NIAAA Director's Report on Institute Activities to the 158th Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

September 9, 2021
Virtual Meeting

George F. Koob, Ph.D.
Director
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health

https://www.niaaa.nih.gov/about-niaaa/advisory-council

Welcome to New NIAAA Staff

Bonnie Hebb joined the Administrative Services Branch as a Program Specialist providing procurement and purchasing support to both intramural and extramural staff. Before joining NIAAA, she most recently served as a purchasing agent with the National Cancer Institute (NCI).

Dr. Nagaraja "Sethu" Balakathiresan joined the Division of Neuroscience and Behavior as a program officer, where he will be responsible for the PTSD and TBI portfolios. Dr. Balakathiresan earned a Ph.D. in Biological Science from the Madurai Kamaraj University in India. He was previously an Assistant Professor of Pathology at the Uniformed Services University of the Health Sciences in Bethesda, Maryland, where he studied the role of PTSD-related rapid eye movement (REM) sleep disturbances and microRNA-based biomarkers for repetitive chronic TBI-induced PTSD.

Sarah Nelson joined NIAAA as a Grants Management Specialist in the Grants Management Branch, where she previously worked as a contractor. In her new position, she will manage a larger grant portfolio.

Welcome to New NIAAA Staff

Division of Intramural Clinical and Biological Research (DICBR)

Dr. Ilse Alonso-Vasquez joined the Laboratory for Integrative Neuroscience as a Post-Doctoral Visiting Fellow. In this position, Dr. Alonso-Vazquez will be performing studies examining effects of alcohol on sleep and cognitive function, and the neuronal and circuit mechanisms underlying these effects.

Dr. Pinaki Bhattacharjee joined the Section on Medicinal Chemistry as a Postdoctoral Visiting Fellow. In this role, Dr. Bhattacharjee will conduct studies on the design, synthesis, and biological investigation of novel cannabinoid modulators for treatment of metabolic and fibrotic disorders.

Dr. Biswajit Kundu joined the Section on Medicinal Chemistry as a Postdoctoral Visiting Fellow. In this role, Dr. Kundu will conduct studies on multi-target agents for treatment of inflammatory disorders.

Internal Transitions

Dr. Bradley Kerridge joined the Division of Epidemiology and Prevention Research, where he will serve as a program officer. Prior to this position, Dr. Kerridge was an epidemiologist in the Epidemiology and Biometry Branch.

Dr. Andrew Kesner converted from a Post-Doctoral IRTA Fellow to a Research Fellow in the Unit on Motivation and Arousal within the Laboratory for Integrative Neuroscience in DICBR.

Dr. Jenica Patterson transitioned to the Medications Development Branch in the Division of Treatment Research. She previously served as a program officer in the Division of Neuroscience and Behavior.

Departing Staff

Patricia Brown retired in April after more than 40 years of public service. Patricia joined NIAAA in 1989 as a Paralegal Specialist when NIAAA was a part of ADAMHA (Alcohol, Drug Abuse and Mental Health Administration). Over the years she has had numerous positions, including Legislative Analyst and Ethics Specialist.

Dr. Patricia Chou retired from federal service in April. She joined NIAAA in 1990 in the intramural Laboratory of Epidemiology and Biometry and later served as Acting Chief of the Epidemiology and Biometry Branch when the laboratory moved to extramural. Dr. Chou played a vital role in the design and analyses of all three waves of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and will continue as a contractor to advise the branch on working with the NESARC datasets.

Dr. Troy Zarcone departed the Science Policy Branch, NIAAA, to serve as Director of the Office of Extramural Policy and Review and the Acting Branch Chief for the Extramural Activities and Initiatives Development Branch at the National Institute on Drug Abuse.

Emily Wilkins, former Program Specialist supporting the Office of the Director, has departed NIAAA for a position as a Management Analyst, Food and Drug Administration.

DICBR Departures

Dr. Miriam Bocarsley, former Research Fellow for the Laboratory Neurobiology of Compulsive Behaviors, has accepted a position as Assistant Professor at Rutgers New Jersey Medical School in the Department of Pharmacology, Physiology, and Neuroscience and a Core Member of Rutgers Brain Health Institute.

Dr. Chuck Chen, former Post-Doctoral Researcher, joined the University of Toronto as a Research Assistant Professor working on genomics of nutrition.

Dr. Lucia Guerri has departed the Laboratory of Neurogenetics and is presently focusing much of her efforts on a neurorobotics startup company.

Dr. Yong He, former Research Fellow in the Laboratory of Liver Disease, has accepted a position as a Principal Investigator at the Shanghai Institute of Materia Medica in Shanghai, China.

Dr. Ji Soo Lee, former Post-Doctoral Visiting Fellow, accepted a job in the pharmaceutical industry in South Korea.

Dr. Daniel Liput, former Research Fellow in the Laboratory for Integrative Neuroscience, has taken a position as a Scientist at Vigene Biosciences, Inc.

FY 2021 Budget

- NIH received a total of $42.9 billion for FY 2021, including:
  - General increases to NIH Institutes and Centers
  - Coronavirus supplemental appropriations
  - Allocations for the HEAL Initiative, the 21st Century Cures Act, the BRAIN Initiative, and research on influenza
  - Continued support for the Gabriella Miller Kids First Act pediatric research initiative
- NIAAA received a total of $554.9 million for 2021.

The budget for 2022 has not been finalized.

Selected Funding Opportunities

(See Director's Report for Complete Listing)

Issued by NIAAA

- **HIV Prevention and Alcohol** (R01/R34) RFA-AA-21-016; RFA-AA-21-017

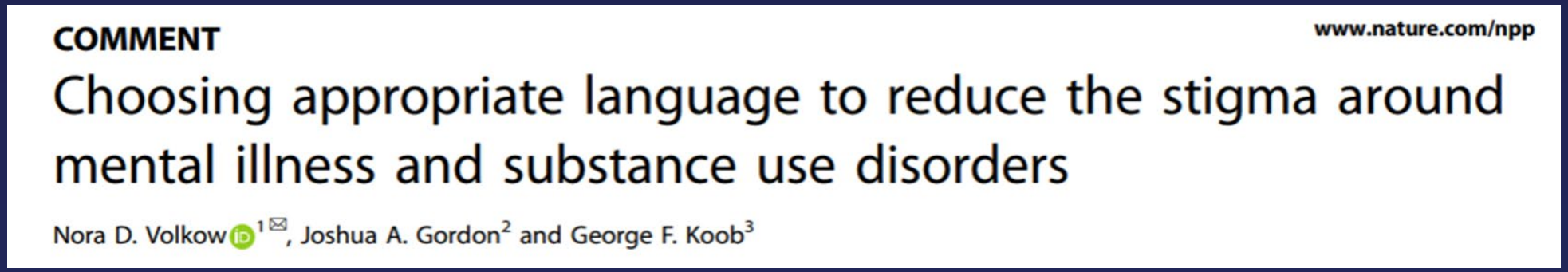
NIH-wide with NIAAA participation

- BRAIN Initiative: New Technologies and Novel Approaches for Recording and Modulation in the Nervous System (R01) RFA-NS-21-026
- Dyadic Interpersonal Processes and Biopsychosocial Outcomes (R01) PAR-21-280; PAR-21-281
- American Women: Assessing Risk Epidemiologically (R01) RFA-AI-21-058
- Notice of Special Interest: Alzheimers-Focused Administrative Supplements for NIH Grants that are Not Focused on Alzheimers Disease NOT-AG-21-018
- Notice of Special Interest (NOSI): Social, Behavioral, and Economic Impact of COVID-19 in Underserved and Vulnerable Populations NOT-MH-21-330

Words Matter: NIAAA Terminology Recommendations

We can help alleviate the stigma associated with alcohol-related conditions by consistently using non-pejorative, non-stigmatizing language to describe these concerns and the people who are affected by them. Some words that are commonly used in society, such as "alcoholic" and "alcohol abuse," are stigmatizing.

