National Institute on Alcohol Abuse and Alcoholism

NIAAA Director's Report on Institute Activities to the 167th Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

Tuesday, September 12, 2024

Hybrid Meeting

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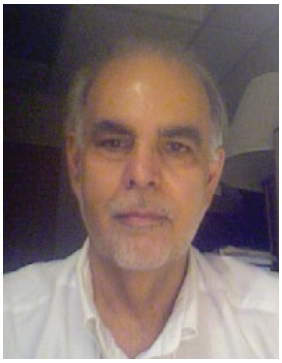
IN MEMORIAM

Dr. George Breese was the John R. Andrews Distinguished Professor at the Bowles Center for Alcohol Studies at the University of North Carolina School of Medicine. Dr. Breese led seminal studies on the anatomical and molecular basis of increased stress emerging from repeated withdrawal from chronic alcohol exposure, including the role of corticotropin-releasing factor in the central amygdala in stress response. Dr. Breese also made important scientific contributions in understanding the role of neuroimmune signaling in alcohol withdrawal-induced stress. His passion for science was remarkable, and his work will continue to inspire the field.

Dr. Klaus A. Miczek was the Moses Hunt Professor of Psychology, Psychiatry, Pharmacology, and Neuroscience at Tufts University. He also served as one of the directors of the Neuroscience Research Center at Tufts. Dr. Miczek's research centered on psychopharmacological and brain mechanisms of aggression, anxiety, social stress, and misuse of alcohol and other substances. He received numerous honors, including the Solvay Duphar Award from the American Psychological Association, a MERIT award from NIAAA, and Silver Medals of the Charles University (Czech Republic). Dr. Miczek was a beloved colleague and highly esteemed scientist who left a lasting impact on the neuropsychopharmacology field.



Dr. Daniel E. Rio was a Senior Scientist/Research Physicist in the Section of Brain Electrophysiology and Imaging of the Laboratory of Clinical Studies at NIAAA from 1996-2015. He made important scientific contributions in neuroimaging data models and analyses. After departing NIAAA, Dr. Rio taught courses in Applied Biomedical Engineering at Johns Hopkins Whiting School of Engineering. He was known as a brilliant, kind, and patient instructor, and many students are lucky to have benefitted from his commitment to teaching.

Dr. Kenneth R. Warren was appointed NIAAA Deputy Director in 2008 and served as NIAAA Acting Director from 2008 to 2014. Following 41 years of Federal service, Dr. Warren retired in 2015, after which he continued to serve as a Special Advisor to the NIAAA Director until 2018. Dr. Warren was a foremost research expert on fetal alcohol spectrum disorders (FASD). He was the lead author on the first U.S. government advisory on alcohol and pregnancy in 1977 and helped lead the first Surgeon General's warning about alcohol and pregnancy in 1981. He received numerous awards, including the Lifetime Achievement Award from the Research Society on Alcohol. He was known as an exceptionally smart, kind, and gentle man, and was a wonderful mentor, friend, and colleague.

NIAAA BUDGET

Fiscal Year (FY) 2024

On March 23, 2024, the President signed H.R. 2882 – Further Consolidated Appropriations Act, 2024. NIH received a total of $47.2 billion, a $0.4 million (0.8%) decrease below the fiscal year 2023 enacted level.

The FY 2024 appropriation for NIAAA provides $595.3 million. This represents a flat appropriation from the FY 2023 budget level. NIAAA estimates it will support a total of 716 Research Project Grants (RPGs) in FY 2024.

FY 2025

The FY 2025 appropriation for NIH and NIAAA has not yet been finalized at this time.

HONORS AND AWARDS

Dr. Olena Bukalo received the 2024 Klaus Gawrisch Travel Award, named in honor of Dr. Klaus Gawrisch who served as Chief of the Laboratory of Membrane Biochemistry and Biophysics until his retirement in 2020.

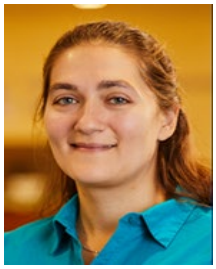
Dr. Robert Freeman received a Department of Health and Human Services Distinguished Service Departmental Award for his contributions to the Rapid Acceleration of Diagnostics Initiative Team.

Meagan Marks received an Outstanding Poster Award at the 2024 NIH Postbaccalaureate Research Day.

Dr. David Haggarty and Dr. Ryan Tyler, postdoctoral fellows in the NIAAA Division of Intramural Clinical and Biological Research, have been chosen as NIGMS Postdoctoral Research Associate Training (PRAT) fellows.

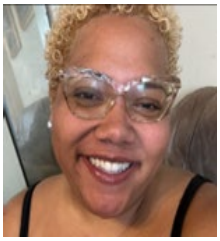
STAFF TRANSITIONS

New Staff



Alicia Caffi joined the Financial Management Branch as the new Budget Officer. Her career with the NIH spans more than 19 years working in budget offices of multiple Institutes and Centers. Ms. Caffi joins NIAAA after serving as the National Human Genome Research Institute Deputy Budget Officer for the past 5 years. Prior to that position, she served as the Deputy Budget Officer at the National Institute of Mental Health, the Budget Officer at the Center for Scientific Review, and a Budget Analyst at the NIH Clinical Center.

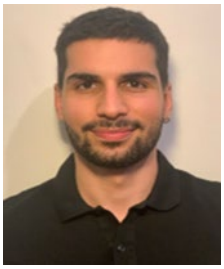
Dr. Subhradeep Dutta joined the Section on Medicinal Chemistry in the Division of Intramural Clinical and Biological Research as a postdoctoral Visiting Fellow. Dr. Dutta will contribute to the synthesis and evaluation of new molecular probes and drug-like molecules for studying G-protein coupled receptors signaling pathways for therapeutics development in alcohol-associated diseases.



