD will never develop a problem with alcohol.

“Not all children of parents with AUD are equally vulnerable,” notes NIAAA grantee Robert Zucker, Ph.D., former director of the University of Michigan Addiction Research Center, and the Substance Abuse Section in the Department of Psychiatry. “Genetic effects never operate in a vacuum,” and scientists are currently investigating how genes may express themselves differently in various environmental contexts and stages of human development.

“Genetic effects often do not operate uniformly at all stages of early life,” says Dr. Zucker. “In addition, interactions with parents and with peers can moderate the genetic vulnerability. In other words, it is not genetics only, it's $G \times E \times D$ —that is, genetics by environment by development—that shapes the child's behavior.”

¹ Center for Behavioral Health Statistics and Quality. *Data Spotlight: More than 7 Million Children Live with a Parent with Alcohol Problems*. Rockville, MD: Substance Abuse and Mental Health Services Administration, February 16, 2012. Available at <http://www.samhsa.gov/data/sites/default/files/Spot061ChildrenOfAlcoholics2012/Spot061ChildrenOfAlcoholics2012.pdf>

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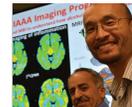


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FEATURE

DR. KOOB RECEIVES FRENCH LEGION OF HONOR AND RSA SEIXAS AWARDS

For NIAAA Director Dr. George F. Koob, June 2016 was an exciting month. After being honored by the Research Society on Alcoholism (RSA) for his extraordinary service in advancing alcohol research, he had to hurry back to Washington, D.C., to become a knight.

Colleagues, friends, and family gathered at the residence of French Ambassador Gérard Araud on June 30, to watch as Dr. Koob was presented with the insignia of Chevalier de la Légion d'honneur (Knight of the Legion of Honor), on behalf of French President François Hollande.

“For your stunning scientific work, for your active contribution to building bridges between the [United States] and France in neuroscience, and for your deep love of French culture, French cuisine, and *art de vivre*, it’s a great pleasure for me to present you with this award,” said Ambassador Araud in his remarks.

Only days before, Dr. Koob had been in New Orleans, Louisiana, for the 39th annual meeting of the RSA, where he was presented with the Seixas Award for Service. The award, normally kept confidential until the final day of the meeting, was announced early to ensure that Dr. Koob could accept in person. The Seixas Awardee is selected by RSA’s Board of Directors, and previous winners include Dr. Ken Warren, currently NIAAA Senior Advisor for Science and Operations, in 1994; Dr. Robert Huebner, Acting Director of NIAAA’s Division of Treatment and Recovery Research, in 2013; and Dr. David Goldman, Acting NIAAA Clinical Director and Chief of the NIAAA Laboratory of Neurogenetics, in 2015.

Dr. Koob is in good company among previous Legion of Honor recipients as



well. France’s premier award has been bestowed upon former Surgeon General C. Everett Koop, M.D., former NIH Director Elias Zerhouni, M.D., and many leaders in academia, politics, and the arts. The Legion of Honor was founded by Napoleon Bonaparte in 1802 to recognize eminent accomplishments of service to France. Dr. Koob received the honor in recognition of his contributions to the development of scientific collaborations between France and the United States.

Dr. Koob is recognized as one of the leaders of the field of addiction research and is internationally renowned for his expertise on alcohol and stress, and on the neurobiology of alcohol and drug addiction. The author of hundreds of articles published in international journals, Dr. Koob has had a long collaborative relationship with Professor Michel Le Moal, M.D., Professor Emeritus of Neuroscience at the University of Bordeaux, France, and a Fellow of the French National Academy of Sciences. With Dr. Le

Moal, Dr. Koob co-authored *Neurobiology of Addiction* in 2006 and *Drugs, Addiction, and the Brain* in 2014. Both books are regarded as major references in the field of addiction research.

Through his association with Dr. Le Moal and other eminent French scientists, Dr. Koob has been able to share his expertise and knowledge of the mechanisms underlying addiction and other psychiatric diseases and behavioral disorders with many French

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A video of Dr. Koob’s Legion of Honor ceremony, produced by the French Embassy, is available here: <https://www.youtube.com/watch?v=TKRszqliDBs>.

