8TH ANNUAL

UNM Brain & Behavioral Health

RESEARCH DAY

Friday, March 31, 2023
9-4 pm
The University of New Mexico,
Domenici Center for Health Sciences Education,
Albuquerque

ABSTRACT BOOK

2023 Event Theme: Substance Use and Brain Health

AGENDA HIGHLIGHTS

9 am Poster Session
70+ posters on current research and community programs from all disciplines in brain & behavioral health

12 pm Keynote Presentation
Blind Drunk: Reporting on New Mexico's Neglected Crisis of Alcohol-Related Deaths

1:00 pm Lunch & Roundtable Discussion
Improving Systems of Care in NM for Substance Use Disorders. *Moderated by Jeremy Lihte, President and Founder of NM Leaders in Recovery*

3:00 pm NM Brain BLAST
TED-style talks focusing on substance use disorders by UNM trainees on their preclinical, clinical, community and health services research

Keynote Speaker
Ted Alcorn, Independent Journalist

Ted Alcorn is a writer raised in New Mexico whose work has appeared in The New York Times, The Atlantic, and The Washington Post Magazine, among other publications.

Welcome

The UNM Brain & Behavioral Health Annual Research Day (formerly, the Neuroscience Day) has been running at UNM since 1985 as an annual event to bring together researchers focused on understanding the nervous system and mechanisms underlying brain health and disorders.

This is the eighth year that Research Day activities have been expanded by the UNM Brain and Behavioral Health Institute (BBHI). The BBHI is being developed as a major priority for the UNM Health Sciences Center. It aims to bring together clinicians, researchers, patients and community members to improve brain and behavioral health of all New Mexicans, across the lifespan. This year we focus on substance use, misuse, and substance use disorders (SUD) as a pressing public health issue affecting our communities.

We are delighted that so many community members and other representatives from advocacy and support groups are able to join us today. One of the main drivers of progress in the previous years has been meaningful, two-way communication between UNM investigators and community stakeholders. We hope that today's activities provide many opportunities for that to continue.

The morning program builds on successes of past research days and emphasizes discussion of ongoing brain & behavioral health research in New Mexico. The poster session includes a broad spectrum of research, from fundamental laboratory work to clinical trials and research in our communities. Community organizations from across the state have been invited to participate in the poster session and poster competition.

We are excited that Ted Alcorn, an independent journalist whose work has appeared in *The New York Times, The Wall Street Journa*l, and *The Atlantic*, will present the keynote presentation on his ongoing investigation of alcohol's impact on the state of New Mexico.

The afternoon session includes a Roundtable Discussion on "Improving Systems of Care in New Mexico for Substance Use Disorder: What are we getting right, what do we need to work on?" The session is moderated by Jeremy Lihte, President and Founder of NM Leaders in Recovery. Immediately following is NM Brain BLAST that features TED-style talks focusing on substance use disorders by UNM trainees and community leaders on their preclinical, clinical, community and health services research.

As you can see from the program, there are a lot of activities going on throughout the day. Please don't hesitate to ask for direction from staff at the registration table.

Thank you!

Sponsors

UNM Brain & Behavioral Health Institute
UNM Cellular and Molecular Basis of Disease (CMBD)
UNM Psychiatry & Behavioral Sciences
UNM Center on Alcohol, Substance use, And Addictions (CASAA)
UNM Neurosciences
UNM Neurology
UNM Center for Memory and Aging
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Event Day - Volunteer Judges

Dr. Amy Gardiner, UNM Cell Biology and Physiology
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Dr. Verlin Joseph, UNM CASAA
Dr. Megan Kirouac, UNM CASAA
Dr. Suzanne Burns, UNM Division of Occupational Therapy
Dr. Afshin Divani, UNM Neurology
Dr. Surojit Paul, UNM Neurology
Dr. Ranjana Poddar, UNM Neurology
Dr. Tyler Kincaid, UNM Division of Community Behavioral Health (CBH)
Dr. Kiran Bhaskar, UNM Brain & Behavioral Health Institute / MGM
Dr. Ludmila Bakhireva, UNM Brain & Behavioral Health Institute / COP

Event Day – Afternoon Session

Ted Alcorn, Independent journalist
Brian Serna, Serna Solutions LLC
Anjali Taneja, Casa de Salud
Jeff Holland, Endorphin Power Company
Jeremy Lihte, NM Leaders in Recovery and Vista Taos Renewal Center
Angie Alley, Central New Mexico Community College
Paul Romo, UNM Psychiatry and Behavioral Sciences
Snehal R Bhatt, UNM Psychiatry and Behavioral Sciences
Donia Hijaz, UNM CASAA
Dylan Richards, UNM CASAA
Alexandria Wiesel, UNM College of Pharmacy SURE Center
Isabella Romano, UNM Molecular Genetics Microbiology
Justine R Zimmerly, UNM Neurosciences

Event Day – General Support

Kenya G Quinonez-Herrera, UNM Center for Memory and Aging
Christopher Wertz, UNM Center for Memory and Aging
Maria Sol Hayes, UNM Center for Memory and Aging
Erika Partridge, UNM Center for Memory and Aging
Sirena Narro, UNM College of Pharmacy

Jasmine Hick, UNM College of Pharmacy
Lidia Enriquez Marquez, UNM College of Pharmacy
Rajani Rai, UNM College of Pharmacy
Margaret Hart, UNM Center for Infectious Disease & Immunology (CIDI)
Luis F Vasquez Porras, UNM Cell Biology and Physiology
Rick Roybal, UNM Neurosciences
Gilbert Cordova, UNM Psychiatry and Behavioral Sciences
Bao V Tran, UNM Psychiatry and Behavioral Sciences
Robin Brinegar, UNM Psychiatry and Behavioral Sciences
Karthikeyan Tangavelou, UNM Molecular Genetics & Microbiology
Kathryn E Sanchez, NM Center for Memory and Aging
UNM Hospital Office of Diversity, Equity & Inclusion

Agenda

9:00 am - 11:30 am Domenici Center	**Poster Session** 70+ posters on current brain & behavioral health research and community programs in New Mexico. *Q&A with the presenting researchers and community organizations.* *Coffee and pastries to be served*
11:45 am - 12:00 pm DCA Auditorium* Zoom Available	**Welcome and Opening Remarks** *Dr. Ludmila N Bakhireva & Dr. Kiran Bhaskar,* *Co-Directors for UNM Brain & Behavioral Health Institute*
12:00 pm - 1:00 pm DCA Auditorium Zoom Available	**Keynote Presentation** *"Blind Drunk: Reporting on New Mexico's Neglected Crisis of Alcohol-Related Deaths"- Ted Alcorn, Independent Journalist*
1:00 pm - 1:30 pm DCNW Room 2710**	**Box Lunch Distribution** *Grab a lunch and join us in DCNW 3740 for the roundtable.*
1:30 pm - 2:45 pm DCNW Room 3740	**Roundtable Discussion** "Improving Systems of Care in New Mexico for Substance Use Disorders. *What are we getting right, what do we need to work on?"* *Moderated by Jeremy Lihte, President and Founder of NM Leaders in Recovery* Panelists • Ted Alcorn, Independent journalist • Brian Serna, Serna Solutions LLC • Jeff Holland, Endorphin Power Company • Dr. Anjali Taneja, Casa de Salud • Dr. Paul Romo, UNM Addiction and Substance Abuse Program (ASAP) & UNM Psychiatry and Behavioral Sciences • Dr. Snehal R Bhatt, UNM Addiction and Substance Abuse Program (ASAP) & UNM Psychiatry and Behavioral Sciences

3:00 pm - 3:45 pm DCNW Room 3740	**NM Brain BLAST** TED-style talks focusing on substance use disorders by UNM trainees & Community Leaders on their preclinical, clinical, community and health services research. *1 slide x 3 min x 4 people.* • **Dylan Richards,** *Sr. Postdoc,* "Understanding why people drink alcohol responsibly." • **Alexandria Wiesel**, *Research Coordinator, "*Over dose-response relations between prenatal alcohol exposure and perinatal outcomes" • **Justine R Zimmerly,** *Graduate Student*, "Prenatal alcohol exposure (PAE) and stress impact neuroinflammation in adulthood." • **Brian Serna,** Community Leader, "Community Reinforcement and Family Training (CRAFT) and Substance Use Disorders"
3:45 pm - 4:00 pm DCNW Room 3740	**Closing Remarks & Poster Awards**

Keynote Speaker

Ted Alcorn, Independent Journalist

Presentation Title (Original)

Blind Drunk: Reporting on New Mexico's Neglected Crisis of Alcohol-Related Deaths

Independent journalist Ted Alcorn will present top-line findings of his ongoing, multipart investigation of alcohol's impact on the state of New Mexico, where drinking kills at a faster clip than anywhere else in the country. He will also provide insight into his reporting process, and his views about the respective roles that journalists, advocates, and government officials play in advancing measures that improve population health and wellbeing.

Ted Alcorn is a writer raised in New Mexico whose reporting on health and justice has appeared in numerous publications. An adjunct at Columbia University's Mailman School of Public Health and NYU's Wagner School of Public Service, he was previously the founding research director of Everytown For Gun Safety and a policy analyst in the New York City mayor's office. He earned graduate degrees at the Johns Hopkins Bloomberg School of Public Health and their School for Advanced International Studies, and lived in Beijing, China as a Henry Luce scholar.

Roundtable Discussion

Improving Systems of Care in New Mexico for Substance Use Disorders: What are we getting right, what do we need to work on?

Moderator:
Jeremy Lihte is the President and Founder of NM Leaders in Recovery and the Director of Community Relations at Vista Taos Renewal Center.

Panelists:
Ted Alcorn is an independent journalist whose reporting on health and justice has appeared in numerous publications. An adjunct at Columbia University's Mailman School of Public Health and NYU's Wagner School of Public Service, he was previously the founding research director of Everytown For Gun Safety and a policy analyst in the New York City mayor's office. He earned graduate degrees at the Johns Hopkins Bloomberg School of Public Health and their School for Advanced International Studies, and lived in Beijing, China as a Henry Luce scholar.

Brian Serna, LPCC, LADAC is the CEO/Founder of Serna Solutions and is a well sought after trainer and consultant in behavioral health issues related to Evidence Based Practices, Cultural Considerations and Ethical Issues. He has an MA in Counseling from the University of New Mexico and a BA in Psychology from New Mexico State University. Mr. Serna has trained and consulted with programs in over twenty different states, five different countries, and sixteen different tribal communities. In addition to his role as the CEO of Serna Solutions he is a founding member and past President of the New Mexico Association of Addiction Professionals (NMAAP), a member of Senator Ben Ray Lujan's Mental Health Consortium and has been appointed to serve on Governor Michelle Lujan Grisham's Council on Racial Justice in Health Subcommittee.

Dr. Anjali Taneja, MD MPH FASAM (@losanjalis) is a family physician and DJ who is passionate about reimagining healthcare and healing. She is the Executive Director of Casa de Salud (@casadesaludnm) in Albuquerque, New Mexico. Casa de Salud is a culturally humble, anti-racist and integrative model of healthcare that works to transform the biomedical model into one of solidarity with community and collective care. Casa integrates accessible and dignified primary care, queer/transgender care, syringe exchange, harm reduction and medication/holistic based opioid addictions treatment, case management, acupuncture, reiki, massage, and healing circles for marginalized communities. Casa has built a sustainable model for low-cost care to patients without insurance (70% of patients) and for patients with Medicaid. Casa also has a rich history of direct service and community organizing around healthcare access, medical debt, addictions care, and community safety — and believes it is the responsibility of healthcare organizations to build power with community. The clinic runs a nationally recognized health apprentice fellowship that trains and mentors primarily young Latinx

people of color interested in healthcare; many go on to become clinicians and healthcare leaders.

Anjali is board certified in family medicine and addiction medicine, and also works in the emergency room of a rural hospital in the Navajo Nation. She completed her family medicine residency at Harbor-UCLA Medical Center in Los Angeles, and medical school at Rutgers New Jersey Medical School. She has lived in New Mexico for a decade. In 2022 Anjali received the NM Ethics in Business Award. and her work was featured on NPR's The Well Women Show. She is an appointed member of both the New Mexico Primary Care Council and the New Mexico Governor's Council on Racial Justice. In 2020, she was selected as one of Go Magazine's 100 Women we Love, featuring LGBTQ+ women who are working for change, and she was interviewed about Casa de Salud, for the How to Survive the End of the World podcast. Over a decade ago, Anjali founded CureThis, an online community space bringing healthcare workers and community members together, for discussion around new models of care, and she is building a team to revive this network and learning space.

Dr. Paul E. Romo, MD is board certified in General and Addiction Psychiatry, and Addiction Medicine. Having completed the entirety of his education and post-graduate training at the University of New Mexico, Dr. Romo understands and is invested in the well-being of all New Mexicans. He currently practices within the UNM Department of Psychiatry serving as Medical Director of the Addiction and Substance Abuse Program (ASAP), including Director for the Dual Diagnosis Clinic within ASAP, and also provides clinical services in other areas of the department.

Dr. Romo's scope of practice extends beyond academia to include the community and the forensic population. This is facilitated through outreach endeavors, ECHO, expert witness services and incarcerated individuals receiving medications for opioid use disorder at the Metropolitan Detention Center (MDC). His research and administrative activities concentrate on forming a continuum of care for patients afflicted with co-occurring psychiatric disorders, primary addictions, and forensics within academia and the private sector locally and throughout the state.

Snehal Bhatt, MD is board certified in General and Addiction Psychiatry, and Addiction Medicine. He received his B.A. in Psychology from The College of New Jersey in 2001, followed by his M.D. from the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School in 2005. He subsequently completed his 4 year residency in General Psychiatry at Robert Wood Johnson Medical School in 2009. Dr. Bhatt then came to the University of New Mexico to complete an additional 1 year of training in Addiction Psychiatry, finishing in 2010.

Dr. Bhatt is passionate about providing equitable, state of the art care to individuals with substance use disorders. Substance use disorders are treatable chronic illnesses that profoundly impact many individuals, their families, and their communities. Unfortunately, these illnesses also remain highly stigmatized, and access to effective treatments can be a major challenge. Dr. Bhatt is motivated by the challenge of helping create systems of care that are patient centered, anti-stigma, equitable, and that offer cutting edge

treatments in trauma-informed and integrated settings. Dr. Bhatt currently serves as the chief of Addiction Psychiatry and Director of the Addiction and Substance Abuse Program (ASAP) at UNM. He provides much of his clinical care at UNMH Addiction and Substance Abuse Programs (ASAP). Additionally, he is very engaged in clinical and implementation research that focuses on improving outcomes for patients with opioid use disorders, and is currently involved in multiple NIDA funded clinical trials, as well as multiple ECHO projects. He is engaged in research that explores the therapeutic potential of psychedelics. Finally, Dr. Bhatt also enjoys teaching, and is involved in clinical teaching of medical students, as well as residents and fellows.

NM Brain BLAST

The 2023 UNM Brain & Behavioral Health Research Day is the pilot year for the NM Brain BLAST. This section was modeled off NM EPSCoR's Research SLAM and Three Minute Thesis (3MT). 3MT was founded by the University of Queensland. 3MT has since been adopted by 85 countries outside Australia.

NM Brain BLAST highlights brain and behavioral health research at UNM and in the community. Speakers for this pilot section were nominated by the faculty advisory committee members for this event. The students trained with **Angie Alley,** CNM professor prior to the event to tailor their message to a non-expert audience. Each presenter has one slide and 3 minutes to speak.

Moderator & Communications Coach

Angie Alley, MA, CNM is Interim Dean for Arts & Sciences and Communications Professor at Central New Mexico Community College, Albuquerque. Angie hails from Colorado, but has called New Mexico home for the past 12 years. She has been a college Communication Instructor for 19 years and loved every moment of it. Her primary focus is Public Speaking and Interpersonal Communication. A couple of years ago, Angie became an Associate Dean for the School of Liberal Arts at CNM, and that has been a wonderful new experience for her. Outside of her job, Angie performs in musical theater, and has performed in 43 musicals. She is also an avid tennis player, and a speaker coach for TEDxABQ.

Speakers:

Dylan Richards, Sr. Postdoc, CASAA
"Understanding why people drink alcohol responsibly."
Dylan K. Richards, Ph.D. is a postdoctoral fellow at the Center on Alcohol, Substance use, And Addictions. His research aims to better understanding the psychology of reducing the harms of alcohol use and other drugs. He is expecting a baby boy May 27th!"

Alexandria Wiesel, Research Coordinator, College of Pharmacy, SURE Center
"Over dose-response relations between prenatal alcohol exposure and perinatal outcomes"
Alexandria Wiesel is a Research Coordinator with the Substance Use Research & Education Center within the College of Pharmacy. She hopes to increase our understanding of substance use during pregnancy and reduce stigma around substance use. She is trained in several martial art forms and is on the path to medical school."

Isabella Romano, Graduate Student, MGM
"Opioid Vaccines
Isabella is a third year PhD student in the Biomedical Sciences Graduate Program. She is currently working on a project to investigate the development of vaccines targeting opioids in the laboratory of Dr. Kathryn Frietze in the department of Molecular Genetics and Microbiology.

Justine R Zimmerly, Graduate Student, UNM Neurosciences
"Prenatal alcohol exposure (PAE) and stress impact neuroinflammation in adulthood."
Justine is a third year PhD student in the Biomedical Sciences Graduate Program. She is currently working on a project to better understand the adverse neuroinflammatory and behavioral consequences of prenatal alcohol exposure and stress in adulthood. When she isn't doing research, she enjoys rock climbing and other outdoor activities.

Brian Serna, Community Leader, Serna Solutions
"Community Reinforcement and Family Training (CRAFT) and Substance Use Disorders"
Brian Serna is the CEO/Owner of Serna Solutions, a behavioral health agency with offices in Santa Fe and Albuquerque. He has been helping families address addiction since 2001 under the mentorship of Dr. Robert J. Meyers (UNM-CASSA retired). He has trained and consulted in the CRAFT model nationally, internationally and in eight different indigenous communities around the world.

Abstract Book

1 Creating a Quality of Life for People with Brain Injuries

Ken Collins

Ken Collins has lived with his brain injury for over 46 years and has worked with people with brain injuries and other disabilities to live independently since 1983: http://www.educationviews.org/ken-collins-reflections-recovery-head-injury/ He is an advocate of developing home and community-based services for people with brain injuries. In 1986-88 he was a VISTA Volunteer and helped develop the first independent living program for people with brain injuries in the U.S. http://www.sheltercare.org/2016/03/uhlhorn-beginnings/ Ken has participated in indigenous healing practices in the treatment of brain injury (Sweat Lodge, Hogan Ceremonies, NAC) and promotes the use of mindfulness-based stress reduction, Emotional Freedom Technique (EFT) tapping, Tai Chi, Yoga for successful integration with western medicine to control anger and other consequences stress and anxiety triggers within the limbic system fight or flight response. Ken has conducted national webinars on using mindfulness-based therapies, meditation, exercise, and nutrition to assist in the brain injury recovery process: http://www.biausa.org/education/altermanwebinars Ken also organized Elders First! to develop elder day services (adult day care) for frail Navajo elders at senior centers on the Navajo Nation. These efforts were supported by two small grants to the Christopher and Dana Reeve Foundation and New Mexico Governor's Commission on Disability for Elders First! to fund focus groups and develop an Elders First! DVD to help educate chapter officials about elder day services at senior centers http://youtu.be/Coth5eeZSu0 The DVD was distributed to key legislative leaders in the Navajo Nation, Navajo Area Agency on Aging (NAAA), and Eastern Agency of the NAAA. Ken also played a leadership role in the passage of the Vulnerable Adult Protection Act "Doris Act" on the Navajo Nation. This legislation was passed by the Navajo Tribal Council on January 24, 2012, and was signed into law in February 2012 by Navajo Nation President, Ben Shelly. Most recently, Ken was elected Chair of the New Mexico State-wide Independent Living Council (NMSILC) and is currently runs the Next Step Program at Rehoboth McKinley Christian Health Care Services (RMCHCS) Behavioral Health Services Treatment Center in Gallup, New Mexico

2 Health Literacy is Linked to Executive Functioning in Older American Indians

Alexis Burks, MS, Anastacia Romero, Macaiah Shendo, Steven P. Verney, PhD

Objective: Health literacy (HL), the ability to understand healthcare information and navigate the healthcare system, is strongly associated with both educational achievement and executive functioning. Many American Indians (AIs) experienced traumatic early education, such as harsh boarding schools, which may impact their educational achievement, and subsequently, HL. Further, AIs disproportionately experience many chronic diseases. This study investigates the relationship between HL and executive functioning in older AIs. Participants and Methods: Participants were recruited from a southwestern urban area who self-identified as AIs aged 55 to 80 (N=43). Participants were asked to complete questionnaires, interviews, and neuropsychological tests over two sessions. The poster investigates the data from participants who completed both sessions. We created a composite variable of HL measures, (Rapid Estimate of Adult Literacy in Medicine, Newest Vital Sign, and Short Test of Functional Health Literacy in Adults verbal and numeracy z-scores). Executive functioning was assessed by WASI Matrix Reasoning and Similarities, Verbal Semantic Fluency (VSF), and Trails Making – B. Results: HL was positively correlated with both WASI Matrix Reasoning and WASI Similarities. Similarly, HL was positively correlated with VSF – Animals and Plants. However, there was no significant correlation between HL and VSF – fruits and Vegetables or HL and Trails Making – B. Conclusions: These findings suggest that HL and executive functioning are linked in older AIs. Discrepancies between the executive functioning tests may be due to resources, culture, and education quality. These findings highlight the need for further investigation of cultural context and development of culturally appropriate measures.