Courtney Kelly joined the Administrative Services Branch as a Purchasing Agent providing procurement support to both intramural and extramural programs within NIAAA. Ms. Kelly previously served as an Extramural Support Assistant for the Center for Scientific Review and has also served as a financial and banking professional outside of NIH for over 3 years.

Dr. Eloise Kuijer joined the Section of Sensory Science and Metabolism in the Division of Intramural Clinical and Biological Research as a postdoctoral Visiting Fellow. Dr. Kuijer will study how internal state shapes chemosensation-guided reward-seeking behavior in mice and its neural correlates using in situ RNA hybridization, behavioral tasks, and in vivo neural activity recordings.

Dr. Sarika Parasuraman joined the Division of Epidemiology and Prevention Research as a Health Scientist Administrator. Dr. Parasuraman previously served as a Health Science Policy Analyst at the NIH Office of Behavioral and Social Sciences Research. Prior to joining NIH, Dr. Parasuraman was a Social Scientist and Chief Evaluation Officer for the Maternal and Child Health Bureau in the Health Resources and Services Administration.



Deniz Seyhan joined the Laboratory of Liver Diseases in the Division of Intramural Clinical and Biological Research as a pre-doctoral Visiting Fellow. Mr. Seyhan will study the molecular and cellular mechanisms underlying alcohol associated liver cancer by using multiplex immunofluorescence staining, RNA sequencing, experimental mouse models, and molecular biology techniques.

Dr. Shoupeng Wei joined the Laboratory for Integrative Neuroscience in the Division of Intramural Clinical and Biological Research as a postdoctoral Visiting Fellow. Dr. Wei will study the mechanisms underlying alcohol actions on the brain and alcohol use disorder in mice using in vitro and in vivo physiological, pharmacological, genetic, and behavioral techniques.

New Post-Baccalaureate Intramural Research Training Award Fellows:

- **Jacob Buursma** – Clinical Neuroimaging Research Core
- **Ailen Costamagna-Soto** – Laboratory of Neuroimaging
- **Lacey Donahue** – Laboratory of Human Psychopharmacology
- **Abigail Holder** – Laboratory for Integrative Neuroscience
- **Ava Mascarenhas** – Office of the Clinical Director
- **Joshua Reitz** - Section on Clinical Genomics and Experimental Therapeutics
- **Natalia Rincon** - Laboratory of Human Psychopharmacology
- **Shanzeh Sadiq** - Laboratory of Behavioral and Genomic Neuroscience
- **Paul Volesky** – Section on Medicinal Chemistry
- **Nicholas Weaver** - Laboratory of Human Psychopharmacology
- **Joshua Zhao** - Laboratory of Neuroimaging

Transitions

Dr. Yonwoo Jung- transitioned from a Visiting Fellow to a Research Fellow in the Laboratory of Neurogenetics. Dr. Jung will identify and quantify regulated genes (RNAs) within intracellular granules after alcohol and cocaine exposure and study the effects of these substances on the RNAs in synapses and oxidative damage.

Dr. Jeong Oen Lee transitioned from a Research Fellow to a Staff Scientist in the Laboratory for Integrative Neuroscience. Dr. Lee conducts studies involving cellular and subcellar imaging in brain slices and in vivo. Dr. Lee will also train new laboratory members in rodent neurosurgery and in the performance and analysis of behavioral studies.

Dr. Bryan Mackowiak transitioned from Postdoctoral Fellow to a Research Fellow in the Laboratory of Liver Diseases. Dr. Mackowiak will continue to study the pathogenesis of alcohol-associated liver disease and explore therapeutic targets for the treatment of alcohol-associated liver disease.

Dr. Wiramon Rungratanawanich transitioned from a Visiting Fellow to a Research Fellow in the Section of Molecular Pharmacology and Toxicology. Dr. Rungratanawanich will continue mechanistic studies of cell or tissue injury caused by binge alcohol drinking and/or a Western-style high fat diet and the role of the gut-liver-brain axis.

Departures

Dr. Ruairi O'Sullivan, a Postdoctoral Visting Fellow in the Laboratory of Behavioral and Genomic Neuroscience departed to work as a data analyst and programmer for an internet-based financial transactions company.

Dr. Angelica Rusilowski, a Postdoctoral Intramural Research Training Award Fellow in the Clinical Neuroimaging Research Core departed to complete a residency in Family Medicine at the University of Illinois Chicago.

Departing Post-baccalaureate Intramural Research Training Award Fellows:

- **Mikayla Bergwood** – Laboratory of Human Psychopharmacology

- **Eva Cullins** - Laboratory of Human Psychopharmacology
- **Natalie Ellis** - Section on Clinical Genomics and Experimental Therapeutics
- **Madelyne Etami** – Laboratory of Neuroimaging
- **Jeffrey Goff** – Laboratory of Behavioral and Genomic Neuroscience
- **Ali Hamandi** - Section on Clinical Genomics and Experimental Therapeutics
- **Natalie Johnson** – Section on Fibrotic Disorders
- **Ethan Kinstler** - Laboratory of Neurogenetics
- **Karli Lefort** – Section of Molecular Pharmacology and Toxicology
- **Nafisa Nawal** – Section of Sensory Science and Metabolism
- **Lauren Park** - Section on Clinical Genomics and Experimental Therapeutics
- **Noa Reuveni** – Laboratory for Integrative Neuroscience
- **Rishika Shah** - Laboratory for Integrative Neuroscience
- **Samay Shivshankar** – Section on Medicinal Chemistry
- **Leah Vines** - Laboratory of Neuroimaging
- **Samuel Vacic** - Laboratory of Neuroimaging
- **Courtney Waters** - Clinical Neuroimaging Research Core

