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SCIENTIFIC REPORT

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The facilities include staff offices and conference rooms, two MRI scanners, open and closed float rooms, and space for psychophysiology, behavioral observation, neuropsychology, transcranial magnetic stimulation (TMS), bioassays and medical assessments.

Research at LIBR is focused on investigating the neural mechanisms underlying anxiety, depression, eating and substance use disorders in diverse populations assessments and prediction tools and develop transdiagnostic interventions to improve mental health outcomes.





MARTIN P. PAULUS, M.D., Scientific Director and President

In reflecting upon the progress of the past year, it motivates me to observe the global progress in psychiatric research and the role the Laureate Institute for Brain Research (LIBR) has played in this journey. The landscape of mental health research and practice is continuously evolving, informed by discoveries and innovative methodologies that seek to bridge the gap between scientific understanding and real-world applications. This letter gives me the opportunity to provide some insights into the strategic alterations we are making at LIBR, the exciting findings from our investigators, and how our research aligns with the broader scientific trends in psychiatry.

The mental health field has witnessed notable advancements that are also important for the mission of LIBR to advance mental health through research. For instance, the application of artificial intelligence (AI) in helping to diagnose schizophrenia using large language models, or the promising potential of psychedelics in reducing PTSD symptoms in veterans, resonate with our commitment to leverage cuttingedge technology and novel therapeutic approaches. Similarly, the burgeoning understanding of the interplay between chronic stress, depression, and inflammation aligns with our core research interests.

Strategically, LIBR embarked on a paradigmatic shift from Individual Level Precision Psychiatry (ILPP) to Population Level Precision Psychiatry (PLPP), a transition aimed at using cutting edge techniques with large data sets to make actionable predictions that improve mental health for many. The focal point has evolved from personalized mental healthcare to a broader, population-centric approach. This strategic overhaul is not merely a shift in perspective; it is a substantial endeavor to enhance the generalizability and real-world applicability of our findings. To that end, we have expanded our team to include data analysts and data scientists within our Population Neuroscience and Genetics (PoNG) Center.

Our aspiration is to transcend the conventional boundaries of psychiatric research by delving into wider mental health trends, risk factors, and their societal implications. Underpinning this transition is a meticulously crafted research program that embodies methodological rigor, multi-center collaborations, real-world clinical utility assessments, and a robust data security infrastructure. These elements are crucial in fostering a trustworthy and effective transition to PLPP, ensuring that our findings are not only scientifically sound but also practically viable.

The digital era we are part of augments our research capabilities exponentially. Big Data, which includes Electronic Health Records, genetic repositories, and symptom databases, serves as a bedrock for our PLPP investigations. These datasets allow us to delve deeper into precision targets like treatment responsiveness, diagnostic accuracy, and relapse prevention, among others. Our engagement with communities and stakeholders ensures that this transition translates into tangible benefits in healthcare, ultimately fostering a more holistic, equitable, and effective mental healthcare ecosystem.

The commendable work of our investigators, as evidenced by the top-cited publications of 2022 and 2023, underscores the multidisciplinary and comprehensive nature of our research endeavors. From employing state-of-the-art neuroimaging techniques (Chun Chieh Fan, Wes Thompson, Haixia Zheng) and computational approaches (Ryan Smith, Maëlle Gueguen) to exploring the inflammatory (Leandra Figueroa-Hall) and neural underpinnings of anxiety (Maria Ironside) and mood disorders (Robin Aupperle, Salvador Guinjoan, Aki Tsuchiyagaito, Masaya Misaki), the breadth and depth of our investigations are truly remarkable. Special attention has been accorded to the delineation of brain-body processing dysfunctions in psychiatric individuals (Sahib Khalsa), integration of AI in mental healthcare (Nick Obradovich), investigation into traumatic brain injuries (Jonathan Savitz), and a thorough examination of substance use on brain processing paradigms (Jennifer Stewart), which are part of our commitment to addressing the multifaceted challenges in psychiatric disorders.

I would be amiss if I did not mention how excited I am about Evan White's evolving research. He was honored with the NIH Director's Pioneer Award (DP1) for his groundbreaking project "Kipiyecipakiciipe – Coming Home." In collaboration with the Shawnee Tribe, Evan's venture melds community-based participatory research with clinical neuroscience to delve into the brain processes affected by traditional cultural engagement concerning substance use disorders. This endeavor not only pioneers the realm of clinical cultural neuroscience but also sheds light on the potential of traditional cultural engagement

in addressing substance misuse. While the data is still being gathered, there's a compelling indication that Evan may be the first American Indian/Alaskan Native recipient of a DP1 award, marking a significant milestone that embodies the essence of diversity and unique contributions in neuroscience and addiction research. This accolade is not merely a recognition of Evan's innovative vision, but also a beacon of inspiration for aspiring researchers from diverse backgrounds, especially within the Native American community. The project holds immense promise for unveiling new insights in neuroscience, enriching the healthcare landscape, and significantly impacting individuals battling substance misuse.



Laureate Institute for Brain Research Campus

The past year has been a period of profound growth, learning, and strategic evolution for LIBR. Our transition to PLPP, buoyed by the stellar work of our investigators and the broader advancements in psychiatry, suggests that there is a promising trajectory towards achieving a substantial, lasting impact on mental health. As we continue to navigate the complex tapestry of mental health challenges, the support and collaborative spirit of the scientific community, stakeholders, and the public are indispensable. Together, we move closer to a future where mental healthcare is more precise, evidence-based, and effective, enriching lives across the globe.



#### **MISSION**

Improving Mental
Health Through
Neuroscience:
To develop products,
which may consist
of new knowledge,
tools, techniques
and interventions for
stakeholders, which
are based on scientific
approaches to improve
mental health
assessment, treatment
and prevention.

#### **VISION**

A clinical neuroscience research institute that recognizes the dignity of each person and leverages leading talent and technology to discover causes of and cures for disorders of mood, anxiety, eating and substance use.

#### VALUES OR GUIDING PRINCIPLES

Understanding of the psychiatric patient requires deeper empirical and quantitative knowledge of psychiatric conditions and is the basis for developing better assessments and treatments for psychiatric disorders.

#### **STRATEGIC AIMS**

To identify, characterize, and develop targetable, disease-modifying processes in mental health. To develop neurosciencebased interventions to improve mental health.

To provide a core service infrastructure to accelerate discoveries by LIBR investigators.

To develop and maintain a workforce of scientific researchers focused on advancing the strategic goals of LIBR.

#### **HISTORY**

LIBR opened on May 1, 2009, and currently houses a multidisciplinary team of scientists and clinical research staff who apply neuroimaging, genetic, pharmacological and neuropsychological tools to investigate the biology of neuropsychiatric disorders. Founded by The William K. Warren Foundation, LIBR's purpose is to conduct studies aimed at developing more effective treatments and prevention strategies for these disorders. The studies are led by scientists from diverse backgrounds, including physics, cognitive neuroscience, psychology, psychiatry, developmental neuroscience, computer science and genetics.



## LIBR BY THE NUMBERS

principal investigators

associate investigators

affiliate

investigators

staff

post-doctoral fellows

graduate students

80+

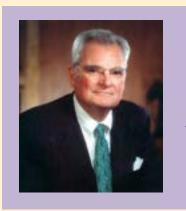
external collaborative investigators

active grants, including clinical trials

new externally funded grants

14+

million dollars in external grant funding



speakers for the William K. Warren Frontiers in Neuroscience lecture series

visiting scientists and distinguished guests

3

Diversity in Mental Health speakers **5,802**inquiries for

inquiries for study participation

1,049

Magnetic Resonance Imaging (MRI) scanning sessions

2,398

participants across all studies

167

participants enrolled in their first MRI study

122

journal article publications by LIBR investigators



## **Scientific Director, COO, CTO**



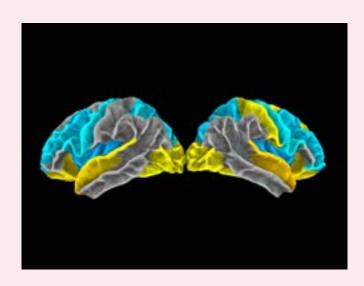
Martin Paulus, M.D.
Scientific Director and President



**Colleen McCallum, M.B.A.**Chief Operating Officer



**Michael Rohan, Ph.D.** Chief Technology Officer



The goal for LIBR is to identify disease-modifying processes (DMP) based on circuits, behavior, or other levels of analysis, which—when modulated—change 1) the risk for, 2) the severity of, or 3) the recurrence of a disease such as mood, anxiety, eating, or substance use disorder.

