National Institute on Alcohol Abuse and Alcoholism

NIAAA Director's Report on Institute Activities to the 159th Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

Thursday, February 10, 2022
Virtual Meeting

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IN MEMORIAM

Richard Saitz, MD, MPH passed away on January 15, 2022. Dr. Saitz made enormous contributions to alcohol research in the domains of prevention and treatment. He was a driving force in developing screening and brief interventions for alcohol and other substance misuse, integrating addiction medicine in routine health care, improving the quality of care in general health settings, ensuring that approaches to address alcohol and other substance misuse are evidence-based, and reducing stigma associated with substance use disorder, particularly through the use of non-stigmatizing language. Dr. Saitz's work transformed the treatment of alcohol withdrawal syndrome and provided support for the treatment of substance use disorders as chronic medical conditions. He served in many leadership roles including directing Boston Medical Center's Clinical Addiction Research and Education (CARE) Unit for over a decade, serving as Chair and Professor of Community Health Sciences at Boston University (BU) School of Public Health, Professor of Medicine at BU School of Medicine, former president of the Association for Multidisciplinary Education and Research in Substance use and Addiction (AMERSA), and editor for many scientific journals. Dr. Saitz was the current editor of the *Journal of Addiction Medicine*. He received many honors and awards during his illustrious career, including AMERSA's W. Anderson Spickard, Jr. Excellence in Mentorship Award and David C. Lewis, MD Service Award; the R. Brinkley Smithers Distinguished Scientist Award, Educator of the Year Award, and James H. Tharp Award from the American Society of Addiction Medicine; and the Research Society on Alcoholism Distinguished Researcher Award. Dr. Saitz was an outstanding, highly innovative researcher, dedicated physician, a beloved mentor, and highly respected colleague.

John J Spitzer, MD passed away on January 20, 2022. Dr. Spitzer was a native of Hungary and a survivor of the Holocaust. Dr. Spitzer immigrated to Nova Scotia where he accepted a position at Dalhousie University Medical School. He later assumed a position at Hahnemann Medical School in Philadelphia, PA from 1961-1973. In 1973, Dr. Spitzer became head of the Department of Physiology at the Louisiana State University Health Sciences Center (LSUHSC), New Orleans, LA, that he led until his retirement in 2001. He strengthened and expanded the department with a focus on collaborative and interdisciplinary research and training. He also maintained continuous NIH support, including two training grants, RO1 awards, a program project grant, and an Alcohol Research Center award. Dr. Spitzer was honored with the prestigious Boyd Professorship, the highest professorial rank awarded by the LSU System, and named as a Richard C. Ashman Professor also by LSU. Dr. Spitzer was a member of many scientific societies including the Research Society on Alcoholism and the Shock Society of which he served as a founding member and President. Dr. Spitzer leaves behind a rich scientific legacy that includes the LSUHSC Comprehensive Alcohol Research Center and the LSUHSC Alcohol and Drug Abuse Center of Excellence that he co-established with Dr. Joseph Moerschbaecher. He will be remembered for his resilience, dedication to mentorship, and commitment to advancing interdisciplinary research.

NIAAA BUDGET

Fiscal Year (FY) 2021

NIAAA closed FY 2021 on September 30. The Institute's final appropriation for FY 2021 was $554.9 million, an $8.2 million or 1.8 percent increase over the FY 2020 budget. The NIAAA appropriation included $6.7 million for the NIH Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative. Below is a summary of key funding actions within this appropriation:

- NIAAA awarded 720 research project grants (RPGs), including 143 competing awards, which corresponds to a success rate of 18.8 percent.
- NIAAA funded 21 research centers at $33.1 million.
- NIAAA funded 183 other research grants at $47.5 million, including career awards, one cooperative clinical agreement, and several resource and conference grant awards.
- NIAAA supported 331 full-time training positions at $16.3 million.
- NIAAA funding for the research and development (R&D) contract portfolio was $33.1 million.
- NIAAA support for intramural research totaled $57.7 million.

FY 2022

NIAAA is currently operating under H.R. 6119, a continuing resolution (CR), until February 18, 2022. Following the NIH policy under the CR, all grants will be funded at 90 percent. This is consistent with the NIH practice during the CRs of FY 2006 to FY 2021. Upward adjustments to awarded levels will be considered after FY 2022 appropriations are enacted, but NIH expects its Institutes and Centers to monitor their expenditures carefully during this period. All legislative mandates that were in effect in FY 2021 remain in effect under the CR.

FY 2023

The preparation of the FY 2023 President's Budget is underway as of January 2022.

HONORS AND AWARDS

Dr. Robert Freeman received a National Institute of Mental Health (NIMH) Director's Award in November 2021 for efforts in planning and conducting a series of research roundtables and a synthesis workshop to inform a prioritized research agenda on risk, resilience, and trajectories in preteen suicide.

Dr. George F. Koob and **Dr. Pal Pacher** were included among the "Highly Cited Researchers 2021," a list produced by the Institute for Scientific Information that reflects highly cited papers during last decade.

Dr. Lorenzo Leggio and **Dr. Falk Lohoff** were recognized as Fellows of the American College of Neuropsychopharmacology in December 2021.

The following NIAAA staff members received the prestigious NIH Director's Award in November 2021:

Dr. Veronica Alvarez as a member of the Distinguished Scholars Program Developers Team.

Dr. Abraham Bautista for efforts as a member of the Katz Early Stage Investigator Award Committee.

Dr. Changhai Cui for extraordinary performance in initiating and managing a critically important project in response to the unanticipated challenge of the COVID-19 pandemic.

Dr. Robert Freeman, Dr. Wenxing Zha, **Judy Fox**, **Dr. Mariela Shirley**, **Dr. Anna Ghambaryan**, and **Dr. Dominique Lorang Leins** for contributions as members of the Rapid Acceleration of Diagnostics Underserved Populations (RADx-UP) Working Group.