RECENTLY ISSUED FUNDING OPPORTUNITIES

Notices of Funding Opportunity (NOFOs) issued by NIAAA

Specialized Alcohol Research Centers: NIAAA solicits Specialized Center grant applications to foster and conduct interdisciplinary, collaborative research on alcohol use disorder (AUD), alcohol misuse and alcohol related problems, and other health related consequences across the lifespan. Topics include, but are not limited to, the nature, etiology, genetics, diagnosis, treatment, and prevention of AUD and alcohol-related end-organ diseases, as well as the related biomedical, psychosocial, and economic consequences across the lifespan and across racial/ethnic groups and other health disparity populations. Centers are also major contributors to the development of research methods, technologies, and approaches that sustain innovative goal-directed research. (P50 Clinical Trial Optional) RFA-AA-24-007. *Contacts: Greg Bloss, Drs. Li Lin, Qi-Ying Liu, Kathy Jung, Antonio Noronha, Mariela Shirley*

Comprehensive Alcohol Research Centers: NIAAA solicits Comprehensive Alcohol Research Centers applications. These Centers must include a dissemination core to initiate and expand community education related to the activities of the Center. The overall purpose of the NIAAA Alcohol Research Center program is to provide leadership in conducting and fostering interdisciplinary, collaborative research on a wide variety of topics relevant to the NIAAA mission. These topics include, but are not limited to, the nature, etiology, genetics, epigenetics, diagnosis, epidemiology, treatment, and prevention of alcohol misuse, AUD, and alcohol-related end organ diseases, as well as the related biomedical, neurochemical, behavioral, psychosocial, and economic consequences across the lifespan and across racial/ethnic groups and other health disparity populations. Centers also are regional or national resources that contribute to the development of new research methods, technologies and approaches that sustain innovative goal-directed research. (P60 Clinical Trial Optional) RFA-AA-24-008. *Contacts: Greg Bloss, Drs. Li Lin, Qi-Ying Liu, Kathy Jung, Antonio Noronha, Mariela Shirley*

NIH-Wide NOSIs, NOFOs and Notices with NIAAA Participation

BRAIN Initiative: Brain Behavior Quantification and Synchronization (R61/R33 Clinical Trial Optional), RFA-MH-26-100.

BRAIN Initiative: Brain-Behavior Quantification and Synchronization Transformative and Integrative Models of Behavior at the Organismal Level (U01 Clinical Trial Optional), RFA-DA-24-040, (U01 Clinical Trials Not Allowed), RFA-DA-24-041.

HEAL Initiative: INTERACT INTEgRAtive Back Pain Longitudinal Cohort Teams (UC2 Clinical Trial Optional), RFA-AR-25-005.

HEAL Initiative: NIH-DOD-VA Pain Management Collaboratory Pragmatic and/or Implementation Science Demonstration Projects ((UG3/UH3) Clinical Trial Required), RFA-AT-24-011.

HEAL Initiative: PainCare Clinician Training Program (PCTP): Mentored Patient-Oriented Research Career Development award (K23 - Clinical Trial Required), PAR-24-220.

HEAL Initiative: PainCare Clinician Training Program (PCTP): Mentored Clinical Scientist Development Awards (K08 - Basic Experimental Studies with Humans (BESH) Required), PAR-24-218., (K08 - Clinical Trials Not Allowed), PAR-24-219, (K08 - Clinical Trials Required), PAR-24-217.

Building Sustainable Software Tools for Open Science (R03 Clinical Trial Not Allowed), RFA-OD-24-010.

Whole Person Research and Coordination Center (Whole Person RCC) U24 (Clinical Trial Not Allowed), RFA-AT-24-010.

Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) Postdoctoral Career Transition Award to Promote Diversity (K99/R00 - Independent Basic Experimental Studies with Humans Required (BESH)), PAR-24-227, (K99/R00 - Independent Clinical Trial Required), PAR-24-226, (K99/R00 Independent Clinical Trial Not Allowed), PAR-24-225.

NIH Research Software Engineer (RSE) Award (R50 Clinical Trials Not Allowed), RFA-OD-24-011.

PHS 2024-2 Omnibus Solicitation of the NIH, CDC and FDA for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44] Clinical Trial Not Allowed), PA-24-245. (Parent SBIR [R43/R44] Clinical Trial Required), PA-24-246.

PHS 2024-2 Omnibus Solicitation of the NIH for Small Business Technology Transfer Grant Applications (Parent STTR [R41/R42] Clinical Trial Not Allowed), PA-24-247., (Parent STTR [R41/R42] Clinical Trial Required), PA-24-248.

Successor-in-Interest (Type 6 Parent Clinical Trial Optional), PA-24-253.

Change of Recipient Organization (Type 7 Parent Clinical Trial Optional), PA-24-254.

Notice of Special Interest (NOSI): Research Opportunities Centering the Health of Women Across the HIV Research Continuum, NOT-OD-24-119.

Notice of Special Interest (NOSI): Ending the HIV Epidemic (EHE), NOT-AI-24-059.

Notice of Special Interest (NOSI): HEAL Initiative: Development and Translation of Diagnostic and Therapeutic Devices via Blueprint MedTech, NOT-NS-24-075.