Researchers are trying to better understand a host of early risk factors. Previous studies have shown that children living in a home with alcohol problems are more likely to suffer negative effects when the alcohol problems are ongoing, and these effects are even more potent when the parents' AUD co-occurs with antisocial behavior—marked by overtly abusive actions or aggression toward others. The situation is considerably worse when both parents have AUD.

Families with AUD tend to have higher rates of conflict, poorer family communication skills, and a lack of stability, all of which can contribute to stress on children.

Dr. Zucker's research suggests that it may be possible to identify at-risk children much earlier, and before the onset of alcohol problems. He and his team have observed differences in brain development among children of people with alcohol problems—functional magnetic resonance imaging (fMRI) scans revealed differences in the impulse control brain circuitry of children of alcoholics. These differences can be seen in childhood, well before problem drinking arises, and persist into adolescence.²

Poor sleep patterns also seem to be linked to later problems for children in homes where parents have alcohol problems. "Sleep problems, even in the preschool years, are predictive of later alcohol problems in adolescence, like earlier onset [of drinking] and more problem drinking in adolescence irrespective of other factors like attentional problems and depression," says Dr. Zucker. Earlier this year, Dr. Zucker co-authored a paper that reported that sufficient sleep is significantly linked to resilient adaptation in children of parents with alcohol problems.³

So what can be done to help children of parents with AUD have the best future possible? According to the National Association for Children of Alcoholics (NACoA), these children can be helped, even if the parent or other family member who has alcohol problems is not receiving help. NACoA is a national non-profit organization whose mission is to eliminate the adverse impact of

parental alcohol and drug use on children and families. Prevention programs can help children reduce stress, deal with emotional issues, and develop self-esteem, coping skills, and social support. Children need to be reminded that their families' problems are neither their fault nor their responsibility. According to NACoA, it is important that these children understand that their own lives can be different and better than that of their family members who have alcohol problems. In fact, this is a significant success story for many children of families with alcohol problems.

All children—both with and without a family history of alcohol problems—can benefit from early screening. NIAAA's *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*, developed in collaboration with the American Academy of Pediatrics, is designed to help health care professionals quickly identify youth at risk for alcohol-related problems in both middle childhood and adolescence. It includes a question about an adolescent's own drinking, as well as a question about the drinking behavior of friends, which can help professionals predict potential risk and target advice effectively.

Ultimately, AUD affects everyone in the family. When the individual with alcohol problems receives treatment, it is important that other family members receive support as well. (See resources to the right.) "If you regard alcoholism simply as a problem for the adults themselves, with no other complications, that only encourages the long-term playing out of these difficulties in the children," says Dr. Zucker. Helping children of families with alcohol problems greatly increases the likelihood that the children will overcome adversity and break the family cycle of AUD.

² Hardee, J.E.; Weiland, B.J.; Nichols, T.E.; Welsh, R.C.; Soules, M.E.; Steinberg, D.B.; Zubieta, J.K.; Zucker, R.A.; and Heitzeg, M.M. Development of impulse control circuitry in children of alcoholics. *Biological Psychiatry* 76(9):708–716, 2014. PMID: 24742620

Resources

National Association for Children of Alcoholics

www.nacoa.org

888-55-4COAS (42627)

Al-Anon Family Groups

www.al-anon.alateen.org

1-888-425-2666 for meetings

Adult Children of Alcoholics

www.adultchildren.org

310-534-1815

Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide

www.niaaa.nih.gov/Publications/EducationTrainingMaterials/Pages/YouthGuide.aspx

Children of Alcoholics: A Guide to Community Action

<http://store.samhsa.gov/product/Children-of-Alcoholics-A-Guide-to-Community-Action/MS939>

³ Hairston, I.S.; Conroy, D.A.; Heitzeg, M.M.; Akbar, N.Z.; Brower, K.J.; and Zucker, R.A. Sleep mediates the link between resiliency and behavioural problems in children at high and low risk for alcoholism. *Journal of Sleep Research* 25(3):341–349, 2016. PMID: 26853891

SPOTLIGHT

NEW STRATEGIC PLAN ESTABLISHES NIAAA'S VISION FOR THE FUTURE OF ALCOHOL RESEARCH



NIAAA is in the final stages of developing a strategic plan outlining its broad priorities for the next 5 years. The plan will serve as a roadmap for optimizing the allocation of the Institute's resources to areas of alcohol research most likely to benefit from additional support and for translating research findings for the benefit of the public. NIAAA will continue to focus on many of its current research priorities, while committing new energy to emerging areas.