Yvonne Horneffer for contributions to the pandemic-related Car Line Team.

Dr. Paule Joseph for contributions to the NIH COVID-19 Call Center and for outstanding accomplishments as a member of NIH's UNITE Initiative.

Dr. Laura Kwako for contributions as a member of the Trans-NIH COVID-19 Mental Health Response Team.

Erin Manor for efforts as a member of the Presidential Transition Preparation Team.

Dr. Philippe Marmillot for efforts as a member of the Stepping Up to Enable COVID Research Team.

Dr. John Matochik for efforts as a member of the NIH Blueprint Neuroimaging Workshop Planning Committee.

Dr. Jenica Patterson for efforts as a member of the Rapid Acceleration of Diagnostics Tech and Advanced Technology Platforms (RADx Tech & ATP) Team.

Dr. Patricia Powell and **Dr. Changhai Cui** for contributions as members of the Rapid Acceleration of Diagnostics Radical (RADx-rad) Working Group.

Joan Romaine for outstanding accomplishments as a member of NIH's UNITE Initiative.

Dr. Bridget Williams-Simmons for contributions as a member of the NIH-Wide Strategic Plan Working Group and as a member of the Trans-NIH Strategic Plan for COVID-19 Research Team.

Cassie Williams for outstanding accomplishments as a member of NIH's UNITE Initiative.

STAFF TRANSITIONS

New Staff

Candice England joined the NIAAA Office of the Director as Executive Secretariat Liaison. In this role, Candice provides administrative support and manages all controlled correspondence for NIAAA. Previously, Candice worked with the NIH Events Management office and the Office of General Counsel providing administrative support and customer service, as well as managing controlled correspondence.

Drennan Lindsay joined the NIAAA Office of the Director as Executive Assistant to the Director, NIAAA. In this role, Drennan coordinates, schedules, and serves as a liaison for NIAAA leadership. Before coming to NIAAA, Drennan served as a senior meeting manager planning large-scale meetings and providing project management, budget administration, contract negotiation, and logistical support.

Dr. Muhammad Arif joined NIAAA as a Postdoctoral Visiting Fellow with a joint appointment in the Laboratory of Cardiovascular Physiology and Tissue Injury led by Dr. Pal Pacher and the Section on Fibrotic Disorders led by Dr. Resat Cinar. Dr. Arif will work on systems biology of inflammatory and fibrotic diseases, including alcohol-induced tissue injury.

Dr. Szabolcs Dvoracsko joined NIAAA as an intramural Postdoctoral Visiting Fellow with a joint appointment in the Section on Medicinal Chemistry led by Dr. Malliga Iyer and the Section on Fibrotic Disorders led by Dr. Resat Cinar. Dr. Dvoracsko's work will focus on the pharmacological characterization of novel synthetic molecules targeting cannabinoid receptors.

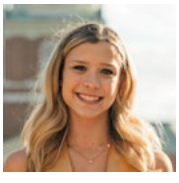
New NIAAA Post-Baccalaureate Intramural Research Training Award (IRTA) Fellows:

Madeline Behee joined NIAAA as a Post-Baccalaureate IRTA Fellow in the Section on Fibrotic Disorders. Madeline's training will explore the pathological mechanisms in alcohol-induced lung injury and pulmonary fibrosis.

Zev Jarret joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory for Integrative Neuroscience led by Dr. David Lovinger. Zev will contribute to the ongoing investigation of brain glia-neuron regulation of alcohol-induced behaviors.

Rodrigo Sandon Veliz joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory of Behavioral and Genomic Neuroscience led by Dr. Andrew Holmes, and will train in the behavioral and genetic analysis of cognition in mice, as well as the effects of alcohol, in various strains of mutant and inbred mice.

Victoria Offenberg joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory of Behavioral and Genomic Neuroscience and will train in the behavioral and genetic analysis of fear in mice as well as the effects of alcohol in various strains of mutant and inbred mice.

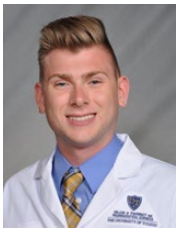


Nina Westcott joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory for Integrative Neuroscience and will conduct research to understand the role of sleep-related neurocircuitry in goal-directed behaviors.

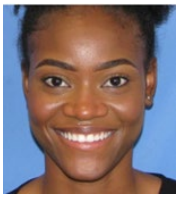
Eli Winkler joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory of Neurogenetics led by Dr. David Goldman and will focus on state-of-the-art techniques including iPSC, CRISPR screening, and functional assays.

Jinpyo Seo joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory of Neuroimaging led by Dr. Nora Volkow and will focus on *in vivo* imaging in the treatment of opioid overdose and addiction using radiotracers.

Carlos Melendez has completed the NIH Academy Program on Health Disparities and transitioned to the Post-Baccalaureate IRTA program in the Laboratory on Human Psychopharmacology led by Dr. Vijay Ramchandani. Carlos's work has focused on research assessments with participants in NIAAA clinical studies, as well as analysis of data on projects examining the impact of early life adversity on alcohol and stress-related outcomes.



Logan Johnson joined NIAAA as a Post-Baccalaureate IRTA in the Section on Medicinal Chemistry led by Dr. Malliga Iyer and will focus on the design and synthesis of novel probes and drug-like molecules for treatment of alcohol-associated disorders.



Josephine Nimely joined NIAAA as a Post-Baccalaureate IRTA in the Section on Medicinal Chemistry and will be involved in projects related to computational chemistry and biological investigations of novel probes and drug-like molecules for treatment of alcohol-associated disorders.