Notice of Correction to PAR-24-219: NIH HEAL Initiative PainCare Clinician Training Program (PCTP): Mentored Clinical Scientist Development Awards (K08 - Clinical Trials Not Allowed), NOT-NS-24-111.

Notice of Intent to Publish a Funding Opportunity Announcement for Blueprint Neurotherapeutics Network (BPN): Biologic-based Drug Discovery and Development for Disorders of the Nervous System (UG3/UH3 Clinical Trial Optional), NOT-NS-24-014.

NIAAA DIRECTOR'S ACTIVITIES

NIAAA Director **George F. Koob, Ph.D.,** gave the following presentations between April – July 31, 2024:

- "Participant Group 4 Therapeutics" at the 2024 Translational Neuroscience 2.0 Meeting in Calistoga, CA on April 7-11, 2024.
- "The Role of Hyperkatifeia in Recovery: A Neurobiological Perspective" at the National Conference on Addiction Recovery Science for the Recovery Research Institute (virtual) on April 24, 2024.
- "Addiction as a 3 Stage Cycle, 3 Domain, 3 Neurocircuit Framework: A Catalyst for Translational Research" at the 3rd Annual Southern California Substance Addiction Research in Los Angeles, CA on April 26, 2024.
- "Changing the Conversation about Alcohol: A Neurocircuit framework for Translational Research" at the International Drug Addiction Research Society Meeting in Rio de Janeiro, Brazil on April 29, 2024.
- "Changing the Conversation about Alcohol in the United States" for the McLean Hospital Keynote Address at the Addictions 2024 Symposium at Harvard Medical School (pre-recorded) on May 17, 2024.
- "Alcohol Use Disorder: The Gain in the Brain is in the Emotional Pain and Implications for Treatment" at the 35th World Congress Collegium Internationale Neuro-Psychopharmacologicum in Tokyo, Japan on May 23, 2024.
- "Neurobiology of Opioid Addiction: Opponent Process, Hyperkatifeia, and Negative Reinforcement" for the 17th Japanese Society of Pharmaceutical Palliative Care and Sciences in Tokyo, Japan on May 25, 2024.
- "Changing the conversation around alcohol in the United States" at the 35th World Congress Collegium Internationale Neuro-Psychopharmacologicum Public Symposium in Tokyo, Japan on May 26, 2024.
- "Hyperkatifeia, negative reinforcement and allostasis: A neglected translational perspective" for the Journée Nationale #Recherche Translationnelle sur les Addictions Keynote for the Ministry of Solidarity and Health in Paris, France on June 3, 2024.

- "Closing the Treatment Gap for Alcohol Use Disorder: A Neurobiological Perspective" for the 18th Congrès International d'Addictologie de l'ALBATROS in Paris, France on June 5, 2024.
- "Neurobiology of Alcohol and Opioid Addiction: A Hyperkatifeia, Negative Reinforcement, and Allostasis Perspective" for the Seminar Bordeaux Neurocampus at the University of Bordeaux in Bordeaux, France on June 10, 2024.
- "Theoretical Framework of the Addiction Cycle in 3 Stages, 3 Domains and 3 Neural Circuits: A Catalyst for Translational Research, An Aid to the Clinic" in the Better Understanding for Better Support Plenary at the Addictions and Sciences Congress for the Addiction Fédération in Bordeaux, France on June 13, 2024.
- "Advancing Alcohol Research: An Update and an Eye Toward the Future" at the 2024 Research Society on Alcohol Conference in Minneapolis, MN on June 23, 2024.
- "Changing the Conversation about Alcohol" at the Mayo Clinic in Rochester, MN on June 26, 2024.
- "Advancing Alcohol Research: An Update and an Eye Toward the Future" for the Council on Addiction Psychiatry, American Psychiatric Association (virtual) on July 10, 2024.

NOTABLE NIAAA STAFF ACTIVITIES

Activities between **April 1, 2024 - July 31, 2024**:

Dr. Bin Gao was featured in NIH's "I am Intramural blog" discussing alcohol-associated liver damage and potential treatments on April 17, 2024.

Dr. Laura Kwako and **Dr. Thekla Ross,** gave presentations on the Healthcare Professional's Core Resource on Alcohol to various groups: On May 22 and June 5, they presented webinars at the Hazelden Betty Ford Summer Institute for Medical Students. On May 31, they presented at the American Medical Students Association annual meeting in Crystal City, VA. On July 17, they presented a webinar sponsored by the American Psychological Association.

Dr. Daniel Falk presented "NIAAA's Medications Development Program to Treat Alcohol Use Disorder" at the Alcohol and Substance Use Disorders Research Program: Pharmacotherapies for Alcohol and Substance Use Disorder Alliance Consortium Programmatic Panel Update and FY24 Vision Setting Meeting, April 2, 2024.

Dr. Tatiana Balachova served as member of the International Advisory Committee for the 9th International Research Conference on Adolescents and Adults with Fetal Alcohol Spectrum Disorders on April 11-14, 2024.

Dr. Sarika Parasuraman served on the panel for a reviewer training meeting for the HHS Children and Youth Resiliency Challenge, on April 23, 2024.

Dr. David Goldman presented "Genetics and Epigenetics of Alcohol Use Disorder" for the NIH Clinical Center Grand Rounds on May 14, 2024.

At the 32nd Society of Prevention Research Annual Meeting, **Dr. Tatiana Balachova** presented in two Scientific Interests Groups: "Prevention Science to Reduce Alcohol-Related Harms: A Dialogue

with NIAAA" with Co-convener **Dr. Robert Freeman,** and "50th Anniversary of FAS/FASD Recognition: How Are We Doing in Prevention?" In addition, Dr. Balachova participated as Co-Convener of SIG Screening, Brief Intervention, Referral to Treatment or Prevention (SBIRT/P) Special Interest Group.