- Use **alcohol use disorder** instead of *alcohol abuse*, *alcohol dependence*, and *alcoholism*
- Use **alcohol misuse** instead of *alcohol abuse* when referring broadly to drinking in a manner that could cause harm
- Use **person-first language** to describe people with alcohol-related problems (e.g., **person with alcohol use disorder** instead of *alcoholic,* **person in recovery** instead of *recovering alcoholic*)
- Use **alcohol-associated liver disease** instead of *alcoholic liver disease*


COMMENT

www.nature.com/npp

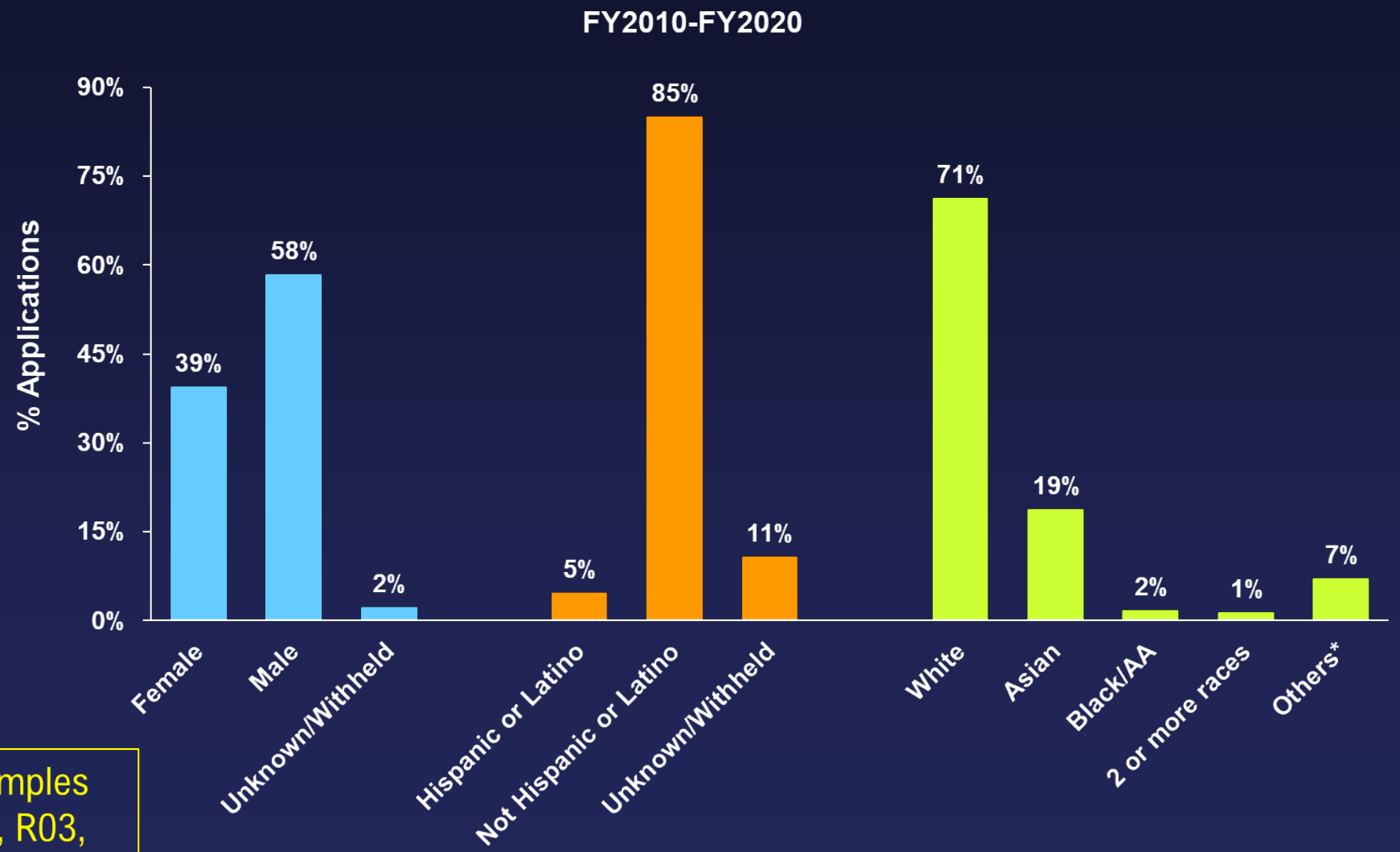
Choosing appropriate language to reduce the stigma around mental illness and substance use disorders

Nora D. Volkow[1], Joshua A. Gordon[2] and George F. Koob[3]

Addressing Diversity, Equity, and Inclusion (DEI) at NIAAA and in the Alcohol Research Community

- Establishment of an internal NIAAA Race and Medicine Interest Group
  - Started by a group of intramural fellows and open to all NIAAA staff, this group provides a forum for discussion and resource sharing
- Continued recruitment of talented and diverse investigators to the NIAAA intramural workforce through the NIH Distinguished Scholars Program and the Lasker Clinical Research Scholars Program
- Exploring establishment of a new training program focused on networking and mentoring (inspired by the SPINES model)
- Increase support for NIAAA's diversity supplement program
- Reinvigorate and expand the National Advisory Council Working Group on Diversity and Health Disparities in the Biomedical Workforce
- Establishment of a steering committee to identify EDI priorities and monitor progress of new and ongoing EDI efforts at NIAAA
- Analysis of NIAAA application and funding data to identify specific points of disparity