The draft plan will be organized into five overarching goals:

- 1: Identify Mechanisms of Alcohol Action and Alcohol-Related Pathology
- 2: Track and Diagnose Alcohol Misuse, Alcohol Use Disorder, and Alcohol-Related Consequences
- 3: Prevent Alcohol Use Disorder and Alcohol-Related Consequences
- 4: Develop and Improve Treatments for Alcohol Misuse, Alcohol Use Disorder, Co-occurring Conditions, and Alcohol-Related Consequences
- 5: Enhance the Public Health Impact of NIAAA-Supported Research

In addition, the Institute has identified the following cross-cutting themes, which are essential to fulfilling NIAAA's mission:

- Addressing Alcohol Misuse Across the Lifespan
- Addressing Co-Occurring Conditions
- Reducing Health Disparities
- Advancing Precision Medicine
- Strengthening Research and Clinical Training

“There has never been a better time to accelerate progress across the spectrum of alcohol research,” said NIAAA Director Dr. George F. Koob. “Our strategic plan will build on the transformative advances that have been made in biomedical research and strengthen the position of NIAAA as the nation's premier source of evidence-based information on alcohol and health.”

The draft plan currently reflects input from the NIAAA Advisory Council, and in the coming weeks the Institute will also solicit feedback from the broader scientific community and the public. Following its completion, the plan will be made available on the NIAAA Web site.

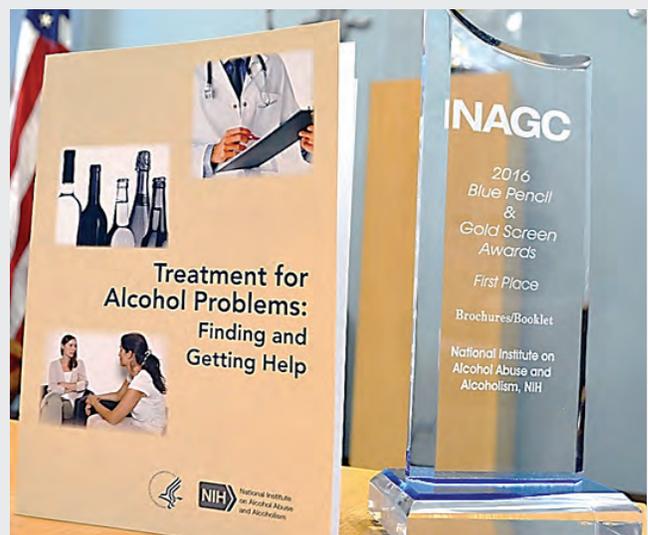
NOTEWORTHY

ORDER OR DOWNLOAD NIAAA'S AWARD-WINNING PUBLICATION

TREATMENT FOR ALCOHOL PROBLEMS: FINDING AND GETTING HELP

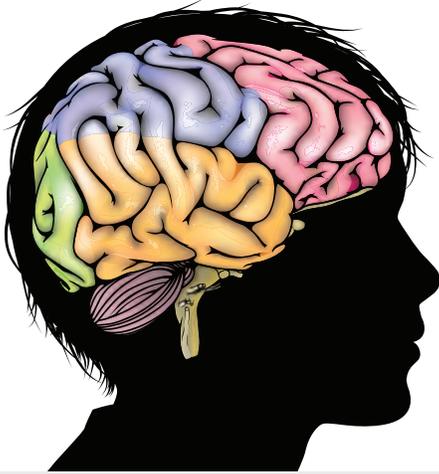
This guide helps readers understand what treatment choices are available for alcohol problems and what to consider when selecting among them.

Visit <http://pubs.niaaa.nih.gov/publications/Treatment/treatment.pdf> for more information.