Ana Oliverio joined NIAAA as a Post-Baccalaureate IRTA in the Laboratory of Physiologic Studies led by Dr. George Kunos and will explore the role of CB1 receptors in nodose ganglion sensory neurons in mouse models of voluntary alcohol intake, and contribute to the development of a transgenic mouse line expressing CB1 receptors in adipocytes.

Departing Staff

Deborah Adams retired after 30 years of service with NIAAA as an Administrative Officer focusing on procurement. Deborah looks forward to traveling and spending time with family.

Jamie Greuber left the NIAAA Office of the Director to join the NIH Center for Scientific Review as Executive Assistant to the Director.

James Loewke retired after 23 years of service with NIAAA. Among his many achievements were contributing to the development of robotic methods that enabled quantitation of fatty acid and lipid compositions (the data were used in analyses of large epidemiological cohorts) and the development of methods for analysis of fatty acids in very small quantities of blood.

RECENTLY ISSUED FUNDING OPPORTUNITIES

Funding Opportunity Announcements (FOAs) Issued by NIAAA

Collaborative Partnership between Research Centers in Minority Institutions (RCMI) and Alcohol Research Centers (U54 – Clinical Trial Optional): This FOA invites U54 applications for the planning and implementation of collaborative partnerships between Research Centers in Minority Institutions (RCMI) and institutions with extensive alcohol research programs, including NIAAA-funded alcohol research centers and consortia (ARC). RFA-AA-21-015 (Scientific contacts: Dr. Hemin Chin and Dr. Elizabeth Powell)

Investigational New Drug (IND)-enabling and Early-Stage Development of Medications to Treat Alcohol Use Disorder and Alcohol-Associated Organ Damage (U43/U44 – Clinical Trial Optional; UT1/UT2 – Clinical Trial Optional): The purpose of this FOA is to provide support to small business concerns (SBC) for the optimization, development, and translation of pharmaceutical research discoveries into new treatments for disorders that fall under the mission of NIAAA. The goal is to advance small molecules, natural products or biologics for alcohol use disorder and alcohol-associated organ damage through the drug development pipeline towards FDA approval and ultimately, commercialization. PAR-22-102; PAR-22-103 (Scientific contacts: Dr. Jenica Patterson and Dr. Svetlana Radaeva)

Notices Issued by NIAAA

Notice of Special Interest (NOSI): Epidemiology and Prevention of Alcohol Misuse in Understudied Young Adult Populations; Military, Workforce, and Community College: The purpose of this solicitation is to balance the NIAAA research portfolio by supporting research on alcohol misuse among persons ages 18 to 29 who are not enrolled in four-year colleges or universities. These persons are commonly in the military, workforce, or community college populations, which are understudied relative to their age peers in four-year colleges. Research on epidemiology, prevention, and screening centered on these understudied populations are all encouraged. NOT-AA-22-001 (Scientific contact: Dr. Bradley Kerridge)

Notice of Special Interest: Administrative Supplements and Urgent Competitive Revisions on Coronavirus Disease 2019 (COVID-19) within the Mission of NIAAA: This NOSI invites administrative supplements and competitive revisions to existing grants and cooperative agreements that advance understanding of critical interactions between alcohol, SARS-CoV-2, and COVID-19. A principal area of focus is research that can improve public health in the near term by informing responses to the current COVID-19 pandemic and its consequences. NOT-AA-22-002 (Scientific contact: Dr. Kathy Jung)

Notice of NIAAA Data-Sharing Guidance for Human Subjects Grants Research Funded by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) [3rd Revision]: The purpose of this notice is to

inform prospective applicants of a policy whereby NIAAA expects investigators and their institutions to provide plans for submitting grant-related human subjects data to a NIAAA-sponsored data repository, the NIAAA Data Archive ($NIAAA_{DA}$). NOT-AA-22-003 (Scientific contact: Dr. Dan Falk)

Request for Information (RFI): Unhealthy Alcohol Use in Active Duty Military: The Military Operational Medicine Research Program (MOMRP), as part of the U.S. Army Medical Research and Development Command (USAMRDC), and NIAAA are requesting information from the broad community of alcohol researchers, clinicians, individual Service Members, and advocates to help identify the most important research questions that may help prioritize future alcohol research investments. The MOMRP and the NIAAA missions and strategic plans provide the current research focus areas for the respective organizations. NOT-AA-21-042 (Scientific contacts: Dr. Jenica Patterson, NIAAA, and Dr. Sarah Maggio, MOMRP)

NIH-Wide FOAs with NIAAA Participation

Research Enhancement Award Program (REAP) for Health Professional Schools and Graduate Schools (R15 – Clinical Trial Required) PAR-21-357

HEAL Initiative: Discovery and Validation of Novel Targets for Safe and Effective Pain Treatment (R01 – Clinical Trial Not Allowed) RFA-NS-22-034

Emergency Awards: HEAL Initiative: Translational Science Career Enhancement Awards for Early and Mid-career Investigators (K18 – Clinical Trials Not Allowed) PAR-22-057

HEAL Initiative: Pilot and Feasibility Trials to Improve Prevention and Treatment Service Delivery for Polysubstance Use (R34 – Clinical Trial Optional) RFA-DA-22-048

HEAL Initiative: Research Networks for the Study of Recovery Support Services for Persons Treated with Medications for Opioid Use Disorder (R24 – Clinical Trial Optional) RFA-DA-22-043

HEAL Initiative: Planning Grants for Efficacy or Effectiveness Trials of Recovery Support Services for Individuals Treated with Medications for Opioid Use Disorder (R34 – Clinical Trial Optional) RFA-DA-22-034

BRAIN Initiative-Related Research Education: Short Courses (R25 – Clinical Trial Not Allowed) RFA-EY-21-003

BRAIN Initiative: Research Resource Grants for Technology Integration and Dissemination (U24 – Clinical Trial Not Allowed) RFA-NS-22-011