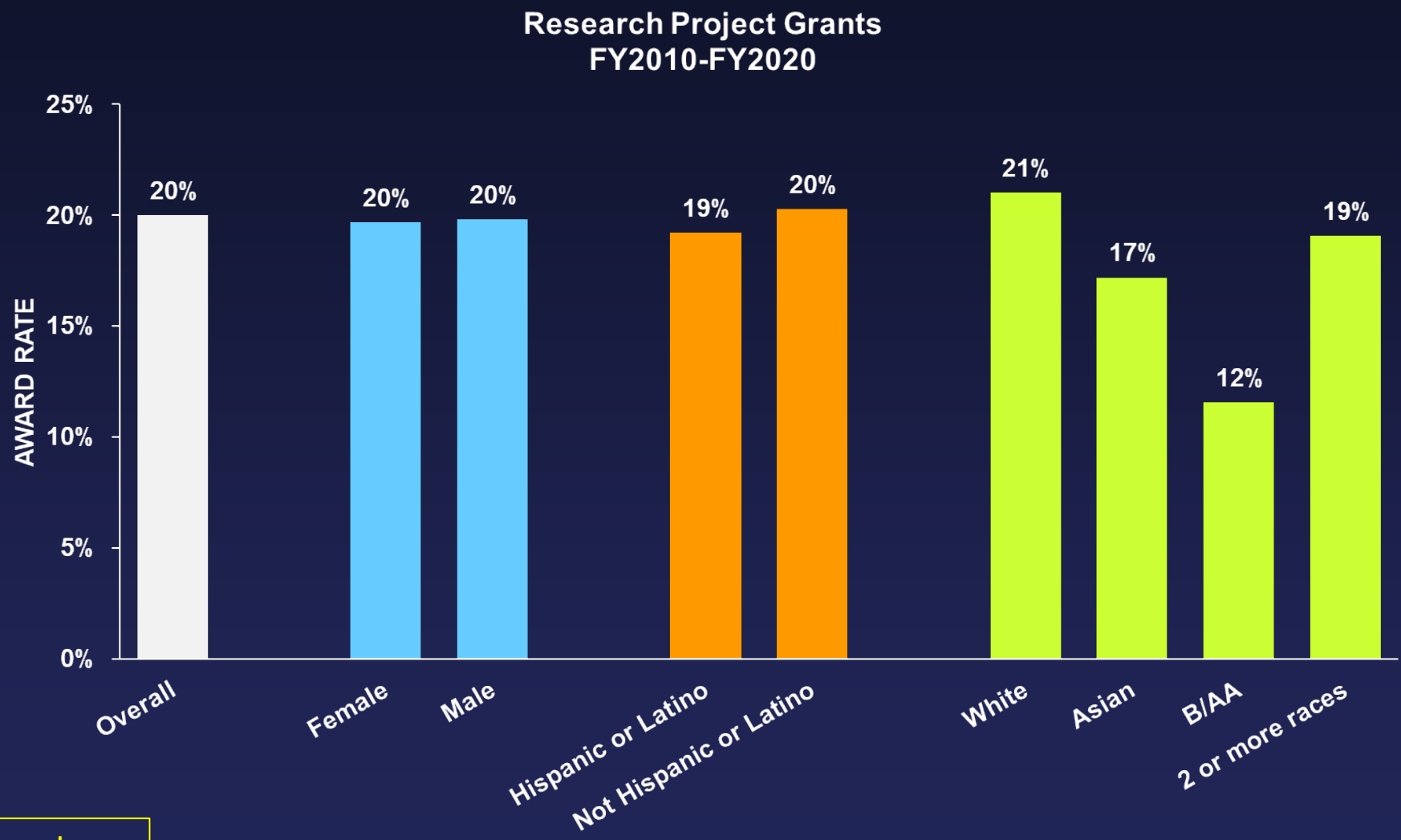
Research Project Grant Application Data



Most common examples of RPGs: R01, R21, R03, R34, R37, R00, U01, P01

* Combined AI/AN, NHOPI, withheld, and unknown

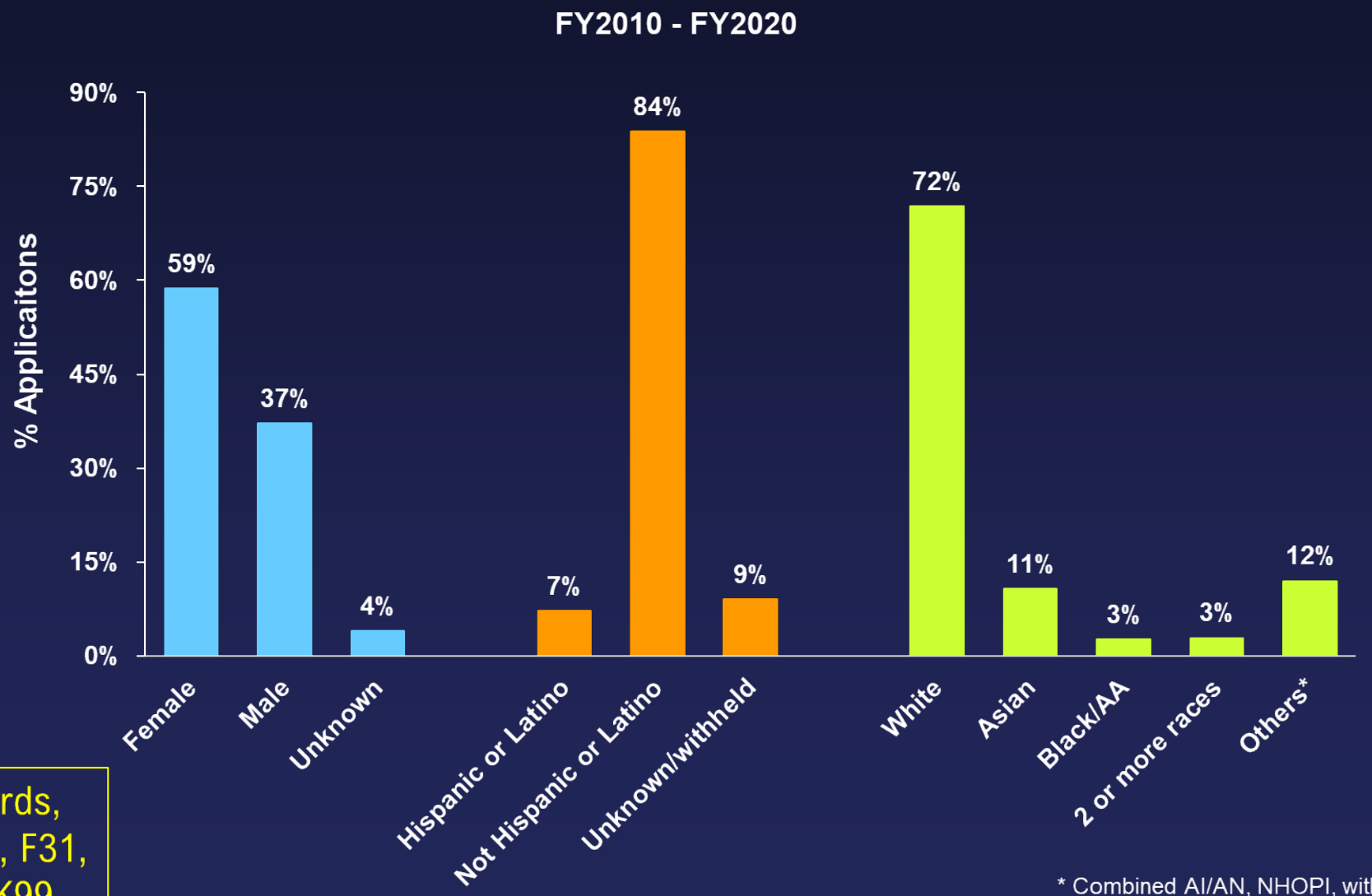
Award Rate by Investigator Demographics



Most common examples of RPGs: R01, R21, R03, R34, R37, R00, U01, P01

Award rate: percentage of funded applications
Applications with multiple PIs counted once for each PI
Resubmissions counted as separate applications