NEWS FROM THE FIELD

NEUROIMAGING SPOTLIGHTS THE IMPACT OF THERAPISTS' WORDS ON TEEN BRAINS



An intriguing new NIAAA-funded study offers a glimpse at how the adolescent brain responds to the language of therapists. Led by Sarah W. Feldstein Ewing, Ph.D., Professor of Psychiatry and Director of the Adolescent Behavioral Health Clinic at Oregon Health & Science University, the study assessed 17 young people ages 15–19 who were self-reported binge drinkers. Following a psychosocial assessment, the youths received two sessions of motivational interviewing aimed at reducing drinking. Between sessions, the participants underwent a

brain scan using functional magnetic resonance imaging, or fMRI.

During the fMRI, the therapist presented two types of statements: one set of “closed questions” based on standard language used within addiction treatment (e.g., “*Do your parents know you were drinking?*”); the other set included more effortful “complex reflections” (e.g., “*You’re worried about your drinking.*”)

Following a psychosocial assessment, the youths received two sessions of motivational interviewing aimed at reducing drinking.

The youth were re-evaluated one month after treatment. At the follow-up evaluation, the youth showed significant reductions in number of drinking days and binge drinking days. Furthermore, in the fMRI sessions, the researchers

observed greater brain activation for complex reflections versus closed questions within the bilateral anterior cingulate gyrus, a brain region associated with decisionmaking, emotions, reward anticipation, and impulse control.

The scientists also noted that greater blood-oxygen level dependent (BOLD) response in the parietal lobe during closed questions was significantly associated with less post-treatment drinking. BOLD response is a way to measure activity in specific brain areas. Previous research has shown that this region’s secondary function is related to a person’s ability to navigate, plan, and make decisions.

The study team also observed lower brain activation in the precuneus was associated with study participants’ post-treatment ratings of the importance of changing their drinking. The precuneus, a subregion of the parietal lobe located inside the fissure that separates the brain’s hemispheres, is related to self-reflection and introspection and is involved in risk behavior. It is

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NOTEWORTHY

NIAAA-NIDA MINI-CONVENTION AT THE SOCIETY FOR NEUROSCIENCE ANNUAL MEETING

NIAAA Director Dr. George F. Koob and NIDA Director Dr. Nora Volkow will co-host a Mini-Convention as part of this year’s Society for Neuroscience Annual Meeting. This year’s theme is relapse and recovery, with an emphasis on integration of preclinical and clinical research and leveraging insights from big data approaches.

Visit <http://apps1.seiservices.com/nida-niaaa/frontiers2016/Default.aspx> for more information.

NEWS FROM THE FIELD

ALCOHOL-INDUCED BLACKOUTS IN YOUNG ADULTS PREDICT OTHER HARMS



Alcohol-induced blackouts are periods of amnesia that occur when the brain stops recording memories of what happens when someone is drinking. People experiencing a blackout are not unconscious, and can walk, talk, and engage in other behaviors, but they will not remember their actions later. Blackouts can be partial or complete

and tend to occur when blood alcohol concentration (BAC) goes up quickly, which is common among young adults. Blackouts tend to occur at BAC levels of 0.15 percent and above, or roughly twice the legal limit for driving a car for those 21 or older. Being female, chugging drinks, drinking on an empty stomach, and individual differences in how memory circuits respond to alcohol can all influence the risk of blackouts.

A recent study funded by several NIH Institutes, including NIAAA, investigated blackouts among young adults to determine whether questions about blackouts are better indicators of the risk of other alcohol-related harms than typical questions about a person's quantity and frequency of drinking. The researchers used data from a 2012–2013 national survey of 2,140 subjects who were one year past high school. Called the NEXT Generation Health Study, this survey also examined respondents' demo-

graphics, substance use behaviors, and other alcohol-related problems.

Researchers found that 53 percent of respondents had consumed alcohol in the past 30 days. Among these past-month drinkers, 75 percent had binged on alcohol at least once and 20 percent experienced a blackout in the previous 6 months. The prevalence of blackouts was higher among individuals who had a lower body weight relative to the other people in the study group. Having any of the following characteristics in the previous 30 days was also linked to an increased risk of blackouts: use of multiple drugs, bingeing more frequently, getting drunk, smoking cigarettes, or living in a college dormitory.