## CURRENT THEMES

#### **Neuroimaging**

Robin Aupperle • Chun Chieh Fan Salvador Guinjoan • Maria Ironside Sahib Khalsa • Jonathan Savitz • Ryan Smith Jennifer Stewart • Wesley Thompson Maelle Gueguen • Masaya Misaki Haixia Zheng

Specialized
Techniques and Novel
Approaches

Salvador Guinjoan (Focused Ultrasound) Leandra Figueroa–Hall (TLR4 System, Intestinal Models) Nick Obradovich (Environmental Mental Health) Aki Tsuchiyagaito (Real-time fMRI Neurofeedback) Mental Health
Disorders: Anxiety,
Depression, PTSD,
Substance Use Disorders

Robin Aupperle • Maria Ironside • Sahib Khalsa Salvador Guinjoan • Jennifer Stewart Evan White • Maelle Gueguen Aki Tsuchiyagaito • Haixia Zheng

Computational Neuroscience and

Ryan Smith • Masaya Misaki Nick Obradovich • Maelle Gueguen Haixia Zheng

**Machine Learning** 



Laureate Institute for Brain Research

Neuromodulation and Treatment Response

Robin Aupperle • Maria Ironside Salvador Guinjoan • Sahib Khalsa Jennifer Stewart • Aki Tsuchiyagaito Masaya Misaki

Clinical and Cultural Neuroscience

> Evan White • Leandra Figueroa-Hall Maelle Gueguen

Population
Neuroscience and
Genetics

Chun Chieh Fan • Wesley Thompson Jonathan Savitz • Haixia Zheng

## **ABCD Study**

The Adolescent Brain Cognitive Development (ABCD) Study<sup>sM</sup> is in its 8th year of research. LIBR is one of 21 sites across the country. The ABCD study is funded by a UO1 grant from the National Institute on Drug Abuse (NIDA), with Drs. Paulus and Aupperle serving as Principal Investigators for the LIBR site. This study originally recruited >11,000 youth ages 9-10 to join the study, which involves tracking of biological, behavioral, and emotional development through adulthood. LIBR is currently working to complete the 5th year assessments, continue the 6th year assessments, and



has recently begun the 7th year assessments with participants, who are now 15-18 years of age.

The study sponsors (NIH Institutes, including NIDA) have continued their dedication to open science and in Spring 2023 the ABCD 5.0 data set was released at NIMH Data Archive. The data release contains the complete data sets for the baseline, 6-month, 1-year, 18-month assessments and partial data for 2-year, 30-month, 3-year, and 42-month assessments. The ABCD consortium, along with scientists from all over the world have been examining the data, available at ABCD Publications. The LIBR group has continued to contribute to this literature through a number of manuscripts published in the past year. This includes (but is not limited to) reports on how the beneficial effect of sleep on behavioral health problems in youth may be disrupted by prenatal cannabis exposure (three led by Dr. Phil Spechler), how brain structural co-development is associated with internalizing symptoms two years later (Dr. Martin Paulus), and how intelligence polygenic scores are predictive of crystallized intelligence measures in the ABCD study (Dr. Chun Fan and Dr. Wes Thompson), as well as a manuscript describing the procedures, characteristics and resources related to ABCD genotype data (Dr. Chun Fan). Additionally, 3 posters featuring ABCD data were presented at the second annual LIBR Research Day by ABCD research assistants. These projects examined the influence of peer and family conflict on suicidal ideation and self-harm behaviors in sexual and gender minority youths (led by Trinity Lasswell), internalizing symptoms

in children of healthcare workers before and during the COVID-19 pandemic (led by Jolene Tay), and the impact of adverse life events on youth sleep (led by Ailis Reavey).

The ABCD team is continuing to change and grow. This year Alexandria Cooper was promoted to Research Specialist in charge of Study Logistics. In 2023, the ABCD team also welcomed Lucy Duran-Camacho and Emily Giovannetti as new research assistants and promoted our former intern, Amanda Schwenke, into a research assistant position. Additionally, Nour El-Sabbagh was promoted from research assistant to Participant Engagement and Support Coordinator for the RECOVER sub-study to examine the impact of long-term effects of the COVID-19 pandemic.



The ABCD team hosted a Family Appreciation Event in October 2023. They invited more than 740 participants' families to visit the Laureate campus. The goal of the event was to provide study updates, answer participants and caregivers' questions about the study, share recent study findings, and provide an opportunity to connect with our youth and family in a relaxed environment while sharing a meal together. Parents were engaged in an active discussion at the end of the evening focusing on topics ranging from the impact of screen or social media on mental health to concerns about the impact of cannabis and other drugs on brain development. This year, the ABCD team, led by Alexandria Cooper (Research Specialist in charge of Logistics), planned a fun evening showcasing art produced by the ABCD team encapsulating "what ABCD means to me" and featuring a photo booth, caricature artist, arts and crafts station, and games to earn raffle tickets and prizes. The annual event was a huge success.

## **Tulsa 1000 Study**



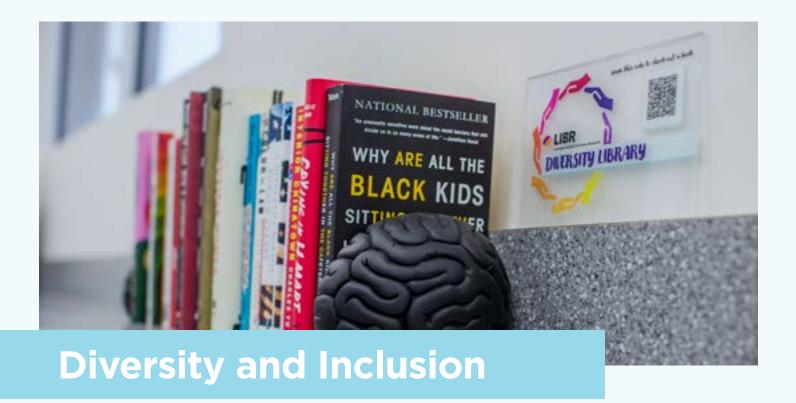
The Tulsa 1000 (T-1000) study, the largest study at LIBR, began in January 2015 and completed baseline enrollment of all 1000 participants in 2018. Participants with disorders of mood and anxiety, eating and substance use completed more than 24 hours of baseline testing including clinical interviews and behavioral and neuroimaging assessments of emotion, cognition, reward and interoception. Longitudinal assessments were conducted with 1-hour follow-up interviews at 3, 6 and 9 months and an 8-hour follow-up session at the 1-year completion mark. Yearly followup assessments continued throughout 2023. The goal for this study is to determine whether neurosciencebased measures can be used to predict outcomes in patients with mental illness. In particular, to determine what factors best predict who will respond well to a particular treatment. The study is a definitive step toward developing a science-based personalized medicine approach in mental health.

To date, more than 40 papers have been published by the T-1000 project authors and their collaborators. Data analysis of the T-1000 variables is ongoing, with more than 30 individual scientific papers in progress for publication. Publications thus far have covered the topics of the relationship between gray matter volume and childhood trauma; behavioral and neural responses during fear conditioning and extinction; the impact of serotonergic medication on interoception; neural processing dysfunctions in depressed individuals with high levels of repetitive negative thinking; the development of automatic pipelines for preprocessing EEG-fMRI data; EEG microstates as

an electrophysiological signature of BOLD resting state networks and characterization of abnormalities in mood and affective disorders; the prediction of brain age from EEG signals using a machine learning approach and the relationship to chronological age; the effect of neighborhood factors on brain structure and function; how body characteristics predict motion in the scanner; how early life stress and adult cytomegalovirus infection are related in mood and anxiety disorders; how processing of body signals differs in individuals with opioid and stimulant use disorders; a potential fMRI-based biomarker for substance use disorder: interoceptive responses in suicide attempters; reward activation with cannabis use in anxious and depressed individuals; elevated peripheral inflammation and reward anticipation in major depressive disorder; polygenic risk scores for neuroticism; rumination circuits within the brain using real-time fMRI functional connectivity neurofeedback; latent variables for brain activation during the monetary incentive delay task; sex differences in inflammatory mediators as a function of substance use disorder; and the distinct oral microbiome pattern in individuals with substance use disorders.

The "Tulsa 1000 Investigators" typically includes the following contributors: Robin Aupperle, Ph.D.; Sahib S. Khalsa, M.D., Ph.D.; Rayus Kuplicki, Ph.D.; Martin P. Paulus, M.D.; Jonathan Savitz, Ph.D.; Jennifer Stewart, Ph.D.; and Teresa A. Victor, Ph.D. For laboratory contributions to analyses of blood/microbiome/saliva, additional contributors include: Kai Ping Burrows, Ph.D. and Leandra Figuerosa-Hall, Ph.D.

In addition to publications, bi-weekly discussions of data analysis pathways and scientific findings with the principal investigators, associate investigators, staff scientists and post-doctoral fellows offer opportunities for new ideas to explore as we work toward developing a personalized treatment approach through the knowledge gained with this comprehensive dataset.