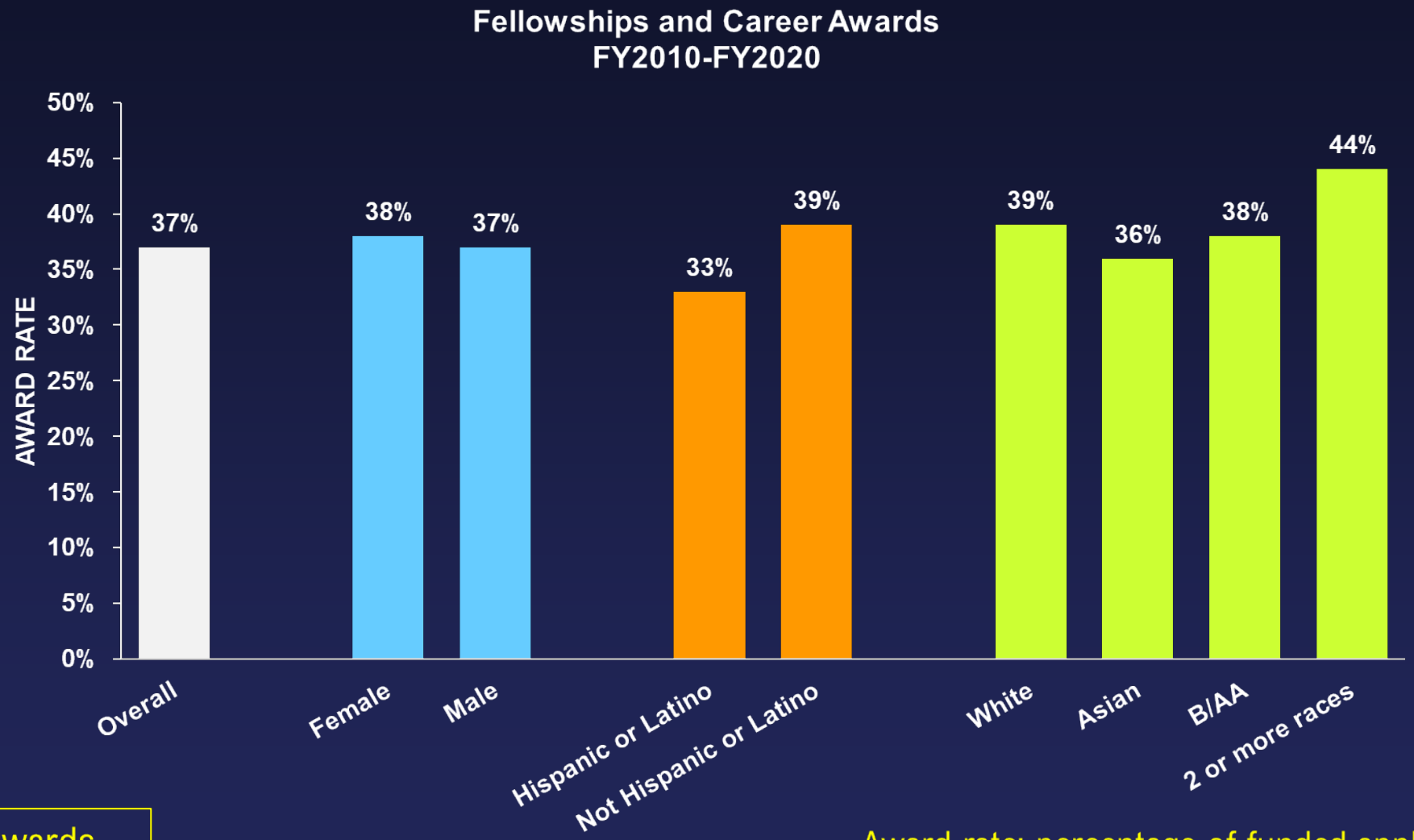
Fellowships and Career Development Application Data



Includes F and K awards, most commonly: F30, F31, F32, K01, K08, K23, K99

* Combined AI/AN, NHOPI, withheld, and unknown

Fellowships and Career Development
Award Rate by Investigator Demographics



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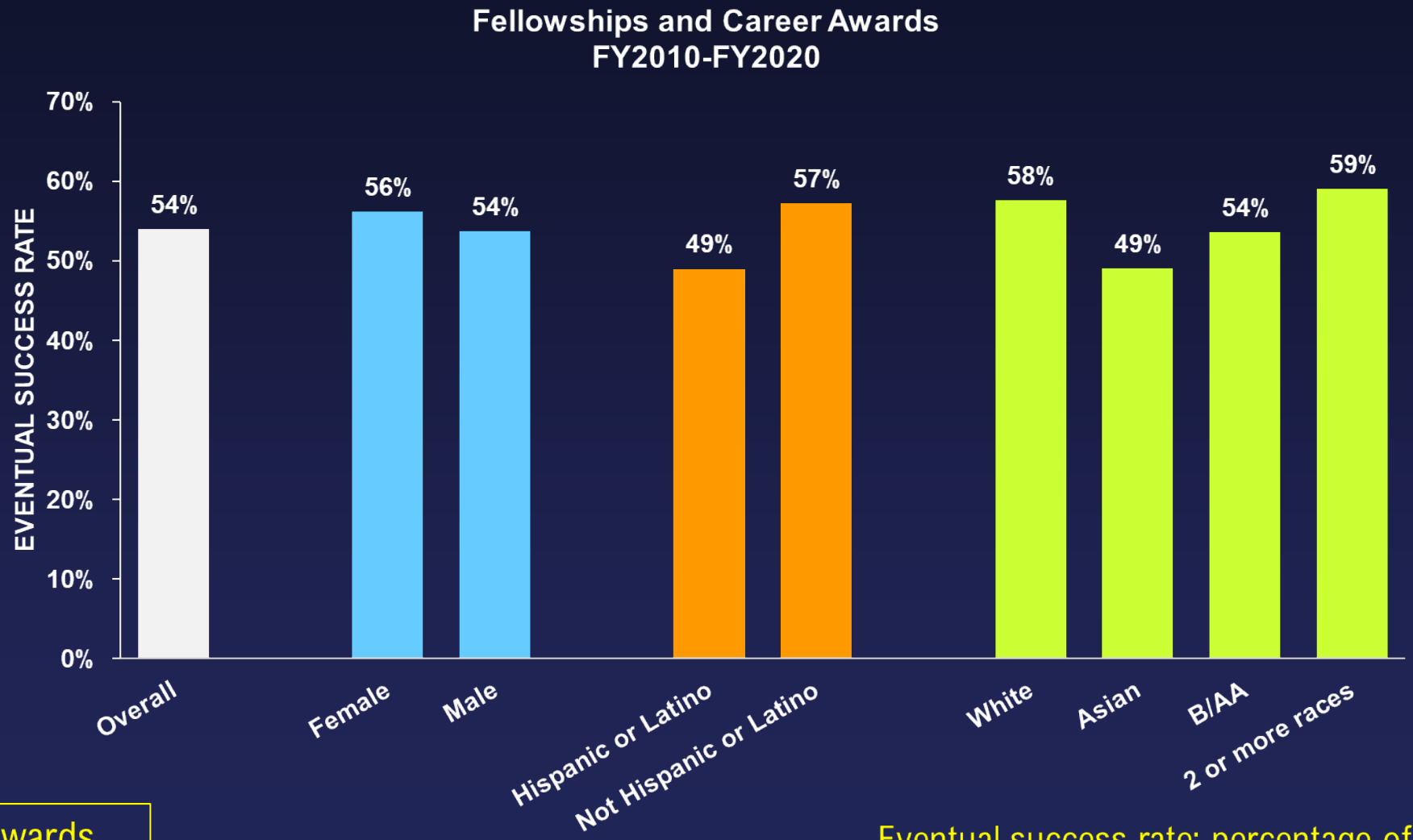
Fellowships and Career Development
Eventual Success Rate by Investigator Demographics



Includes F and K awards, most commonly: F30, F31, F32, K01, K08, K23, K99

Eventual success rate: percentage of funded projects
Projects with multiple PIs counted once for each PI
Submissions/A1s counted as one project

Recent Webinars

CollegeAIM Webinar Series

NIAAA and the International Town and Gown Association hosted a series of webinars, "The Updated College Alcohol Intervention Matrix (CollegeAIM): What Colleges and Communities Need to Know Now," in April, May, and August. Panelists included Jason Kilmer, Ph.D., Jessica Cronce, Ph.D., and Alicia Baker.