3 Peer Support Model to Address Substance Use Disorders Treatment Engagement in Rural Communities

J.L Saavedra1, A.S Crisanti1, C.M. Caswell1, A.J. Jaramillo1, STTEP Research Group

Background: New Mexico (NM) leads the nation in alcohol-related and drug overdose deaths. This project aims to implement and test a model of telehealth-substance use disorder (TH-SUD) treatment to reach underserved rural, Hispanic, and Native American (NA) populations in Sandoval, San Juan, McKinley, Cibola, Valencia, and Santa Fe Counties. The overall goal is to reduce the consequences of substance use in culturally relevant ways. Our population of focus is rural, Hispanic, and NA adult patients with an SUD presenting to the emergency department (ED) or inpatient units of the University of New Mexico Sandoval Regional Medical Center located in Sandoval County. Methods: The evidence-based, culturally informed, and trauma-focused TH-SUD treatment includes Medication Addiction Treatment (MAT), Seeking Safety (SS), and psychosocial supports. Using motivational interviewing, Peer Support Workers (PSWs) are responsible for in-person patient screening and navigation from the ED or inpatient units to outpatient TH-SUD treatment. PSWs deliver SS and psychosocial supports and MAT is provided by medical professionals. Results: Data are being collected from participants prior to starting TH-SUD treatment and every 60 days thereafter on outcomes including treatment engagement/retention, types of services received, substance use, substance craving, quality of life, PTSD symptom severity, hospital utilization, motivation to change, self-stigma, and perceptions of recovery. The preliminary costs associated with the intervention and potential cost-savings are also being determined. Discussion: Data on participant outcomes are currently being collected and it remains to be determined whether implementing a TH-SUD treatment program in a hospital setting is an effective approach to reducing the consequences of SUD. While there have been challenges, there have also been successes. Given the lack of resources in rural communities, more research on providing SUD treatment to these populations is necessary. Our poster will provide an overview of the intervention and summarize preliminary data and challenges/successes. Funding: Research reported in this presentation was supported by Congressionally Delegated funds administered by the Substance Abuse and Mental Health Services Administration (SAMHSA) Award Number 1H79FG000817-01.

4 Quality of Education & Level of Education in Association with Executive Functioning in Older American Indians

Eunice Kim, BA, Alexis Burks, MS, Katherine Edwards, BA, Maria McCready, BA, Emily Kuehn, Jezreel Romero, & Steven P. Verney Ph.D.

Objective: Level of educational achievement is often associated with executive functioning (EF) and overall health. However, education level does not account for the quality of education, which may be a better educational index for older American Indians (AIs). Many older AIs have suffered traumatic educational experiences, such as forced boarding schools and relocation focused on cultural assimilation rather than subject knowledge. This study investigated the relationship between EF and quality of education in older AIs. Participants and Methods: Participants were recruited from a southwestern urban area who self-identified as AI aged 55 to 80 years (N=42). Participants completed questionnaires, interviews, quality of education (Wide Range Achievement Tests, WRAT) and executive functioning tests (WASI and verbal semantic fluency, VSF) over two sessions. Results: Both education quality and level were significantly associated with WASI Matrix scores and VSF plants. Only education level was positively correlated with VSF fruits and vegetables and only quality of education was positively correlated with VSF animals. Regression analyses revealed that quality of education yielded significant regression equations for VSF animals, VSF plants, and WASI Similarities. Conclusions: Education quality accounted for the variance in several EF tests over and beyond education level in this sample. This suggests quality of education may better explain EF test performance in older AIs than educational achievement.

5 Striving Towards Universal Treatment: The Novel “Full Spectrum People-With-Opioid-Use-Disorder Care Model."

Richard Gadomski, Snehal Bhatt, Jessica Gross, Tony Dixon, Phillip Fiuty, Max Shapiro, Rafael Fernandez-Mancha, & Julie Salvador.

Background: People with Opioid Use Disorder (PWOUD) represent an underserved and marginalized population. Low-barrier programs like mobile care units and street outreach programs have yielded increased access to buprenorphine and social services, however OUD pertinent co-occurring behavioral health and medical conditions are frequently left unaddressed. A novel, tailored, comprehensive care delivery model may reduce disparities and improve access to care across a range of pathologies in this historically difficult to reach population and enhance efforts to provide universal treatment access.
Methods: Descriptive data was collected and analyzed regarding patient demographics, retention in treatment and services rendered at a new, wrap-around, low-barrier buprenorphine clinic established at an existing harm reduction site in New Mexico between August 1, 2020 and August 31, 2021.
Results: 203 people used any service at the newly implemented program, 137 of whom specifically obtained medical and/or behavioral health care services including prescriptions for buprenorphine at least once from the physician onsite. Thirty-seven unique medical and psychiatric conditions were treated, representing a total of 565 separate encounters. The most common service utilized was buprenorphine treatment for opioid use disorder (81%), followed by treatment for post-traumatic stress disorder (62%), anxiety (44.5%) and depression (40.9%). Retention in buprenorphine treatment was 31.5% at 6 months.
Conclusions: An innovative, multidisciplinary, buprenorphine-centric care model, which targets a wide range of OUD pertinent pathologies while employing a harm reduction approach, can enhance utilization of these services among an underserved PWOUD population in a manner which moves our health system toward universal OUD treatment access.

6 Guidance on methadone for opioid use disorder in older adults: current practices

Madalyn Dankocsik, Shreeti Patel, Alexandria Viszolay, Ellen Green, Catherine Smith

Introduction: Opioid use disorder is highly prevalent and treatment is becoming more complex with the emergence of fentanyl. Methadone is a highly effective medication and full agonist of the opioid receptor allowing treatment of patients with high opioid tolerance. The proportion of adults over 65 is increasing and will rise to 77 million by 2034. In geriatric populations up to 50% of Medicare recipients take at least five medications a day. This polypharmacy and physiologic changes of metabolism puts this population at a higher risk of adverse events. In this study, we aim to determine the current practice of methadone treatment of older adults to address gaps of care within the geriatric community. Methods: In order to determine current medical practice around the care of older adults (^{3} 65 years old) in Opioid Treatment Programs (OTPs) who provide methadone as a medication for opioid use disorders (MOUD), phone calls were made to 21 certified centers throughout New Mexico. Survey inquiry included instigators of dose changes and monitoring protocols for older adults in addition to standard annual history, physical, and electrocardiogram. For an in-depth analysis of a patient population taking methadone, a retrospective chart review of patients at the University of New Mexico (UNM) OTP called the Addiction and Substance Abuse Program (ASAP) was performed. Results: Of these 335 adults on methadone, 13% (n=44) were ^{3} 65 years old with a maximum methadone of 200 mg, 75% of whom qualified for ^{3} 2 weeks of take-home doses compared to only 45% of patients < 65. Discussion: Older adults face unique risk factors with methadone treatment due to polypharmacy, metabolic changes, and comorbidities. To address both the chronic condition of OUD effectively and acknowledge the unique biology of the aging population, further guidance is imperative.

7 Validation of the Substance Use Protective Strategies Scale (SUPSS) among U.S. College Students

Jakub Greń, Matthew R. Pearson, Dylan K. Richards & Addictions Research Team

Protective Behavioral Strategies (PBS) are behaviors that effectively reduce the likelihood of experiencing substance-related harms. Despite the fact that most individuals use more than one substance, previous research on PBS has been limited to substance-specific measurement, i.e. alcohol-specific (e.g., PBSS) and cannabis-specific (e.g., PBSM). We developed the Substance Use Protective Strategies Scale (SUPSS) to measure more general substance use PBS, which was preliminary validated among Polish young adults (aged 18-30) using various substances (Greń et al., 2023), sand sought to its further examination. Participants (N=1856) took part in a multisite research of substance use among college students recruited from 10 universities located in 8 US states (AK, CA, CO, ID, NM, TX, VA, and WA). Analyses were restricted to those who reported substance use in the past month (n=1208; 88.4% alcohol, 43.9% cannabis, 3.8% stimulants). Based on previous psychometric testing, we examined a series of 3- and 4-factor models (with and without hierarchical factors or bifactors) using Confirmatory Factor Analysis (CFA) and Exploratory Structural Equation Modeling (ESEM). Based on fit statistics and factor interpretation, 3-factor solution was selected with ESEM, which is ideal when small (non-zero) cross-loadings are expected. Across models, the SUPPS factors accounted for significant variance in substance-related outcomes (cannabis use disorder symptoms, R-square=.129; alcohol use disorder symptoms, R-square=.074; cannabis-related consequences, R-square=.065; alcohol-related consequences, R-square=.054). SUPSS (total score) was moderately correlated with established substance-specific measures for both alcohol (PBSS; r=.36) and cannabis (PBSM; r=.45), supporting its concurrent validity. Although our sample was relatively large, we will continue to gather data as part of this ongoing multisite study to explore measurement models that failed to converge in the present sample (e.g., bifactor CFA model). Overall, we found further support for assessing general substance use PBS, which complements and extends the examination of substance-specific PBS use.

8 The Neurodevelopmental Outcomes for Children Participating in Navajo Birth Cohort Study.

Heather Krapf, Brandon Rennie

Background: There are many (>500) abandoned mines on Navajo Nation with lots of families living within a short distance (within 10 km) of an abandoned site. Research has indicated higher concentrations of heavy metals among many individuals on Navajo Nation. The Environmental Influences on Child Health Outcomes (ECHO), a seven-year initiative funded by the National Institute of Health (NIH), allowed us to build on the Navajo Birth Cohort Study (NBCS) and continue to follow-up with existing participants. A main aim of NBCS/ECHO has been to examine the effects of environmental exposures such as heavy metals on childhood developmental outcomes. This has been accomplished by tracking the trajectories of childhood neurodevelopmental and physical outcomes. Methods: Comprehensive neurodevelopmental assessments were performed for children aged 3-5 (n=138) and 7-8 (n=65). These assessments were conducted in five different locations across Navajo Nation. Children were assessed using parent rating scales, direct assessment, parent interview, and a medical exam. Following the assessment, children were provided with a clinical best estimate diagnosis when applicable. Our results indicate much higher rates of neurodevelopmental disorders in both age groups, with language disorder and speech-sound disorder being the most prevalent diagnoses for each age group. For example, the rate of language disorder diagnoses seen in the 3-5-year old group is 34.1% while in the general population the rate is 3.3%. Conclusion: Rates of neurodevelopmental disorders are higher amongst our study population relative to the general population. Further research is needed to understand the contributing factors, including metal exposure, to the onset of these conditions and the developmental trajectories.

9 Improving the detection of behavioral health conditions through positive and unlabeled learning: self-harm and opioid use disorder

Praveen Kumar; Jonathan K. Tsosie; Christophe G. Lambert

Accurate detection and estimation of behavioral health conditions, such as self-harm and opioid use disorder (OUD), is crucial for identifying at-risk individuals, determining treatment needs, tracking prevention and intervention efforts, and finding treatment-naive individuals for clinical trials. Despite the underdiagnosis and undercoding of these conditions in electronic health records (EHRs), our work aims to accurately estimate both the probability of a given patient having these conditions and the overall population prevalence. We have developed a novel machine learning algorithm, "Positive Unlabeled Learning Selected Not At Random (PULSNAR)", to estimate the prevalence of undiagnosed or unrecorded behavioral health conditions. Positive unlabeled learning differentiates between labeled positive instances and a mix of positive and negative instances (unlabeled). Our algorithm addresses the limitations of traditional methods, which do not accurately reflect the true prevalence of behavioral health conditions due to the fact that known, coded cases are not representative of undetected cases. Cases are generally not selected at random, for example, because more serious cases are more likely to generate a healthcare encounter. In a study of 6,037,479 commercially insured patients with major mental illness (MMI) and 1,329,120 veterans, our PULSNAR algorithm estimates 3.97% visit-level self-harm among patients with MMI and 10.46% lifetime self-harm among Veterans, compared to the 0.453% and 1.85% coded in their EHR data, respectively. Chart review of 97 unlabeled individuals among the Veteran population confirmed that PULSNAR provides well-calibrated classification. In a study of 1,000,000 patients with at least one opioid prescription fill, PULSNAR estimated 5.3% (53,144) of patients have OUD, compared to the 2.0% (20,079) that have a recorded diagnosis of OUD. PULSNAR accurately estimates the prevalence of underdiagnosed/unrecorded behavioral health conditions, including self-harm and OUD. This has the potential to inform public health, guide screening efforts, identify health disparities, and reduce the negative impacts of these conditions.

10 Association of neurofascin155 with severe, rapidly progressive sensory axonal polyneuropathy in a cohort of Native American women: A novel case series and review of the literature

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Objective: Paranodal antibodies against neurofascin155 (NF155) have been well-described in chronic and acute demyelinating diseases of both the central and peripheral nervous system, but have not yet been associated with acute axonal pathology1. Here we characterize the demographic, clinical, laboratory, and electrodiagnostic features in a cohort of adult women of Native American ethnicity who presented with rapidly progressive, severe, subacute painful paresthesias and were found to have axonal polyneuropathy associated with positive serum NF155 antibody. Methods: Five patients presented with severe, rapidly progressive, symmetric, painful paresthesias, and were found to have sensory greater than motor axonal polyneuropathy. All patients were tested with the Washington University sensory and motor neuropathy panel which includes NF155 and contactin-1. All five patients underwent EMG/NCS testing. Demographic and clinical data were collected. Results: All cases presented with rapidly progressive distal neuropathic pain, sensory ataxia, areflexia, and mild symmetric distal weakness. All were women of self-reported full or partial Native American ethnicity. All had evidence of severe axonal polyneuronopathy on EMG/NCS. Four of the five cases were seropositive for NF155. Seropositive patients were trialed on a course of IVIg with two of these patients subsequently receiving plasmapheresis. This treatment led to a mild subjective and clinical improvement in just one of the patients. Clinical follow up is ongoing in three of the five patients. Two patients have since died from unrelated causes. Conclusions: This series highlights rapidly progressive axonal polyneuronopathy associated with NF155 in a small cohort of women of Native American ethnicity. To our knowledge, this is the first time these antibodies have been described in association with acute axonal pathology.

11 Identifying Profiles of Cannabis Users Based on Their Motivations to Use Cannabis Responsibly: An Application of Self-Determination Theory

Joey C. Mok, Jakub D. Gren, Haydee Andujo, Ricardo A. Rubio, Dylan K. Richards, Matthew R. Pearson, & Addictions Research Team

Based on self-determination theory (SDT), motivation can be understood as existing on a continuum from the most to the least self-determined (autonomous motivation, introjected regulation, external regulation, amotivation) with more self-determined motivations associated with positive health outcomes, and less selfdetermined motivations associated with negative health outcomes. Using a newly developed measure of motivations to use cannabis responsibly (TRSQ), we sought to identify unique subpopulations of cannabis users based on their motivations to use (or not use) cannabis use responsibly, positing that those with more selfdetermined motivations would report higher use of cannabis protective behavioral strategies (PBS) and lower cannabis use/problems. A sample of 408 past month cannabis users were recruited from a multisite study of college students (n=1856). We used latent profile analysis to determine the number of unique subpopulations based on these motivations, which supported a 5-profile solution. Consistent with our hypotheses, the class with the highest level of autonomous motivation and lowest level of amotivation ("Self-Determined Class", n=40, 10.4% of the sample) reported the highest cannabis PBS use (z=.67) and lowest cannabis use (z=.31), and lowest cannabis use disorder symptoms (z=-.22). Further, the class with the highest level of amotivation and lowest level of autonomous motivation ("Amotivated Class", n=83, 21.5% of the sample) reported the lowest cannabis PBS use (z=-.22) and highest cannabis use (z=-.16), highest consequences (z=.22), and highest cannabis use disorder symptoms (z=.27). Similar to previous research that has demonstrated that latent profile analysis can be used to distinguish individuals based on their motivational profiles for drinking responsibly, our results support subtyping individuals based on their motivations to use cannabis responsibly. Additional research with larger sample sizes is needed to determine the level of generalizability of these motivational profiles, and longitudinal studies are needed to identify if these classes predict outcomes in the long-term.

12 Everyday stressors in association with mental health evaluation in Cheyenne River Sioux Tribal community members

Elena O'Donald, Rae O'Leary, Brandi Fink, Sharon Rulyak, Marcia O'Leary, Kendra Enright, Esther Erdei

Background:

This pilot study analyzed mental health (SCL-90-R), discrimination, everyday stressor and societal factor measures implemented to an ongoing heavy metal toxicants risk assessment evaluation. The P50 Center supported sub-study was a response to community concerns of the Cheyenne River Sioux Tribe in South Dakota. National Institute of Mental Health reported that in 2020, U.S. adults had a prevalence rate of serious mental illness 5.6% overall, while Native Americans had even higher rate of 6.6%.

Methods: Out of 225 CRST Tribal participants, 57 completed all pilot survey tools, including socioeconomic measures, discrimination survey, everyday stressors, adverse childhood event (ACE) history, and SCL-90-R symptom checklist. Based on the expert review (by B.F.) of participants' responses, we created 10 main, 2 additional, and 1 global mental health domains: including Somatization, Depression, Anxiety and Suicide/death/obsession. Quantile regression modeling examined association between serum/urinary metal/micronutrient concentrations and mental health domains. Everyday stressors, perception of discrimination, adverse childhood event (ACE) history, and demographic factors were also investigated.

Results: We found that 40% of the participants had elevated ACE score (4 or higher) and mean everyday stressor weight score was 0.49. Discrimination based on ethnicity, gender, race, age, was prevalent and reported by 47%, 19%, 28%, and 21% of community members, respectively.

Everyday stressor weight score predicted Global Severity Index, Anxiety, Depression, Somatization, and Bodily/somatic symptoms. Discrimination weight score was also associated with Obsessive compulsive and Interpersonal sensitivity. Serum manganese concentrations predicted Somatization response. Elevated ACE score was linked to Global Severity. Racial discrimination responses were associated with Interpersonal sensitivity. Weight/obesity-related discrimination was linked to Hostility and Suicide/death/obsession. All reported above relationships were direct and statistically significant at $\alpha=0.01$.

Conclusions: Everyday stressors, discrimination, ACE history, and serum manganese adversely affect mental health. Younger and lower educated people are more vulnerable to Hostility and Phobic anxiety conditions, respectively.

13 A Novel Methodological Approach of Studying Heart Rate Variability during Still Face Paradigm in Infants of ENRICH Prospective Birth Cohort Study.