Dr. Daniel Falk presented "NIAAA Update: Focus on Medications Development for the Treatment of Alcohol Use Disorder" at the American Society of Clinical Psychopharmacology Annual Meeting, May 31, 2024.

Dr. Malliga Iyer was featured in the NIH Record for her lab's studies on drug targets in the endocannabinoid system for the Record's intramural inventor series for Makers Month on June 7, 2024.

Dr. Robert Freeman was a member of the Planning Committee for the National Institute on Mental Heath Workshop on Sexual and Gender Minority Youth, held virtually on June 10-11, 2024.

Dr. Robert Freeman presented "IPV Research at the National Institute on Alcohol Abuse and Alcoholism," at the HHS Violence Against Women Intimate Partner Violence (IPV) Research Showcase, Meeting of the Intergovernmental Steering Committee on Violence Against Women, Washington, DC, on June 18, 2024.

Dr. Ralph Hingson gave a virtual presentation on "Trends in and Interventions That Work to Prevent Underage and College-age Drinking" for the Groton Alliance for Substance Use Prevention on June 24, 2024.

The 47th Annual Research Society on Alcoholism Scientific Meeting was held on June 22-26, 2024, in Minneapolis, Minnesota.

- **Dr. Tatiana Balachova** presented on the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders and **Dr. Bill Dunty** gave the NIAAA Update at the FASD Study Group Meeting, on June 22, 2024.
- **Dr. Kathy Jung** served as a discussant at the "Wearable Alcohol Sensors in Research: Expert Presentations and Interactive Discussion on Progress, Hurdles, and Innovative Solutions" satellite session on June 22, 2024.
- **Dr. Mark Egli** presented "Funding Opportunities Related to Pain and Alcohol" at the Symposium on Pain and Alcohol: Bridging Preclinical and Clinical/Translational Research on Alcohol and Pain on June 22, 2024.
- **Dr. Elizabeth Powell** served as the discussant for the "Alcohol and Large-Scale Brain Networks in Human and Preclinical Studies" symposium on June 23, 2024.
- **Dr. Changhai Cui, Dr. Peter Gao, Dr. Li Lin, Dr. Philippe Marmillot, and Dr. Abbas Parsian** co-chaired the NIAAA-Supported Research: Grant Skills Workshop on June 24, 2024.
- **Dr. Daniel Falk** presented on the "Potential Pipeline of Pharmacotherapies for Treatment of AUD in Patients with ALD" roundtable on June 24, 2024.
- **Dr. Peter Gao** served as the discussant for the "Novel Insights into the Molecular Mechanisms and Biomarkers of Alcohol-Induced Carcinogenesis" session on June 24, 2024.
- **Dr. Robert Freeman** chaired a Symposium on "Advances in Mobile Health Interventions for Preventing Alcohol-Related Violence" on June 26,2024.

Dr. Paule Joseph became co-director of the newly established NIH Smell and Taste Center (NSTC) in July 2024, which also includes investigators from the National Institute on Deafness and Communicative Disorders and the National Institute on Aging. The NSTC is dedicated to advancing understanding of the chemical senses (smell and taste) and related disorders through comprehensive research, patient care, and education.

Gregory Bloss presented "Trends in and Prevention of Underage and Emerging Adults Drinking and Consequences" at CADCA's 23rd Annual Mid-Year Training Institute on July 14-18, 2024.

Dr. Mark Egli discussed the NIAAA pain research portfolio in the virtual session "Know Your IC: National Institute on Alcohol Abuse and Alcoholism (NIAAA)" for the NIH Helping to End Addiction Long-term (HEAL) PURPOSE Pain Network meeting on July 26, 2024.

NIAAA Scientific Meetings and Resources

NIAAA held a workshop titled **Reducing Alcohol-associated Liver Disease Burden through Early Screening and Management in the General Population** on April 17-18, 2024. This workshop focused on the prevention of severe alcohol-associated liver disease (ALD) through early detection and management. Topics included target patient population selection, current and emerging ALD and alcohol use screening tools and protocols, intervention management, including pharmacotherapy, and pathways of inter-specialty care delivery.

What's Ahead?

The **7th European FASD Alliance Conference** will be held on September 20-26, 2024, in Madrid, Spain.

The 2024 **NIAAA Public Liaison Meeting** will be held virtually on October 2, 2024.

The **NIDA-NIAAA Frontiers in Addiction Research Mini-Convention** will be held in person on October 4, 2024, in Chicago, Illinois. The agenda for the Mini-Convention includes scientific sessions on Psychedelics and Empathogens for Treatment of Alcohol and Substance Use Disorders, GLP-1 Receptor Agonists for the Treatment of Substance Use Disorders, and the Habenula as an Anti-Addictive Circuit Hub.

NIAAA Research Highlights

Factors Underlying the Neurofunctional Domains of the Addictions Neuroclinical Assessment Assessed by a Standardized Neurocognitive Battery

Significance: The Addictions Neuroclinical Assessment (ANA) is a neurobiologically-informed framework designed to understand the etiology and heterogeneity of alcohol use disorder (AUD). Previous studies validated the three neurofunctional domains of ANA: incentive salience (IS), negative emotionality (NE) and executive function (EF) using secondary data. In this study, a more

streamlined assessment battery was devised to evaluate the three ANA domains and was tested in a prospective sample of adults across the AUD spectrum. This research provided novel findings on the underlying factor structure of the three domains and the clinical utility of these factors in classifying individuals with and without AUD. These results revealed additional dimensionality to the ANA domains, bringing together different constructs from the field into a single cohesive framework.