Innovations in Treating Stress & Trauma in Women with Alcohol Use Disorder

Panelists discussed the link between recent increases in rates of AUD in women and stress and trauma, focusing on vulnerable populations of women and advances in treatment. Presenters included Tracy Simpson, Ph.D., Geetanjali Chander, M.D. M.P.H., and Sherry McKee, Ph.D.

This event is archived at https://videocast.nih.gov/watch=42248

Alcohol Research: Current Reviews
Published a 14-Article Topic Series, "Recovery from AUD"

- Dr. Brett Hagman (NIAAA) and Dr. John Kelly (Recovery Research Institute) were co-editors
- The series includes articles on topics such as:
  - *What Is Recovery?*
  - *Sex and Gender Effects in Recovery from Alcohol Use Disorder*
  - *Brain Structure and Function in Recovery*
  - *Natural Recovery by the Liver and Other Organs After Chronic Alcohol Use*
  - *Racial/Ethnic Disparities in Mutual Help Group Participation for Substance Use Problems*
  - *Impact of Continuing Care on Recovery From Substance Use Disorder*
  - *The Role of the Family in Alcohol Use Disorder Recovery for Adults*

To view the complete series, visit:

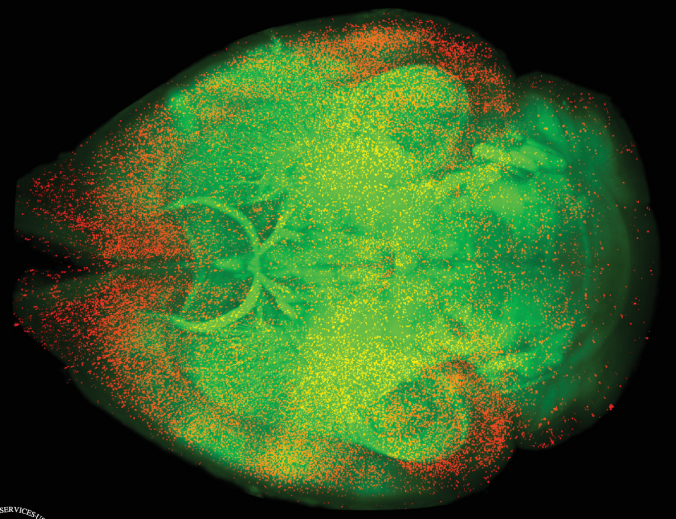
https://arcr.niaaa.nih.gov/topic-series/recovery-alcohol-use-disorder

What's Ahead?

The National Institute on Drug Abuse &
The National Institute on Alcohol Abuse and Alcoholism
Present...

2021 NIDA-NIAAA Mini-Convention

FRONTIERS
IN ADDICTION RESEARCH



Virtual Meeting

November 1–2, 2021 • 11 a.m. – 3 p.m.

NIH National Institute on Drug Abuse

NIH National Institute on Alcohol Abuse and Alcoholism

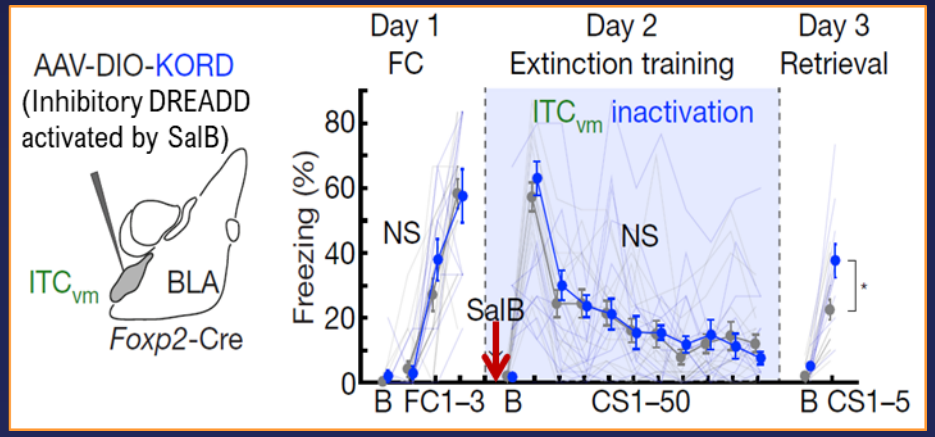
Scan the QR code to view the agenda and speaker lineup.

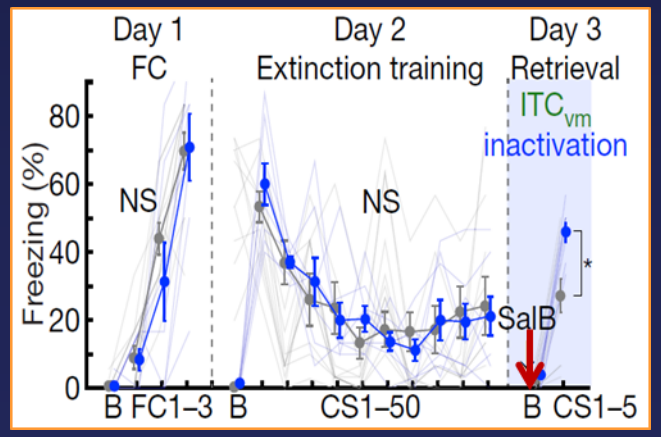
Research Highlights

Intercalated Amygdala Clusters Orchestrate a Switch in Fear State

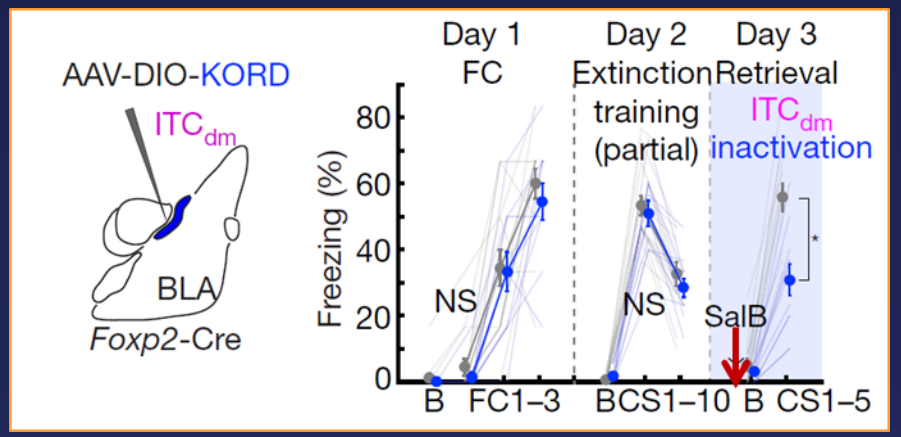
Effective extinction of fear memories prevents persistent, excessive reactions to threats that are associated with anxiety or trauma-related disorders. Researchers identified two clusters of neurons in the amygdala, ventral and dorsal intercalated cell masses (ITCs), that differentially mediate the acquisition and retrieval of fear extinction memory in mice. Inhibition of the ventral ITCs impaired both extinction memory formation and retrieval, whereas inhibition of the dorsal ITCs strengthened retrieval of extinction. Investigators also demonstrated that the two clusters have direct, selective access to major cortex-amygdala loops that regulate fear extinction. Collectively, the results suggest aberrant ITC function could contribute to susceptibility to various psychiatric conditions and may have implications for understanding the neuropathological basis for post-traumatic stress disorder.