The Diversity and Inclusion Workgroup focuses on 3 main initiatives:

- To enhance our assessment and understanding of context and environment (e.g., social determinants of health) in relation to mental health problems and neuroscientific findings.
- To make an effort to diversify our workforce so that we can bring as many perspectives to our research as possible.
- To work with community stakeholders to arrive at better research questions that can solve problems that affect racial and ethnic minority groups.

This work will continually be a process, without a specific finish line. This year, Dr. Maria Ironside reflected on how enriching and inspiring the interactions have been with the diverse perspectives invited to LIBR as part of this initiative and communicated her enthusiasm for her fellow committee members' consistent perseverance in pursuit of this long-term goal.

In 2023, our quarterly seminar series dedicated to Diversity in Neuroscience brought to Tulsa three talented investigators. Dr. Negar Fani from Emory University discussed her work focused on understanding the neurobiological mechanisms of race-related trauma and pathways for vulnerability and strategies for resilience. Dr. Micah Johnson from the University of South Florida discussed his work examining trauma, substance misuse, and

juvenile justice, and the impact of sociodemographic and sociopolitical factors contributing to outcomes for youth. Dr. Nii Addy, an accomplished researcher as well as Director of Scientist Diversity and Inclusion at Yale School of Medicine, spoke about his work on L-type calcium channel mechanisms in relation to substance use and mood disorders, in addition to his work promoting diverse, equitable and inclusive work environments.

The Diversity and Inclusion Workgroup also leads an ongoing, monthly reading and discussion group, where all faculty and staff at LIBR are invited to join a discussion of readings. Over the past year, this has included discussing articles related to the role of religion and faith in mental health and science; racial and ethnic differences in the effects of adverse childhood experiences on substance misuse; consideration of types of diversity training that may do more harm than good; the history of conversion therapy in psychological research; historical trauma effects and healing in the context of the Tulsa Race Massacre: the detrimental mental health impacts of Native American mascots; and the different factors that may be important to consider when studying suicide risk in diverse communities. The purpose of these discussion groups is to increase our comfort with engaging in difficult conversations in science and broaden our perspectives concerning the factors to consider in research related to mental health and neuroscience.

The Diversity and Inclusion Workgroup also supported the continuation of the Diversity in Research and Multidisciplinary Neuroscience (DREAM-Neuro) Fellowship and the LIBR Advanced Summer Research (LASR) internship, both of which have been successful in not only supporting undergraduate and post-baccalaureate students in their educational and professional goals but also in recruiting new talent to LIBR. These training efforts are currently being led by Dr. Leandra Figueroa-Hall. We also identified a free online training program for all mentors at LIBR to use to enhance their mentorship skills when working within scientific labs, provided through the National Research Mentoring Network that was originally developed via funding from the National Institutes of Health (NIH). We hope to continue to increase our inclusion as well as mentorship of diverse talent at all levels of our organization.

Research endeavors have been initiated that would incorporate some of the ideas generated through the discussion groups, conversations with visiting scientists, and local community partnerships. Dr. Robin Aupperle will be initiating a small pilot study in concert with Lizbeth Rojas (current DREAM-Neuro fellow) and Elisabeth Akeman (MA, LPC) to conduct focus groups with potential research participants, who are primarily Spanish-speaking, to obtain input on the obstacles and opportunities for increasing engagement with Spanish-speaking communities in future research efforts. Dr. Evan White, in collaboration with Cherokee Nation Behavioral Health, brought in a collaborator—Dr. John Markowitz (Columbia University)—to provide an interpersonal psychotherapy training workshop. The goal of this effort is to support

future collaborations between LIBR and Cherokee Nation for clinical outcome and potential treatment adaptation studies. In July 2023, Dr. White's DP1 proposal titled "Kipiyecipakiciipe - Coming Home: Establishing clinical cultural neuroscience as a tool for understanding the role of traditional cultural engagement in mitigating substance misuse and disorder" was funded. This project combines a communitybased participatory research approach with clinical neuroscience methods to establish neuroscientific indicators of cultural protective factors against substance use and addiction. Relationship building with the Shawnee Tribe has been critical to the development of this project. The Shawnee Tribe, as well as a community advisory board comprised of Shawnee adults, will help guide culturally appropriate work and ensure the community-level impact of the efforts.

Within the larger U.S. neuroscience community, Drs. White and Aupperle serve on the Culture and Environment Workgroup for the multi-site Adolescent Brain and Cognitive Development (ABCD) Study<sup>SM</sup>, for which LIBR is also a site. Dr. White is also serving as the chair of the Native American Issues in Behavior Therapy and Research Special Interest Group of the Association for Behavioral and Cognitive Therapies. Through the Diversity and Inclusion Workgroup, we have also increased our presence in the local Tulsa community, attending events such as the American Foundation for Suicide Prevention Out of Darkness Walk, the Tulsa Mental Health Walk, Tulsa Pride, and multiple Pow Wows in the region. We also organized donation drives for school supplies to support the local TTCU Project School Supplies and for Christmas gifts for children of women in the Women in Recovery (WIR) program. Within LIBR, we have also increased our efforts to recognize and encourage celebration of culturally relevant holidays like the Mid-Autumn Festival and Día de los Muertos.

The Diversity and Inclusion Workgroup is not only proud of the accomplishments achieved since being established in 2020 but also has numerous goals for 2024 and into the future. We look forward to establishing new community partnerships, increasing the representation of under-represented groups in science, and further enhancing our research through the consideration of modifiable factors that may increase risk or protect against mental health problems for individuals of diverse races, ethnicities, cultures, and backgrounds.



The Electroencephalography (EEG) Core is among the newest additions to LIBR's Core services, established in January 2022 and previously operated under LIBR MRI and EEG Neuroimaging Core since June 2010. The EEG Core provides LIBR researchers and external collaborators with easy access to state-of-art equipment, tools, resources, technical support, and preprocessing needed for research including EEG techniques. Our goal is to implement best practices of EEG acquisition, data processing, and analysis to enable investigators to conduct world-class EEG research.

The EEG Core is equipped with two complete sets of up to 128-channel, high-density, MRI-compatible BrainAmp-MR-plus EEG systems for measuring brainwaves within MRI scanners. Also, the Core supports standalone, 32-channel BrainAmp EEG systems for recording standard EEG brainwaves outside MRI scanners for more traditional EEG protocols. Each recording system can be paired systems for recording physiological signals simultaneously. The functionality of main hardware, accessory equipment, and consumables are maintained and inspected regularly by EEG Core staff to ensure the quality of each scanning session. Recorded raw neurophysiological data are digitized online and stored on the LIBR server.

The EEG core supports preprocessing through standard and customizable pipelines using BrainVision Analyzer software or Matlab based EEG/ERPLAB. Most processing is done by trained EEG Core staff to ensure processed data meets the standard of specific field and researcher needs. Our staff also provide services such as onboarding training for research assistants and staff on EEG data acquisition (capping, recording, etc.) and basic processing, consultation for study design, data collection, stragetic analyses, assisting with institutional review board (IRB) applications, pipeline customization, programming, grant methods, and result interpretation upon request. Since the facility was established, we have hosted a hybrid EEG training workshop, several in-person data acquisition training courses, and research consultation sessions.

The EEG Core is directed by Dr. Evan White, LIBR Principal Investigator, an expert in EEG/eventrelated potentials (ERPs) and clinical translation psychophysiology, supported by staff scientist Dr. Xi Ren, who specializes in EEG/ERP analysis and source localization, and research assistant Eric Mann, B.A.







# Magnetic Resonance Imaging (MRI) Core

Established in July 2009 and in research operation since June 2010, the Magnetic Resonance Imaging (MRI) Core provides advanced state-of-the-art structural MRI, functional MRI (fMRI), simultaneous electroencephalography (EEG) recording with fMRI, and real-time neuroimaging capabilities. Two MRI scanners are fully dedicated to research and provide an advanced capacity for the latest quantitative imaging of the human brain structure and online monitoring of brain activity in real-time. The two scanners can also be synchronized and integrated for hyperscanning, where EEG and fMRI signals of two interacting subjects are measured simultaneously.

The MRI Core provides all of the latest technology, tools, and resources necessary to conduct and support brain neuroimaging studies focused on advancing clinical research to discover novel interventions for mood, anxiety, eating, and memory disorders.

In 2023, LIBR purchased a new magnetic resonance system, a Siemens 3.0 Tesla Prisma NX, to replace the original system installed in 2009. The arrival of this new system with state-of-the-art radiofrequency (RF) coils and methods will support more powerful imaging results in the coming decade. The new system is the focus of several NIH grants and LIBR projects awarded in 2023. It complements the ongoing work supported by the second scanner, a General Electric 3.0T Discovery 750.