R Rai, J DiDomenico, SM Rodriguez, J Maxwell, J Lowe, C Aragón, LN Bakhireva, JM Stephen

Introduction: Prevalence of Fetal Alcohol Spectrum Disorders (FASD) among school age children in the U.S. might be as high as 1-5%. Diagnosis of FASD is often delayed as higher-order cognitive deficits manifest later. The inability to regulate autonomic activity during social interactions is believed to contribute to social and emotional dysregulation in children. Heart rate variability (HRV) consists of changes in the time intervals between consecutive heartbeats called interbeat intervals. It is regulated by Autonomic Nervous System through synergistic activity of the sympathetic and parasympathetic branches. Still Face Paradigm (SFP) is used as an experimental social stressor paradigm to access mother infant interaction, infant self-regulation and emotional dysregulation. Autonomic dysregulation is a risk factor for future dysregulation of stress reactivity. Self-regulation is one of the key behavioral deficits in children diagnosed with FASD. HRV can be a strong predictor of Self-regulation. Objective: Our goal was to evaluate changes in HRV in response to SFP as a social stressor. Methods: Participants were 86 mother-infant dyads, recruited prenatally and completed the HRV data collection along with SFP when infants were 6 /9 months of age. EKG and respiratory recordings were collected during five 2-minute SFP episodes (three play and two Still face episodes) preceded by one baseline episode for one minute. Based on prospective repeated assessment of maternal alcohol use in pregnancy the infants were divided into two groups: 1) healthy control and 2) prenatal alcohol exposed. The time and frequency domain indices of HRV were calculated from continuous EKG recordings from each infant group. Results/Conclusion: To date we have successfully collected 74 infant's HRV data. First two episodes of SFP had greater success rate of HRV collection. Significant differences in HRV among SFP episodes were identified. HRV may be used as a specific marker for Self-regulation in infants.

14 Development of a Smartphone Application Able to Capture Patient-Centered Outcome (PCO) Measures for Dystonia

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Introduction: Botulinum neurotoxin (BoNT) is a first line therapy for many types of dystonia and results in significant improvement, yet approximately one-third of patients discontinue use of BoNT suggesting that BoNT therapy may not fully address patient expectations. Symptom Snap was developed to capture Patient-Centered Outcome (PCO) measures across motor, disability, and psychosocial domains, enabling clinicians and researchers to characterize the therapeutic response to BoNT therapy over time on a frequent basis. Methods: In collaboration with TekSynap, we developed a smartphone application able to capture PCO measures tailored for three major dystonia subtypes: cervical dystonia (CD), blepharospasm (BP), and laryngeal dystonia (LD). The app is accessible to users on both Android and iOS operating systems. We also developed a web-based admin panel able to track all data entered in the app. The admin panel is accessible to study personnel only. The admin panel is also used for generating login credentials.

15 Modification of Existing Head Circumference Charts for New Mexico Native American Children

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Background: Current Centers for Disease Control (CDC) and World Health Organization (WHO) growth charts are based on normative data that do not adequately represent the distinct pattern of head growth observed by providers for New Mexican Native American children.1 Therefore, Native American children with normal but larger head circumferences (HC), can be inaccurately diagnosed with macrocephaly and undergo unnecessary diagnostic workups.2 The purpose of this study is to evaluate whether HCs for Native American children in New Mexico distribute differently than established growth charts.
Methods: This is an IRB-approved retrospective chart review of all Native American well-child visits from ages 0 to 2 seen at the UNM Hospitals and Clinics. 1,513 patients were screened, and 1,214 patients were included. Data for gestational age, sex, zip code, date of birth, date of visit, HC, CDC and WHO percentile were recorded. HC curves were calculated using quantile regression.
Results: A total of 8,569 HCs and their corresponding CDC and WHO percentiles were recorded. The 99th, 95th, 90th, 75th, 50th and 25th CDC and WHO HC percentile curves were compared with the estimated corresponding Native American HC percentile curves for males and females. For all percentiles, the Native American HC curve naturally crosses percentiles within the first four months.
Conclusion: In this preliminary analysis, New Mexico Native American children HCs are not adequately represented by current growth curves. Of particular concern is the trend that Native American HCs appear to naturally cross percentiles within the first four months, which causes unnecessary workups for increasing HC. Further analysis will focus on increasing data collection to create a refined New Mexico Native American HC model.

16 The Bronze Age Armenian Artifact Decoded via CBB (discovered in Lake Sevan, Armenia, during the 1950s by archeologists)

April Vihilidal

Background: Within the research paradigm in the cognition, brain, and behavior (CBB) group includes studies of sensation and perception, learning and memory, attention, mental imagery,and conceptual representation. The Bronze Age Armenian Artifact is an example of humans from the past using (CBB) to communicate with humans of the present. The artifact dates to the 11th-12th centuries BCE. There are five ancient archeological sites related to the Bronze Age Armenian artifact via the planet's ley lines:
1) Mount Nemrut, Turkey, dates from the 1st century BCE.
2) Lake Sevan, Armenia, where the artifact was discovered.
3) Carahunge dates back 7,500 years.
4) Karahan Tepe is at least 11,000 years old
5) Göbekli Tepea, Turkey dates between c. 9500 and 8000 BCE.
Methods: Address the research question via observation and analysis, "How does the Bronze Age Armenian Artifact act as a holographic measuring device, create synchronistic connections between 1) itself, 2) Google Maps, and 3) an analemma of Lake Sevan, Armenia that allow for the deciphering of meaningful geodesic geometry that connects the aforementioned to reveal encoded knowledge about the artifact itself and its relationship to ancient archeological sites in the same vicinity of its discovery?" Results: Archeological discoveries from 3,200 to 12,000 years ago are changing how modern man sees his ancestors. Increased archeological evidence shows immense astronomical sophistication that has yet to be recognized with academic aplomb. Therefore, research is accomplished to create a tertiary academic paradigm shift. Conclusions: The ancient archeological sites and the ancient artifact from the eastern side of the earth reveal information concerning the western side of the world. Connected via the planet's ley lines on the earth's grid, the ancients who designed the artifact encoded where on the planet a person with a like mind, via CBB, is decoding the Bronze Age Armenian Artifact.

18 The Risk Analysis Index Has Superior Discrimination Compared to the Modified Frailty Index-5 in Predicting Worse Postoperative Outcomes for the Octogenarian Neurosurgical Patient

Alyssa Yocky, Oluwafemi Owodunni, Evan Courville, Syed Faraz Kazim, Meic Schmidt, Susan Gearhart, Naomi George, Diana Greene-Chandos, Christian Bowers

Background: Healthcare systems continuously strive to improve quality and value of care. Advances in surgical technologies, enhanced perioperative surgical planning, and multidisciplinary care strategies are increasing the number of elective procedures in the geriatric population. However, frail older adults are still more likely to have poor postoperative outcomes. We examined the discriminative thresholds for the risk analysis index (RAI), modified frailty index-5 (mFI-5) and increasing patient age for predicting adverse postoperative outcomes. Methods: Octogenarian neurosurgery patients undergoing spine, cranial, and other procedures, captured in the ACS-NSQIP between 2012-2020 were included. We employed receiver operating characteristic (ROC) curve to examine the discriminative thresholds of RAI, mFI-5, and increasing patient age. Multivariable analyses were performed. Our primary outcomes were 30-day mortality, extended length of stay (eLOS [75th percentile]) and continued inpatient care >30 days (pLOS). Secondary outcomes were skilled care facility (SNF) discharges and readmissions. Results: 20,710 octogenarians were included, with a mean age of 83 years (SD, 2.5), and a male (52.7%), and white (79.8%) majority. The RAI had higher predictive discriminative thresholds for 30-day mortality (C-statistic of 0.743), eLOS (C-statistic: 0.692), and pLOS (C-statistic: 0.697) compared to the mFI-5 (C-statistic: 0.574, 0.556, and 0.550 respectively), and increasing patient age (C-statistic: 0.577, 0.546, and 0.504 respectively), P<0.001. On multivariable analyses, RAI showed a larger effect size with adverse postoperative outcomes by increasing frailty strata than mFI-5 and increasing patient age. Nonetheless RAI showed decreased risk for SNF discharges. Conclusion: We found that RAI was a more accurate predictor than mFI-5 and increasing patient age for 30-day mortality, eLOS, and pLOS in octogenarian neurosurgery patients. More research is needed on RAI's performance in different specialized neurosurgical populations. It is increasingly clear that comprehensive risk assessment strategies tailored to optimize perioperative care should be prioritized to potentially improve outcomes for this at-risk population.

19 Using the 55-word story method of reflection and writing about not Losing Hope in Humanity

Pearl Huynh MSI, Ricardo Falcon MD, Tim Petersen PhD, Codruta Soneru MD

Creative writing with 55-word stories can encapsulate key experiences. It stimulates reflection and professional growth. Their brevity adds insight and impact.

I have so many mixed feelings about everything going on in the world right now. There is so much disagreement on everything and to me it feels like we can never get everyone on the same page. Whether it be political things, health care, Roe v. Wade, world hunger, vaccines, violence, etc.. Being a first-year medical student, it can be easy to forget about everything going on in the world as you are so busy trying to study and stay afloat. I forget about everything going wrong for a while until I open a news article or Facebook and see another school shooting happening not too long from the last one that occurred. My hope in humanity had been continuing to decrease as I continued seeing all the bad news. As I continued forgetting away in my studies, I completely forgot that I needed to make an appointment for my dad to see his surgeon regarding a procedure he had awhile back on his arm -- I felt extremely guilty that I didn't find time to make it for him. A week later, I had dinner with him and asked how his doctor's appointment went (this was with his oncologist who knows nothing about his surgical procedure), he told me it went well and that the doctor went out of her way to ask about his arm and even asked to call and make his appointment for him. Him telling me this made me cry. It was so touching to me that his oncologist went out of her way to make his appointment for him when it had nothing to do with her care. Amid all this chaos, my dad, who does not speak English, received help. I thought to myself, maybe hope in humanity still exists.

First drafts have no length limit; editing distills key components and implicit ideas. The final version:

55 words: Politics, healthcare, abortion, violence. The world will never be on the same page. My hope for humanity diminishes. One day, an oncologist made an appointment for my dad through his cellphone about his missed orthopedic appointment. My mind changed. She didn't need to do that. I thought to myself, maybe hope in humanity still exists. Discussion: Verbalizing strong feelings was hard. I adore my parents, who left wartime Vietnam seeking a better life and future. I feel guilty about spending little time with them, and not always helping my non-English-speaking dad with appointments. We live in stressful, conflicting times. My story helped pinpoint the essence; cutting to 55 words was cathartic. Reflecting on the good instead of focusing on the negative is okay.

20 KSRP Reduces the Migration and Invasion of Glioblastoma Cells and Restricts Angiogenesis of Human Brain Microvascular Endothelial Cells

Pearl Huynh, Robert Oliver, Gabriela Perales, Roxana Gutierrez, and Amy S. Gardiner

Glioblastoma multiforme (GBM) is a highly aggressive and invasive brain tumor that has been continuously challenging to treat. Combined treatment strategies, including surgical resection, radiotherapy, and chemotherapy, have improved patient outcomes, however, median survival time is less than 15 months. Thus, there is a critical need for new therapeutic targets and approaches. KSRP is a multi-functional RNA-binding protein that acts post-transcriptionally to regulate mRNA stability, splicing, and transport, as well as the biogenesis and function of microRNAs and other non-coding RNAs. Several studies have shown that KSRP expression is significantly associated with prolonged survival of glioblastoma patients. We recently identified novel KSRP-dependent RNA targets, which are altered in glioblastoma cells. We are currently examining how KSRP interacts with and regulates its targets in glioblastoma cells. In addition, we are studying the effect of modulating KSRP and its targets on cellular processes such as tumor cell migration, invasion, and angiogenesis. This project will further our understanding of the molecular mechanisms by which KSRP and its targets impact tumor development and progression. In addition, this work may lead to strategies for targeted therapies against novel molecules and pathways.

21 Continuous cerebral autoregulation measurement and outcomes in aneurysmal subarachnoid hemorrhage

Masoom Desai, Ali Alsarah, Thomas Jones, Bert Davis, Chad Cole, Andrew P Carlson

Background:
Impaired cerebral autoregulation has been associated with worse outcomes in patients with aneurysmal subarachnoid hemorrhage (aSAH). Recent data demonstrated that oxygen reactivity measured by either parenchymal probes or near infrared spectroscopy (NIRS) may be associated with worse clinical outcomes and occurrence of spreading depolarization events. Methods: We prospectively collected continuous multimodality monitoring recordings in patients with aneurysmal treated at our institution between 2011 and 2021. Physiologic data were linked using the Moberg Component Neuromonitoring system (CNS) and clinical data were obtained by chart review. Continuous autoregulation indices were calculated using the CNS Envision software retrospectively for all available data sources (intracranial pressure either from ventriculostomy tranducer or parenchymal monitor of Hummingbird bolt, PbtO2 from Licox, cerebral blood flow from Bowman probe, or cerebral oximetry from NIRS). These led respectively to the following autoregulation indices available for analysis: PRx (ventriculostomy), PRx (Hummingbird), CBFRx, ORx, and OSRx (right, left, and mean). Outcome was assessed by discharge modified Rankin Score as good (0-2) or poor (3-6). Descriptive statistics and logistic regression were used to estimate the association of various impaired autoregulation indices and functional clinical outcomes, controlling for admission variables. Results: We identified 332 subjects with at least one multimodality of physiologic monitoring. Age, Admission GCS, Admission WFNS, and impaired ORx and OSRx were strongly associated with worse clinical outcomes ($p<0.0001$). On multivariable analysis, age (OR=1.043, 95%CI 1.020-1.067) and OSRx (OR=112.516, 95%CI= 4.188- >999) were the only variables that remained significant in the model. Conclusion: Cerebral autoregulation as calculated from continuous measurement of brain oxygenation parameters appears to have the strongest association with clinical outcomes. These may offer targeted approaches to individualize blood pressure management to avoid secondary injury in aSAH patients and such strategies should be incorporated into clinical trials.

22 A peptide mimetic of tyrosine phosphatase STEP: a potential therapeutic agent for treatment of stroke under hypertensive condition

Seong Won Choi, Sathyanarayanan Rajagopal, Prabu Paramasivam, Ranjana Poddar, Surojit Paul

Background: Hypertension is a complex multifactorial disease that is influenced by both genetic and environmental factors. Although hypertension can develop at any age, the prevalence of hypertension is particularly evident in the aging population. It is also the most common comorbid condition in ischemic stroke patients and accounts for ~54% of all strokes. Despite advances in understanding the pathophysiology of stroke, current pharmacologic therapies are still limited to rapid reperfusion using thrombolytic agents, and neuroprotective approaches that can reduce the consequences of ischemic and reperfusion injury are still not available. To bridge this gap, we have evaluated the long-term efficacy of a novel peptide-based neuroprotectant TAT-STEP, derived from the brain-enriched and neuron specific tyrosine phosphatase STEP. Methods: The study utilized spontaneously hypertensive (SHR) rats as an animal model of ischemic stroke, which was induced through transient occlusion of the middle cerebral artery for 60 min followed by reperfusion. The STEP-derived peptide (TAT-STEP) was administered intravenously 6h after the onset of the insult and brain infarct size was evaluated at 1, 7 and 28 days after the insult using the non-invasive magnetic resonance imaging (MRI) approach. Functional deficits were also assessed using a battery of motor, sensory and cognitive tests. Results: Our findings show that a single intravenous administration of the peptide reduces mortality rate. In the surviving rats, MRI scans show significant reduction in infarct size and improvement of structural integrity within the infarcted area following peptide treatment. Behavioral assessments show significant improvement in motor coordination, sensory motor function and spatial memory following peptide treatment. Conclusion: The study demonstrates for the first-time efficacy of a peptide mimetic derived from the tyrosine phosphatase STEP in attenuating ischemic brain damage under hypertensive condition and facilitating long-term recovery.

23 Deficiency in interleukin-1 receptor accessory protein (IL-1RAP) alleviates tau pathology

Somayeh Dadras, Kiran Bhaskar

Neuroinflammation is associated with hyperphosphorylation and aggregation of tau, which results in the formation of neurofibrillary tangles in tauopathy brains. However, the precise mechanisms of how brain inflammation drives this process remains unclear. Previously, we have reported that tau pathology is induced in neurons through microglia-derived IL-1. It is unclear how IL-1 signaling is regulated in a cell-specific manner and at the receptor level. An important factor in IL-1/IL-1R1 signaling is IL-1 receptor accessory protein (IL-1RAP). In response to IL-1β, IL-1R1 engages IL-1RAP and activates NF-kB or p38 MAPK leading to downstream effects. In this study, we aimed to determine if IL-1RAP deficiency has any effect on tau pathology and neurodegeneration. We assessed tau pathology in hippocampi of LPS-injected mice with global IL-1RAP knockout and PS19 mice with myeloid/microglial IL-1RAP knockout by western blot, immunofluorescence, and immunohistochemistry, and Gallyas silver staining. Both LPS-injected IL-1RAP global knockout mice and PS19 mice with myeloid conditional knockout showed a significant decrease in their ptau levels compared to their controls. Our data suggests that global deletion of IL-1RAP decreases tau pathology in an LPS model of systemic inflammation. IL-1RAP deficiency in myeloid/microglial cells in PS19 mice also results in reduction of ptau levels which suggests that the myeloid/microglial knock out of IL-1RAP is sufficient to bring down the ptau levels in the brain. This might be due to how the IL-1 signaling is regulated in different cells and at the receptor level which needs further investigation.

24 Urine Anxiety Chronic Pain Model

Karin High, Sascha Alles, and Marena Montera

Chronic stress is linked closely with mood disorders such as anxiety and depression. These behaviors can be measured to understand chronic pain more effectively. Previous studies have shown that similar pathways are used to treat both chronic pain and chronic anxiety. In this study a predatory stress model offers a non-physical pain stimulus as an avenue to invoke an anxiety response. To mimic a predatory situation, the behavior of BALB/c mice in response to regular exposure to coyote urine was analyzed. The use of a non-physical stressor elicits a similar response to the stress that an adult experiences daily. This model offers new insight into a different type of chronic pain and its response to treatment. The common side effects of extended stressors, anxiety and depression, are easily measured in the behavior of mice. This study aimed to first identify if coyote urine could be used to elicit a predatory response that is consistent with physical chronic pain models. These responses would then be tested against the effects of a cholecystokinin B receptor antagonist. Using an antagonist of CCKBR offers a non-opioid treatment for chronic anxiety. The CCKBR is shown to be up-regulated during chronic neuropathic pain models and by blocking this ligand, it's hoped to decrease pain responses. Our study finds trends that support CCKBR as an avenue to reduce mood disorders in mice experiencing chronic anxiety. Three anxiety behavior models were used in this study; the Light/Dark Box, the Sucrose Test, and the Zero Maze. These anxiety models assess the rodents behavior against normal performance. Anxious and depressive moods often result in the mice varying from the baseline in vehicle groups and returning to baseline for treated. Behaviors such as grooming, rearing, aversion to light, and aversion to novel areas were all analyzed. The coyote urine study was a short chronic anxiety model conducted over five weeks. The findings suggest trends that the coyote urine did result in chronic anxiety. The Chronic Anxiety Urine Paradigm shows a variance from baseline for both the vehicle and treated groups. The Light/Dark Assay shows the effects of CCKBR antagonist bringing the treated mice back to baseline levels. The study brings light to the effectiveness of coyote urine as a model while also suggesting the success of CCKBR antagonist as a novel therapeutic for treating both chronic pain and chronic stress.

25 Comparison of novel virus-like particle vaccines against tau in a mouse model of Alzheimer's disease.

Jonathan Hulse. Niccole Maphis. Julianne Peabody. Bryce Chackerian. Kiran Bhaskar.