Inhibition of ventral ITCs impairs extinction memory formation and retrieval of extinction memory (enhanced fear response during retrieval)





Inhibition of dorsal ITCs enhances retrieval of extinction memory (reduced fear response during retrieval)

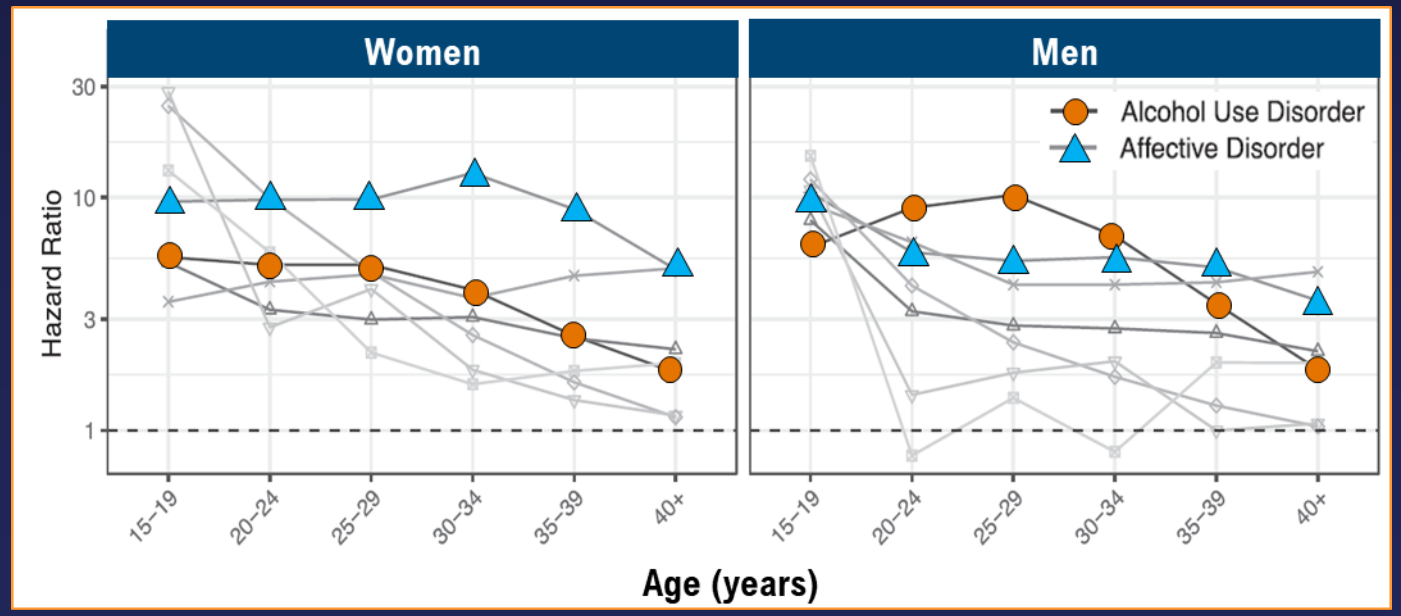


Citation: Hagihara KM, Bukalo O, Zeller M, Aksoy-Aksel A, Karalis N, Limoges A, Rigg T, Campbell T, Mendez A, Weinholtz C, Mahn M, Zweifel LS, Palmiter RD, Ehrlich I, Lüthi A, Holmes A. Nature. 2021 Jun;594(7863):403-407.

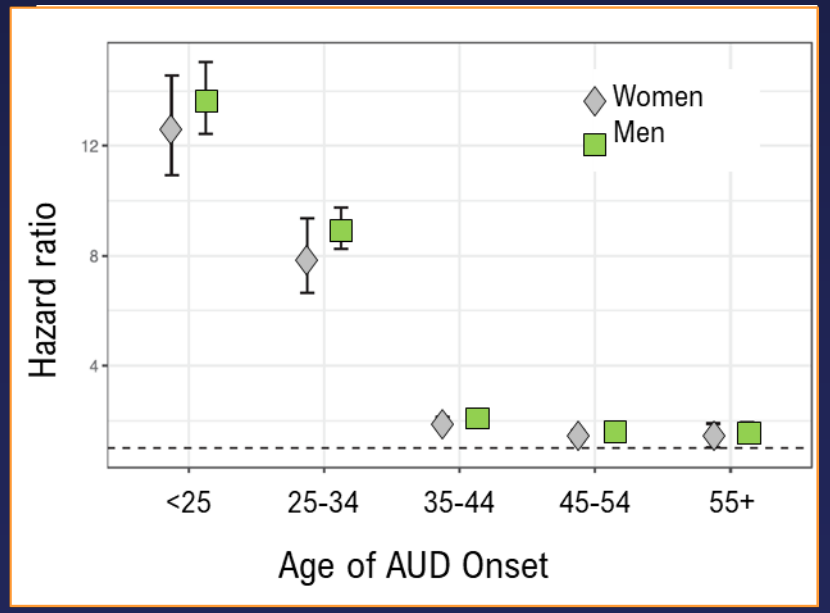
Alcohol Use Disorder and Non-Fatal Suicide Attempt: Findings from a Swedish National Cohort Study

Analysis of longitudinal nationwide Swedish registry data showed that AUD was robustly associated with suicide attempt after adjusting for sociodemographic factors and psychiatric comorbidity. Sex differences and age-of-onset effects were observed, with early-onset AUD more strongly associated with suicide attempt. AUD appears to be an important predictor of suicide attempt, results that have clinical implications for screening for suicidality risk on AUD diagnosis.

Risk of first suicide attempt among women and men with AUD or an affective disorder: Whereas risk for suicide attempt gradually declined across age for women with AUD, risk increased from age 15 to 29 before declining in men with AUD.



For both men and women, risk of lifetime suicide attempt was lower among those with later AUD onset relative to onset by age 25.



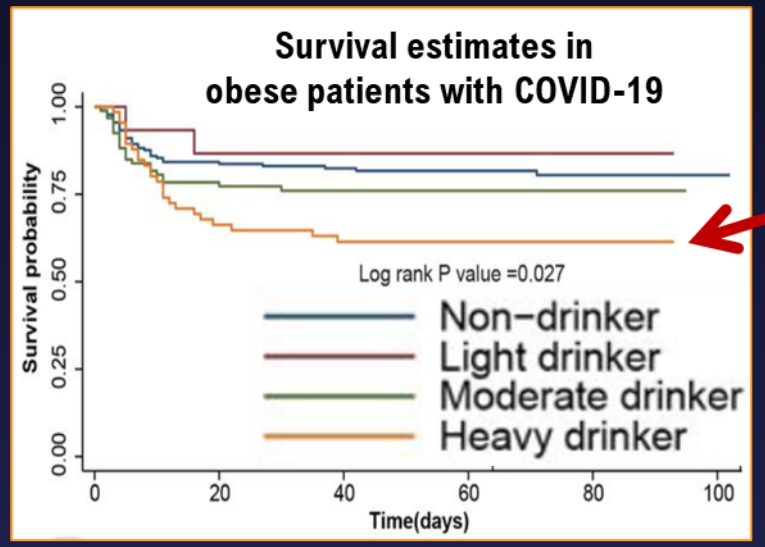
Citation: Edwards AC, Ohlsson H, Mościcki E, Crump C, Sundquist J, Kendler KS, Sundquist K. Addiction. 2021 Jun 22.