LIBR's custom-made data management system allows for automatic handling of large amounts of neuroimaging data and real-time integration of fMRI, physiological data (respiration, pulse oximetry, or electrocardigram waveforms), and EEG data simultaneously acquired with fMRI. These capabilities enable live monitoring of ongoing brain activation in real-time with extensive multimodal information.

LIBR employs a custom, real-time imaging system that provides continuous, scan-quality monitoring, resulting in superior functional MRI. This real-time system is also an integral part of a neurofeedback system, in which subjects are trained to self-modulate their thoughts and brain activity using feedback that is calculated from their own scans in real time. Neurofeedback is being investigated as a potential treatment for psychiatric disorders. Neurofeedback also provides online optimization of brain stimulation with simultaneous transcranial direct or alternating current stimulation (tDCS/tACS) during fMRI.

The advanced combination and customization of state-of-the-art MRI, RF coils, EEG, and brain stimulation technologies, along with custom-developed software solutions and a wide range of auxiliary computerized equipment, offer a unique potential for conducting advanced brain research. The MRI Core also supports collaborative neuroimaging research with researchers from local academic institutions, including The University of Oklahoma and The University of Tulsa.

The MRI Core is directed by Michael Rohan, Ph.D., an expert in functional imaging systems and methods. It operates with the technical support of Masaya Misaki, Ph.D., an expert in multimodal neuroimaging data analysis and information technology and under the management of Julie Arterbury, Chief MRI Technologist. Additional staff includes two MRI technologists, Leslie Walker and Amy Ginn.

The MRI Core was founded and built by Jerzy Bodurka, Ph.D., and is named in his honor.

# **Biomedical Laboratory Core**



The Biomedical Laboratory Core houses four laboratory rooms dedicated to human blood processing, long-term specimen biobanking, bioassays, and extracellular vesicle (EV) research. Human blood and saliva are routinely collected, and blood is processed for serum, plasma, and peripheral blood mononuclear cells (PBMCs), aliquoted, and appropriately stored for LIBR investigators.

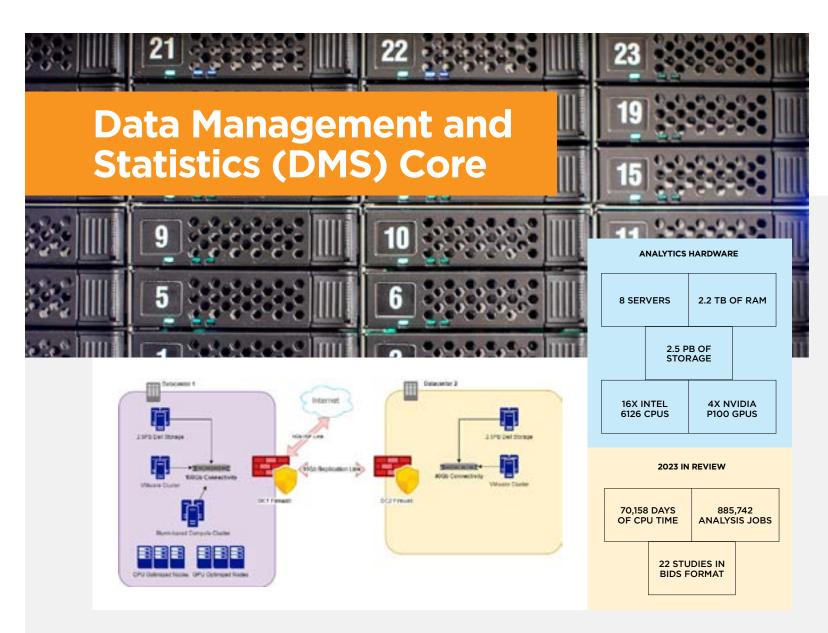
#### Laboratory Rooms

The specimen sample processing room contains recently purchased state-of-the-art equipment including 1) a Biosafety Level 2 (BSL-2) laminar flow cabinet for making sterile aliquots of samples; 2) a Beckman Coulter Avanti J-15R refrigerated centrifuge for blood cell processing; 3) small clinical centrifuges for serum and plasma processing; 4) Invitrogen Countess 3 Automated Cell Counter for cell counting; and 5) a label-maker for labeling storage vials.

The biobanking room contains three recently purchased, large ultralow (-80°C) temperature freezers for specimen biobanking and long-term storage, and a mini -80°C freezer for temporary storage of unfilled specimen boxes to avoid frequent opening and closing of biobank freezers. The biobanks are in secure rooms with access given only to approved personnel. All freezers used for biobanking are on continuous generator backup power. The freezers are monitored 24 hours per day with Sensaphone technology and Monnit Smart Monitoring Systems that send emails, text messages, and phone calls to staff scientist Dr. Kaiping Burrows in case of any disruption in power, sensor disconnection, or change in temperature. The biobanks are monitored and tracked by biorepository monitoring and inventory software (Freezerworks) and kept on the LIBR server. In addition to electronic inventories, handwritten logbooks are securely stored in the laboratory in case of server loss of function.

The bioassay room is mainly used to measure blood or saliva-based biomarkers using enzyme-linked immunosorbent assay (ELISA) to assess immune, metabolic and stress-related markers. This room also serves as a second blood processing room. Other experiments such as ribonucleic acid (RNA) extraction and complementary deoxyribonucleic acid (cDNA) transcription are conducted in this room. The equipment/software in this room includes 1) a BioTek 50 TS automated microplate washer for ensuring rapid and even washing of plates; 2) a BioTek 800 TS Absorbance Microplate Reader with onboard software through a color touchscreen interface, and Gen5 software for ELISA data reading; 3) a small BSL-2 laminar flow cabinet for RNA extraction, and other experiments to prevent contamination; 4) a NanoDrop for micro-volume analysis of purified nucleic acids; 5) an undercounter refrigerator and freezer (-20°C) for storing ELISA kits or reagents that require 2°C to 10°C, or < -20°C controlled temperatures; 6) 3 refrigerated and unrefrigerated centrifuges for RNA extraction. processing PBMCs, or centrifuging plasma, serum, or saliva samples after defrosting; and 7) single and multichannel pipettors for bioassay precision and accuracy.

The EV research room is designed to isolate and characterize brain-enriched EVs from human serum or plasma. Major equipment in this room includes 1) a nanoparticle size analyzer to measure exosome size and concentrations: 2) a gEV Automatic Fraction Collector (AFC) for precise EV isolation using size exclusion chromatography methods; 3) a large laboratory refrigerator for storing reagents and preforming experiments (e.g., rotating samples overnight at 4°C) that require 2°C to 10°C controlled temperatures; 4) a freezer (-20°C) and an ultralow temperature freezer (-80°C) for storing samples or reagents that require < -20°C or < -70°C controlled temperatures; and 5) an ice maker to create ice flakes for defrosting frozen plasma/serum samples and keeping some reagents cold during lab experiments. Other equipment in the EV research room includes a sonicator for resuspending pellets, centrifuges for EV isolation, and a rotating mixer for gentle to vigorous mixing of laboratory samples.



The Data Management and Statistics (DMS) Core makes research at LIBR possible by providing services from data collection and organization through production of final results.

Hardware: LIBR maintains a powerful, remotely accessible analysis cluster running the SLURM batch scheduler. This allows researchers to run hundreds of jobs spread across an array of servers in a fraction of the time it would take on a local workstation. For example, 8 analysis servers give researchers access to about as much computing power as 50 typical workstations. LIBR also has a newly upgraded, massive network-attached storage system complete with off-site backup in Oklahoma City. This system provides superior performance and security on-site plus a recovery plan should there be a disaster at the LIBR campus.

**Data Analysis and Statistics:** The DMS Core provides consultation and support to every lab at the institute and is responsible for processing several shared datasets including the Tulsa 1000 and CoBRE Core. Services in this area include study design and project planning through the development of custom analysis pipelines and interpretation of results.

Data Management: All studies conducted at LIBR are organized according to the Brain Imaging Data Structure (BIDS). BIDS is a standard providing best practices for the organization and documentation of complex neuroimaging and related datasets. BIDS has become the de facto standard used across institutes, and data sharing arrangements are increasingly contingent on the format. The DMS Core also facilitates compliance of funded studies with the new NIH data-sharing policy.

## Population Neuroscience and Genetics (PoNG) Center





PoNG Center Directors:

Drs. Chun Chieh Fan and Wesley Thompson

The LIBR Population Neuroscience and Genetics (PoNG) Center remains committed to its mission of advancing the field of population neuroscience through innovative research and collaboration. Our achievements in 2023 serve as a strong foundation for our future endeavors, and we look forward to another year of groundbreaking research and discovery. This report outlines the significant advancements we have made in our core aims.

## Aim 1: Development and Adaptation of Statistical Methods

Throughout 2023, our team has made considerable strides in refining statistical methods for neuroscience research.