Abstract: The Addictions Neuroclinical Assessment (ANA) is a neurobiologically-informed framework designed to understand the etiology and heterogeneity of Alcohol Use Disorder (AUD). Previous studies validated the three neurofunctional domains of ANA: Incentive Salience (IS), Negative Emotionality (NE) and Executive Function (EF) using secondary data. The present cross-sectional observational study assessed these domains in an independent, prospective clinical sample. Adults across the drinking spectrum (N = 300) completed the ANA battery, a standardized collection of behavioral tasks and self-report assessments. Factor analyses were used to identify latent factors underlying each domain. Associations between identified domain factors were evaluated using structural equation models. Receiver operating characteristics analyses were used to determine factors with the strongest ability to classify individuals with problematic drinking and AUD. We found (1) two factors underlie the IS domain: alcohol motivation and alcohol insensitivity. (2) Three factors were identified for the NE domain: internalizing, externalizing, and psychological strength. (3) Five factors were found for the EF domain: inhibitory control, working memory, rumination, interoception, and impulsivity. (4) These ten factors showed varying degrees of cross-correlations, with alcohol motivation, internalizing, and impulsivity exhibiting the strongest correlations. (5) Alcohol motivation, alcohol insensitivity, and impulsivity showed the greatest ability in classifying individuals with problematic drinking and AUD. Thus, the present study identified unique factors underlying each ANA domain assessed using a standardized assessment battery. These results revealed additional dimensionality to the ANA domains, bringing together different constructs from the field into a single cohesive framework and advancing the field of addiction phenotyping. Future work will focus on identifying neurobiological correlates and identifying AUD subtypes based on these factors.

Gunawan T, Luk JW, Schwandt ML, Kwako LE, Vinson T, Horneffer Y, George DT, Koob GF, Ramchandani VA, Diazgranados N, Goldman D. Factors underlying the neurofunctional domains of the Addictions Neuroclinical Assessment assessed by a standardized neurocognitive battery. Transl Psychiatry. 2024 Jul 2;14(1):271. doi: 10.1038/s41398-024-02987-9. PMID: 38956031

Designing Clinical Trials to Address Alcohol Use and Alcohol-Associated Liver Disease: An Expert Panel Consensus Statement

Significance: In the absence of Food and Drug Administration-approved treatments for alcohol-associated liver disease (ALD), only alcohol cessation can prevent further liver disease progression and improve long-term patient outcomes. The recognition that ALD is co-morbid with AUD has led the hepatology field to work toward the integration of care and treatment for both disorders. Some specialized clinics offer integrated care from multi-disciplinary teams of hepatologists and addiction medicine providers. Yet, optimizing integrated treatment of ALD and AUD requires additional research and clinical trials. To inform the design and conduct of such trials, national and international hepatologists, addiction specialists, clinical trial specialists,

statisticians, and regulatory experts convened by NIAAA developed recommendations on how to combine research and clinical practices for AUD and ALD in single clinical trials.

Abstract: Most patients with alcohol-associated liver disease (ALD) engage in heavy drinking defined as 4 or more drinks per day (56 g) or 8 (112 g) or more drinks per week for women and 5 or more drinks per day (70 g) or 15 (210 g) or more drinks per week for men. Although abstinence from alcohol after diagnosis of ALD improves life expectancy and reduces the risk of decompensation of liver disease, few studies have evaluated whether treatment of alcohol use disorders will reduce progression of liver disease and improve liver-related outcomes. In November 2021, the National Institute of Alcohol Abuse and Alcoholism commissioned a task force that included hepatologists, addiction medicine specialists, statisticians, clinical trialists and members of regulatory agencies to develop recommendations for the design and conduct of clinical trials to evaluate the effect of alcohol use, particularly treatment to reduce or eliminate alcohol use in patients with ALD. The task force conducted extensive reviews of relevant literature on alcohol use disorders and ALD. Findings were presented at one in-person meeting and discussed over the next 16 months to develop the final recommendations. As few clinical trials directly address this topic, the 28 recommendations approved by all members of the task force represent a consensus of expert opinions.

Lee BP, Witkiewitz K, Mellinger J, Anania FA, Bataller R, Cotter TG, Curtis B, Dasarathy S, DeMartini KS, Diamond I, Diazgranados N, DiMartini AF, Falk DE, Fernandez AC, German MN, Kamath PS, Kidwell KM, Leggio L, Litten R, Louvet A, Lucey MR, McCaul ME, Sanyal AJ, Singal AK, Sussman NL, Terrault NA, Thursz MR, Verna EC, Radaeva S, Nagy LE, Mitchell MC. Designing clinical trials to address alcohol use and alcohol-associated liver disease: an expert panel Consensus Statement. Nat Rev Gastroenterol Hepatol. 2024 Jun 7. doi: 10.1038/s41575-024-00936-x. PMID: 38849555

Reduction of APOE Accounts for Neurobehavioral Deficits in Fetal Alcohol Spectrum Disorders

Significance statement: Findings from this study suggest that controlling levels of a gene that encodes apolipoprotein E (APOE) may be a potential treatment for neurobehavioral deficits in fetal alcohol spectrum disorders (FASD). The investigators identified an epigenetic mechanism that drives the reduction in brain APOE in a mouse model of prenatal alcohol exposure (PAE). Postnatal administration of an APOE receptor agonist rescued both learning deficits and anxiety in PAE mice. Furthermore, a functional polymorphism in the *APOE* enhancer was identified as a genetic risk factor that augments the effects of PAE on cognitive performance. This reduction in APOE levels was identified in the plasma of children who had PAE and correlated with lower cognitive performance. These data suggest that APOE replenishment with an agonist may serve as a potential therapy for patients with FASD. More research is needed to support clinical translatability.