Alzheimer's disease (AD) is characterized by the accumulation of tau tangles and amyloid-β plaques in the brain with accompanied neurodegeneration. Phosphorylation of tau at specific sites occurs early in the disease process and has been shown to drive tau pathology which correlates with disease progression. Promoting the clearance of pathological tau may be a useful therapeutic strategy. Previously, we developed Qβ bacteriophage virus-like particle (VLP) vaccines displaying phosphorylated Thr181 tau peptides that promoted robust immune response, tau clearance, and improved memory. Here we report characterization and comparison of a Qβ-PHF-1-VLP and a Qβ-AT8-VLP vaccine. Transgenic rTg4510 mice were administered three bi-weekly intramuscular injections of Qβ control or Qβ conjugated to peptides corresponding to the tau PHF-1 site or the tau AT8 site. Serum antibody titers were assessed using ELISA. Cognitive function was assessed using Morris Water Maze (MWM) and Novel Object Recognition (NOR) tasks. Western blot and immunohistochemical analyses were performed to assess the levels of phosphorylated and aggregated tau. Both Qβ-PHF-1 and Qβ-AT8 vaccination induced a robust antibody response compared to Qβ control. Qβ-PHF-1 significantly reduced phosphorylated and Sarkosyl-insoluble tau in the brain compared to Qβ control while Qβ-AT8 did not. Qβ-PHF-1 vaccination ameliorated delay-dependent memory deficits assessed by NOR but did not rescue spatial memory deficits assessed by MWM (unlike Qβ-pT181 which also rescues spatial memory-PMID: 31428463). Qβ-AT8 failed to rescue any deficits in delay-dependent or spatial memory. Qβ-PHF-1 also reduces inflammatory microgliosis observed by immunohistochemistry compared to Qβ control. In summary, Qβ-PHF-1 vaccine outperforms the Qβ-AT8 vaccine, but both are less efficacious than Qβ-pT181.

26 Preoperative frailty measured by risk analysis index predicts complications and poor discharge outcomes after Brain Tumor Resection in a large multi-center analysis

Rachel Thommen, Syed Faraz Kazim, Kavelin Rumalla, Alexander J. Kassicieh, Piyush Kalakoti, Meic H. Schmidt, Rohini G. McKee, Daniel E. Hall, Richard J. Miskimins & Christian A. Bowers

Background: To evaluate the independent effect of frailty, as measured by the Risk Analysis Index-Administrative (RAI-A) for postoperative complications and discharge outcomes following brain tumor resection (BTR) in a large multi-center analysis. Methods: Patients undergoing BTR were queried from the National Surgical Quality Improvement Program (NSIQP) for the years 2015 to 2019. Multivariable logistic regression was performed to evaluate the independent associations between frailty tools (age, 5-factor modified frailty score [mFI-5], and RAI-A) on postoperative complications and discharge outcomes. Results: We identified 30,951 patients who underwent craniotomy for BTR; the median age of our study sample was 59 (IQR 47–68) years old and 47.8% of patients were male. Overall, increasing RAI-A score, in an overall stepwise fashion, was associated with increasing risk of adverse outcomes including in-hospital mortality, non-routine discharge, major complications, Clavien-Dindo Grade IV complication, and extended length of stay. Multivariable regression analysis (adjusting for age, sex, BMI, non-elective surgery status, race, and ethnicity) demonstrated that RAI-A was an independent predictor for worse BTR outcomes. The RAI-A tiers 41–45 (1.2% cohort) and >45 (0.3% cohort) were ~4 (Odds Ratio [OR]: 4.3, 95% CI: 2.1–8.9) and ~9 (OR: 9.5, 95% CI: 3.9–22.9) times more likely to have in-hospital mortality compared to RAI-A 0–20 (34% cohort). Conclusions: Increasing preoperative frailty as measured by the RAI-A score is independently associated with increased risk of complications and adverse discharge outcomes after BTR. The RAI-A may help providers present better preoperative risk assessment for patients and families weighing the risks and benefits of potential BTR.

27 Neurodevelopmental Transcription Factors Promote Proliferation, Regulate Cell Type, and Play Opposing Roles in Cellular Migration in Glioblastoma

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Glioblastomas (GBM) make up ~50% of primary brain tumors and prognosis has not improved over the last 30 years. Despite the inherently high inter- and intratumoral heterogeneity of GBMs, basic-helix-loop-helix (bHLH) transcription factors, ASCL1 and OLIG2, are present in the majority of tumors. Previously, we showed in patient-derived GBM xenograft (PDX-GBM) that ASCL1 binds to promoter and enhancer regions of cell cycle genes, as well as neurodevelopmental transcription factors including OLIG2. Similarly, we showed that OLIG2 binding overlaps with the majority (~90%) of ASCL1 binding sites, including at promoter and/or enhancer regions of ASCL1 and OLIG1/2 loci, illustrating their potential redundant and/or feed-forward function in GBM. It has been proposed that ASCL1 and OLIG2 contribute to the neural stem cell-like properties of tumor cells, which may promote tumor growth and progression but also the treatment resistivity and high recurrence rate of GBMs in patients. Using an immune competent glioma mouse model, we are able to efficiently induce tumors from glial progenitors surrounding the lateral ventricle while altering the levels of ASCL1 and OLIG2 to assess their combinatory roles in GBM progression. Remarkably, we found that loss of both Ascl1 and Olig2 prevents tumor formation, whereas the loss of only Ascl1 resulted in reduced cellular migration from the tumor bulk while the loss of Olig2 promotes a highly migratory phenotype. Conversely, elevating the levels of Ascl1 increased both tumor cell proliferation and migration similar to the loss of OLIG2. Using single cell RNA-sequencing, we found that tumor cells which express high levels of Ascl1 exhibit neural stem cell/astrocytic gene signatures, which supports ASCL1's role as a marker of glioma-stem-cells. Collectively, these findings illustrate the role of ASCL1 and OLIG2 in regulating GBM initiation, proliferation, and migration where ASCL1 may directly be responsible for the highly invasive and proliferative phenotype of GBMs.

28 Alzheimer's Disease-associated circHomer1 can inhibit the expression of long APP and MAPT mRNA isoforms in the frontal cortex via competing for binding to HuD.

Madison Otero, Grigorios Papageorgiou, Sophie E Eckel, Marissa R Westenskow, Ibrahim El-Sharkawy, Niko Nykänen, Bruno A. Benitez, Carlos Cruchaga, Nikolaos Mellios.

Circular RNAs (circRNAs) are a novel category of non-coding RNAs derived from the back-splicing and covalent joining of exons or introns. Recent studies have suggested that circRNAs are preferentially generated from synaptic plasticity-related genes and are particularly enriched in the brain. Although some circRNAs have been found to sequester microRNAs and others to associate with RNA-binding proteins (RBPs), the mechanism of action of most circRNAs remains poorly understood. Moreover, little is known about the potential involvement of circRNAs in Alzheimer's disease (AD). Using circRNA-specific quantification, we had previously found that circHomer1, a neuronal-enriched circRNA derived from Homer protein homolog 1 (HOMER1) capable of regulating cognitive function, is significantly downregulated postmortem brains of patients with AD and robustly associated with clinical dementia ratings and AD-associated neuropathology. Here we show that in vivo knockdown (KD) of circHomer1 in mouse frontal cortex results in a significant upregulation of long Amyloid precursor protein (APP) and microtubule-associated protein tau (MAPT) mRNA isoforms, of which accumulation of their respective encoded proteins are the pathological hallmark of AD. Furthermore, we show that circHomer1 is predicted to directly bind to both of these mRNA isoforms, potentially competing for binding with ELAV-like protein 4 (ELAVL4 or HuD), an RBP associated with AD and known to both bind to circHomer1 and associate with the long APP mRNAs, to promote their stability. Lastly, we demonstrate that circHomer1 is reduced in iPSC-derived neurons from subjects with AD and in the cortex of the 5xFAD model of AD. Ongoing experiments are aimed at further investigating the role of circHomer1 in APP and MAPT gene regulation and AD-associated pathogenesis and examining the effects of different drugs on brain circHomer1 expression. Taken together, our work introduces novel molecular networks with potential importance for AD.

29 Tyrosine phosphatase STEP is a key regulator of post-ischemic inflammatory response under hypertensive condition

Prabu Paramasivam, Seong Won Choi, Ranjana Poddar, Surojit Paul

Background: Hypertension, the most common comorbid condition in stroke patients worsens stroke outcome. The canonical pathway of stroke-induced brain damage involves excessive glutamate receptor activation. Post-ischemic inflammation further contributes to the pathogenesis of stroke outcome under comorbid conditions. In earlier studies we developed a novel therapeutic target TAT-STEP, derived from the brain-enriched and neuron specific tyrosine phosphatase STEP, which has been shown to be effective in reducing stroke induced brain damage in the absence of any associated comorbidities. In the current study we evaluated the post-ischemic inflammatory pathways that contribute to the exacerbation of ischemic brain injury under hypertensive conditions and further assessed whether the STEP-derived peptide can attenuate such post-ischemic inflammatory response. Methods: Transient ischemic stroke was induced in both normotensive and hypertensive rats by occlusion of the middle cerebral artery for 60 min followed by reperfusion. In a subset of these rats the STEP-derived peptide was administered intravenously at the onset of reperfusion. Coronal brain sections were processed for histopathological studies and cortical lysates from the ischemic hemisphere were processed for RNA preparation or immuno-blotting. Results: Evaluation of ischemic brain damage by Fluoro-Jade staining show an early onset and exacerbation of ischemic brain damage under hypertensive condition. An early onset in post-ischemic inflammatory response is also evident under hypertensive condition that involves sustained activation of ERK MAPK/ADAM10 signaling in neurons, increased expression of the neuronal chemokine, CX3CL1 and specific cytokines, increased microglial activation and blood-brain barrier permeability. Restoration of STEP signaling attenuates these post-ischemic inflammatory responses. Conclusions: The ability of the STEP-derived peptide to attenuate such increase in post-ischemic inflammatory response under hypertensive conditions could lead to a new direction for stroke treatment that could reduce the detrimental impact of inflammation in the early stages of ischemia, without affecting its beneficial factors in the recovery phase.

30 Repeated concussions and spreading depolarizations are associated with acute behavioral deficits

Natalie J Pinkowski, Betty Fish, Carissa J Mehos, and Russell A Morton

It is estimated that more than 42 million individuals have a concussion or mild traumatic brain injury every year. These injuries are accompanied by acute symptoms including disorientation, impaired motor coordination, and altered mental state. These symptoms are attributed to neurological impairment caused by disruptions in ion gradients and neurotransmitters. Recently, spreading depolarizations (SDs) have been shown to occur in concussion model injuries. SDs are massive waves of chemical and electrical changes that spread slowly in a unique way through grey matter of the brain. Our previous work found that an SD is sufficient to produce the acute symptoms of a concussion in a preclinical model. In those studies, SDs were initiated from a concussion model, and compared to those initiated without mechanical force: chemically with a KCl injection, and optogenetically with light stimulation on a transgenic mouse. The SDs with and without mechanical pressure onto the head resulted in the same acute behavioral symptoms in an open field arena and on a series of neurological severity score tasks (Wald-$\chi 2$=11.751, p=0.003). Our current research is investigating repeated concussions, comparing no injury, a single injury, and two injuries at different time intervals. To investigate the neuroimmune response following repeated impacts, we are analyzing astrocyte and microglia activation in the brain, in addition to acute behavioral symptoms in open field and on the neurological severity score tasks. These data show an increase in behavioral deficits and an increase in mitochondria activation after repeated concussive injuries. Future studies will add repeated SDs initiated with optogenetic stimulation to compare to the SDs induced with concussion models.

31 Syllable Diadochokinesis in Professional Boxers and Mixed Martial Artists

Amy Neel, Ninel Hernandez, Jessica Richardson, Lauren Bennett, Sarah Banks, Aaron Ritter, Charles Bernick

Syllable Diadochokinesis in Professional Boxers and Mixed Martial Artists. Background: Recent studies in our laboratory have documented slower speech rates in passage readings for boxers and mixed martial artists (MMAs) compared to healthy controls. Diadochokinetic rate tasks (DDK), where syllables are repeated as quickly as possible, more directly measure speech motor abilities than reading or spontaneous speech tasks (e.g., less cognitive/linguistic confounds). We investigated DDK rates for professional boxers, MMAs, and controls with no history of RHI. Methods: Participants were 27 professional boxers, 37 professional MMA fighters, and 30 controls ranging in age from 20 to 77 years of age from the Professional Athletes Brain Health Study. They were asked to repeat the syllable /kΛ/ as rapidly and evenly as possible for at least 10 seconds. Three measures for each set of /kΛ/ repetitions were obtained: average syllable repetition rate (DDK avr) and two measures of regularity: coefficient of variance of period and coefficient of variance of intensity. Results: The three groups differed significantly in DDK avr, $H(2) = 23.01$, $p < .01$, and the effect size was large ($d = 1.1$). DDK rate for boxers was 4.85 syls/s (SD = 1.13, range = 2.1 – 7.3), for MMAs was 5.48 (SD = 0.9, range = 3.2 – 6.7), and for controls was 6.33 (SD = 1.10, range = 4.1 – 9.5). Boxers produced slower DDK rates than controls, $H(1) = -34.31$, $p < .01$ but did not differ significantly from MMAs, $H(1) = -13.82$, $p = .27$. MMAs also produced slower repetition rates for /kΛ/ than controls, $H(1) = -20.48$, $p = .02$. Measures of stability showed little difference among the groups was found. Discussion: The average DDK rate for boxers was nearly 1.5 syllables per second slower than for controls, and MMA fighters averaged 0.85 syllables per second slower than controls. Professional fighters exhibited evidence of speech motor impairment associated with RHI. Speech DDK tasks show promise for assisting in the diagnosis of subtle motor impairment in head injury, even for individuals with no overt speech impairment.

32 Apoptosis-associated speck-like protein containing a CARD (ASC) as a potential biomarker of dementia in cerebrospinal fluid

Kathryn Sánchez, Shanya Jiang, Sasha Hobson, Jeff. F. Thompson, Sharina P. Desai, Gary A. Rosenberg, and Kiran Bhaskar

Dementia impacts about fifty-five million individuals world-wide, and this number is expected to double every twenty years according to the World Health Organization. Though amyloid beta plaques and neurofibrillary tangles comprised of the hyperphosphorylated microtubule-associated protein tau are established hallmarks of dementia, inflammation is critical to its pathology. In a pathological state, microglia, which are the innate immune cells of the brain, assemble a multiprotein complex called the inflammasome. The inflammasome is composed of the NACHT, LRR, and PYD domain-containing protein 3 (NLRP3); the adaptor protein apoptosis-associated speck-like protein containing a CARD (ASC); and inflammatory caspase 1 (cysteine-dependent aspartate-directed protease 1). The ASC and pro-caspase 1 components of the complex lead to the activation of caspase-1, which can facilitate the cleavage of IL-1β and IL-18. Upon labeling for ASC, the inflammasome complex appears as a speck. This visualized "ASC-speck" is approximately 1 μm in diameter, secreted into the extracellular space, and is capable of cross-seeding in a prionoid-manner. Our recent study in a small patient population (PMID: 34551296) detected ASC-specks in the cerebrospinal fluid (CSF) of patients with tauopathies. However, it is unclear if ASC-specks could serve as a potential biomarker in a larger patient cohort. To determine if ASC is a feasible biomarker of disease, flow cytometry was utilized to quantify ASC specks in CSF. Here, we report for the first time to our knowledge that levels of ASC specks are significantly increased (p= 0.0033) in the CSF samples of dementia patients (n=18;1.9x104 specks/μL ± 1918) in a group primarily comprised of AD patients compared to community member controls (n=11; 1x104 specks/μL ± 1756). Preliminary investigations suggest that the amount of ASC in the CSF correlates with phosphorylated threonine 181 tau (pT181+ tau). Together, these studies suggest that ASC-speck levels could serve as a valid inflammatory biomarker for dementia diagnosis and supplement pT181+ tau levels in the CSF.

33 Pathological tau regulates autophagy and inflammation in microglia

Karthikeyan Tangavelou, Shanya Jiang, Michael A Mandell, Rakez Kayed and Kiran Bhaskar

Hyperphosphorylated tau monomers and its conformers - oligomer, paired helical filaments (PHFs), and neurofibrillary tangles (NFTs) can be cleared by brain-resident immune cells "microglia". However, microglial function is dysregulated in Alzheimer's disease (AD) and other tauopathies, causing "cytokine storm" and spreading of protein aggregation in various regions of the brain. Autophagy is well known for its anti-inflammatory function by degrading inflammasome components besides its role in protein homoeostasis, which is impaired in neurodegenerative diseases. Here, we found impaired autophagy (accumulation of p62 and LC3B-II) in human microglial cell line and iPSC-derived human microglia cells (iMGLs) treated with lysates from hTau, but not non-transgenic, mouse brain, and purified tau monomer. Surprisingly, a canonical inflammatory NF-kB pathway inhibitor protein, IkBα was also coincidentally accumulated, suggesting that autophagy likely regulates NF-kB-inflammation. Next, mouse bone marrow macrophage cells (BMM) treated with human tau oligomers and PHFs showed accumulation of galectin 3 (marker of endo-membrane damage) and p62 (autophagy receptor) puncta, suggesting that endocytosed pathological tau damages membranous vesicles or intracellular organelles. Activation of inflammatory NF-kB pathway by pathological tau was also confirmed by NF-kB luciferase reporter assay in mouse microglia BV2, astrocyte C8D1A, and BMMs. Together, these results suggest the gain-of-toxic-function of tau in driving NF-kB-mediated inflammation via impairing autophagy.

34 Differential Contributions of GluN2A- and GluN2B- containing NMDA Receptors to Tissue Recovery after SD

Jordan E. Weisend, C.W. Shuttleworth

Spreading depolarizations (SDs) are now recognized as a principal source of excessive glutamate accumulation in stroke. It is not yet known whether different NMDA receptor (NMDAR) subtypes contribute to progression of SD or damaging effects of SD in vulnerable tissues. We examined possible contributions of GluN2A- and GluN2B-containing NMDARs to SDs in healthy and vulnerable tissues. Focal microinjection of KCl was used to initiate SDs in the hippocampal CA1 subregion of murine brain slices. Intrinsic optical signals (iOS) monitored SD propagation and tissue swelling. Extracellular potential changes ("DC shifts") were used to examine prolonged depolarizations previously linked to neuronal injury. Field excitatory postsynaptic potentials (fEPSPs) provided an additional measure of functional recovery. DC shifts, iOS, and fEPSPs were fully recoverable after SD in healthy recording conditions, but are persistently suppressed in vulnerable tissues where metabolic substrate supply was reduced by flow restriction. Non-selective inhibition of NMDARs (MK801 or APV) caused concentration-dependent inhibition of SD initiation/propagation and reduced the duration of DC shifts. Selective inhibition of GluN2A-containing NMDARs (NVP-AAM077, 300nM) slowed SD propagation (4.2±0.8 vs. 3.4±0.8 mm/min, control vs NVP-AAM077, $P<0.05$, n=7), while GluN2B inhibition (Ro 25-6981, 1μM) was without effect. Neither GluN2A- nor GluN2B- antagonism affected fEPSP recovery rate in healthy tissues (n=4-6, $P=0.38$). In vulnerable tissues, GluN2B-antagonism did not protect tissues from SD induced injury, but GluN2A-antagonism significantly improved fEPSP recovery rate (24.3±9.8 vs 101.4±51.2% baseline, control vs NVP-AAM077, $P< 0.05$, n=7) and iOS recovery (110.9±6.3 vs 127.9±6.1, control vs NVP-AAM077, $P< 0.05$, n=6) after SD. While previous work has often implicated GluN2B-containing receptors in damaging excitotoxicity, these results suggest instead that GluN2A-contining NMDARs activated by SD-induced increases in extracellular glutamate is more likely to contribute to tissue detriment. Selective targeting of these receptor subtypes during SD events may provide an adjunct approach to limiting progression of stroke.