Drug Discovery For Nervous System Disorders (R01 – Clinical Trials Not Allowed) PAR-22-031; (R21 – Clinical Trials Not Allowed) PAR-22-032

Opportunities for Collaborative Research at the NIH Clinical Center (U01 – Clinical Trial Optional) PAR-21-343

Pre-application: Opportunities for Collaborative Research at the NIH Clinical Center (X02 – Clinical Trial Optional) PAR-21-342

Administrative Supplements to Promote Diversity in Small Businesses-SBIR/STTR (Admin Supp – Clinical Trial Not Allowed) PA-21-345

Innovation Corps (I-Corps™) at NIH Program for NIH and CDC Translational Research (Admin Supp – Clinical Trial Not Allowed) PAR-22-073

Research on Biopsychosocial Factors of Social Connectedness and Isolation on Health, Wellbeing, Illness, and Recovery (R01 – Clinical Trial Required) PAR-21-352; (R01 – Clinical Trials Not Allowed) PAR-21-350; (R01 – Basic Experimental Studies with Humans Required) PAR-21-349

Chronic, Non-Communicable Diseases and Disorders Across the Lifespan: Fogarty International Research Training Award (NCD-LIFESPAN) (D43 – Clinical Trial Optional) PAR-21-230

NIH-Wide NOSIs with NIAAA Participation

BRAIN Initiative: Translation of Groundbreaking Technologies from Early-stage Development through Early Clinical Study via Blueprint MedTech NOT-NS-22-052

Administrative Supplement for Research and Capacity Building Efforts Related to Bioethical Issues (Admin Supp – Clinical Trial Optional) NOT-OD-22-026

Availability of Administrative Supplements for Research on Pathobiological Mechanisms of Post-Acute Sequelae of SARS-CoV-2 Infection NOT-OD-22-038

Administrative Supplements for Research on Sex and/or Gender Influences (Admin Supp – Clinical Trial Optional) NOT-OD-22-030

Administrative Supplements for Embedded Ethicists into BRAIN Initiative Supported Research NOT-MH-22-040

NIAAA Director's Activities

NIAAA Director **George F. Koob, Ph.D.,** gave the following virtual presentations between August 1 and December 31, 2021:

- "Trends and Increases in Alcohol Consumption and Sales as Impacted by the COVID-19 Pandemic" at the Substance Abuse and Mental Health Services Administration (SAMHSA) National Advisory Council on August 30, 2021
- "Neurobiology of Addiction: Hyperkatifeia, Deaths of Despair and Covid-19" for the California Society of Addiction Medicine (CSAM) 2021 Review Course in Addiction Medicine on September 1, 2021
- "The Negative Emotional Side of Addiction: The Gain in the Brain is in the Pain" for the Division of Internal Medicine at UT MD Anderson Cancer Center Research Grand Rounds on September 15, 2021
- "NIAAA Updates" for the American Psychiatric Association's Council on Addiction Psychiatry on September 30, 2021
- "Conceptual Framework of Alcohol Addiction" for the Fall e-School of Alcohol Addiction Research of the Réseau National de Recherche en Alcoologie (REUNIRA) on October 28, 2021

- "Hyperkatifeia, Negative Reinforcement and the Negative Emotional Side of Addiction" for the Eighth Annual Symposium of the Stanford University Wu Tsai Neurosciences Institute on October 21, 2021
- "Neurobiology of Addiction, Pain and Hyperkatifeia: The Negative Emotional Side of Addiction" for the Canadian Society of Addiction Medicine Annual Conference on October 23, 2021
- "The Neurocircuitry of Alcohol Use Disorder" for Vereniging voor Verslavingsgeneeskunde Nederland (VVGN) on October 25, 2021
- "Telehealth Now, During the Pandemic, and Beyond" for the Friends of NIAAA webinar on Telehealth and Digital Therapeutics for Treatment of Alcohol Use Disorders during the COVID-19 Pandemic and Beyond on November 3, 2021
- "Alcohol Use Disorder as a Coping Response: Hyperkatifeia, Deaths of Despair and COVID-19" for the Addiction Policy Forum on November 4, 2021
- "Updates from Key Leaders in NIH" for the American Association for the Study of Liver Diseases (AASLD) NIH-focused session on November 13, 2021
- "Hyperkatifeia, Negative Reinforcement and the Negative Emotional Side of Addiction" for Ground Rounds, Department of Psychiatry, University of South Carolina-Greenville on November 17, 2021
- "Alcohol Use Disorder: The Gain in the Brain is in the Pain" for the International Society of Addiction Medicine on November 20, 2021
- "The Neurocircuitry of Addiction: A Heuristic Framework" for the NeuroSchool Aix Marseille Universite on November 30, 2021
- NIAAA Update: Institute Directors Briefing for the American College of Neuropsychopharmacology on December 5, 2021
- "Alcohol Misuse: Scope of the Problem, Effects on Health, Closing the Treatment Gap" for the U.S. Senate Committee on Health, Education, Labor and Pensions on December 13, 2021
- "Words Matter: New and Better Ways to Discuss Alcohol Issues" for the Association of Health Care Journalists on December 15, 2021
- "Alcohol and Drug Addiction: Hyperkatifeia, Negative Reinforcement and Loss of Control" for the 2021 Japanese Alcohol, Nicotine & Drug Addiction Conference on December 18, 2021

NOTABLE NIAAA STAFF ACTIVITIES

Dr. Tatiana Balachova and **Dr. Deidra Roach,** along with staff from other ICCFASD member agencies, established the ICCFASD Screening and Brief Intervention for Pregnant and Postpartum People (ISBI) Working Group.

Dr. Bill Dunty gave the "NIAAA Update" during the 2021 summit of the National Organization on Fetal Alcohol Syndrome (NOFAS) (now known as FASD United) on September 29, 2021.