Abstract: A hallmark of fetal alcohol spectrum disorders (FASD) is neurobehavioral deficits that still do not have effective treatment. Here, we present that reduction of Apolipoprotein E (APOE) is critically involved in neurobehavioral deficits in FASD. We show that prenatal alcohol exposure (PAE) changes chromatin accessibility of Apoe locus and causes reduction of APOE levels in both the brain and peripheral blood in postnatal mice. Of note, postnatal administration of an APOE

receptor agonist (APOE-RA) mitigates motor learning deficits and anxiety in those mice. Several molecular and electrophysiological properties essential for learning, which are altered by PAE, are restored by APOE-RA. Our human genome-wide association study further reveals that the interaction of PAE and a single nucleotide polymorphism in the APOE enhancer which chromatin is closed by PAE in mice is associated with lower scores in the delayed matching-to-sample task in children. APOE in the plasma is also reduced in PAE children, and the reduced level is associated with their lower cognitive performance. These findings suggest that controlling the APOE level can serve as an effective treatment for neurobehavioral deficits in FASD.

Hwang HM, Yamashita S, Matsumoto Y, Ito M, Edwards A, Sasaki J, Dutta DJ, Mohammad S, Yamashita C, Wetherill L, Schwantes-An TH, Abreu M, Mahnke AH, Mattson SN, Foroud T, Miranda RC, Chambers C, Torii M, Hashimoto-Torii K. Reduction of APOE accounts for neurobehavioral deficits in fetal alcohol spectrum disorders. Mol Psychiatry. 2024 May 11. doi: 10.1038/s41380-024-02586-6. PMID: 38734844.

Negative Affect, Harassment and Problematic Alcohol Use in Young Adults

Significance: This study looked at the role of negative affect (emotions such as anxiety and sadness) in the relationship between harassment and alcohol misuse. Following harassment experiences, college students reported more alcohol-related problems and increased negative affect. Analysis suggested that negative affect may be a mediating mechanism between the harassment experience and subsequent alcohol problems. Thus, understanding how individuals deal with their negative affect may help to design interventions to reduce alcohol-related problems among college students.

Abstract: *Background:* While research suggests that both negative affect and alcohol use are impacted by exposure to harassment (i.e., sexual harassment, generalized harassment or bullying), less is known about the effect of harassment on negative affect subsequently leading to alcohol consumption, particularly in young adults. We examined the mediating role of negative affect on the relationships between sexual and generalized harassment at school and alcohol misuse. *Methods:* Participants were 2899 incoming freshmen in fall of 2011 who completed a Web-based survey assessing demographics (T0), sexual and generalized harassment at school (T0-T2), negative affect (T3), and problems associated with drinking, binge drinking, and drinking to intoxication (T0, T4, T5). Separate hybrid path models were fitted in Mplus v.8.8 for generalized harassment and sexual harassment and each outcome. *Results:* Mediation analyses showed a small but significant indirect effect for the sexual harassment model (beta = 0.05, S.E. = 0.01, $p < 0.001$) and generalized harassment (beta = 0.03, S.E. = 0.01, $p < 0.01$), indicating that negative affect partially mediated the associations between harassment early in students' college experience and later problems associated with drinking. No significant indirect effects were found for the binge drinking or intoxication models. *Conclusions:* High levels of negative affect associated with harassment may contribute to longer term impact on problematic use of alcohol in young adults, providing evidence that the effects of harassment on drinking may partly stem from harassment's lingering effects on negative affective pathways.

Hallihan H, Ghalyoun H, Moilanen KL, Lee S, Rospenda K. Negative Affect, Harassment and Problematic Alcohol Use in Young Adults. Subst Use Misuse. 2024;59(10):1556-1564. doi: 10.1080/10826084.2024.2360109. Epub 2024 May 29. PMID: 38812117.

Relationships of State Alcohol Policy Environments with Homicides and Suicides

Significance: Alcohol use is involved in a large proportion of homicides and suicides each year in the U.S. To understand how alcohol policies influence violence, this study used a composite measure of state-level alcohol policies (Alcohol Policy Scale) and data on deaths from the National Vital Statistics System in a sample including data from all 50 states. Results indicate that a 1 standard deviation change in the Alcohol Policy Scale was associated with a 6% decline in homicide rates both overall and for firearm homicides specifically. There was no clear association of alcohol policy with suicides. The model predicts that a nationwide increase in alcohol restrictions equivalent to a shift from the 25th to 75th percentile of the scale's distribution would result in almost 1,200 fewer homicides annually. Alcohol policies may provide a promising approach to homicides in the U.S. More research is needed to identify specific policies that are most effective and the mechanisms through which policies affect homicide rates.