35 Rodent Models of Subconcussive Brain Injury

Colin M. Wilson, Russell Morton, Afshin A. Divani, Kimberly Byrnes, Reed Selwyn

Subconcussion has been defined as a cranial impact or rapid acceleration-deceleration that does not result in clinically observable neurological signs or symptoms that would typically indicate a diagnosis of mild traumatic brain injury (mTBI) or concussion. Low-level subconcussive impacts due to soccer ball heading have been reported to cause an acute, transient dysfunction in vestibular processing, which returns to baseline levels within 24 hours. Although one or even several subconcussive impacts may have no lasting effects, there is increasing evidence that repeated subconcussive exposure over an extended period has the potential to cause significant neurological deficits. Among former professional contact-sport athletes, repetitive head impact (RHI) exposure has been associated with increased rates of neurodegenerative disease, leading to chronic traumatic encephalopathy (CTE) dementia or death. Strong evidence of a causal link between RHI and the development of CTE has been established using a combination of human neuropathological examinations and animal models. While mild traumatic brain injury has been an active area of research for more than 20 years, relatively little is known about subconcussive brain injury. However, a growing body of literature suggests that it may also pose a health risk for the general public. Structural and functional alterations have been observed in amateur contact-sport athletes as young as adolescents, often with no concussion history. Neuroimaging studies have detected longitudinal white matter changes in athletes sustaining subconcussive head impacts that correlate with head impact exposure.Youth athletes exposed to repetitive head impacts demonstrate impaired cognitive performance, and cumulative impact exposure strongly predicts neurocognitive impairment and neuropsychiatric dysfunction later in life. In recent years, novel models of subconcussive brain injury have been developed to better understand this phenomenon. This presentation will provide an overview of emerging rodent models of subconcussive brain injury, including a summary of recent behavioral, histopathological, and biomarker findings.

36 Do you need equipment and/or resources to complete your research? We are here to help you and your team!

J. Kevin Wilson, MS, Jude Chavez, BS, Karen Luo, BS, John Romero, BS, Ethan Campbell, MS, Janet Adams, MS, Marcus Sterling, BS, Sarah Ward, BS, Adam Littleton, BS, Michel Torbey, MD, Jeremy Hogeveen, PhD, Jessica D. Richardson, PhD, CCC-SLP, Davin Quinn,

The Center for Brain Recovery and Repair was established as a clinical and preclinical neuroscience Center of Biomedical Research Excellence. Our Clinical Core is an Albuquerque based, user-friendly human participants research hub. We provide expert consultation, mentoring/training, cutting-edge electrophysiological, neurostimulation, neuroimaging, and neuropsychological instrumentation, and technical support on a fee-for-use basis for clinical neuroscience investigators seeking to advance discoveries and treatments that will lead to improved outcomes for those affected by brain and behavioral conditions.

37 Progressive endothelial S1PR1 disruption and BBB dysfunction in cerebral microvasculature induced by chronic hypoxic hypoperfusion

Yi Yang , Jeffrey Thompson, Kelsey Duval, Sasha Hobson, Karen SantaCruz K, Michael Griego

Background: Clinical and neuroimaging studies suggested a fundamental role of BBB leakage in the progressive development of cerebral small vessel disease (SVD) pathology. The capillary barrier and survival are regulated by sphingosine-1-phoshate (S1P) and its receptor isoforms (S1PRs). Disruption of endothelial S1P signalling leads to capillary dysfunction, BBB breakdown, and perivascular inflammation. Aim: To test the hypothesis that chronic hypoxic hypoperfusion down-regulates capillary endothelial S1P receptor 1 (S1PR1), compromising BBB integrity and leading to neuroinflammation, we used a rat model of SVD. Method: Spontaneously hypertensive stroke-prone rats underwent unilateral carotid artery occlusion (UCAO) followed by a Japanese permissive diet (JPD) for up to 9 weeks. Selective S1PR1 agonist SEW2871 was used to activate S1PR1. MRI, Western blot, and histology were used for measurements. Results/Conclusions: Significant reduction of endothelial S1PR1 was detected at 4 and 9 weeks following UCAO/JPD onset. The endothelial S1PR1 reduction was also seen in human SVD brains. We also found that significant accumulation of pTau in cortex neurons at 9 weeks, when the rats developed extensive inflammation. The timeline of the accumulation of pTau is consistent with significant reduction of S1PR1 seen at 9 weeks. S1PR1 activation by SEW2781 treatment reduced white matter lesions, preserved cerebral blood flow, and significantly reversed the loss of endothelial tight junction proteins induced by the UCAO/JPD. This protective role of the SEW2871 are associated with changes in PI3K/Akt/Rac signalling pathway. Our data suggest that hypoxic hypoperfusion triggers disruption of S1P-S1PR1 signalling, leading to endothelial injury and BBB dysfunction in SVD.

38 The RPL/RPS gene signature of melanoma CTCs associates with brain metastasis

Bowley, T., Lagutina, I., Francis, C., Sivakumar, S., Selwyn, R., Taylor, E., Yan Guo, Bridget N. Fahy, Bernard Tawfik, and Dario Marchetti

Melanoma brain metastasis (MBM) is linked to poor prognosis and low overall survival. We hypothesized that melanoma circulating tumor cells (CTCs) possess a gene signature significantly expressed and associated with MBM. Employing a multi-pronged approach, we provide first-time evidence identifying a common CTC gene signature for ribosomal protein large/small subunits (RPL/RPS) which associate with MBM onset and progression. Experimental strategies involved capturing, transcriptional profiling and interrogating CTCs, either directly isolated from blood of melanoma patients at distinct stages of MBM progression or from CTC-driven MBM in experimental animals. Second, we developed the first Magnetic Resonance Imaging (MRI) CTC-derived MBM xenograft model (MRI-MBM CDX) to discriminate MBM spatial and temporal growth, recreating MBM clinical presentation and progression. Third, we performed the comprehensive transcriptional profiling of MRI-MBM CDXs, along with longitudinal monitoring of CTCs from CDXs possessing/not possessing MBM. Our findings suggest that enhanced ribosomal protein content/ribogenesis may contribute to MBM onset. Since ribosome modifications drive tumor progression and metastatic development by remodeling CTC translational events, overexpression of the CTC RPL/RPS gene signature could be implicated in MBM development. Collectively, this study provides important insights for relevance of the CTC RPL/RPS gene signature in MBM, and identify potential targets for therapeutic intervention to improve patient care for melanoma patients diagnosed with or at high-risk of developing MBM.

39 The Littlest Thinkers: Neonatal Cognitive Development Investigation Using EEG

Kate Cody-Cavanagh, Aaron Cardon, Jessie Maxwell, Dawn Novak, Neurodiagnostics Lab

This is an ongoing research study investigating neonatal cognitive development using EEG (electroencephalogram) and auditory event-related potentials (AERPs). Very little is known about the cognitive brain development in neonates, and even less is known about neonates who have neurologic concerns, as they are often excluded from participation in other developmental studies. We used a non invasive and non participatory method for analyzing cognition by way of the mismatched negativity (MMN) event related potential. This is a cortically evoked electrophysiological response to the brain's awareness of a change in auditory stimuli. The negative EEG deflection that occurs between 150-400ms after a time-locked surprising sound is highly sensitive to cognitive abilities. We expect a more robust AERP response to negatively correlate with the neonate's clinical outcome such as length NICU stay, duration of supplemental oxygen, and time to full nipple feeds. To date we have collected data on three participants. All three were on HIE cooling protocol and completed the task while on cooling, and again once rewarmed.
Aim#1- Gather within subject AERPs on neonates who are receiving an EEG during both the cooling and rewarming phases for neonatal therapeutic hypothermia. Aim#2- Run the MMN paradigm on neonates that are receiving an electroencephalogram as part of their clinical management to investigate how neurologic concerns, such as seizures, influence their AERP response. Aim#3- Gather characteristics from those participants who attend a follow up exam a few months after discharge from the NICU. Neonatal characteristics to be collected include, but are not limited to age, weight, MRI (magnetic resonance imaging) results, cerebral ultrasound brain characteristics, temperature, medications, respiratory support, feeding method, date of full nipple feeds, NICU discharge date, and birth complications.

40 Observed Differences In Goal-Directed Actions Among Individuals Affected By Covid-19

Jude Chavez, Kevin Wilson, Karen Luo, Sarah Ward, Marcus Sterling, Adam Littleton, John Romero, Ethan Campbell, Darbi Gill, Richard Campbell, Jeremy Hogeveen, Jessica Richardson, Davin Quinn

The neurological complications of COVID-19 are fearsome and not understood Ischemic strokes, meningo-encephalitis, peripheral nerve damage, agitated delirium, dysosmia, and psychiatric disturbances have all been extensively documented. SARS-CoV-2 appears to directly invade neural tissue and triggers states of hypercoagulability, immune system activation, and hypoxemia, all of which contribute to severe brain dysfunction and possible damage in the acute phase. The motivation to initiate action is central to adaptive functioning but is impaired in a variety of neurological and psychiatric disorders. In particular, a significant number of patients with traumatic brain injury (TBI) demonstrate clinically-significant apathy - i.e., a negative change in goal-directed actions-which can significantly impact patients' lives and persist long after the injury event. We hypothesize that individuals with COVID-19 diagnosis will show an increase in apathy along with a decrease in willingness to explore novel choice options and greater effort-based discounting of rewards. Here, we merged computational modeling of 'explore-exploit; decision-making (i.e, flexibly deciding whether to explore a novel option versus exploiting a familiar one) and effort-based decision-making during fNIRS in patients with COVID-19 diagnosis. Behavioral results indicated that COVID-19 patients with elevated apathy demonstrate the reduced exploration of novel choice options, and greater effort-based discounting of rewards, suggesting that the anticipated costs associated with flexible decision-making may interact to shape apathy in COVID-19 diagnosis. fNIRS analyses are ongoing but will test the hypotheses that neural computations critical for explore-exploit decision flexibility and effort estimation are both disrupted in individuals with COVID-19 diagnosis and increased levels of apathy. A greater understanding of the neurocomputational bases of apathy in COVID-19 diagnosis could shape the design of more effective brain-based interventions for normalizing goal-directed behavior in patients affected by COVID-19.

41 A Novel Methodological Approach of collecting MRI in newborns and infants without sedation in a multi-site consortium pilot study.

Lidia Enriquez Marquez; Tracey Wick; Crystal Almeida; Alexandria Wiesel; Arvind Caprihan; John Phillips; Ludmila Bakhireva; Andrew R. Mayer

Background: The HEALthy Brain and Child Development (HBCD) is a multi-site research study (25 sites) designed to prospectively examine brain and behavioral development beginning prenatally through mid-childhood. The study will determine the impacts of a variety of risk and resilience environmental factors, including prenatal exposure to substances, from a diverse sample of pregnant individuals and their live-born children. The study incorporates repeated neuroimaging and neurophysiological measures (magnetic resonance imaging, MRI). One aspect of the HBCD pilot phase focuses on optimizing non-sedation techniques to facilitate MRI data acquisition in newborns (<1 month) and infants (≤9 months).
Methods: Concerted efforts were devoted to maximize scanning rates in young populations at the national and local levels. At the New Mexico site, an MRI preparation room was developed specifically focusing on families with young children. Participants in both age groups were scanned without sedation at the Mind Research Network (MRN). MRI sequences included structural (T1/T2), diffusion, resting state, quantitative, and MR spectroscopy. Data was transmitted to the HBCD Data Coordinating Center where it underwent QC/QA processes. Results/Conclusions: Data from 3 newborns and 4 infants were collected. Participants were scheduled for evaluation either during a daily nap or evening sleep times. The highest number of successful frames (framewise displacement < 0.3 mm) for resting state and diffusion scans were 207/261 and 29/76 respectively. With respect to patient-related facilitators, flexibility and adaptability were crucial. A detailed sleep questionnaire helped facilitate success rates. Parents were allowed to stay in the room with the child during the MRI along with a designated baby monitor/RA for the duration of the scan. Additional comforting techniques utilized included debriefing the family, feeding and swaddling, infant immobilizer, use of MRI-safe weighted blanket, deformable wax plugs, pediatric MiniMuffs, and headphones playing white noise, minimizing interaction with the child and a low stimulation environment.

42 Effect of Recorded Maternal Voice on Quantitative EEG in the Preterm Newborn

Meghan Groghan, MD, Aaron Cardon, MD, Kate Cavanaugh, REEGT, Dawn Novak, MD

Background: Despite continued advances in quality medical care for premature infants, neurodevelopmental delay remains one of the most common complications of prematurity. It is also known that early diagnosis and intervention for developmental delays leads to improved outcomes. More recently, quantitative electroencephalogram (qEEG) has shown potential as a prognostic tool for identifying delays in preterm infants but remains an underutilized assessment. Maternal voice exposure has positive effects on autonomic stability and feeding vigor/tolerance in preterm infants. This novel study aims to investigate the effects of recorded maternal voice on qEEG patterns in preterm neonates. Methods: Prospective, randomized, placebo-controlled clinical trial with planned enrollment of 40 infants. Infants born at 24 0/7 - 32 3/7 weeks gestation, without congenital/neurologic anomalies, and admitted to the Newborn Intensive Care Unit (NICU), are eligible to participate. Enrolled infants have a baseline qEEG performed just prior to 33 weeks corrected gestational age (cga). A recording of their mother's voice or a blank control recording is then played for the infant (1 hour daily) for a 2-week intervention period (from 33-35 weeks cga). A second qEEG is obtained in the infant following the intervention period (from 35-36 weeks cga). The qEEG data is processed for quantitative spectral analysis. Results: Enrollment is ongoing, with n=7 at time of submission. We hypothesize that infants exposed to their mother's recorded voice will have an increase in higher-frequency alpha and beta spectral powers on qEEG. This has previously been shown to correlate with long-term neurodevelopmental outcomes. If pattern differences match previously published results, recorded maternal voice may be a useful addition to NICU developmental care strategies, and the use of qEEG as a screening/prognostic tool in the neonatal population could be further explored.
Next Steps: Continued enrollment, data collection and analysis.

43 Altered Neuronal Firing Following a Spreading Depolarization: an in vivo Study

Brandi R. Hess, Natalie J. Pinkowski, Carissa J. Mehos, Betty Fish, Russell A. Morton

Spreading Depolarizations (SD) are slowly propagating waves of tissue depolarization that result in the suppression of neuronal firing for multiple minutes. SDs are known to occur in rodents suffering from moderate or severe traumatic brain injuries and are also associated with visual auras that often-proceeded migraines. Our previous work established that SDs initiate in a closed skull concussion model in mice. The presence of SDs in our injury model is tightly associated with acute behavioral deficits that last hours. The behavioral deficits are attributed to neurological impairment, but a mechanistic understanding of that impairment remains unclear. We hypothesize that there is a period of altered neuronal firing that is associated with the period of acute behavioral symptoms of a concussion. Using two-photon microscopy we will investigate individual neuronal function with genetically encoded calcium indicators (GCaMP). The purpose is to measure the firing rate of an individual neuron prior to, during, and immediately after the acute recovery to assess baseline firing and recovery of individual neurons following an SD. In our preliminary data we have confirmed the complete suppression of neuronal firing immediately following the SD. We aim to determine the amount of time until neuronal firing returns to baseline rates following an SD.

44 Midbrain Degeneration and Cognition in Parkinson's Disease

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Neuromelanin imaging is an emerging biomarker for PD as it captures degeneration of the midbrain. Currently, it is unknown whether this degeneration contributes to cognitive dysfunction in PD beyond dysfunction associated with fronto-subcortical systems. Here, we examine whether neuromelanin signal is associated with broader cognitive dysfunction in PD patients with varying degrees of cognitive impairment: PD with normal cognition (PD-NC), PD with mild cognitive impairment (PD-MCI), and healthy controls (HC). 12 PD-NC, 18 PD-MCI and 19 HC underwent an MRI scan that included a neuromelanin-sensitive (NM-MRI) sequence. Contrast-to-noise-ratio of the substantia nigra pars compacta (SNc) and ventral tegmental area (VTA) was calculated. Analyses indicated a significant main effect of group ($p < 0.001$) for both SNc CRmode and VTA CRmode. PD-MCI patients exhibited significantly reduced SNc CRmode relative to HC. The same pattern was observed for the VTA CRmode whereby PD-MCI exhibited significantly reduced VTA CRmode relative to HC. PD patients exhibited decreased neuromelanin in the SNc and VTA relative to healthy controls, confirming the ability of the NM-MRI sequence to map neurodegeneration in Parkinson's Disease. There is a generally consistent relationship between SNc and VTA degeneration in PD, with SNc degeneration more strongly associated with worse cognitive performance in working memory and executive functioning tasks than VTA degeneration. These findings warrant further examination of the SNc and VTA in PD patients with varying levels of cognitive impairment.

45 Post-error adjustment enhances task-positive visual processing

Mark Lavelle, James F. Cavanagh

Our ability to discern multiple, simultaneous latent processes during the exertion of control is limited by rudimentary combinations of manifest behavior. We hypothesized that EEG could provide unique evidence that control can simultaneously alter behavioral output (i.e. decision threshold) as well as sensory gain (i.e. drift rate). This study includes EEG data from 21 young adults who completed a Flankers task where the luminance of the stimuli varied trial-wise against a black background. Conflict was associated with lower drift and lower threshold, as well as increased frontal midline theta power. Controlling for these effects, lower drift rate and threshold were signaled at the single trial level by enhanced peri-response frontal midline theta. Increased luminance was associated with higher drift as well as increased alpha-beta power in visual cortex. Visual alpha power, in turn, was associated with greater drift and threshold, with an even greater power-parameter slope for brighter stimuli. While trials following errors were associated with higher threshold but unchanged drift rate, visual alpha-beta power was significantly enhanced following errors. This suggests adaptations to errors involved enhancement of attention that was masked in behavior. Future work will investigate the role of frontal control systems in this attentional enhancement as well as localize the visual attention effects using MEG source estimation.

46 Comparison of Right vs Left Accelerated Resting-State fMRI-Guided Theta Burst Stimulation to the DLPFC for Late-Life Depression: A Pilot Study

Jude Chavez, Karen Luo, Crystal Garcia, Christopher Abbott, Davin Quinn

Background: While trials of accelerated, neuronavigated repetitive transcranial magnetic stimulation (rTMS) to the left dorsolateral prefrontal cortex (DLPFC) for depression have shown efficacy for depression, there has not yet been validation of this technique for late-life depression (LLD). Additionally, no studies have tested accelerated intermittent theta burst stimulation (iTBS) to the right DLPFC for depression, although it may benefit depression and anxiety. Methods: We enrolled 36 elderly patients (ages 50-79 years) with a diagnosis of pharmacoresistant depression of at least 6 months. Each participant received 45 sessions (5 treatments/day over 9 days) of iTBS to their functional MRI (fMRI) determined target. Additionally, each patient underwent fMRI and behavioral assessment pretreatment and after 15th and 45th treatments. The Inventory of Depressive Symptoms (IDS-30-C) measured changes in depressive symptoms and the Generalized Anxiety Disorder-7 (GAD-7) measured changes in anxiety symptoms. IDS-30-C was elicited at one and three months after treatment. Results: Mean age was 65 ± 6.9 years (36 patients). Mean IDS-30-C and GAD-7 scores decreased throughout study protocol: IDS-30-C – V1: 38.97 ± 9.6; V2: 31 ± 9.3; V3: 20.4 ± 10.2; GAD-7 – V1: 10.4 ± 5.4; V2: 8.9 ± 4.8; V3: 5.6 ± 5.1. There was a 18.6 point decrease in mean IDS-30-C scores from Visit 1 to Visit 3. Of 18 patients (mean age 63 ± 7.4 years), depression scores remained below pretreatment values at one and three months (20.34 ± 14.15). Updated right-vs-left stimulation data will be reported on conference day. Conclusions: Preliminary results showed accelerated fMRI-guided iTBS to the right DLPFC in patients with LLD was effective in reducing symptoms of depression and generalized anxiety. Updated right-versus-left sided stimulation conclusions will be reported on conference day.

47 Is There an Association Between Anxiety and Response Confidence?

Sofia Miranda, Garima Singh, Mark Lavelle, James F. Cavanagh

This project investigates the neuro-behavioral relationship between anxiety, error monitoring, and decision confidence. Individuals with heightened anxiety have larger neurobiological action monitoring signals, such as the Error Response Negativity (ERN) or Correct-Response Negativity (CRN): negative deflections in the trial-averaged EEG that occur when participants commit an erroneous or correct choice, respectively. Anxiety is associated with larger ERN amplitudes and lower decision confidence. Yet, response confidence is associated with both higher CRN amplitude as well as faster response time. It remains unknown how anxiety is related to these neural systems underlying decision confidence. The current study investigated ERN and CRN amplitudes in a sample of 69 individuals with varying levels of self-reported anxiety. Response times and ERN and CRN signals were investigated as participants completed a probabilistic learning task. We found that individuals with higher anxiety levels did not have any difference in post-error response slowing or post-correct response speeding. While there was no significant association between anxiety levels and CRN amplitude, there was a larger ERN signal in those with higher anxiety levels. Together, these findings indicate that anxiety affects internal error monitoring, but not reactive behaviors following errors. Together, these findings suggest that anxiety affects the experience but not the external expression of error monitoring.