Notably, we introduced the Zero Inflated Variance (ZIV) estimator, an innovative approach for interpreting brain imaging data through questionnaire responses. Furthermore, we crafted a novel algorithm capable of integrating spatial molecular annotations of the human brain, significantly enhancing our interpretation capabilities of brain imaging data.

2023 has seen the successful application of our analytical tools to large-scale datasets, a testament to our collaborative efforts with international registries. We have published impactful papers using registries from Denmark and Taiwan, providing deeper insights into the biological mechanisms and heterogeneity of neuropsychiatric outcomes at the population level.

Aim 3: Application of Analytical Tools

to Large-Scale Data

for Multidisciplinary Research

The PoNG Center has further established itself as a pivotal hub for researchers from various disciplines. Our organization of a hackathon at LIBR has been particularly notable, offering guidance to early investigators on obtaining their K grants and fostering a collaborative environment for innovation.

Aim 4: Establishment as a Hub

## Aim 2: Integration of Whole-Brain Imaging with Molecular Assays

Our commitment to bridging whole-brain imaging with detailed molecular assays has been fruitful. The publication of several imaging genetics papers, featuring our novel analytic techniques, underscores this success. Key discoveries include the identification of molecular factors that influence astrocyte function and their role in shaping the human brain, as well as factors affecting iron accumulation in motor neurons.





The Laureate Institute for Brain Research (LIBR) is home to the world's first research laboratory investigating the effects of floatation therapy on both the body and the brain, as well as exploring its potential as a therapeutic treatment for improving mental health and well-being in individuals with various forms of psychiatric disorders inlcuding anxiety, depression, or eating disorders.

The Float Clinic and Research Center (FCRC) is directed by Dr. Sahib Khalsa and currently in its 7th year of operation. Initial studies published in 2018 found that floating appears to guickly reduce levels of stress, muscle tension, and blood pressure in individuals with anxiety and depression. A study published in 2020 led by Dr. Khalsa found floating to be safe in outpatient individuals with eating disorders, and lowered levels of anxiety, stress, and blood pressure, as well as improved body image. A study published in 2021 found patterns of reduced functional connectivity between regions of the brain involved in mapping body sensation and selfrepresentation in healthy individuals. This study provided the first functional neuroimaging evidence of the effects of floating on brain function. Another study published in 2022 found changes in heart rate variability and blood pressure during floating, providing further evidence that it lowers sympathetic arousal and alters the balance of autonomic nervous system functioning toward a parasympathetic state.

Building from this base of knowledge, two studies published in 2023 led by Dr. Khalsa reported on the feasibility and tolerability of floatation therapy as a technique for reducing anxiety and depression in individuals with high levels of anxiety and depression. One of these studies, published in the first issue of the Journal of Mood and Anxiety Disorders, demonstrated that floatation therapy was associated with anxiolytic and antidepressant effects lasting for up to 2 days in some individuals. Also in 2023, a LIBR-funded clinical trial led by Dr. Khalsa was published examining the efficacy of floatation therapy as a technique for reducing body image disturbance and anxiety in individuals with anorexia nervosa hospitalized for inpatient treatment at the Laureate Eating Disorders Program. This study was first-authored by Dr. Emily Choquette, who joined LIBR as an Associate Investigator at the end of 2023, and conducted in partnership with Dr. Scott Moseman, the medical director of the Laureate Eating Disorders Program, and the clinical staff from the program. Importantly, at the end of 2023, Dr. Choquette also received a mentored career development (K23) award from the National Institute of Mental Health (mentored by LIBR investigators Drs. Sahib Khalsa and Robin Aupperle), to study the integration of floatation therapy with evidencebased psychotherapy for body image in inpatient women with anorexia nervosa. This new approach, called float-assisted psychotherapy, seeks to boost the body image improvement effects seen in each individual therapy, and could result in a new form of mind-body treatment for eating disorders.

Overall, 2023 was a very fruitful year for the FCRC, with studies showing evidence of safety, feasibility, or clinical impact for 3 major types of psychiatric conditions.



Over the course of 2023, LIBR has explored the utility of a new transcranial, low-intensity focused ultrasound (LIFU) device for the modulation of brain circuit activity in a safe, noninvasive, and reversible manner. After obtaining a Non-Significant Risk determination from the Food and Drug Administration for our study protocol, we have completed recruitment of patients who suffer from major depression and are affected by rumination of different intensities. In a preliminary analysis of the initial group of patients with major depression, we have demonstrated that sonication of white matter tracts produces reliable modulation of their gray matter destinations. Thus, employing resting-state functional MRI, we observed functional disconnection between thalamus or striatum, and different regions of the prefrontal cortex, including cingulate and orbitofrontal regions. If confirmed in the whole sample of patients (and a group of healthy controls which is close to completion), this observation would pave the way to a new, safe, noninvasive, and financially efficient method to explore brain mechanisms of symptom generation in psychiatric disorders, and possibly its application with therapeutic purposes in the not-so-distant future. This approach aligns optimally with LIBR's aims and objectives, in its quest to understand the neurobiological bases of psychiatric conditions and potential treatments for them.

In LIFU, a transducer converts electrical into mechanical energy in the form of high frequency soundwaves (250-500 kHz), able to traverse the skin and the cranium and focus on a certain region of the brain. Since the device used at LIBR permits steering the depth of the

ultrasound focus, the resulting mechanical energy can be concentrated in a relatively small region with anatomical precision. This is done with the help of a neuronavigator, a complex optical system and software which guides the operator by computing the position of the transducer and the location of the tissue to be modulated, in a similar way to a Global Positioning System (GPS). Although this is an emerging method and the field is still pursuing a standardization of stimuli, these characteristics make LIFU a human neuroscience research tool whose potential is unmatched by any other available technique.

The multidisciplinary team of this study includes Megan Cole, Lindsay Bailey, Dara Critten, and Courtney Boone in the assessment of participants, whereas the operation of the experiments is done jointly by Dr. Aki Tsuchiyagaito and Dr. Salvador Guinjoan, who acts as responsible investigator.

#### Dr. Evan White's Lab



LIBR received funding through the National Institutes of Health (NIH) Director's Pioneer Award (DP1 Mechanism) for an innovative collaborative research project "Kipiyecipakiciipe - Coming Home" between the LIBR and the Shawnee Tribe. The research will be led by Dr. White, Principal Investigator and **Director of Native American Research** at LIBR. This partnership, which is supported by a \$5.9 million, 5-year NIH DP1 grant (DP1DA058986), aims to establish clinical cultural neuroscience as an indispensable tool in communitydriven research to reduce substance misuse and disorder.

Danielle Bethel received the Fan Favorite Award at the 2nd Annual LIBR Research Day for her poster on "Development and Validation of American Indian Cultural Identity Stimulus Set: Implications for Future Research and Addressing Mental Health Disparities.

#### Dr. Leandra Figueroa-Hall's Lab



Dr. Figueroa-Hall was selected to participate in the Early Career Reviewer program at the Center for Scientific Review, National Institutes of Health. Dr. Figueroa-Hall attended her first scientific grant review meeting as an adhoc reviewer for the Cellular and Molecular Biology of Glia Study Section in October 2023.

Dr. Figueroa-Hall received travel and registration benefits to attend the 2023 American College of Neuropsychopharmacology (ACNP) Annual meeting in Tampa, Florida, where she presented a poster titled, "Astrocyte-enriched extracellular vesicle vascular injury proteins and hsa-let-7f-5p expression after in vivo immune challenge in major depressive disorder."

#### Dr. Maria Ironside's Lab



Dr. Ironside received an R01 grant from the NIMH entitled: "Processes and circuitry underlying threat sensitivity as a treatment target for comorbid anxiety and depression" and became a member of the British Association of Psychopharmacology.

#### Dr. Robin Aupperle's Lab



Dr. Aupperle received an R34 grant from NIAAA entitled "Developing and Evaluating a Positive Valence Treatment for Alcohol Use Disorder with Anxiety or Depression" (Co-PI with Dr. Charles Taylor at UCSD).

Dr. Aupperle also received funding through the U.S. Department of Defense Congressionally Directed Medical Research Program (CDMRP) for a project entitled "SMART-CPT for PTSD and History of Concussion: A Pragmatic Implementation Trial" (Site PI, study PI: Dr. Amy Jak, San Diego VA).

Dr. Timothy McDermott completed his Ph.D. in Clinical Psychology at The University of Tulsa. He began a position as a postdoctoral research fellow at Emory University, funded through an NIH F32 fellowship award.

Dr. Kelly Cosgrove completed her Ph.D. in Clinical Psychology at The University of Tulsa. She began a position as postdoctoral research fellow in the Developmental Psychobiology Research Group T32 Training Program at the University of Colorado School of Medicine.