Dr. Bill Dunty presented the NIAAA Pediatric Research portfolio to the NIH Pediatric Research Consortium on November 16, 2021.

Dr. Anna Ghambaryan led NIAAA's outreach activities at the NIH Virtual Seminar on Program Funding and Grants Administration on November 1-4, 2021. Other staff who contributed to NIAAA's participation included **Alexis Pelt, Katherine Masterton, Cara Anjos Breeden, Gregory Roa, Judy Fox, Celia Herlihy, Lauren Early, Jeff Thurston, Deb Hendry, Megan Ryan,** as well as **Drs. Laura Manella, Dan Falk, Ivana**

Grakalic, Mariela Shirley, Gary Murray, Luis Espinoza, RV Srinivas, Tatiana Balachova, Elizabeth Powell, Dominique Lorang-Leins, Jenica Patterson, Changhai Cui, Philippe Marmillot, I-Jen Castle, and **Shailesh Kumar**.

Dr. Shailesh Kumar, Dr. Dominique Lorang-Leins, Dr. Ivana Grakalic, and Dr. Mariela Shirley representing NIAAA on the NIH Sleep Research Coordinating Committee, gave a virtual presentation at the Sleep Disorders Research Advisory Board meeting on December 2, 2021.

Dr. Laura Kwako co-moderated a conference discussion forum at a trans-HHS Working Group Conference on Dissemination and Implementation on December 15 and 16, 2021.

Dr. Laura Kwako presented "Telehealth Priorities at NIAAA" for FedTel, a trans-HHS meeting from NIH and HRSA on January 6, 2022.

Dr. John Matochik was the Co-Chair of the NIDA-NIAAA Frontiers in Addiction Mini-Convention held virtually on November 1 and 2, 2021. He was also the Chair for the Early Career Investigator Showcase.

Dr. Andras Orosz co-chaired a scientific session of the NIH Common Fund Cellular Senescence (SenNet) Kick-Off Meeting on November 4, 2021.

Dr. Jenica Patterson co-organized, with staff from NIDA and NIMH, the workshop "Psychedelics as Therapeutics: Gaps, Challenges and Opportunities" on January 12-13, 2022.

Dr. Elizabeth Powell was the Co-Chair for the scientific session on "Brain, Behavior and Environment as a Complex System in SUD/AUD" at the NIDA-NIAAA Frontiers in Addiction Mini-Convention held virtually on November 1 and 2, 2021.

Dr. Patricia Powell and Dr. Tatiana Balachova organized and led the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD) Executive Meeting on November 15, 2021.

Dr. Deidra Roach served as a co-organizer of the NHLBI-sponsored virtual workshop "Building Unifying Systems of Care Addressing Comorbidities in Women and Girls" and served as organizer and moderator of the session "Building the Infrastructure for Integrative Health Care Systems for Women and Girls" on December 16 and 17, 2021.

WHAT'S AHEAD?

The Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD) 2022 Public Meeting will be held virtually on April 1, 2022. The meeting will be organized and led by Dr. Patricia Powell, Chair, and Dr. Tatiana Balachova, ICCFASD Scientific Coordinator and Executive Secretary. Dr. Bill Dunty is the NIAAA representative to the ICCFASD, and Dr. Deidra Roach is the alternate member.

The Gordon Research Conference (GRC), "Alcohol-Induced End Organ Disease," will be held in Ventura, California, April 24–29, 2022. Dr. Andras Orosz will be the discussion leader of the "Cancer Stem Cells and Alcohol-Associated Cancer" session.

Epigenome-Wide Association Study of Alcohol Consumption in N = 8161 Individuals and Relevance to Alcohol Use Disorder Pathophysiology: Identification of the Cystine/Glutamate Transporter SLC7A11 as a Top Target

Significance: Chronic heavy alcohol consumption is strongly associated with alterations in DNA methylation, a process that influences gene transcription. Identification of alcohol-associated methylome variation might provide novel insights into pathophysiology and innovative treatment targets for alcohol use disorder (AUD). Using the largest epigenome-wide association study of alcohol consumption to date (N=8161), investigators identified 2504 methylation sites with the five leading gene targets including SLC7A11, JDP2, GAS5, TRA2B, and SLC43A1. Biological validation and follow-up studies confirmed a substantial role for the cystine/glutamate transporter SLC7A11 in AUD. Given the prominent function of glutamate signaling in brain and liver, the results identify SLC7A11 as a novel target for therapeutic intervention in AUD.