48 Emotional faces and working memory in children with high autistic and anxiety traits

Teagan Mullins, Jeremy Hogeveen

While the impact of anxiety and autism on working memory has been investigated, conflicting findings have been reported. For both conditions, working memory has been reported to be intact, impaired, or improved, or variously modulated by other factors, including emotional content of stimuli, and neuroimaging findings have been varied. When looking at the combined effect of comorbidity, the picture is even less clear. Here, we determined whether a classic finding in the cognitive neuroscience of anxiety—increased salience and attention to negative emotional stimuli—varies across children who do or do not also have elevated autistic traits. Specifically, we used the Adolescent Brain Cognitive Development (ABCD) study dataset to compare threat or negative emotion bias across 4 well-matched subgroups of 9–10-year-old children: 1) high anxiety and low autistic traits (ANX;N=54), 2) high autistic traits and low anxiety (AUT; N=48), 3) high anxiety and autistic traits (ANX+AUT; N=51), and 4) low anxiety and low autistic traits (CTRL; N=52). We examined an n-back task that probed visual working memory and utilized emotional face stimuli (EN-Back), which allowed us to look at the behavioral and neural correlates of emotional faces on working memory in these groups. Behavioral Results showed no group differences in accuracy, reaction time, or d-prime scores across groups, indicating preserved working memory across groups, but main effects of stimuli were present, showing that emotional faces did alter working memory. Amygdala recruitment was sensitive to faces but not valence. Some modest evidence for enhanced neural recruitment in response to negative stimuli in high anxious and dual groups. This did not impact behavior.

49 Compensatory Functional Activation During Motion Discrimination in Parkinson's Disease

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Objective

PD patients commonly exhibit cognitive dysfunction early in the disease course which may or may not predict further cognitive decline. In contrast, early emergence of visuospatial and memory impairments are more consistent predictors of an evolving dementia syndrome. Prior studies using fMRI have demonstrated that PD patients exhibit hyperactivation dependent on the degree of cognitive impairment, suggestive of compensatory strategies. No study has evaluated whether PD patients with normal cognition (PD-NC) and PD patients with Mild Cognitive Impairment (PD-MCI) exhibit compensatory activation patterns during visuospatial task performance. Participants and Methods: 10 PD-NC, 12 PD-MCI, and 14 age and sex-matched HC's participated in the study. PD participants were diagnosed with MCI based on the Movement Disorders Society Task Force, Level II assessment (comprehensive assessment). FMRI was performed during a motion discrimination task that required participants to identify the direction of horizontal global coherent motion embedded within dynamic visual noise under Low and High coherence conditions. Behavioral accuracy and functional activation were evaluated using 3 × 2 analyses of covariance (ANCOVAs) (group [HC, PD-NC, PD-MCI] × Coherence [High vs. Low]) accounting for age, sex, and education. Results: PD-MCI (0.702± 0.269) patients exhibited significantly lower accuracy on the motion discrimination task than HC (0.853 ± 0.241; p = 0.033) and PD-NC (0.880 ± 0.208; p =0.039). A Group × Coherence interaction was identified in which several regions, including orbitofrontal, posterior parietal and occipital cortex, showed increased activation during High relative to Low coherence trials in the PD patient groups. HC showed default mode deactivation and frontal-parietal activation during Low relative to High coherence trials that were not evident in the patient groups. Conclusions: PD-MCI patients exhibited worse visuospatial performance on a motion discrimination task than PD-NC and HC participants and exhibited hyperactivation of the posterior parietal and occipital regions during motion discrimination, suggesting possible compensatory activation.

50 MEG reveals multiple sources to the Reward Positivity, only one of which is affected by Major Depression

Christopher J.H. Pirrung, Garima Singh, Davin Quinn, Jeremy Hogeveen, James F. Cavanagh

Anhedonia is a primary symptom of Major Depressive Disorder (MDD). In order to better understand this phenotypic dimension, we investigated a marker of reward that is sensitive to information content and valence, the Reward Positivity (RewP). This study used concurrent EEG and MEG to establish the source of the RewP in control and MDD participants. The RewP emerged as a distributed network involving ventromedial prefrontal cortex (vmPFC), anterior midcingulate cortex (aMCC), and bilateral insulae. Only the vmPFC differed between groups, whereas the aMCC/insula "salience network" areas were similarly responsive to reward prediction error. This suggests specific deficits in affective valuation in MDD. To further understand this pattern, we examined fMRI resting state functional connectivity analysis of these regions in the same participants. While vmPFC and aMCC were positively correlated at rest, this coupling was anticorrelated with depressive symptom scores within the MDD+ group. These findings suggest that, in addition to hypoactivation of vmPFC in response to reward, heavily depressed individuals may have a deficit in their ability to effectively balance the relative contributions of value and salience networks.

51 Depression Severity Relates to Lower Information Encoding in the RewP Following High Positive-Affect Feedback

Garima Singh1, Trevor C.J. Jackson1, Mark Lavelle1, Darin R. Brown2, James F. Cavanagh1

The Reward Positivity (RewP) is a positive deflection in the EEG sensitive to reward receipt. Recent evidence suggests that the RewP is modulated by both reward probability as well as affective valuation ("liking"). We hypothesize that this latter "liking" feature is specifically affected in major depression. We recruited 69 participants (MDD =35, Control= 34) who completed a reinforcement learning task (green or red screen feedback) with concurrent affective images. We specifically examined the modulation of the RewP when paired with hedonically preferred images (puppies) vs. less-preferred images (cows). There was no group difference in "liking" ratings of puppy or cow pictures, nor were there differences in RewP between groups. Our next hypothesis was that the affective information encoding (EEG-RPE Correlation) will be affected by depression severity. Across all participants, we found a significant correlation between BDI score and EEG-RPE encoding for hedonically affective imagery in depression group (win puppy; $r= -0.39$, $p=0.02$) confirming our hypothesis. Our results indicate an inter-individual influence of self- reported depression on Prediction Error Correlation for hedonic imagery. These findings suggest a motivation- specific diminution of hedonic encoding and responsiveness in people with high symptoms of depression.

52 It's all in your head": Abnormal visual processing during magnetoencephalography is associated with mild traumatic brain injury in US Veterans

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53 Slc7a5 (LAT1) inhibition alleviates chemotherapy-induced neuropathic pain

Sachin Goyal; Ian M. Adams; Sascha R.A. Alles

Background: Chemotherapy-induced neuropathic pain (CINP) is a debilitating and difficult-to-treat side effect of chemotherapeutic drugs. Effective, non-addictive, non-opioid therapeutics are urgently needed for the treatment of chemotherapy associated chronic pain. Slc7a5 (Lat1), also known as system L-neutral amino acid transporter, is involved in a number of physiological processes related to inflammation. Transcriptomics studies have shown that Slc7a5 and its binding partner Slc3a2 are expressed in neurons of the dorsal root ganglia (DRG) and spinal dorsal horn, which are critical to the initiation and maintenance of nociception and pathophysiology of chronic pain. Here, we investigate the role of Slc7a5 in the chemotherapy-induced peripheral neuropathy (CIPN) in rodents mainly using the Slc7a5 blocker, JPH203. Methods: The mice model of CIPN was established by 5 consecutive intra-peritoneal injections of oxaliplatin (1.0 mg/kg) in every alternative week for five weeks. CIPN mice were treated with either Slc7a5 blocker, JPH203 (12.5 mg/kg), or vehicle, administered intrathecally in a blinded, randomized manner. Pain behavior assessment was made by conducting paw withdrawal mechanical threshold (PWMT) test using von Frey filaments. The effects of JPH203 on nociceptor excitability were measured using whole-cell current clamp electrophysiology of isolated dorsal root ganglion (DRG) neurons. Conclusions: We found that blocking Slc7a5 with intrathecal administration of the drug JPH203 alleviated oxaliplatin induced mechanical allodynia. Using whole-cell current-clamp electrophysiology, we observed that JPH203 treatment reduced excitability of DRG neurons from chemotherapy-induced peripheral neuropathy (CIPN) mice, in agreement with its behavioral effects. Altogether, these results demonstrate that Slc7a5 is dysregulated in oxaliplatin induced chronic neuropathic pain and can be targeted to provide relief of hypersensitivity.

54 ASCL1 regulates astrocyte and oligodendrocyte cell fate, proliferation, and migration in the dorsal cortex.

Luis E Paez-Beltran; Milindu Lyanapathirana; Tou Y Vue

Background: Astrocytes and oligodendrocytes are part of the macroglia cell family, which is the most abundant cell type in the CNS. Glia progenitor cells (GPC) give rise to both lineages by differentiating in either astrocyte precursor cells (APC) or oligodendrocyte precursor cells (OPC), fate determined mainly by a few master regulators. ASCL1, a basic-helix-loop-helix (bHLH) transcription factor, is one of these developmental regulators expressed in progenitors' cells during neurogenesis and gliogenesis, but its specific role in fate, migration and proliferation remains yet to be elucidated. Methods: We employed an initial descriptive study to examine ASCL1 and OLIG2 distribution in the developing brain of E17.5, P0 and P2 mice (N=4). We notice the highest number of ASCL1+ cells at the upper SOX2- region of the ventricular zone (VZ) and opposing gradients of expression of ASCL1 and OLIG2. Next, we did a lineage tracing study of GPCs from each stage, E17.5, P0 and P2, and examine their progeny two days later and at P30. Spatiotemporal labeling of the litters from the crossed Ascl1CreERT2 and Ai14(RCL-tdT)-D transgenic mice lines was possible thanks to the CreER-loxP system induced temporally by tamoxifen and limited spatially to the ASCL1-expressing cells (N=4). We found that ASCL1+ GPCs give rise to both astrocyte and oligodendrocyte lineages that populate the gray and white matter of the adult mice brain at each labeled stage. Furthermore, GPCs from each stage exhibit different homing patters of their progeny such as significantly reduced labeled cells coming from E17.5 progenitors, and a dorsal-ventral cortical distribution pattern as development progresses. Conclusions: We found that ASCL1 is essential for determining the type, number and destination of glia cells in the mature mice brain. Further experiments analyzing downstream targets of ASCL1 are needed to identify the direct effectors of cell fate, migration and proliferation changes and evaluate their roles in mice neurodevelopment.

55 Renalase agonist, BP1002, alleviates visceral hypersensitivity and reduces excitability of pancreas-innervating neurons in a mouse model of acute pancreatitis.

Ian M. Adams; Marena Montera; Barry Berkowitz, PhD; Karin N. Westlund, PhD; Sascha R.A. Alles, PhD

Acute pancreatitis (AP) is a life-threatening gastrointestinal condition with many possible causes, the most common being chronic alcohol consumption. Severe epigastric pain is the most common presenting symptom of AP. Management of this pain relies on opioids and NSAIDs, and there is a need for alternatives for pain management in AP. We are studying the efficacy of novel therapeutic peptide and renalase agonist, BP1002, for treating pain in a mouse model of acute pancreatitis. BP1002 potentiates the activity of renalase, an enzyme with pro-survival and anti-inflammatory activities that has been found to be positively associated with better outcomes in both mice and humans. Our lab has demonstrated that administration of BP1002 in vivo reduces visceral pain response in a mouse model of AP. In this study we use whole-cell patch clamp electrophysiology to assess if administering BP1002 will reduce excitability of pancreas-innervating dorsal root ganglia neurons in mice with AP. Male BALB/c mice received injection of CTB555 into the long head of the pancreas to label afferent nerve terminals in the pancreas. After 2 weeks mice received BP1002 or vehicle injection at the beginning of a course of hourly injections of cerulein over two days (14 injections total). Bilateral thoracic dorsal root ganglia (T9-12) were then removed, enzymatically and mechanically dissociated and plated for overnight incubation. Whole-cell current clamp recordings were obtained from DRG neurons that contained the fluorescent CTB555 label. The firing frequency of recorded neurons was decreased in the mice that received BP1002, indicating a decrease in neuronal excitability. Future work will examine the molecular and cellular nature of pancreas-innervating neuronal subtypes implicated in the mechanism of action of BP1002. This study has far reaching clinical implications for the treatment of acute pancreatitis.

56 Preliminary Psychometric Testing of the Treatment Self-Regulation Questionnaire for Assessing Motivations for Responsible Cannabis Use: An Application of Self-Determination Theory

Haydee Andujo, Jakub D. Gren, Joey C. Mok, Ricardo A. Rubio, Dylan K. Richards, Matthew R. Pearson, & Addictions Research Team

Cannabis use protective behavioral strategies (PBS) are cognitive–behavioral strategies used before, during, and/or after cannabis use to reduce cannabis use and related problems. Self-determination theory (SDT) provides a potentially useful framework to understand motivations for responsible cannabis use, which is operationalized in the present study as PBS use. In the present study, we examined the relation of motivations for responsible cannabis use, as assessed by the 15-item Treatment Self-Regulation Questionnaire (TSRQ), with cannabis PBS use and other cannabis-related outcomes. A sample of 408 past month cannabis users were recruited from a multisite study of college students (n=1856). Consistent with SDT and previous studies of the TSRQ for drinking responsibly, we found support for a 4-factor structure of the TSRQ via Exploratory Structural Equation Modeling (CFI=.974, RMSEA=.047): autonomous motivation (important conscious valuing; “Because I personally believe it is the best thing for my health”), introjected regulation (internal rewards/punishments; “Because I would feel guilty or ashamed of myself if I did not use cannabis responsibly”), external regulation (external rewards/punishments; “Because others would be upset with me if I did not”), and amotivation (lacking intent; “I really don't think about it”). Consistent with SDT, introjected regulation was positively associated with cannabis PBS use (beta=.373, p<.001) and external regulation was negatively associated with cannabis use (beta=-.258, p<.001). Unexpectedly, autonomous motivation (beta=.142, p=.092) and amotivation (beta=-.012, p=.842) was not significantly related to cannabis PBS use. Our overall model (motivation→PBS use→cannabis use→consequences/symptoms) accounted for a substantial portion of the variance in cannabis-related outcomes including frequency of cannabis use (R-square=.301), negative cannabis-related consequences (R-square=.189), and cannabis use disorder symptoms (R-square=.441). Overall, our results partially support the predictions of SDT, suggesting the need for further development and refinement of the TRSQ for assessing responsible cannabis use.

57 Examination of Self-Determination Theory-Based Motivations for Using Cannabis Responsibly and Cannabis Use Motives as Predictors of Cannabis-Related Outcomes among College Students

Ricardo A. Rubio, Jakub D. Gren, Joey C. Mok, Haydee Andujo, Dylan K. Richards, Matthew R. Pearson, & Addictions Research Team

Cannabis use motives, or reasons people choose to use cannabis, are well-established risk factors for cannabis use and related negative consequences and include (in order of most to least risky) using cannabis to reduce negative affect (coping motives), increase positive affect (enhancement motives), to avoid negative social experiences (conformity motives), to enhance social experiences (social motives), and to expand one’s experiences (expansion motives). Our current research also examines motivations to use cannabis responsibly based on self-determination theory (SDT), which includes (in order of most to least protective) consciously valuing responsible use (autonomous motivation), seeking/avoiding internal rewards/punishments (introjected regulation), seeking/avoiding external rewards/punishments (external regulation), and lacking conscious motivations (amotivation). We examined the relationship between cannabis use motives and motivations for using cannabis responsibly as well as their unique and incremental associations with outcomes (cannabis protective behavioral strategies, cannabis use frequency, negative consequences, and cannabis use disorder symptoms). A sample of 408 past month cannabis users were recruited from a multisite study of college students (n=1856). External regulation for using cannabis responsibly was strongly correlated with conformity use motive (r=.47) and was significantly correlated with each of the other cannabis use motives (.12<rs<.27); autonomous motivation to use responsibly was significantly correlated with expansion use motive (r=.18). Thus, these constructs were modestly related, highlighting little redundancy. As expected, motivation to use responsibly was most strongly associated with PBS use, whereas cannabis use motives were most strongly related to cannabis use/problems. Both motivational constructs predicted cannabis-related outcomes beyond the other, but cannabis use motives generally accounted for more variance. Integrating motivation in relation to both cannabis use and responsible cannabis use responsibly may lead to a better understanding of cannabis-related behaviors and the associated negative consequences among college students, which can be used to inform the development and tailoring of effective cannabis interventions.

58 Cognitive Behavioral Therapy is an Empirically Supported Treatment for Substance Use Disorder

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Cognitive behavioral therapy (CBT) is a commonly used treatment for a variety of substance use disorders (SUD) but has not been evaluated using the American Psychological Association's "Tolin Criteria" which serves as the current standard for determining the empirical basis of psychological treatments. The current systematic review of reviews evaluated five meta-analyses of CBT for SUD. One meta-analysis had sufficient quality to be considered in the evaluation of effect sizes. CBT produced small to moderate effects on substance use, including quantity and frequency, when compared to inactive treatment and was most effective at early follow-up (1-6 months post-treatment; grange = 0.18-0.42) compared to late follow-up (8+ months post-treatment; g = 0.05). Sensitivity analyses including all five meta-analyses found a similar pattern of results. A "strong" recommendation was provided for CBT as an empirically supported treatment for SUD, based on the intervention's effects on substance use, quality of the evidence, and consideration of additional contextual factors (e.g., efficacy in diverse populations, efficacy across multiple substances, and efficacy across a variety of settings). This evaluation offers the first examination of the status of CBT for SUD as an empirically supported treatment according to the Tolin Criteria. Formal recognition may help encourage insurance reimbursement for CBT and inspire further dissemination of and training in CBT

59 Development of opioid vaccines using bacteriophage virus-like particles

Isabella G. Romano, Bryce Chackerian, Matthew Campen, Kathryn Frietze

Oxycodone is the most abused prescription opioid and a common cause of opioid use disorder and overdose. Despite the availability of different treatment options, opioid overdose rates have skyrocketed to a staggering 80,000 deaths in 2021. Vaccines against opioids have been proposed as a novel strategy for preventing overdose and several studies have established the feasibility of this approach. Here, we report our efforts to engineer a vaccine against oxycodone that elicits high-titer antibodies with protective functionality against oxycodone. We accomplish this using a bacteriophage Qβ virus-like particle (VLP) platform to display oxycodone in a highly immunogenic and multivalent format. The repetitive nature, small particulate size, and excellent safety profile of Qβ VLPs makes them a promising platform for vaccine design. The oxycodone hapten was chemically modified to include a short peptide linker (GGGG-C) to enable conjugation to Qβ VLPs. Mice and rhesus macaques were immunized with Qβ-oxycodone or unconjugated Qβ control. Qβ-oxycodone elicited high-titer antibodies after one immunization, with high-avidity IgG antibodies elicited after two immunizations. In future studies, we will investigate drug distribution in the blood and brain, as well as protection from oxycodone-induced anti-nociception and opioid induced respiratory depression.

60 Third-wave treatments for impulsivity in addictive disorders: A narrative review of the active ingredients and overall efficacy

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Purpose of Review: The goal of this review was to (1) synthesize recent studies that have examined impulsive behaviors in third-wave behavioral treatments, including Acceptance and Commitment Therapy, Mindfulness-Based Interventions, and Dialectical Behavior Therapy, and (2) examine the efficacy of these third-wave treatments in modifying impulsivity among individuals with addictive disorders.
Recent Findings: Recent studies indicate the potential for third-wave treatments in both treating addictive disorders and targeting the underlying neurocognitive mechanisms of impulsivity. Concerns around the conceptualization of impulsivity as a construct warrant the use of improved measurement of impulsive behaviors in future work. Summary of Results: Through shared emphases on mindfulness, acceptance, and emotion regulation, third-wave treatments offer great promise in the alleviation of suffering resulting from impulsive and addictive behaviors. Rigorous research with improved methodological designs, larger samples, and sound measurements of specific impulsive behaviors is needed to clarify the utility of third-wave interventions in targeting impulsivity.