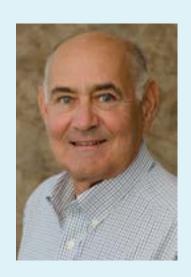
Dr. Hannah Berg received a Career Development Leadership Program Award from the Anxiety and Depression Association of America (ADAA) and a conference travel award from the Association of Behavioral and Cognitive Therapies (ABCT).

**Dr. Emily Choquette** was awarded a K23 Patient Oriented Career Development Award entitled "Interoceptive mechanisms of body image disturbance in anorexia nervosa."



#### In Remembrance of Dr. William "Bill" Yates

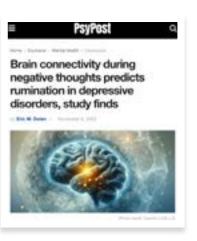
With profound sadness, LIBR shared in the grief of the sudden passing of our colleague, Dr. William "Bill" Yates, on January 19, 2023. Bill was a member of the Laureate Institute for Brain Research Board of Directors and had been a core supporter of LIBR from the very beginning. He was a member of the Department of Psychiatry, University of Oklahoma College of Medicine, Tulsa, and the lead investigator for the local site of the highly influential STAR\*D trial. Bill continued to work with staff at LIBR to improve diagnostic assessment, provided thoughtful comments about proposed studies at LIBR, and helped to support the establishment of the Tulsa 1000 (T-1000) study. In his private life he was an expert birder and photographer, who loved to spend time in different parts of the country taking amazing photographs. We will miss his genuine warmth and kindness to all, and the depth of his psychiatric expertise gifted to our community.





## 10th Annual LIBR Investigator Retreat

LIBR Investigators gathered at Shangri-La Resort for their 2023 annual scientific retreat. The gathering was a time to reflect on the progress of the institute over the past year and look ahead to future research endeavors through open discussion and engagement.



## PsyPost.org Connected with Dr. Masaya Misaki to Discuss His Research Published in the Journal of Affective Disorders

"Repetitive negative thinking (RNT), a cognitive process characterized by a passive, repetitive, and evaluative focus on distressing thoughts, is associated with significant distress in several mental disorders, including major depressive disorder," said Dr. Misaki, associate investigator at LIBR. The patterns of brain activity when people with major depressive disorder (MDD) engage in repetitive negative thinking can predict how prone they are to such thoughts. The findings provide new insights into the neurobiological processes underlying depression.

Brain Connectivity During Negative Thoughts Predicts Rumination in Depressive Disorders November 6, 2023, PsyPost | Read the full article.

Dr. Nick Obradovich Contributes to Annual Health and Climate Change Report Published in The Lancet

Read the full article.



The Lancet Countdown 2023 Report revealing the human cost of climate inaction was covered by numerous media outlets including ABC, the AP, Axios, El Pais, CNN, The Guardian, NBC, the NYT, and the Washington Post. Dr. Nick Obradovich, a contributing author and Chief Scientist for Environmental Mental Health at LIBR said:

"We know from an increasingly large body of research that environmental stressors like extreme heat, flooding, and large storms impede our physical and mental health. They simply make it harder for us to be well, a fact we observe via our indicator on social media sentiments that decline in response to adverse climatic conditions. The broad efforts by our Lancet Countdown team to trace and monitor the myriad manners in which climatic stressors are altering human well-being represent an important undertaking. I'm pleased to be a part of this project and look forward to ever more high-quality research feeding into the process and informing the indicators and metrics we monitor going forward."

Dr. Obradovich's work on sleep and climate change was covered by the Washington Post:

The Unexpected Force That May Make Us Get Less Sleep May 21, 2023, Washington Post | Read the full article.

Dr. Nick Obradovich contributed to an **NPR 1A podcast segment** that discussed emerging research on how heat can affect our mental health and ways to prepare for a heat wave's effect on not only our bodies, but our brains as well.

Listen to the podcast segment.





## Innovative Therapy for Anorexia Nervosa Shows Promise

Can a novel, non-pharmacological treatment help with body image and anxiety in anorexia nervosa? LIBR's latest study of floatation-REST suggests that it can, offering a promising new treatment direction for eating disorders.

"The study showed that after each floatation-REST session, participants in this group reliably had reduced body image dissatisfaction," said Dr. Sahib Khalsa, who serves as Director of Clinical Operations at LIBR. "Overall, these reductions remained 6 months after floatation-REST intervention. There were also large reductions in anxiety after each floatation-REST session."

Congratulations to the Khalsa Lab, co-first authors Drs. Emily Choquette and Michael Flux, and collaborators at the Laureate Eating Disorders Program and Float Research Collective on their trailblazing new research published in eClinicalMedicine, a part of The Lancet Discovery Science initiative.

Read the full article.

LIBR Received the NIH
Director's Pioneer Award
for Innovative Research
Collaboration with
the Shawnee Tribe led
by Dr. Evan J. White

Read the full article.

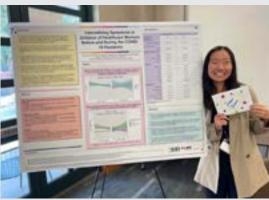




An innovative, collaborative research project "Kipiyecipakiciipe - Coming Home" between LIBR and the Shawnee Tribe received funding through the prestigious National Institutes of Health (NIH) Director's Pioneer Award (DP1 Mechanism) awarded to Dr. Evan J. White, Principal Investigator and Director of Native American Research at LIBR. The goal of the project is to address substance use problems that impact Native American people at higher rates than the general population. "Being involved in traditional ways of life has many benefits, and research shows that reducing and preventing substance use is one benefit," said Dr. White. "Our goal is to use modern clinical neuroscience to help understand the way this impacts the brain to promote substance use recovery and prevention."







#### 2nd Annual LIBR Research Day

"LIBR Research Day" has quickly become one of LIBR's favorite summer events. The 2nd annual poster session was filled with bright and talented LIBR trainees sharing their research methods and results, building presentation skills and engaging with the local community. Special thanks to the organizers and judges for another successful event.

## Understanding the Gut-Brain Connection

A pioneering study conducted by LIBR researchers made significant strides in understanding the elusive gut-brain connection, a complex relationship that has long puzzled scientists due to the difficulty of accessing the body's interior. The study, "Parieto-occipital ERP indicators of gut mechanosensation in humans," appeared in the peer-reviewed scientific journal Nature Communications. "We were able to localize most of the capsule stimulations to the gastroduodenal segments of the digestive tract using abdominal X-ray imaging," said Dr. Sahib Khalsa, senior author on the study.

"This finding is crucial as it provides

a more precise understanding of where these gut-brain interactions are originating."

Read the full article.





## 2023 Zarrow Mental Health Symposium Speakers

Several LIBR researchers participated as speakers in the 2023 Zarrow Mental Health Symposium "New Horizons in Brain Science" organized and hosted by the Mental Health Association Oklahoma on September 20–23, 2023.

#### **Neurobiology and Eating Disorders**

Scott Moseman M.D., CEDS Sahib Khalsa M.D., Ph.D.

#### Practical and Neuroscientific Perspectives of Behavioral Therapy

Robin Aupperle, Ph.D. Elisabeth Akeman Hannah Berg, Ph.D.

#### A Window Into the Depressed Brain

Leandra Figueroa-Hall, Ph.D., MSc, BSc Kaiping Burrows, Ph.D.

#### Focused Ultrasound: An Emerging Neuromodulation Tool

Salvador Guinjoan, M.D., Ph.D. Aki Tsuchiyagaito, Ph.D.

#### **ACTIVE GRANTS**

#### National Institutes of Health (NIH): National Institute of Drug Abuse (NIDA)

15/21 Adolescent Brain Cognitive Development (ABCD)— USA Consortium: Research Project Site at LIBR 04/15/2020 – 03/31/2027

 $\label{eq:principal investigators: Martin Paulus, M.D., and Robin Aupperle, Ph.D. \\$ 

Plasticity of Aversive Salience in Opioid Use Disorder 03/01/2021 – 12/31/2025
Principal Investigator: Jennifer Stewart, Ph.D.

"Kipiyecipakiciipe – Coming Home: Establishing clinical cultural neuroscience as a tool for understanding the role of traditional cultural engagement in mitigating substance misuse and disorder"

07/01/2023 - 05/31/2028

Principal Investigator: Evan White. Ph.D.

Interoceptive mechanisms of body image disturbance in anorexia nervosa 12/01/2023 – 11/30/2028

**Principal Investigator: Emily Choquette** 

#### NIH: National Institute of Mental Health (NIMH)

Neural Response to Inflammatory Challenge in Major Depressive Disorder 05/14/2021 – 04/20/2026
Principal Investigator: Jonathan Savitz, Ph.D.

A Neurocomputational Assay of Gastrointestinal Interoception in Anorexia Nervosa

09/01/2021 - 06/20/2027

Principal Investigator: Sahib Khalsa, M.D., Ph.D.