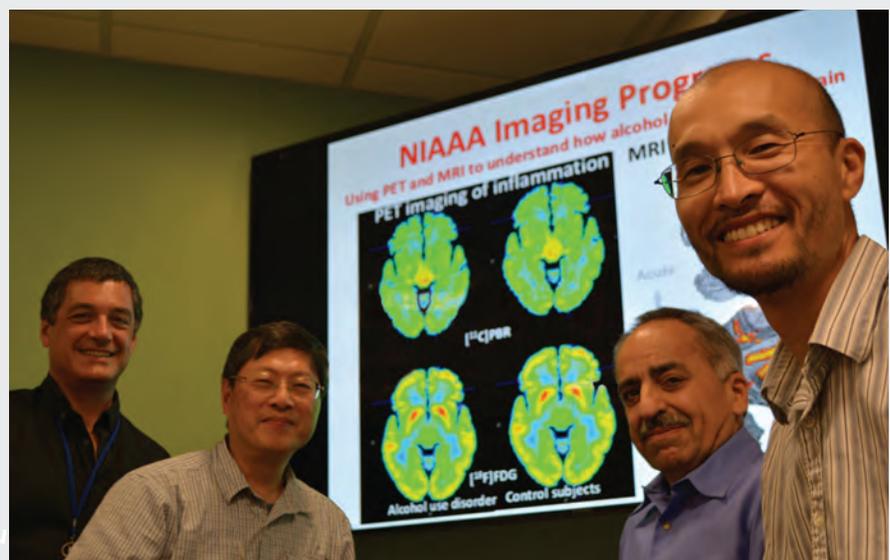
After controlling for drinking levels, having a blackout was the strongest independent predictor for most other alcohol problems experienced by

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COMPUTER IMAGING AT NIAAA

Reviewing digital brain scans are, from left to right, Dardo Tomasi, Ph.D., Gene-Jack Wang, M.D., Reza Momenan, Ph.D., and Sunny Kim, Ph.D. Drs. Tomasi, Wang, and Kim work in the NIAAA Laboratory of Neuroimaging, while Dr. Momenan leads the Clinical Neuroimaging Research Core. Digital imaging helps NIAAA researchers understand how alcohol affects the human brain. Here, positron emission tomography (PET) scans illustrate the inflammation associated with alcohol use disorder. On the right, magnetic resonance imaging (MRI)



NEWS reveals how acute and chronic blackouts and alcohol use alter brain connectivity.

5 QUESTIONS WITH . . .

VIJAY RAMCHANDANI, PH.D.

Chief, NIAAA Section on Human Psychopharmacology



1 You are the head of the Intramural Division's Section on Human Psychopharmacology. What does your team study?

Our Section's research focuses on understanding the genetic and environmental sources of individual variation in the pharmacological effects of alcohol in people and tries to elucidate the relationship between these sources of variation and the risk for alcohol use disorder (AUD). We are also conducting studies to develop human laboratory models that can be used to screen novel medications for the treatment of AUD.

2 Careful administration of alcohol is key to many of your studies. How is that done?

The usual method for administering alcohol in human research studies is orally. However, there is a 3- to 4-fold variation in breath alcohol levels following oral alcohol, making the design and interpretation of data from oral alcohol challenge studies problematic. To avoid this problem in our studies, we use intravenous (IV) alcohol administration combined with a physiological model-based algorithm that provides exquisite precision in the rate, level, and duration of alcohol exposure. This computer-

assisted infusion system (CAIS), developed collaboratively with Sean O'Connor at Indiana University School of Medicine, provides a unique platform for studying the effects of alcohol with minimal variation in breath (and therefore brain) alcohol exposure.

Two IV alcohol administration methods form the foundation of our work: (1) the "alcohol clamp," and (2) intravenous alcohol self-administration or "IV-ASA." The alcohol clamp method uses a dosage and rate that are pre-calculated to provide a precise and prescribed profile of steady-state alcohol exposure. This approach offers unique opportunities to time-lock the presentation of stimuli and assessment of behavioral and imaging-based outcomes to specific phases and levels of brain alcohol exposure. The IV-ASA method gives subjects the flexibility to choose when to push a button to receive alcohol, while the investigator can control the breath alcohol level achieved. Therefore, this method allows the assessment of alcohol-seeking and consumption behavior that is driven mainly by the pharmacological effects of alcohol.