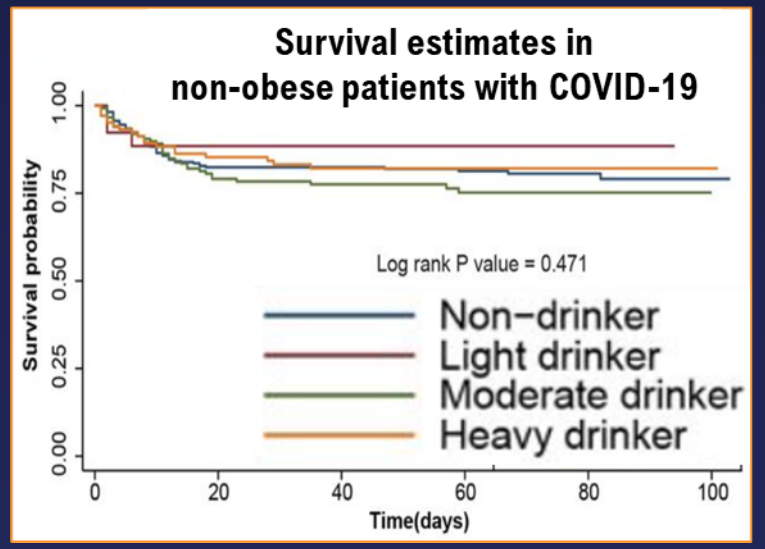
Alcohol Consumption Is Associated with Poor Prognosis in Obese Patients with COVID-19: A Mendelian Randomization Study Using UK Biobank

Using the UK Biobank cohort, this study examined the association between alcohol consumption and odds of SARS-CoV-2 infection and risk of death, using both traditional regression analyses (of self-reported alcohol consumption data) and Mendelian randomization analyses (of relevant genetic variants as a proxy for alcohol consumption).

Alcohol consumption was not associated with either increased or decreased risk of SARS-CoV-2 infection. However, in white patients with obesity, frequent alcohol consumption, especially heavy drinking, was associated with greater risk for worse COVID-19 clinical outcomes (ICU admission and death).

The findings suggest that alcohol can worsen the prognosis in patients with other risk factors for dying from COVID-19, such as obesity.





Citation: Fan X, Liu Z, Poulsen KL**, Wu X, Miyata T, Dasarathy S, Rotroff DM, Nagy LE. Nutrients. 2021 May 10;13(5):1592.

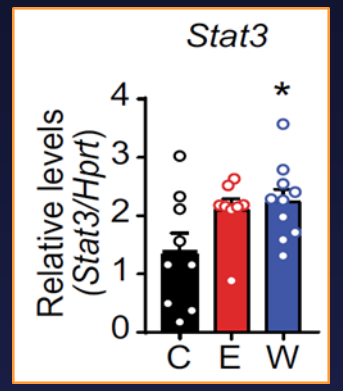
**NIAAA career development awardee

Transcriptomics Identifies STAT3 as a Key Regulator of Hippocampal Gene Expression and Anhedonia during Withdrawal from Chronic Alcohol Exposure

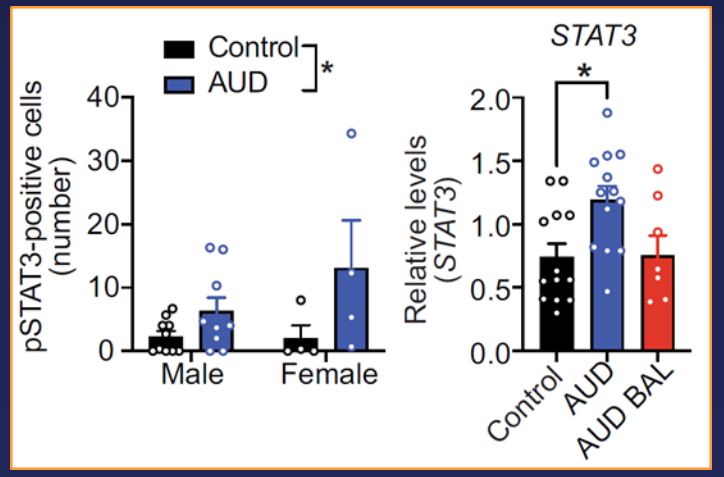
Investigators collected hippocampal tissue from rats during withdrawal from chronic alcohol exposure. RNA sequencing followed by network analysis identified the transcription factor STAT3 gene as a central node in a cluster of genes.

Stat3 was not only elevated in rat hippocampus during withdrawal, but increased expression of pSTAT3-labeled cells was also observed in the post-mortem hippocampus of humans with AUD. Inhibition of STAT3 reversed the post-withdrawal anhedonia phenotype in rats, suggesting that STAT3 signaling in the hippocampus may contribute to negative affect associated with AUD.

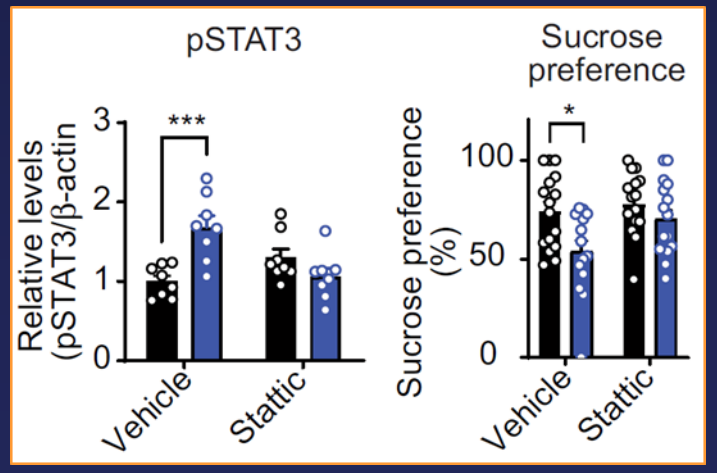
Stat3 expression was elevated in the hippocampus of EtOH-withdrawn ("W") rats



Increased pSTAT3-labeled cells and STAT3 was also observed in the post-mortem hippocampus of human subjects with AUD



STAT3 inhibitor Stattic reduced pSTAT3 levels and reversed withdrawal-related anhedonia (indexed by sucrose preference)



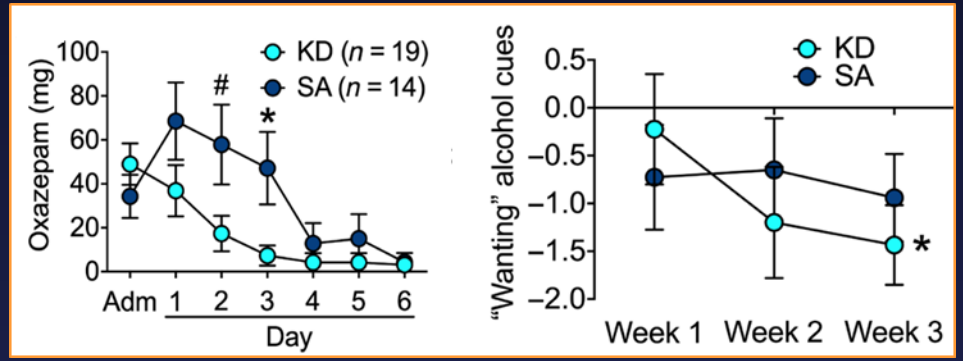
Citation: Chen WY, Chen H, Hamada K, Gatta E, Chen Y, Zhang H, Drnevich J, Krishnan HR, Maienschein-Cline M, Grayson DR, Pandey SC, Lasek AW. Transl Psychiatry. 2021 May 20;11(1):298.