(co-funded by the National Institute for General Medical Science (NIGMS))

An Approach-Avoidance, Computational Framework for Predicting Behavioral Therapy Outcome in Anxiety and Depression

07/01/2020 - 06/30/2025

Principal Investigator: Robin Aupperle, Ph.D.

Neural Basis of Meal Related Interoceptive Dysfunction in Anorexia Nervosa 05/01/2017 – 03/31/2023

Principal Investigator: Sahib Khalsa, M.D., Ph.D.

In vivo inflammatory challenge to elucidate the roll of the toll-like receptor 4 pathway in depression

04/01/2022 - 03/31/2024

Principal Investigator: Leandra Figueroa-Hall, Ph.D.

Effects of pandemic-related disruption to social connectedness on the brain and emotional wellbeing in adolescents

06/01/2022 - 12/30/2026

Principal Investigators: Chun Chieh Fan, M.D., Ph.D., and Wesley Thompson, Ph.D.

Identifying and quantifying genetic effects on neurodevelopmental trajectories in adolescents

06/01/2022 - 01/31/2025

Principal Investigator: Chun Chieh Fan, M.D., Ph.D.

#### NIH: National Institute of General Medical Sciences (NIGMS)

The Center for Neuroscience-based Mental Health Assessment and Prediction (NeuroMAP) 09/15/2017 - 06/30/2023

Principal Investigator: Martin Paulus, M.D.

#### NIH: National Institute on Minority Health and Health Disparities (NIMHD)

Neuroscientific Exploration of Cultural Protective Factors in American Indians 12/01/2022 – 11/30/2025

Principal Investigator: Evan White, Ph.D.

#### **Brain and Behavior Research Foundation (formerly NARSAD)**

Examining the Utility of Frontoparietal Synchronization to Modulate Drug Craving to Enhance Self-Control to Cue Induced Cravings in Individuals with Opioid Use Disorder 01/15/2019 — 01/14/2023

Principal Investigator: Hamed Ekhtiari, M.D., Ph.D.

#### Presbyterian Health Foundation (PHF)

(University of Oklahoma)

Structural and Functional Markers of Injury in Cervical Spinal Compression 07/01/2020 – 06/30/2023
Principal Investigators: Martin Paulus, M.D., and Zachary Smith, Ph.D.

#### Wellbeing for Planet Earth Foundation, Japan

Using active inference to uncover the neurocomputational mechanisms that contribute to well-being and their potential differences across diverse populations 04/09/2022 – 04/08/2025

Principal Investigator: Ryan Smith, Ph.D.

#### **ACTIVE SUBAWARDS**

#### National Institutes of Health (NIH): National Institute of Mental Health (NIMH)

Road Map to Precision Psychiatry: Comprehensive Investigation of Chromosomal Anomalies (PsychMap)

04/01/2021 - 02/28/2026

Prime Awardee: Region Hovedstaden, Denmark – Thomas Werge, Ph.D. LIBR Subaward PI: Wesley Thompson, Ph.D.

Estimating the Fraction of Variance Explained by Genetics and Neuroanatomy in Neuropsychiatric Conditions

08/15/2022 - 06/30/2027

Prime Awardee: University of California San Diego — Armin Schwartzman, Ph.D. LIBR Subaward PI: Wesley Thompson. Ph.D.

Population-Level and Mechanistic Dissection of 17q21 Structural Variant Association with Psychiatric Traits

06/01/2022 - 04/30/2025

Prime Awardee: University of Pennsylvania – Michael Gandal, Ph.D. LIBR Subaward PI: Wesley Thompson, Ph.D.

#### NIH: National Institute of Drug Abuse (NIDA)

ABCD-USA Consortium Data Analysis Informatics and Resource Center 09/30/2015 – 03/31/2027

Prime Awardee: University of California San Diego – Anders Dale, Ph.D. LIBR Subaward Pl: Wesley Thompson. Ph.D.

Interpretable Deep Forecasting of Hazardous Substance Use During High School 09/30/2022 – 08/31/2027

Prime Awardee: Stanford University – Kilian Pohl. Ph.D.

LIBR Subaward PI: Wesley Thompson, Ph.D.

Healthy Brain and Child Development National Consortium Data Coordinating Center 07/01/2022 – 06/30/2026

Prime Awardee: Washington University – Christopher Smyser LIBR Subaward PI: Wesley Thompson, Ph.D.

#### NIH: National Institute on Alcohol Abuse and Alcoholism (NIAAA)

NCANDA Data Analytics

08/10/2022 - 06/30/2027

Prime Awardee: Stanford University — Kilian Pohl, Ph.D.

LIBR Subaward PI: Wesley Thompson, Ph.D.

#### Department of Defense (DoD)

SMART-CPT for PTSD and History of Concussion: A Pragmatic Implementation Trial 06/15/2023 – 06/14/2027

Prime Awardee: University of California San Diego – Amy Jak, Ph.D. LIBR Subaward PI: Robin Aupperle, Ph.D.

#### Private: Oklahoma Clinical and Translational Science Institute

Prognostic Utility of MRI Based Bio-Markers in Degenerative Cervical Myelopathy 11/01/2021 – 10/31/2024

Prime Awardee: University of Oklahoma – Yuan Yang, Ph.D.

LIBR Subaward PI: Martin Paulus, M.D., and Michael Rohan, Ph.D.

#### **2023 DONORS**

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Grand Addiction Recovery Center (ARC), formerly 12&12, Inc., continues to solidify its position as the leading Comprehensive Community Addiction Recovery Center (CCARC) in Oklahoma. With a 35-year legacy of helping individuals overcome addiction and co-occurring mental health disorders. Grand ARC remains dedicated to providing comprehensive care and supporting individuals throughout their recovery journey.

#### This past year, Grand ARC has made significant strides in:

- Expanding treatment options: Grand ARC now offers a full continuum of care, including detoxification, intensive residential treatment, outpatient and intensive outpatient treatment, counseling, transitional living, and sober living. This allows them to tailor treatment plans to meet the individual needs of each client.
- Fostering research collaboration: Grand ARC is actively involved in research initiatives aimed at improving addiction treatment outcomes. This includes collaborating with the LIBR substance use team to provide clients with access to cutting-edge research opportunities.

Raela Baxter, Lead Chemical Dependency Technician (CDT), continues to play a crucial role in Grand ARC's success. As the liaison for the LIBR substance use team, Raela ensures that clients who are interested in participating in research studies have a seamless and positive experience.



The Tulsa Day Center in Tulsa, Oklahoma, connected with LIBR as a community research collaborator in 2023. Tulsa Day Center provides services to individuals experiencing homelessness and those at risk of homelessness. The center typically offers services such as shelter, meals, hygiene facilities, case management, mental health support, job assistance, and access to resources for housing assistance.

LIBR has collaborated with the Tulsa Day Center to initiate a novel research study for individuals experiencing homelessness with schizophrenia or bipolar disorder that involves regular case manager meetings and a focus on obtaining goals that may ultimately improve housing outcomes.





Emily Choquette., Ph.D.

Associate Investigato Laureate Institute for Brain Research

Scott Moseman, M.D. Medical Director Laureate Eating Disorders Program

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### **Laureate Eating Disorders Program Collaboration**

The LIBR research team and Laureate Eating Disorders Program (LEDP) reside in the same building on the Laureate campus. This allows for a symbiotic partnership between the research teams led by Dr. Sahib Khalsa and Dr. Emily Choquette and the treatment program led by Dr. Scott Moseman.

LEDP strives to provide excellence in eating disorder treatment and care. The research conducted on eating disorders at LIBR aims to inform best care practices. From functional neuroimaging investigations of brain functionality in individuals with eating disorders, to body image therapies and diagnostic evaluation, LIBR remains on the cutting edge of investigation into eating disorder neurobiology and intervention.

When an individual receiving treatment at LEDP qualifies for ongoing research studies, they may be offered the opportunity to participate. The clinical team assists in evaluating how participation will support their recovery and whether the individual might benefit from engaging in the study. Current areas of research include a National Institutes of Health (NIH)-funded study focused on identifying abnormal gut-brain interactions in anorexia nervosa, and a recently NIH-funded study led by Dr. Emily Choquette focused on developing float-assisted psychotherapy, a new form of mind-body treatment that combines floatation-REST (Reduced Environmental Stimulation Therapy) with evidence-based psychotherapy for body image disturbance in anorexia nervosa. LIBR has made important discoveries relevant to individuals struggling with eating disorders as well as to those who love, support, and provide treatment for these individuals.

# CLINICAL AND COMMUNITY COLLABORATORS





#### Women In Recovery (WIR)

Laureate Institute for Brain Research and Women in Recovery (WIR) have been closely collaborating since 2016 to conduct research that will:

Determine how the brain recovers from trauma, substance use, depression, and/or anxiety.

Identify factors that may predict success within the Women in Recovery program.

Inform modifications to the program in order to potentially enhance success for future clients.