Alcohol misuse is common in many societies worldwide and is associated with extensive morbidity and mortality, often leading to alcohol use disorders (AUD) and alcohol-related end-organ damage. The underlying mechanisms contributing to the development of AUD are largely unknown; however, growing evidence suggests that alcohol consumption is strongly associated with alterations in DNA methylation. Identification of alcohol-associated methylomic variation might provide novel insights into pathophysiology and novel treatment targets for AUD. Here we performed the largest single-cohort epigenome-wide association study (EWAS) of alcohol consumption to date (N = 8161) and cross-validated findings in AUD populations with relevant endophenotypes, as well as alcohol-related animal models. Results showed 2504 CpGs significantly associated with alcohol consumption (Bonferroni p value < 6.8 × 10-8) with the five leading probes located in SLC7A11 (p = 7.75 × 10-108), JDP2 (p = 1.44 × 10-56), GAS5 (p = 2.71 × 10-47), TRA2B (p = 3.54 × 10-42), and SLC43A1 (p = 1.18 × 10-40). Genes annotated to associated CpG sites are implicated in liver and brain function, the cellular response to alcohol and alcohol-associated diseases, including hypertension and Alzheimer's disease. Two-sample Mendelian randomization confirmed the causal relationship of consumption on AUD risk (inverse variance weighted (IVW) p = 5.37 × 10-09). A methylation-based predictor of alcohol consumption was able to discriminate AUD cases in two independent cohorts (p = 6.32 × 10-38 and p = 5.41 × 10-14). The top EWAS probe cg06690548, located in the cystine/glutamate transporter SLC7A11, was replicated in an independent cohort of AUD and control participants (N = 615) and showed strong hypomethylation in AUD (p < 10-17). Decreased CpG methylation at this probe was consistently associated with clinical measures including increased heavy drinking days (p < 10-4), increased liver function enzymes (GGT (p = 1.03 × 10-21), ALT (p = 1.29 × 10-6), and AST (p = 1.97 × 10-8) in individuals with AUD. Postmortem brain analyses documented increased SLC7A11 expression in the frontal cortex of individuals with AUD and animal models showed marked increased expression in liver, suggesting a mechanism by which alcohol leads to hypomethylation-induced overexpression of SLC7A11. Taken together, our EWAS discovery sample and subsequent validation of the top probe in AUD suggest a strong role of abnormal glutamate signaling mediated by methylomic variation in SLC7A11. Our data are intriguing given the prominent role of glutamate signaling in brain and liver and might provide an important target for therapeutic intervention. (Lohoff FW, Clarke TK, Kaminsky ZA, Walker RM, Bermingham ML, Jung J, Morris SW, Rosoff D, Campbell A, Barbu M, Charlet K, Adams M,

Lee J, Howard DM, O'Connell EM, Whalley H, Porteous DJ, McIntosh AM, Evans KL. Epigenome-wide association study of alcohol consumption in N = 8161 individuals and relevance to alcohol use disorder pathophysiology: identification of the cystine/glutamate transporter SLC7A11 as a top target. *Mol Psychiatry*. 2021 Dec 2. doi: 10.1038/s41380-021-01378-6.)

Development and Validation of a Postnatal Risk Score that Identifies Children with Prenatal Alcohol Exposure

Significance: Investigators developed and validated an efficient and easily calculable risk score to identify an individual's risk of having been exposed prenatally to alcohol. Unlike previously published clinical tools for fetal alcohol spectrum disorder (FASD) assessment, the proposed risk score relies on measures that can be easily obtained, comprising physical measures (dysmorphology) as well as parent-reported measures of adaptive functioning and behavior for a total score of 0–5. With preliminary testing, the risk score shows promise in distinguishing alcohol-exposed children from control subjects, while correlating with cognitive outcomes. The risk score could be easily deployed in a clinical setting as an early screening tool for FASD.

Background: This study aimed to develop an efficient and easily calculable risk score that can be used to identify an individual's risk of having been exposed to alcohol prenatally. Methods: Data for this study were collected as part of the Collaborative Initiative on Fetal Alcohol Spectrum Disorders, Phases 2 and 3. Two cohorts (ages 5 to 17 years) completed a comprehensive neurobehavioral battery and a standard dysmorphology exam: a development cohort (DC; n = 325) and a comparative cohort (CC; n = 523). Both cohorts included two groups: those with histories of heavy prenatal alcohol exposure (AE-DC, n = 121; AE-CC, n = 177) and a control group that included subjects with minimal or no prenatal alcohol exposure (CON-DC, n = 204; CON-CC, n = 346). Behavioral assessments and physical exam data were combined using regression techniques to derive a risk score indicating the likelihood of prenatal alcohol exposure. Subjects were then divided into two subgroups: (1) low risk and (2) high risk. Chi-square ($\chi 2$) determined classification accuracy and ROC curves were produced to assess the predictive accuracy. Correlations between risk scores and intelligence quotient and executive function scores were calculated. Results: Subjects were accurately classified in the DC ($\chi 2 = 78.61$, $p < 0.001$) and CC ($\chi 2 = 86.63$, $p < 0.001$). The classification model also performed well in the DC (ROC = 0.835 [SE = 0.024, $p < 0.001$]) and CC (ROC = 0.786 [SE = 0.021, $p < 0.001$]). In the AE-CC and CON-CC, there were modest but significant associations between the risk score and executive function (AE-CC: $r = -0.20$, $p = 0.034$; CON-CC: $r = -0.28$, $p < 0.001$) and intelligence quotient (AE-CC: $r = -0.20$, $p = 0.034$; CON-CC: $r = -0.28$, $p < 0.001$). Conclusion(s): The risk score significantly distinguished alcohol-exposed from control subjects and correlated with important cognitive outcomes. It has significant clinical potential and could be easily deployed in clinical settings. (Bernes GA, Courchesne-Krak NS, Hyland MT, Villodas MT, Coles CD, Kable JA, May PA, Kalberg WO, Sowell ER, Wozniak JR, Jones KL, Riley EP, Mattson SN; CIFASD. Development and validation of a postnatal risk score that identifies children with prenatal alcohol exposure. *Alcohol Clin Exp Res*. 2021 Nov 21. doi: 10.1111/acer.14749.)

Resting Hypoconnectivity of Theoretically Defined Addiction Networks during Early Abstinence Predicts Subsequent Relapse in Alcohol Use Disorder

Significance: The present study investigated resting-state functional connectivity in brain networks related to three addiction domains (incentive salience, negative emotionality, and executive functioning) during early abstinence in predicting relapse in alcohol use disorder (AUD). Compared to those individuals who

remained abstinent, those who relapsed had significantly lower functional connectivity during early abstinence in all three brain networks, which predicted subsequent relapse using both dichotomous and continuous measures of relapse. The brain networks also predicted time to relapse, whereas clinical self-reports were not reliable predictors. The findings highlight the value of functional brain connectivity as a biomarker of vulnerability for relapse and the potential of modulating functional connectivity in addiction networks as a treatment for AUD.