Ketogenic Diet Reduces Alcohol Withdrawal Symptoms in Humans and Alcohol Intake in Rodents

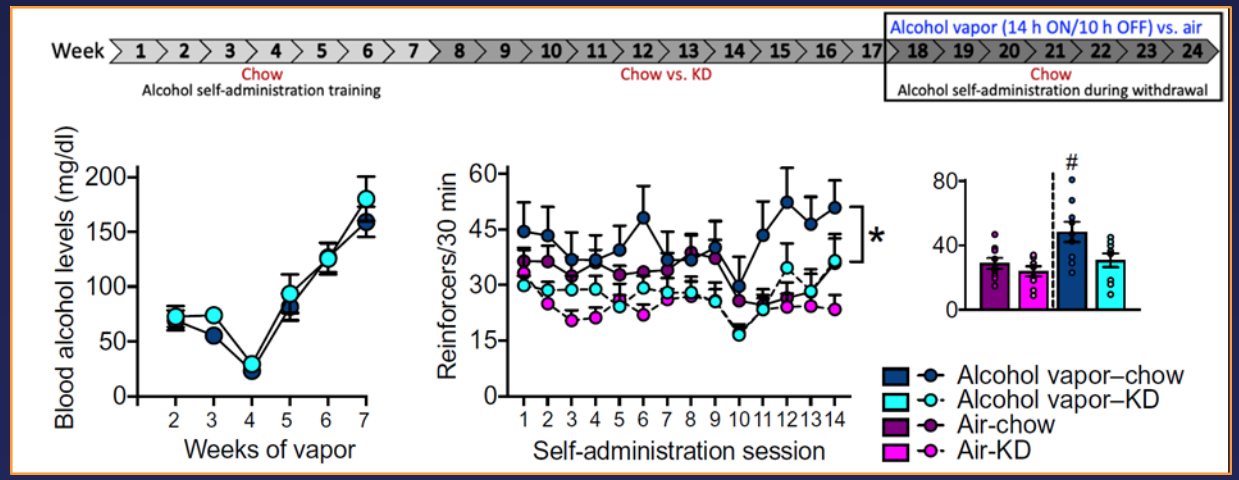
During alcohol withdrawal, acetate plasma levels fall, causing an energy deficient state. To test the hypothesis that a deficit in energy from acetate in the brain contributes to symptoms of alcohol withdrawal and increased alcohol drinking, investigators assessed the impact of a high-fat, low-carbohydrate "ketogenic diet" intervention in patients with AUD undergoing alcohol detoxification.

Patients on the ketogenic diet needed fewer benzodiazepines to treat alcohol withdrawal and showed less alcohol craving compared with patients who consumed a standard American diet. Rats with a history of a ketogenic diet self-administered significantly less alcohol compared to those on a regular chow diet. The study provides clinical and preclinical evidence that a ketogenic diet may offer a unique AUD treatment option to alleviate withdrawal symptoms and to lower alcohol craving and consumption.

Compared to those on a standard American (SA) diet, patients on the ketogenic diet (KD) needed less benzodiazepine administration during the first week of withdrawal and demonstrated reduced cue-induced craving.



Compared to rats fed regular chow, rats on the KD self-administered less alcohol following intermittent vapor exposure (i.e., a model of alcohol dependence)



Citation: Wiers CE, Vendruscolo LF, van der Veen JW, Manza P, Shokri-Kojori E, Kroll DS, Feldman DE, McPherson KL, Biesecker CL, Zhang R, Herman K, Elvig SK, Vendruscolo JCM, Turner SA, Yang S, Schwandt M, Tomasi D, Cervenka MC, Fink-Jensen A, Benveniste H, Diazgranados N, Wang GJ, Koob GF, Volkow ND. Sci Adv. 2021 Apr 9;7(15):eabf6780.

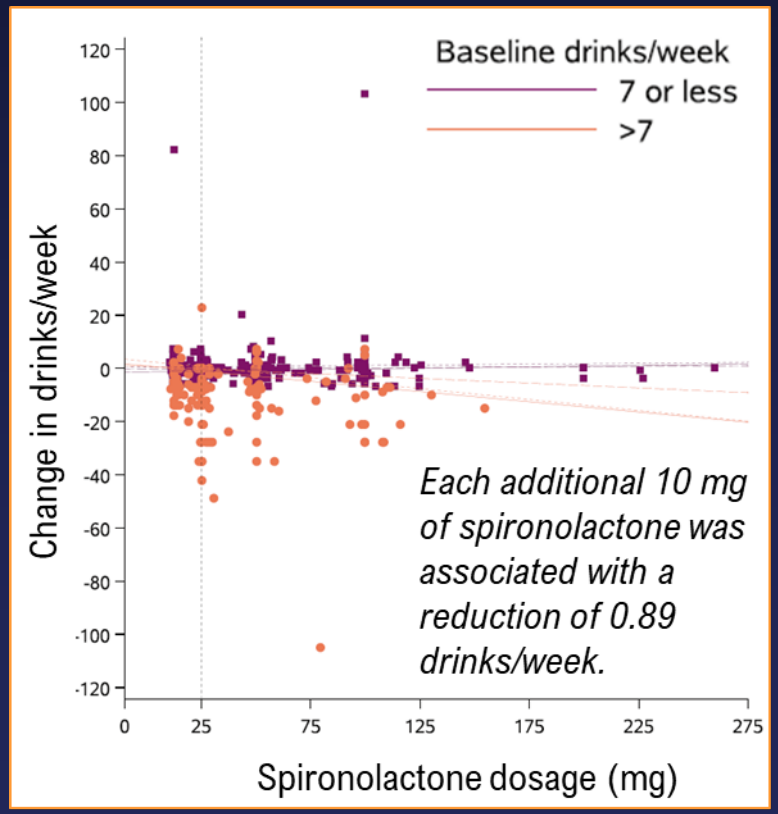
Effectiveness of Spironolactone Dispensation in Reducing Weekly Alcohol Use: A Retrospective High-Dimensional Propensity Score-Matched Cohort Study

Spironolactone is mineralocorticoid receptor (MR) antagonist that is widely used in primary and specialty care settings to treat a variety of health conditions such as essential hypertension, heart failure, primary hypoaldosteronism, hypokalemia, and nephrotic syndrome.

To test the hypothesis that MRs may represent a novel pharmacological treatment for alcohol use disorder (AUD), investigators conducted a pharmacoepidemiologic retrospective cohort study to examine whether dispensation of spironolactone (≥90 continuous days), for any indication, was associated with changes in weekly alcohol use about 6 months later.

For patients who drank >7 drinks/week at baseline, those treated with spironolactone (vs untreated patients) reported a reduction in weekly alcohol use by around four drinks. No significant difference was observed among patients who drank less at baseline. Spironolactone (or other MR antagonists) may hold promise as a pharmacotherapy for AUD.

Dose-response relationship between spironolactone dose and change in drinks/week



Citation: Palzes VA, Farokhnia M, Kline-Simon AH, Elson J, Sterling S, Leggio L, Weisner C, Chi FW. Neuropsychopharmacology. 2021 Aug 2.

THANK YOU!

Special thanks to:

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