3 Please tell us about some of the research advances your team has achieved in recent years.

We recently completed a study examining the effect of varenicline, a smoking cessation medication, on brain function, using a novel functional magnetic resonance imaging task and IV alcohol self-administration in heavy drinkers. We found that varenicline, compared to placebo, significantly reduced the brain response in regions associated with motivation for reward and emotional arousal. These results suggest a mechanism by which varenicline may reduce alcohol intake, and complement the findings of a recent clinical trial supported

by NIAAA's extramural Division of Medications Development. This study demonstrated the efficacy of varenicline in reducing alcohol use in individuals seeking treatment for AUD.

4 Looking forward, what are some promising developments on the horizon?

We have just completed a study characterizing IV alcohol self-administration in a sample of nearly 200 drinkers. We are conducting a number of data analyses to examine the effect of factors associated with the reward, stress, and cognitive domains of alcohol response in this sample. Initial findings suggest some interesting and potentially important genetic and environmental underpinnings of these alcohol responses derived from the IV alcohol self-administration model.

We are also conducting a pharmacogenetics study examining the effect of nalmefene (a medication that modulates opioid receptor function) on neuroimaging measures of reward and stress processing, as well as alcohol self-administration, in heavy drinkers. We believe this study might provide some important information on the mechanism underlying the clinical effectiveness of these opioid medications, and examining the pharmacogenetics of nalmefene may lead to personalized medicine approaches in the treatment of AUD.

5 If you weren't a scientist at NIAAA, what might you be doing?

Interesting question... I think if I wasn't a scientist at NIAAA, I might be working as a chef in a Michelin-starred restaurant in Paris!

FEATURE: Dr. Koob Receives Honor . . . Continued from page 2

investigators. Throughout his career, Dr. Koob has created strong links between French and American researchers, and he has hosted and trained a large number of young scientists from France, including 13 post-doctoral fellows.

“I am extremely grateful for, and humbled by, this recognition,” said Dr. Koob, who has served as NIAAA director since January 2014. “My collaborations and interactions with scientists in France have been deeply

gratifying, both personally and professionally, and I look forward to ongoing scientific camaraderie between our countries in the years ahead.”

NEWS FROM THE FIELD: Adolescent Brains . . . Continued from page 5

considered to be a hub of the brain’s key resting-state network.

The researchers also noted what they did not find from the brain scans—any link between treatment outcome and activation of the frontal lobes, which are a region tied to complex reasoning. The authors commented that this lack of activation might be because the frontal lobes of the adolescent brain are still

developing, making it difficult for teens to bring their frontal lobes “online.”

The study authors note that their findings have important implications for the treatment of addiction in adolescents and can improve our understanding of youth brain systems and inform how to influence mechanisms of behavior change in this population.

Reference:

Feldstein Ewing, S.W.; Houck, J.M.; Yezhuvath, U.; Shokri-Kojori, E.; Truitt, D.; and Filbey, F.M. The impact of therapists’ words on the adolescent brain: In the context of addiction treatment. *Behavioural Brain Research* 297:359–369, 2016. PMID: 26455873

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

respondents in the past six months. Such problems included missing class or work, getting behind in school or work, doing something that was later regretted, arguing with friends, experiencing an alcohol overdose, etc. Having a blackout was also an independent predictor of hangovers, damaging property, getting hurt, and trouble with the police. Researchers note that future studies should examine the frequency of blackouts, as well as the relationship

between alcohol-related blackouts and harm to other people.

Because blackouts indicate drinking at levels that result in significant cognitive and behavioral impairment, questions about blackouts could serve as important, simple screeners for the risk of experiencing other alcohol-related harms. The authors note that limits of their study included the use of self-report, which can be influenced by individuals’ memory recall and fear of stigmatization. Additional research

could examine whether questions about blackouts could be useful additions to national surveys of drug and alcohol use, as well as in screening instruments for healthcare settings.

Reference:

Hingson, R.; Zha, W.; Simons-Morton, B.; and White A. Alcohol-induced blackouts as predictors of other drinking related harms among emerging young adults. *Alcoholism: Clinical and Experimental Research* 40(4):776–784, 2016. PMID: 27012148

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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