Theoretical models of addiction suggest that alterations in addiction domains including incentive salience, negative emotionality, and executive control lead to relapse in alcohol use disorder (AUD). To determine whether the functional organization of neural networks underlying these domains predict subsequent relapse, we generated theoretically defined addiction networks. We collected resting functional magnetic resonance imaging data from 45 individuals with AUD during early abstinence (number of days abstinent M = 25.40, SD = 16.51) and calculated the degree of resting-state functional connectivity (RSFC) within these networks. Regression analyses determined whether the RSFC strength in domain-defined addiction networks measured during early abstinence predicted subsequent relapse (dichotomous or continuous relapse metrics). RSFC within each addiction network measured during early abstinence was significantly lower in those that relapsed (vs. abstained) and predicted subsequent time to relapse. Lower incentive salience RSFC during early abstinence increased the odds of relapsing. Neither RSFC in a control network nor clinical self-report measures predicted relapse. The association between low incentive salience RSFC and faster relapse highlights the need to design timely interventions that enhance RSFC in AUD individuals at risk of relapsing faster. (Camchong J*, Haynos AF, Hendrickson T, Fiecas MB, Gilmore CS, Mueller BA, Kushner MG, Lim KO. Resting Hypoconnectivity of Theoretically Defined Addiction Networks during Early Abstinence Predicts Subsequent Relapse in Alcohol Use Disorder. *Cereb Cortex*. 2021 Oct 20:bhab374. doi: 10.1093/cercor/bhab374.)

*NIAAA career development award recipient

Quantifying COVID-19's Impact on Telemedicine Utilization

Significance: COVID-19 pandemic-era restrictions regarding in-person care led to widespread adoption of telemedicine-based healthcare. To investigate trends in telemedicine utilization over the course of the pandemic, researchers analyzed data from doxy.me, the largest free telemedicine platform, and the NIH Clinical Center, the largest U.S. clinical research hospital. Analysis revealed that, nationally, use of telemedicine peaked in April 2020 at 291 million minutes, stabilizing at 200-220 million monthly minutes from May to November 2020. State-level data also revealed a correlation between states with early expansion of telemedicine capacity (i.e., New England and Mid-Atlantic states) and greater overall telemedicine expansion during the pandemic. Results paint a picture of how telemedicine has evolved throughout the pandemic.

Background: While telemedicine has been expanding over the past decade, the COVID-19 pandemic era restrictions regarding in-person care have led to unprecedented levels of telemedicine utilization. To the authors' knowledge, no studies to date have quantitatively analyzed both national and regional trends in telemedicine utilization during COVID-19, both of which have key implications for informing health policy. Objective: To investigate how trends in telemedicine utilization changed across the course of the COVID-19 pandemic. Methods: Using data from doxy.me, the largest free telemedicine platform, and the NIH Clinical Center, the largest U.S. clinical research hospital, we assessed changes in total telemedicine minutes, new provider registrations, monthly sessions, and average session length from March-November

2020. We also conducted state-level analysis of how telemedicine expansion differed by region. Results: National telemedicine utilization peaked in April 2020 at 291 million minutes and stabilized at 200-220 million monthly minutes from May to November 2020. Surges were strongest in New England and weakest in the South and West. Greater telemedicine expansion during COVID-19 was geographically associated with lower COVID-19 cases per capita. The nature of telemedicine visits also changed, as the average monthly visits per provider doubled and average visit length decreased by 60%. Conclusions: The COVID-19 pandemic led to an abrupt and subsequently sustained uptick in telemedicine utilization. Regional and institute-level differences in telemedicine utilization should be further investigated to inform policy and procedures for sustaining meaningful telemedicine use in clinical practice. (Vogt EL, Welch BM, Bunnell BE, Barrera JF, Paige SR, Owens M, Coffey P, Diazgranados N, Goldman D. Quantifying COVID-19's Impact on Telemedicine Utilization. *Interact J Med Res*. 2021 Sep 6. doi: 10.2196/29880.)

Integrative Data Analysis of Self-Efficacy in 4 Clinical Trials for Alcohol Use Disorder

Significance: Self-efficacy has been proposed as a key predictor of alcohol treatment outcomes and a potential mechanism of success in achieving abstinence or drinking reductions following alcohol treatment. The present study examined the effect of treatment on self-efficacy across four different treatment studies (Project MATCH; COMBINE; and two studies of telephone continuing care, TEL1 and TEL 2). All active treatments, including cognitive-behavioral treatment, a combined behavioral intervention, medication management, motivation enhancement treatment, telephone continuing care, 12-step facilitation, and relapse prevention, were associated with significant increases in self-efficacy from baseline to posttreatment that were maintained for up to a year. Treatment as usual in community settings, which consisted of weekly group therapy that included addiction counseling and 12-step recovery support, was not associated with significant increases in self-efficacy.

Background: Self-efficacy has been proposed as a key predictor of alcohol treatment outcomes and a potential mechanism of success in achieving abstinence or drinking reductions following alcohol treatment. Integrative data analysis, where data from multiple studies are combined for analyses, can be used to synthesize analyses across multiple alcohol treatment trials by creating a commensurate measure and controlling for differential item functioning (DIF) to determine whether alcohol treatments improve self-efficacy. Method: The current study used moderated nonlinear factor analysis (MNLFA) to examine the effect of treatment on self-efficacy across four different treatment studies (N = 3720; 72.5% male, 68.4% non-Hispanic white). Self-efficacy was measured using the Alcohol Abstinence Self-Efficacy Scale (AASE) in the COMBINE Study (n = 1383) and Project MATCH (n = 1726), and the Drug Taking Confidence Questionnaire (DTCQ) in two studies of Telephone Continuing Care (TEL Study 1: n = 303; TEL Study 2: n = 212). DIF was examined across time, study, treatment condition, marital status, age, and sex. Results: We identified 12 items from the AASE and DTCQ to create a commensurate measure of self-efficacy using MNLFA. All active treatments, including cognitive-behavioral treatment, a combined behavioral intervention, medication management, motivation enhancement treatment, telephone continuing care, twelve-step facilitation, and relapse prevention, were associated with significant increases in self-efficacy from baseline to posttreatment that were maintained for up to a year. Importantly, treatment as usual in community settings, which consisted of weekly group therapy that included addiction counseling and twelve-step recovery support, was not associated with significant increases in self-efficacy. Conclusions: Alcohol self-efficacy increases following treatment and numerous evidence-based treatments are associated with significant increases in self-efficacy, which are maintained over time. Community treatment that focuses solely on addiction counseling and twelve-step support may not promote increases