Abstract: *Introduction***:** Alcohol use is involved in a large proportion of homicides and suicides each year in the U.S., but there is limited evidence on how policies targeting alcohol influence violence in the U.S. context. Extant studies generally focus on individual policies in isolation of each other. This study examines the impacts of changes in states' alcohol policy restrictions on overall homicide and suicide rates and firearm-related homicide and suicide rates using a holistic measure of states' alcohol policy environments. *Methods***:** Using a composite measure of state-level alcohol policies (Alcohol Policy Scale) and data from the National Vital Statistics System from 2002 to 2018, this study applied a Bayesian time series model to estimate the impacts of alcohol policy changes on overall and firearm-involved homicide and suicide rates. The analysis was performed in 2023 and 2024. *Results***:** A 1 SD change in the Alcohol Policy Scale was associated with a 6% decline in homicide rates both overall (incident rate ratio=0.94; 95% credible interval = 0.89, 1.00) and for firearm homicides specifically (incident rate ratio=0.94, 95% CI=0.88, 1.01). There was no clear association of alcohol policy with suicides. The model predicts that a nationwide increase in alcohol restrictions equivalent to a shift from the 25th to 75th percentile of the scale's distribution would result in almost 1,200 fewer homicides annually. *Conclusions***:** Increases in the restrictiveness of state-level alcohol policies are associated with reductions in homicides. More restrictive alcohol policy environments may offer an opportunity to reduce homicides.

Murphy JP, Smart R, Schell TL, Nicosia N, Naimi TS. Relationships of State Alcohol Policy Environments With Homicides and Suicides. Am J Prev Med. 2024 Aug;67(2):193-200. doi: 10.1016/j.amepre.2024.04.002. Epub 2024 Apr 10. PMID: 38604458.

NIAAA Communications and Public Liaison Activities

News Media

Dr. Koob and other NIAAA scientists completed 50 media interviews from April 2024 through July 2024 with media outlets such as CNN, the New York Times, Medscape, Radio Bilingüe, and National Geographic.

NIAAA posted news stories and NIAAA Director's blogs including NIAAA Releases Strategic Plan for Fiscal Years 2024-2028, Play it safe this summer and be mindful of alcohol's effects on the body, NIAAA Expands Social Media Presence to LinkedIn, and In Memoriam: Dale Hereld, MD, PhD.

Major Activities, Partnerships, Events, and Products

- NIAAA's Alcohol and Your Brain Virtual Reality (VR) experience received the 2024 Achievement in Audio Description – Public Sector Award from the American Council of the Blind's Audio Description Project. This award celebrates outstanding contributions to the quality, availability, and understanding of audio description. The video version that provides audio descriptions for users with low or no vision and captions for viewers who are hard of hearing is available on YouTube.
- NIAAA College Working Group – Presentations highlighting the College Alcohol Intervention Matrix (*CollegeAIM)* are being planned.
- American Society of Addiction Medicine Podcast – Dr. Koob recorded a segment for Alcohol Awareness Month.
- Research Society on Alcohol – The annual conference included signage promoting NIAAA products. Also, the RSA National Advocacy and Public Education Committee highlighted resources available on NIAAA's website, specifically information and tools relevant to adolescents and young adults.
- University of Michigan – Communication and Public Liaison Branch worked with Dr. Megan Martz to share NIAAA resources in a talk to the Addiction Center, Department of Psychiatry, titled, "NIDA and NIAAA Resources for Practitioners, Patients, and the Public."

Top NIAAA Educational Resources

From April to July 2024:

- Top print publications: Rethinking Drinking and Treatment for Alcohol Problems;
- Top online publications: Understanding the Dangers of Alcohol Overdose and Understanding Alcohol Use Disorder
- Top webpages: Alcohol's Effects on the Body and Drinking Levels and Patterns Defined.

- New and updated resources include Treatment for Alcohol Problems: Finding and Getting Help, Strategic Plan for Fiscal Years 2024-2028, and Multilingual Health Information page.

Social Media Highlights

- During Alcohol Awareness Month, NIAAA posted a new video to illustrate that alcohol impacts organs and systems throughout the body.
- For Alcohol Awareness Month, social media efforts generated almost 2 million impressions and 123,000 engagements, including 40,000 complete plays through video content. For example, a post about the dangers of alcohol and swimming generated 56,000 impressions. A post to foster interest in participating in clinical trials generated 310,000 impressions and 1,800 clicks to the clinical trial webpages.

Notable Pickup of NIAAA Content

The Department of Health and Human Services (HHS), NIH, NIH Office of Research on Women's Health, Medline Plus, USA.gov, Centers for Disease Control and Prevention (CDC), Research Society on Alcohol (RSA), Community Anti-Drug Coalitions of America (CADCA), American Academy of Addiction Psychiatry, Michigan Medicine, and others shared NIAAA resources. Examples include:

- The HHS Office of Disease Prevention and Health Promotion X, Health.gov, posted about Alcohol and Your Brain VR experience.
- Research Society on Alcohol featured the NIAAA Strategic Plan in its Weekly E-news email.
- NIH Office of Women's Health reposted an X message about NIAAA Facts About Teen Drinking.
- NIH Newsletter (April) highlighted NIAAA Facts About Teen Drinking and (June) featured Dr. Koob's summer blog and NIAA's web resource about alcohol's effects on the body.
- CDC's Division of Adolescent and School Health X reposted a NIAAA message about alcohol and the adolescent brain.
- NIH News in Health highlighted NIAAA Facts About Teen Drinking.
- CADCA's Coalitions Online highlighted Short Takes with NIAAA: What are the Dangers of Underage Drinking, NIAAA's alcohol's effects on the body, and Strategic Plan.

- The NIH Record featured NIAAA's 2024 Achievement in Audio Description – Public Sector Award from the American Council of the Blind's Audio Description Project for the VR experience.
- HHS X posted NIAAA's spring and summer messages about alcohol and cutting back on drinking.

- NIH X and Medline Plus X highlighted NIAAA's messages about alcohol and swimming. This messaging was also highlighted on the homepage of the NIH website.
- USA.gov in Espanol X translated and reposted a NIAAA summer safety message.
- American Academy of Addiction Psychiatry highlighted Short Takes at NIAAA: What Should Older Adults Know About Alcohol?.