61 Agonizing the 5-HT2c receptor attenuates methamphetamine-induced conditioned place preference in adolescent male rats

Nicole C. Reyna & Nathan S. Pentkowski

Methamphetamine use disorder (MUD) and other stimulant use remains high in the Western area of the United States, with New Mexico having one of the highest stimulant use percentages in adolescents, at 11.4%. Additionally, adolescence is a time of enhanced sensitivity to drug reward and there are currently no FDA approved treatments for MUD. Therefore, there is a critical need to develop effective interventions for adolescents using methamphetamine. The present study utilized a conditioned place preference paradigm (CPP) for determining if agonizing the serotonin-2C (5-HT2c) receptor attenuates expression of methamphetamine reward in adolescent Sprague-Dawley rats (PND 30). Rats were randomly assigned into four separate groups: 2c agonist-low/Meth, 2c-agonist high/Meth, Vehicle/Meth, and Vehicle/Saline. During conditioning rats were given methamphetamine (1 mg/kg, i.p.) for 2 conditioning sessions/day for 4 consecutive days following baseline preference testing. Rats received injections (s.c. ;0.3, 1 mg/kg) of the 5-HT2c agonist, CP809101, or a saline vehicle 30 minutes before final expression testing. Similar to previous studies examining cocaine, rats that received the high dose and low dose of CP809101 demonstrated reduced expression of methamphetamine-induced CPP. These findings suggest that agonizing the 5-HT2c receptor may be an effective pharmacotherapy intervention for those diagnosed with MUD.

62 A bacteriophage virus-like particle vaccine against heroin generates protective antibody responses

Isabella G. Romano, Brandi Johnson-Weaver, Hermann Staats, Bryce Chackerian, Kathryn Frietze

Opioid use disorder (OUD) and opioid overdose are urgent public health crises, with opioid overdose rates tripling within the last decade in the United States. Current treatments have limited efficacy, and challenges associated with implementation. Vaccines against opioids have recently been proposed as novel treatments, with some vaccine strategies showing promising pre-clinical data. Here, we report our efforts to engineer a vaccine against heroin that elicits high-titer and long-lasting antibodies with protective functionality. We utilized bacteriophage Qβ virus-like particles (VLPs) to display drug targets in a highly immunogenic and multivalent format. The active metabolites of heroin, morphine and 6-aceyl-morphine, were chemically modified to include a short peptide linker (GGGG-C) allowing for chemical conjugation to Qβ VLPs. BALB/c mice (n=6) were then immunized with 2 doses of Qβ-morphine (20µg), Qβ-6-acetyl-morphine (20µg), or a combination vaccine (20µg Qβ-morphine + 20µg Qβ 6-acetyl-morphine) . We studied kinetics of elicited antibody responses via Enzyme Linked Immunosorbent Assays (ELISAs) and show the generation of high-titer antibodies against morphine and 6-acetyl-morphine. A dose response study was conducted in naïve animals to determine the heroin dose used in subsequent anti-nociception challenges. Animals were challenged with subcutaneous heroin (0.5mg/kg, as determined via the dose response study) and anti-nociceptive responses were studied in tail-flick assays. We found that both the Qβ-6-acetyl-morphine and the combination vaccine candidates significantly reduced the anti-nociceptive effects of heroin in a tail flick assay.

63 Participation in ECHO is Associated with Expanding Buprenorphine Treatment for Opioid Use Disorder in Rural Primary Care

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Context: Access to medications for opioid use disorders (MOUD) is limited, especially in rural communities. Documented barriers limit integration of treatment for opioid use disorder (OUD) in primary care settings, inhibiting provider training and delivery of treatment. Innovative delivery mechanisms are needed to enhance integration of services. Objective: Examine impact of participation in the Extensions for Community Healthcare Outcomes model (ECHO) intervention on expansion of OUD treatment using buprenorphine among rural primary care providers. Study Design: Quasi-experimental single group design to assess achievement of benchmark measures related MOUD expansion. Analysis: We estimated the strength of the association between participation in MOUD-focused ECHO sessions and expansion of MOUD treatment using logistic regression. Setting: Rural primary care providers in New Mexico and border areas in surrounding states (TX, AZ, CO). Population Studied: Medical Doctors, Doctors of Osteopathic Medicine, Nurse Practitioners, and Physician Assistants. Intervention/Instrument: A 12-session curriculum using the ECHO model providing education, support and consultation on key areas to help start and expand buprenorphine treatment including details on prescribing, psychosocial treatment, recovery support, and clinic functioning. Outcome Measures: Primary outcome measures were the following MOUD implementation benchmarks: 1) obtaining DATA 2000 waiver, 2) obtaining license X number, 3) prescribing buprenorphine to first patient, 4) adding additional patients onto provider's buprenorphine panel. Results: We detected a positive relationship between participation in the ECHO and expansion of MOUD treatment. Specifically, there is a positive relationship to achieving any of the above benchmarks 1-5 ($p<.001$), and in particular the benchmark of starting to prescribe buprenorphine ($p=.003$). Participation: 81 prescribers across 49 clinics in rural areas of NM, CO, and TX participated in the study. Sixty-five percent (53/81) advanced to accomplish at least one benchmark, and 47% (38/81) have started adding additional patients to their buprenorphine panel.

64 Examining the Psychometric Properties of the Reward and Relief Inventory of Drinking Situations

Victoria R. Votaw, Rylee Brachle, Jenny Fillebrown, Matthew Lopez, Ethan Van, Isabel Weisberg, & Katie Witkiewitz

Recent work has examined the extent to which individuals seek alcohol to enhance positive experiences (reward drinking) or relieve aversive states (relief drinking), and processes underlying reward/relief drinking correspond to neurobiological adaptations within the addiction cycle. Previous findings indicate the utility of reward/relief drinking phenotypes in matching patients to AUD pharmacotherapies, with high reward drinkers responding better to naltrexone versus placebo. Practical reward/relief drinking measures with good psychometric properties are needed to translate these findings to clinical practice. We examined the reliability and construct validity of a recently developed brief measure of reward /relief drinking, the Reward and Relief Inventory of Drinking Situations (RR-IDS). Sixty-five individuals (51% female; 77% White, 8% multiracial, 6% American Indian, 9% other racial identities; 49% Hispanic; mean age=31.6 years) with high-risk alcohol use based on the AUD Identification Test were recruited in New Mexico. The RR-IDS reward (α=.866-.897) and relief (α=.905-.917) subscales demonstrated good internal consistency and test-retest reliability over one month (reward intraclass correlation coefficient (ICC)=.652; relief ICC=.722). The RR-IDS reward subscale was associated with greater social and enhancement motives, reward responsiveness, and sensation seeking ($ps<0.05$). Conversely, the relief subscale was associated with greater age, AUD severity, alcohol craving, coping motives, negative urgency, and depression and anxiety, and lower age of alcohol initiation and positive affect ($ps<0.05$). Pending additional information on the RR-IDS' predictive validity and clinical utility, implementing this measure in clinical settings might help match patients to AUD treatments that work best for them.

65 Investigating Mechanisms of COVID-19 Neuropsychological Dysfunction

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Background: Severe acute respiratory syndrome coronavirus (SARS-CoV-2) is a highly pathogenic human coronavirus that typically causes respiratory infection. Evidence suggests that 10-15% of patients experience chronic neurologic symptoms, such as fatigue, headaches, and cognitive impairment.10 SARS-CoV-2 is thought to invade neural tissue, triggering immune system response, which may lead to brain dysfunction.7 The resulting brain dysfunction may be demonstrated through abnormal MRI and electroencephalography (EEG).4,8,9 Objective: This study aims to establish foundational knowledge about the subacute and chronic neurocognitive effects of COVID-19, determine the pathologic mechanisms associated, and develop effective tools to guide and enhance treatment. Hypothesis: Neuro-positive COVID patients are predicted to have significantly greater deficits in fronto-parietal control network domains of executive function compared to controls and neuro-negative COVID patients. Additionally, neuro-positive COVID patients are expected to have lower activation amplitudes of event-related potentials on EEG, and lower levels of oxyhemoglobin in bilateral prefrontal cortices on Functional Near-Infrared Spectroscopy, (fNIRS). Neuropsychological Testing: Neuropsychological testing aims to measure psychological functions linked to specific brain pathways. Examples of neuropsychological tests that will be administered in this study include: Test of Memory Malingering (TOMM); Hopkins Verbal Learning Test (HVLT); WAIS-IV: Digit Span; WAIS-IV: Symbol Coding, etc. Functional Near-infrared Spectroscopy (fNIRS) The application, fNIRS is used as a safe, optical brain imaging modality that measures the selective absorption of photons by oxyhemoglobin and deoxyhemoglobin in small vessels near the cortical surface. During fNIRS assessments, participants complete numerous active tasks. Electroencephalography (EEG) EEG detects and measures the brain's electrical activity. Electrodes on the participant's scalp can detect the electrical charges produced. During EEG assessments, participants complete numerous active tasks.

66 The Effects of Moderate Prenatal Alcohol Exposure on Navigation in a Delayed Non-Match-To-Place Spatial Alternation Task by Adult Male and Female Rats

Gabriela Acosta, Benjamin J. Clark, Dan D. Savage, Suzy Davies

Prenatal Alcohol Exposure (PAE) has been found to result in structural alterations to regions of the brain involved in spatial memory, including the thalamus and hippocampus. Previous studies have shown that spatial memory is impaired after moderate PAE (mPAE; ~60-80 mg/dL) and damage to the limbic thalamus and hippocampus. Recent work has shown that visual-spatial discrimination memory is impaired after mPAE in a sex-specific manner such that female mice exhibit greater deficits after 15sec retention intervals. It is unclear whether similar-sex specific deficits would be observed in tests of spatial memory or in a rat model of mPAE. Thus, the present study tested the hypothesis that mPAE would produce sex-specific deficits in a delayed non-match-to-place variant of a spatial alternation task. Saccharine (n=8; 4 female and 4 male) and mPAE (n=8; 4 female and 4 male) adult Long-Evans rats were trained to alternate from a reference point to the outbound arms of an M-maze. Animals were required to encode recently learned spatial cues during the initial trajectory and subsequently recall their initial trajectory after a 15sec retention interval. After the delay, rats navigated to the opposite (alternate) arm for a food reward. Rats performed 10 training trials each test day. The behavioral measures of task performance were quantified by accounting for the number of errors in each session of 10 trials in addition to the number of sessions until the criteria were met (criteria = 90% correct for two consecutive days). After criteria was met, rats were given two probe tests in which the delay was randomly varied between 15sec and 30sec. Preliminary results indicate that mPAE did not specifically impair performance, however female rats were generally slower to reach criteria. The results of the study suggest that this task variant is sensitive to sex differences in spatial behavior.

67 IMPACT OF TWO DIFFERENT RODENT DIETS ON MATERNAL ETHANOL CONSUMPTION, SERUM ETHANOL CONCENTRATION AND PREGNANCY OUTCOME MEASURES.

Suzy Davies, Danika E Nelson, Daniel D Savage.

Recent studies have reported that varying levels of ethanol consumption by rodents maintained on different commercially available laboratory diets, may impact offspring outcome measures. Here, we compared ethanol consumption by rats maintained on the Envigo 2920 diet used in our lab, with an isocalorically equivalent PicoLab 5L0D diet, used in some alcohol consumption studies. Compared to the 5L0D diet, female rats maintained on the 2920 diet consumed 14% less ethanol during the daily four-hour drinking sessions prior to pregnancy and 28% less ethanol during gestation. While this difference did not affect litter size, maternal weight gain during pregnancy by 5L0D dams decreased by 5%. However, their offspring birth weights increased by 10% compared to the 2920 dams. A subsequent study revealed that hourly ethanol consumption was not different between diets during the first two hours, but was significantly reduced in 2920 rats at the end of the third and fourth hours. The mean serum ethanol concentration at two hours was 46 mg/dL in 5L0D dams compared to 25 mg/dL in 2920 dams. Further, ethanol consumption at the two-hour blood sampling time was more variable in 2920 dams compared to 5L0D dams. An in vitro analysis mixing each powdered diet with 5% ethanol in acidified saline revealed that 2920 diet suspension adsorbed more aqueous medium than 5L0D suspension diet. The total ethanol remaining in the aqueous supernatant of 5L0D mixtures was nearly twice the amount in supernatants of the 2920 mixture. These results suggest that 2920 diet expands to a greater extent in aqueous medium than 5L0D diet. We speculate that increasing adsorption of water and ethanol by the 2920 diet may reduce or delay the amount of ethanol absorbed and may decrease serum ethanol concentration to a greater extent than would be predicted from the amount of ethanol consumed.

68 Prenatal Alcohol Exposure and Placental Insufficiency Result in Altered Dendritic Complexity in Medial Frontal Cortical Neurons in Adult Rat Offspring

Brooke Dunn, Nathaniel Pavlik, Clement Jose, Jessie Newville, Suzy Davies, Daniel Savage, Jessie Maxwell

Prenatal Alcohol Exposure (PAE) results in deficits in executive functioning. PAE is also associated with placental abnormalities in function and perfusion, deemed placental insufficiency (PI). PI independently contributes to neurodevelopmental deficits. The impact on the combined effects of PAE and PI is unknown. We hypothesized that voluntary moderate PAE+PI would result in decreased neuronal complexity within the medial frontal cortex, a region critical to executive functioning, assessed through use of a three-dimensional (3D) Sholl analysis. To establish a model of moderate PAE and PI, pregnant Long-Evans rats voluntarily drank 5% ethanol or saccharin water until embryonic day 18 (E18). On E19, an open laparotomy was performed to induce PI via occlusion of the uterine artery for 60 minutes. Pups delivered normally on E22 and weaned on postnatal day 24 (P24). At P100, brains were extracted, and Golgi-Cox staining conducted. Coronal sections of the medial frontal cortex (mFC) were imaged by confocal microscopy using z-stacking capabilities to render 3D images. 3D Sholl analysis was conducted with Imaris software to examine complexity between neurons in the mFC and area 25 of the cingulate cortex (A25).
Analysis of mFC neurons at P100 demonstrated increased proximal apical complexity after PI only, while PAE only and combined PAE+PI demonstrated diminished complexity compared to control. Basal projections of mFC neurons in PAE only and PI only offspring also showed increased complexity relative to controls. Analysis of A25 neurons demonstrated increased proximal apical branching complexity in PAE only compared to PI only and controls, and decreased complexity in PI only compared to combined PAE+PI. The basal dendritic complexity of A25 was not significantly different. This paradigm demonstrated changes in dendritic complexity within the mFC and A25 that persist into adulthood. Abnormal dendritic arborization may impact the functional circuitry of these regions. Supported by K08 AA030080 and P50 AA22534

69 MODERATE PAE-INDUCED DEFICITS IN LTP AND GLUTAMATE LEVELS IN THE DENTATE GYRUS. ENHANCEMENT IN LTP WITH THE HISTAMINE H3 RECEPTOR INVERSE AGONIST SAR153954

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The hippocampus is susceptible to the effects of prenatal alcohol exposure (PAE) which can result in persistent cognitive impairments. Although there have been many investigations, deficits in synaptic plasticity remain poorly understood. Previous studies have identified deficits in long-term potentiation (LTP) in the perforant pathway (PP) to dentate gyrus synapses as a robust consequence of PAE. Currently, there are no known, clinically effective pharmacotherapeutic interventions for these deficits. This study sought to investigate the effects of PAE on the pre-synaptic mechanisms involved in LTP. We first investigated differences in extracellular glutamate levels following stimulation of the PP (n=20/PAE = 10). In vivo electrophysiology was conducted along with glutamate biosensor implants in the DG. The fractional amplitude measure revealed less change in the PAE group compared to controls ($p = 0.033$). These observations suggest that deficits in LTP following PAE may be related to alterations in the presynaptic mechanisms associated with LTP. A second experiment examined the effects of two doses of an H3R inverse agonist, SAR152954, on PAE-induced LTP deficits in the dentate gyrus, as a possible agent to reverse those deficits. Rats were given a single injection of SAR152954 (0.1 or 1.0 mg/kg) or saline (vehicle) 30 min prior to the recording session. Saline-treated PAE rats displayed reduced LTP relative to controls ($p = 0.05$). Control rats receiving 0.1 mg/kg SAR152954 displayed decreased LTP relative to VEH. PAE rats receiving 0.1 mg/kg SAR152954 did not show a reversal of PAE-induced deficits ($p > 0.8$). However, the 1.0 mg/kg dose reversed PAE-induced deficits to levels comparable to the control animals ($p > 0.7$) and greater than PAE animals that received either the vehicle or low dose SAR152954 conditions ($p = 0.02$). Together these experiments suggest deficits in the presynaptic mechanisms of LTP and offer a possible pharmacological intervention for those deficits.

70 EFFECT OF PRENATAL ETHANOL EXPOSURE ON HISTAMINE H3 RECEPTOR-EFFECTOR COUPLING AND SIGMA-1 RECEPTOR MODULATION OF HISTAMINE H3 RECEPTOR FUNCTION.

DE Nelson, S Davies and DD Savage

We have reported that the histamine H3 receptor (H3R) inverse agonist ABT-239 ameliorates prenatal alcohol exposure (PAE)-induced deficits in synaptic plasticity and learning. It has been reported that different H3R inverse agonists have variable affinities for also binding to Sigma-1 receptors (S1Rs), including ABT-239, which is roughly equipotent at both receptor types. Given this dual action of ABT-239 and other H3R inverse agonists on both H3Rs and S1Rs, we examined whether PAE would affect that actions of the more selective H3R inverse agonist JNJ5207852 compared to the specific S1R agonist PRE-084 on H3R receptor-effector coupling. Radiohistochemical studies of [^{35}S]-GTPγS (GTP) binding were conducted using sagittal brain sections from five-month-old control and PAE rat offspring. Sections were incubated in the presence of an EC_{80} concentration (500 nM) of the H3R agonist alpha-methylhistamine (αMH), in the absence or presence of increasing concentrations either JNJ-5207872 or PRE-084. In the absence of either agent, moderate PAE significantly increased αMH-stimulated GTP binding in dentate gyrus and cerebrocortical brain regions, as we reported previously. JNJ-5207852, dose-dependently inhibited αMH-stimulated GTP binding in a similar manner in both control and PAE rats. These results suggest that PAE does not affect the ability of H3R inverse agonists to inhibit H3R receptor-effector coupling. PRE-084 dose-dependently *elevated* H3R agonist-stimulated GTP binding in various brain regions. In contrast, PRE-084 *reduced* H3R agonist-stimulated binding to binding levels similar to controls in the absence of either drug. These results suggest that PAE reduces the ability of S1R agonists to modulate the function of H3Rs. Given that S1Rs act as chaperone proteins to enhance many different neurobiological processes including, NMDA receptor function, neurotransmitter release, hippocampal neurogenesis and learning, all of which are diminished in PAE rodents, these results suggest that PAE may diminish S1R modulation of many neurobiological processes involved in brain function and behavior. Supported by 1P50AA022534.

71 Long-term effects of Prenatal Alcohol Exposure on GABAergic system in posterior parietal cortex

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Fetal Alcohol Spectrum Disorders (FASDs) are a group of neurobehavioral deficits including physical, cognitive, learning and behavioral disabilities that persist throughout the lifespan. Our recent investigation showed that moderate prenatal alcohol exposure (PAE) during first and second-trimesters equivalent impairs cognitive control on a touchscreen continuous performance task accompanied by frontal and cortical power alterations. The literature to date had extensively investigated the molecular abnormalities underlying the PAE impairments in cognitive functions mediated by cortical areas, but there are no studies exploring the long-term effects of PAE in the posterior parietal cortex (PPC). The PPC represents one of the major cortical association areas involved in multiple cognitive processes. To address this knowledge gap, using behaviorally naïve control and PAE mice we characterized the GABAergic transmission in PPC. The triple immunostaining revealed that low PAE (BAC of dams ~ 30 mg/dl) induces a significant reduction of parvalbumin (PV+) and calretinin (CR+)-expressing GABAergic interneurons in adult animals (~ 3 months old). Next, in order to understand how this interneuronopathy modulates the GABAergic transmission, using a different set of littermates we conducted whole-cell patch clamp recordings in pyramidal neurons expressed in PPC layer 5. Spontaneous inhibitory postsynaptic currents (sIPSCs) were pharmacologically isolated using 50 μM AP5 and 10 μM CNQX to block NMDA and AMPA receptor-mediated currents. Surprisingly, the data collected revealed non-significant changes in sIPSCs measured in PAE animals. Since the PV+ interneurons produce strong inhibition on pyramidal neurons generating large sIPSCs, we separated small and large events and the analysis did not show a significant treatment effect. Taken together, these findings suggest that the molecular mechanisms underlying the cognitive impairments observed in PAE mice might be mediated by the reduction of interneurons even though there is not a significant alteration in GABAA function measured in pyramidal neurons. General Summary:
The cognitive deficits observed in Fetal Alcohol Spectrum Disorder (FASD) children can have catastrophic consequences across the lifespan, for this purpose, it is necessary to find targeted therapies. Posterior parietal cortex is a critical brain region involved in multiple cognitive processes including sensorimotor integration, spatial navigation, decision-making, and movement planning. Investigating the effects of gestational alcohol exposure in this area could provide an important tool for developing new effective therapies.