in self-efficacy. (Kruger ES, Serier KN, Pfund RA, McKay JR, Witkiewitz K. Integrative data analysis of self-efficacy in 4 clinical trials for alcohol use disorder. *Alcohol Clin Exp Res*. 2021 Nov;45(11):2347-2356. doi: 10.1111/acer.14713.)

NIAAA Communications and Public Liaison Activities

Media Interviews:

Dr. Koob and other NIAAA scientists completed 44 interviews from August 1 to December 31, 2021. Noteworthy media outlets included: *JAMA News*, *AARP Bulletin*, Yahoo! News, Medical News Today, *TIME*, *The Chronicle of Higher Education*, *USA Today*, *Financial Times*, *The Scientist*, *The Philadelphia Inquirer*, iHeart Radio, and NBC.

NIAAA News Items:

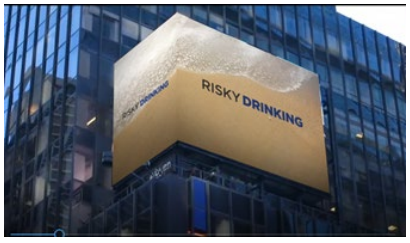
- College students head back to campus in an uncertain time (September 2, 2021)
- September 9 is International Fetal Alcohol Spectrum Disorders Awareness Day (September 3, 2021)
- Embracing Community and Culture to Prevent Underage Drinking (November 10, 2021)
- National Institute on Alcohol Abuse and Alcoholism Launches Video Series (December 14, 2021)

NIAAA Director's Blog Posts:

- December 2021 - Rethinking Your Holiday Drinking
- November 2021 - Embracing Community and Culture to Prevent Underage Drinking. This blog originally appeared on the National Institute on Minority Health and Health Disparities' *NIMHD Insights* webpage. In recognition of Native American Heritage Month, Dr. Koob discussed NIAAA-supported research demonstrating the importance of community-based interventions in preventing underage drinking among American Indian and Alaska Native youth.

Major Events:

- FASD United Twitter Chat for FASD Awareness Month (September 21, 2021)
- American Society of Addiction Medicine (ASAM) National Addiction Treatment Week All-Day Twitter Conversation on Ending Stigma (October 20-21, 2021)
- Association of Health Care Journalists (AHCJ) "Words Matter: Responsible Reporting on Alcohol Use and Misuse" webinar (December 15, 2021)
- NIAAA Summer Safety billboard in Times Square (July, August, and September)



- **New video series: "Short Takes with NIAAA."** This series consists of brief 60-second videos that explain the meaning of commonly used–but often misunderstood–alcohol terms in a way that is easy to understand. The first installment includes videos on alcohol use disorder, blackouts, alcohol overdose in both Spanish and English, and binge drinking. NIAAA promoted the Short Takes via social media, email, the NIAAA website, and television displays at the NIH Clinical Center. In addition to promotion through our non-federal and federal partners, Short Takes will be featured in the salud.NIH.gov newsletter and website in February 2022.

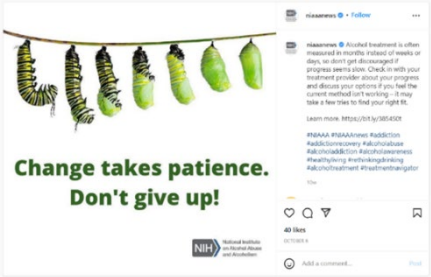
Publications and web activities:

- NIAAA publications elicited about 772,137 website pageviews, 12,204 downloads, and more than 16,000 print copies ordered. The most viewed NIAAA publications were Alcohol Facts and Statistics, the Understanding the Dangers of Alcohol Overdose factsheet, and Treatment for Alcohol Problems: Finding and Getting Help brochure. The most frequently downloaded publication was the Alcohol Use Disorder factsheet. The most ordered NIAAA publications were the English versions of the Treatment for Alcohol Problems: Finding and Getting Help and Harmful Interactions: Mixing Alcohol with Medications booklets.
- New website features include:
  - Evidence-based alcohol interventions for young adults
  - Historical milestones in NIAAA's history
- Major updates were made to the following publications:
  - Alcohol and Your Pregnancy trifold, available in English and Spanish, and version geared to American Indian/Alaska Native populations
  - Rethinking Drinking: Alcohol and Your Health booklet and website, available in English with a Spanish translation forthcoming
- New Translations:
  - Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide (Spanish)
  - Alcohol Use Disorder: A Comparison Between DSM-IV and DSM-5 factsheet (Spanish and 15 other languages commonly used at NIH and/or in the U.S. Census)

Social Media Highlights:

The NIAAA Twitter account (@NIAAAnews) currently has approximately 27,600 followers, an increase of about 2.4 percent since August 2021. The NIAAA Instagram account (@NIAAAnews) now has 2,159 followers, an increase of about 7 percent since August 2021. Facebook (@NIAAAgov), NIAAA's newest social media account, currently has more than 819 followers, growing by over 23% since August.

Top Instagram post



Top Facebook Post