72 Alcohol consumption during early adulthood in a preclinical mouse model of Alzheimer's disease leads to gait impairments, dysregulated circadian rhythm, alterations in tauopathy and brain-region-specific transcriptional alterations

Nicole M. Maphis, Dominic Furlano, Seth A. David, & David N. Linsenbardt

Alzheimer's disease (AD) is a leading cause of cognitive dysfunction and death in the US attributable in part to the accumulation and spread of pathologically modified tau (pTau). Recently, excessive alcohol use, particularly binge drinking, has emerged as a risk factor for the development of AD. However, the neurobiological consequences underlying how excessive alcohol exposure might lead to the accumulation and/or progression of pTau and associated neurobehavioral deficits has not been fully explored. We used the binge-alcohol drinking paradigm, 'drinking-in-the-dark' (DID), in the P301S mouse model of tauopathy to test the hypothesis that excessive voluntary alcohol consumption during young adulthood would exacerbate pTau-induced alterations in behavioral decline as a consequence of the recruitment of unique neurobiological genes/gene networks. We found that excessive alcohol use in the P301S mice altered the presentation of pTau, shortened circadian rhythm, impaired right hind paw gait characteristics, and led to brain-region-specific transcriptional alterations. Of particular interest, we identified a well-characterized thyroid transport gene, Transthyretin (Ttr), recently found to regulate microtubule dynamics and has a strong connection to Alzheimer's, that was downregulated in the hippocampus of alcohol consuming P301S males compared with alcohol consuming male nTg littermates. These findings support alcohol consumption as a factor that interacts with pTau and pTau-associated behavioral decline as well as reveals some potential targetable neurobiological mechanisms underlying these changes.

73 Microvascular structure and blood brain barrier function are compromised in developing cortices following prenatal alcohol exposure

Gabriela Perales, Marissa Westenskow, and Amy S. Gardiner

Fetal Alcohol Spectrum Disorders (FASD) occur due to in utero alcohol exposure. FASD presents as a wide range of neurocognitive deficits that may be caused by abnormal vascular development in the brain and expression of factors that regulate vessel formation. We and others have shown that miR-150-5p alters pathways important for vascular development, including angiogenesis and integrity of the blood-brain barrier (BBB). In an established mouse model of moderate prenatal alcohol exposure (PAE), we found that brain microvascular endothelial cells (BMVECs) isolated from cortices of EtOH-exposed pups at embryonic day 18 (E18) contained significantly higher levels of miR-150-5p compared to saccharin (SAC)-exposed controls. To assess the structure of the developing microvasculature, we used CLARITY, an imaging technique that renders tissue optically transparent. After tissue clearing and staining of the vasculature, 3D images were taken with the Leica TCS SP8 confocal microscope, fitted with a long working distance objective designed for imaging thick tissue sections. Imaris cell imaging software was used for image visualization and quantification. We found that PAE E18 cortices displayed significant reductions in vessel area, volume, and mean vessel diameter. Further, intracerebroventricular (ICV) injection of miR-150-5p inhibitors could reverse some of the vascular deficits. To assess BBB function, TRITC-labeled dextran tracers were injected into embryonic livers. This was followed by immunohistochemistry and confocal microscopy of the embryonic cortices. A permeability index was calculated from the dextran signal found outside the blood vessels compared to the total dextran signal for each cortex. We found that PAE cortices had an increased permeability index compared to controls, indicating compromised BBB function. Our work suggests that PAE-mediated elevation of miR-150-5p within BMVECs alters molecular pathways affecting angiogenesis and BBB permeability during development and may contribute to neurodevelopmental deficits seen in patients with FASD.

74 PRENATAL ALCOHOL EXPOSURE EXAGGERATES NLRP3 INFLAMMASOME-DEPENDENT IMMUNE INTERACTIONS POST MORPHINE TREATMENT INCREASING THE CHRONICITY OF PATHOLOGICAL PAIN IN MICE.

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In utero alcohol exposure can lead to Fetal Alcohol Spectrum Disorder (FASD) which can result in a range of neurobehavioral deficits. Prenatal Alcohol exposure (PAE) can lead to chronic central nervous system (CNS) immune dysfunction during adulthood. Our prior work has demonstrated that adult PAE rat offspring with minimal nerve injury develop pathological light touch sensitivity or allodynia due to aberrant peripheral and spinal glial-immune interactions resulting in increased levels of pain inducing proinflammatory cytokine, IL-1β. We suspect that PAE-related adaptations may “prime” CNS glial-immune cells to over-respond to subtle immune challenges through innate immune receptors, TLR4 and Nod-like receptor family pyrin domain containing 3 (NLRP3) signaling. Interestingly, morphine is known to be the standard opioid used as a pain therapeutic. In addition to signaling via μ-opioid receptor, recent literature suggests that morphine can activate glial TLR4 leading to NLRP3 inflammasome activation resulting in an increased production of mature IL-1β protein. These overlapping immune interactions from PAE and morphine lead us to hypothesize that morphine treatment following adult-onset peripheral nerve injury may paradoxically prolong allodynia in PAE offspring through an aberrant NLRP3 activation and if true, selectively blocking the NLRP3 inflammasome activity would reverse the morphine-prolonged allodynia in PAE mice. Our data suggest that morphine (10 mg/kg, 5 subsequent days) treatment in PAE mice with a minor nerve injury significantly increased the duration of allodynia, in comparison to nerve injured PAE mice without morphine treatment. We also confirmed that this morphine-induced prolongation of allodynia in PAE mice is sex-independent. Moreover, treatment with a small-molecule inhibitor of NLRP3, MCC950 (i.p. 10 mg/kg) resulted in full reversal of morphine induced allodynia with as soon as 90 minutes post- injection, compared to the vehicle treated mice. MCC950-mediated reversal of allodynia persisted at 24 hours post- injection. At this timepoint, pain-relevant brain regions and spinal cord tissues were collected. Our ongoing work is focused on evaluating differential expression of immune molecules related to the TLR4-NLRP3 pathway in the presence of morphine and PAE. These data provide evidence that in PAE and morphine interactions involve aberrant NLRP3 activation, which may be predictive of adverse responses to opioids intended to treat pain in individuals with FASD.

75 NOWS in COVID - Neonatal opiate withdrawal hospital course after implementation of COVID-19 infection control practices.

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Background: The SARS-COVID-19 pandemic requires hospitals to increase infection control practices and implement policies calling for universal face masks. These policies dramatically changed the hospital milieu for newborns as visitors were either limited or entirely restricted. For newborns experiencing neonatal opiate withdrawal syndrome (NOWS) due to exposure to opioids during pregnancy, hospitalization is often prolonged. Protocols for care for infants with NOWS emphasize the importance of non-pharmacologic care as first-line treatment, recommending holding infants, swaddling, and rooming-in caregivers. With changes to infection control policies, providers are concerned infants with NOWS are experiencing complications including longer stays and more complex clinical courses, which may put this group at higher risk for long-term developmental delays. Methods: A retrospective chart review was performed on infants with NOWS admitted to the UNMH for the 8 months prior to the SARS-CoV-2 pandemic (6/1/2019-2/1/2020) [Cohort 1], and for the 8 months following the implementation of infection control practices (4/30/2020-12/31/2020) [Cohort 2]. Data: Infant charts were reviewed and admission characteristics were recorded. The cohorts were controlled for gestational age, birthweight and significant pregnancy, delivery and hospital complications. The outcomes are length of stay, medications required for treatment of NOWS symptoms, and whether or not infants needed feeding support with naso-gastric feeds or a speech consult. Conclusion: Infants with prenatal opiate exposure are already at risk for developmental delays, but this cohort with an environment lacking in access to care-givers' faces, may be at higher risk. We hypothesize that these newborns may experience longer hospital stays, more medications and more feeding complications, all of which may lead to future developmental issues. We hope to follow the development, health, and social outcomes of these populations long-term.

76 Enrichment-mediate neurogenesis is impaired in the ventral hippocampus in a mouse model of fetal alcohol spectrum disorder (FASD) and potential therapeutic intervention.

Arasely M. Rodriguez; Lu Li; Lee Anna Cunningham

Fetal alcohol spectrum disorder (FASD) is a leading cause of preventable intellectual disability and neural developmental disorders. Depression and anxiety are the most common mental illness in people with FASD. These disorders are related to ventral hippocampus function. The hippocampus is unique in its ability to produce new neurons throughout life. In fact, part of the therapeutic effect of some common antidepressants is to increase neurogenesis. Previous research conducted by our lab has shown that in a mouse model of FASD, enriched-environment (EE) mediated neurogenesis in the dorsal hippocampus is inhibited, this correlates with impaired pattern discrimination learning (Gustus et al., 2020). However, EE mediated neurogenesis of the ventral hippocampus has not been studied in a FASD model. Here, we tested the hypothesis that EE-mediated neurogenesis is impaired in the ventral hippocampus of prenatal alcohol exposed PAE mice. We utilized Nestin-CreERT2:tdTomato mice as a means to label adult-generated hippocampal DGCs after PAE and placement in EE. tdTom+ DGCs in the ventral hippocampus were quantified histologically. We found that PAE had no significant (Tukey Post-Hoc, P=0.97) impact on neurogenesis under SH conditions (SAC-SH: M=93.0, SD = 56.91, N=5; PAE-SH: M=81.75, SD = 33.45, N=4), but significantly impaired (P= 0.01) the neurogenic response to EE (SAC-EE: M=173.9, SD = 21.44, N=5; PAE-EE: M=76.55, SD = 24.77, N=4). As ventral and dorsal EE mediated neurogenesis is impaired in PAE mice, we are currently studying if the use of the antidepressant fluoxetine will reinstate this neurogenesis.

77 Placenta programing of fetal HPA axis

Elizabeth Solomon, Ludmila Bakhireva, Melissa Roberts, Xingya Ma, Erin Milligan

Background: Maternal stress and prenatal alcohol exposure (PAE) alter fetal programming of hypothalamic-pituitary-adrenal (HPA) axis, including glucocorticoid regulation of the stress response in placenta, leading to lifelong health issues. While preclinical studies began underlining the importance of placenta-mediated programming of the glucocorticoid signaling system in PAE, clinical studies are extremely limited. The amount of cortisol that crosses the placenta is a function of relative expression of 11-β hydroxysteroid dehydrogenases (11β-HSD): 11β-HSD2 oxidizes active maternal cortisol into inactive 11-dehydrocortisone, while 11β-HSD1 acts as a reductase and converts inactive 11-dehydro-corticostisone to active cortisol. Down regulation of 11β-HSD2 is associated with altered glucocorticoid programming. Methods: In the prospective cohort study, conducted at the University of New Mexico, we evaluated the effect of maternal stress, mental health, and PAE on key placenta targets of HPA axis and corresponding downstream markers in umbilical cord blood. PAE was assessed by prospective repeated TLFB interviews and a battery of ethanol biomarkers. Maternal stress and mental health were assessed by the Perceived Stress Scale (PSS), Generalized Anxiety Disorder-7 screener (GAD-7), PTSD symptoms (PCL-5), Edinburgh Postnatal Depression Scale (EPDS), and Adverse Childhood Experience (ACE-Q). Placenta specimens were collected within 5 hours of delivery; tissue excised from grossly normal areas of the villous parenchyma, excluding the decidua basalis and chorionic plate, flash frozen, and stored at -80°C. Placenta protein was isolated via fractional centrifugation, treated with protease/phosphatase inhibitors, producing lysates enriched with cytosolic proteins, and analyzed by ELISA for 11β-HSD type 1, 11β-HSD-type 2, and their ratio. Cortisone, cortisol, and cortisone/cortisol ratio was evaluated in umbilical cord blood, collected at birth, as a downstream measure of fetal HPA axis dysregulation. T-test was conducted to assess differences in the mean expression of the HPA axis biomarkers among PAE and control participants and those with ≥2 binge drinking episodes vs. < 2 binge episodes. Spearman correlation examined an association between biomarkers and continuous scores on maternal stress and mental health scales. Results: In 85 placenta samples (27 with PAE and 58 controls) analyzed to date, higher 11β-HSD2/11β-HSD1 ratio was observed in participants with PAE (p=0.02), ACE≥4 (p=0.03), and those with ≥2 binge drinking episodes (p=0.07). Additionally, significant correlation was observed between 11β-HSD2 and PSS (rho=0.277; p=0.01), GAD-7 (rho=0.273; p=0.01), and PCL-5 (rho=0.224; p=0.04). In analysis of 101 samples of umbilical cord plasma, higher cortisone/cortisol ratio was observed in participants with ≥2 binge drinking episodes (p=0.04). Conclusion: These data demonstrate the importance of placenta-mediated programming of the fetal glucocorticoid signaling system, and the effect of maternal stress and alcohol exposure on HPA axis. The focus on placenta, as a key interactive endocrine entity linking maternal and fetal HPA axes is expected to leade to identification of early markers of impaired stress reactivity/regulation in affected children.

78 Mechanisms contributing to aberrant vascular development in the brain following prenatal alcohol exposure through elevation of miR-150-5p

Marissa Westenskow, Roxana Gutierrez, Gabriela Perales, Amy Gardiner

Fetal Alcohol Spectrum Disorders (FASD) are conditions impacting development in children exposed to alcohol in utero. Among other associated anatomical defects, the organization of the brain microvasculature is altered in severe forms of FASD. Other vascular anomalies such as defective angiogenesis, permeability, vessel reactivity, and blood flow are found in animal models of prenatal alcohol exposure (PAE). The underlying mechanisms of these vascular defects are not fully understood. We previously found miR-150-5p to be upregulated in brain microvascular endothelial cells (BMVECs) isolated from embryonic mouse cortices following moderate PAE. We identified targets of miR-150-5p in BMVECs and demonstrated that miR-150-5p inhibition could counter alcohol-mediated effects in vitro on BMVECS and in vivo on the cortical microvasculature. Here, we investigate mechanisms that contribute to miR-150-5p elevation in BMVECs following PAE. We hypothesized that multiple mechanisms contribute to increased miR-150-5p abundance in BMVECs following ethanol (EtOH) exposure. We previously determined that EtOH exposure reduces exosomal secretion of miR-150-5p from BMVECs. We investigated the vacuolar protein sorting-associated protein 4 A (VPS4A), which controls the loading of some miRNA cargo, including miR-150-5p, into exosomes. VPS4A was reduced in primary BMVECs following PAE and in vitro following EtOH treatment. Overexpression of wild-type VPS4A reduced intracellular levels and increased exosomal levels of miR-150-5p, while overexpression of a dominant-negative form of VPS4A did the opposite. These results indicate that VPS4A mediates intracellular and exosomal miR-150-5p distribution in BMVECs. Additionally, we investigated the RNA-binding protein KSRP, which binds the stem-loop of select pre-miRNAs, including pre-miR-150, to promote their maturation to miRNAs. KSRP is increased in primary BMVECs following PAE and following in vitro EtOH treatment. Ongoing studies will determine whether PAE affects KSRP binding of pre-miR-150 and miR-150-5p levels. In summary, our research implicates multiple mechanisms of miR-150-5p regulation that may contribute to brain microvascular defects following PAE.

79 Prenatal Alcohol Exposure (PAE) and Stress Alter Levels of Circulating Corticosterone and Expression of Corticotropin-Releasing Factor (CRF) In Adult Brain

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Prenatal alcohol exposure (PAE) results in a constellation of negative consequences clinically known as fetal alcohol spectrum disorders (FASD), which include disorders of mood, behavior, and cognition. The hypothalamus and amygdala influence the stress response of the hypothalamic-pituitary-adrenal (HPA) axis. Glucocorticoids (CORT) released into circulation following HPA activation exert negative feedback by activating glucocorticoid receptors (GR) that inhibit further HPA activation and CORT release. Stress-induced production of corticotropin-releasing hormone (CRH) in the brain initiates HPA activation, a process also associated with the activation of astrocytes and production of proinflammatory cytokines such as interleukin-1β (IL-1β). We hypothesize that PAE alters brain astrocyte and cytokine actions in response to acute stress in adulthood. Dexamethasone (DEX), a synthetic GR agonist, was administered to mimic glucocorticoid negative feedback in response to stress. 1.5-hr prior to 30-min restraint stress, subcutaneous vehicle (DMSO; 1:100 in sterile phosphate buffered saline, (PBS), pH 7.4) or DEX (25 µg in DMSO:PBS) was given to 3–5-month-old female C57BL/6 mouse offspring that underwent prenatal control exposure (saccharine; SAC) or PAE (10% EtOH). Tail vein blood collection occurred immediately after stress. The hypothalamus and amygdala were collected 24-hr or 3-hr after stress. Messenger RNA (mRNA) expression levels of CRH, IL-1β, and glial-fibrillary-acidic-protein (GFAP; for astrocyte activation) and NR3C1 (GR gene) were assessed by RT-qPCR. Glucocorticoid levels were assayed by quantification of blood plasma CORT via enzyme-linked immunosorbent assay (ELISA). In both SAC and PAE, stress increased circulating CORT levels. DEX pretreatment blunted CORT levels in both SAC and PAE. At 3 hours, the PAE-stressed hypothalamus revealed blunted CRH mRNA expression. At 24 hours, the PAE-stressed hypothalamus revealed elevations in GFAP mRNA expression levels. The results of this study indicate that the peripheral GR response is functional, and that astrocytes may play a role in the dysregulation of the PAE brain-stress response.

80 Effects of ethanol exposure on oligodendrocyte development in the brain

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Background: Prenatal Alcohol Exposure (PAE) occurs when an expecting mother consumes alcohol. PAE will lead to children to develop fetal alcohol spectrum disorders (FASDs), which are a group of conditions that can include a wide range of physical deformities and/or intellectual disabilities. Glial cells such as oligodendrocyte precursor cells (OPCs) are responsible for generating oligodendrocytes to myelinate neuronal axons, which is essential for proper conduction of action potentials. Studies in both humans and animal models showed that decrease myelination in the brain are prominent features of PAE. In this project, we propose that pups exposed to ethanol at the third trimester during the height of OPC generation will show reduced differentiation into mature myelinating oligodendrocytes. Methods: Our project used the vapor chamber to expose mouse pups to either air (control) or ethanol (experimental) vapor for 4 hours/day (10:00 – 14:00) under reversed dark-light cycle from postnatal day (P) 4 to P8. At day P3, pups were injected with tamoxifen to induce Cre and label OPCs with YFP reporter to demonstrate that they were present at the time of exposure. Pups were either perfused at P8 or kept alive till P30 to study long term effects. Immunohistochemistry was used to study PAE effects on OPC differentiation into oligodendrocytes in the cortex and corpus callosum. Oligodendrocyte markers OLIG2, MBP, CC1, and cleaved Caspase 3 (CC3), a cell death marker, were used. Conclusions: Pups that experienced PAE showed decreased myelination at P8 based on MBP expression, while the number of mature YFP-labeled oligodendrocytes as labeled by CC1 was also decreased at P30 compared to air exposed control mice. CC3 showed that these decreased was not due to an increase in the death of OLIG2+ OPCs or oligodendrocytes. These findings demonstrate that PAE prevents the differentiation of OPCs into oligodendrocytes.