#### These goals have been supported by several collaborative projects:

## **Predictions and Mechanisms** of Recovery

This project was conducted as part of the Tulsa 1000 study and primary investigators on this study include Drs. Paulus and Aupperle. A total of 169 women enrolled in the study. Several publications have come from this collaboration in previous years and there continues to be further insights and manuscripts from this study reporting on cognitive and neurobiological mechanisms relating to substance use. For example, substance use may

relate to altered learning rates and less precise action selection when making decisions to seek reward or reduce uncertainty, as well as elevated decision uncertainty and reduced avoidance drives during approach-avoidance conflict decision-making (Smith et al., 2022, 2023). In 2023, Dr. Ryan Smith and Ms. Claire Lavalley also led an analysis that identified how individuals with current substance use disorders show difficulty adjusting beliefs about the reliability of interoceptive (bodily) signals. Dr. Jennifer Stewart led a paper reporting that the factors contributing to substance use may have

nuanced differences for biological males and females, with female amphetamine users having more difficulty planning ahead and male amphetamine users exhibiting compensatory recruitment of left insula activation to support inhibitory processing (Stewart et al., 2023). Lastly, Dr. Aupperle and a previous graduate student (Sonalee Joshi, Ph.D.) presented results at the Anxiety and Depression Association of America (ADAA) describing how 1) relationships between striatal reactivity to reward and impulsivity is moderated by PTSD symptoms reported by women in the WIR program, and 2) changes in ventral striatum reactivity to reward from baseline to 1-year into the WIR program relates to the changes in impulsivity—suggesting that enhancing neural reactivity to non-drug rewards could be one potential clinical target for future research.

## PASO (Plasticity of Aversive Salience in Opioid Addiction) Study

Investigators have completed year 3 of a 5-year grant funded by the National Institute on Drug Abuse examining how the brain, body, behavior, and clinical symptoms (emotional experiences, depression, anxiety, pain) change during early abstinence in men and women with opioid use disorder enrolled in treatment at WIR or Grand Addiction Recovery Center (ARC). Participants complete neuroimaging scans, behavioral testing, physiology (heart rate, respiration, skin conductance), questionnaires, and interviews at 4 timepoints: baseline and 1-, 2-, and 3-month followup visits. Researchers Dr. Stewart (Principal Investigator), Dr. Kuplicki (Co-Investigator), and Dr. Paulus (Co-Investigator) aim to identify how cognitive, emotional, and physiological responses change as a function of abstinence in early recovery and how these changes compare to controls without a history of opioid use over time. Thus far we have recruited more than 145 individuals with opioid use disorder into the PASO study. Data processing is ongoing as we plan to recruit a total of 200 individuals from WIR and ARC for final analyses.

#### Aims for the Future

Dr. Khalsa and Dr. Stewart completed a pilot study examining the safety and acute effects of floatation therapy for individuals receiving inpatient treatment for amphetamine use disorder, including women from WIRwhich will hopefully inform future NIH grant submissions. Dr. Maëlle Gueguen will be initiating a study at the beginning of 2024 to examine the impact of positive emotions on decision-making behavior for individuals in amphetamine use recovery. Dr. Ryan Smith completed a pilot study examining how anxiety induction alters decision-making in those with amphetamine use disorders and recently submitted an R01 grant application to NIDA to explore how differences in sensitivity to this effect may predict vulnerability to relapse. In addition, LIBR investigators and staff (Robin Aupperle, Ph.D., Emily Choquette, Ph.D., Elisabeth Akeman, MA, LPC) conducted focus groups with WIR staff and clients to identify the next steps in collaboration on research to clinical translation. The aim of these focus groups has been to enhance the clinical-research translation and inform the next stage of collaboration—which will focus on conducting research examining intervention modifications that may enhance outcomes for Women in Recovery.





Over Tim Collins'
14-year tenure leading the assessment team, the team has successfully managed and executed screening assessments and study visits integral to all LIBR research studies.

#### The assessment team prioritizes 4 key objectives:

- Recruitment of Participants: The team employs a comprehensive, multi-faceted approach to recruit participants residing in the Northeastern Oklahoma region on behalf of all LIBR investigators. Utilizing channels such as social media, digital platforms, radio advertising, on-site facility recruitment, direct engagement at the Laureate Psychiatric Clinic and Hospital, and in-person activity-based strategies, the team ensures a diverse and engaged pool of interested participants.
- Clinical Assessment of Participants: The clinical team, consisting of three Masters-educated licensed interviewers (licensed therapists or licensed social workers), conducts diagnostic interviews following DSM-5 criteria to ascertain accurate diagnoses for each participant. In-depth discussions regarding current and past suicidal thoughts and self-harm attempts are facilitated, alongside comprehensive assessments of symptom severity.
- Medical Assessment of Participants: The medical team, comprising 3 registered nurses and 3 medical research technicians, conducts thorough interviews to establish the medical history of participants. This includes an examination of chronic, recent, and current medical conditions, ensuring a comprehensive understanding of each participant's health status.
- Completion of LIBR-Based Studies: The assessment team plays a pivotal role in supporting LIBR's research endeavors. This involves meticulous coordination and collaboration to meet the study-specific requirements of each investigator.

In addition to the 4 key objectives, the assessment team conducts clinical interviews, clinical ratings, and blood collections, further contributing to the depth and richness of the research data.

Over the past 3 years, the assessment team has achieved significant milestones, including:

11,205

potential subjects contacting LIBR

3,489

screening consents signed

1,068

collections

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These impressive numbers underscore the team's commitment to engagement, precision, and efficiency in carrying out their responsibilities within the LIBR research framework. The assessment team continues to be a cornerstone in advancing the institute's research objectives and contributing valuable insights to the mental health field.

#### Assessment Team Highlight: Megan Cole, RN



My passion for mental health ignited during my first psychiatric rotation in nursing school. After graduating with my Bachelor of Nursing from Langston University, I pursued this passion by working as an RN on the Laureate Adult Inpatient Unit. It was there that I gained valuable experience in caring for individuals with mental health conditions. After a year, I was presented with an exciting opportunity to not only provide direct care but also contribute to the future of mental health research as an RN Research Coordinator with the Laureate Institute for Brain Research.

Since joining LIBR in 2011, I have had the privilege of working on innovative studies exploring various treatment options for mental health disorders including medications, transcranial ultrasounds, and exercise programs. These experiences have deepened my understanding of the field and instilled in me a strong commitment to improving mental health outcomes for all. I am confident that my continued work at LIBR will allow me to contribute meaningfully to the advancement of mental health care and support the overall well-being of the community.

## **Training and Mentoring**

LIBR Accelerated Summer Research (LASR)
Internship Program. Drs. Evan White and Ricardo
Wilhelm coordinated LIBR's 3rd annual summer
internship program, which enabled students to be
full-time paid research interns at LIBR for 2 months.
Interns successfully worked with a lab mentor on
developing a research question, analyzing data to answer
that question, and presenting their results in a poster
format to LIBR staff. Interns also participated in career
development workshops with LIBR staff members.



Athena Klein graduated from Northeastern
State University with a B.S. in psychology and a minor in political science.
Athena worked with
Dr. Robin Aupperle

on secondary data analysis exploring the potential risk and protective factors that contribute to anxiety and depression in individuals identifying as LBGTQIA+ minorities. Results indicated LGBTQIA+ individuals reported greater levels of depression, anxiety, and prior trauma. These indicate trauma and other social determinants of health, such as socioeconomic status, as key factors contributing to adverse mental health in LGBTQIA+ individuals. Athena is drawn to social psychology, as her research interests include investigating gender role traits and LGBTQIA+ populations. Athena plans to get her Ph.D. in Experimental Psychology and aspires to conduct research at an institution or a university in the future.



Catherine Scales graduated from the University of Arkansas majoring in psychology with a minor in philosophy. Catherine worked with Dr. Robin Aupperle on

secondary data analysis of a study examining striatal activity (recorded via MRI) and P300 amplitudes

(recorded via EEG) during anticipatory reward processing on a monetary incentive delay task as potential predictors of substance use treatment completion for women. Results showed that P300 amplitudes during gain and no gain processing (but not striatal function) predicted a trend for improved completion of the recovery program. Catherine remains interested in neurophysiological predictors of affective and other psychiatric disorders, as well as predictors of treatment success or barriers to positive treatment outcomes. After graduation, she will be pursuing post-baccalaureate research positions prior to applying to clinical psychology Ph.D. programs.



Ethan Cheraghpour graduated from the University of Maryland, College Park with a B.A. in psychology. Ethan worked with **Dr. Maria Ironside** on secondary data analysis

examining whether individuals with major depressive disorder (MDD) and comorbid MDD and anxiety disorder(s) (ANX) exhibited reductions in cortical, subcortical, and whole brain gray matter volume (GMV) relative to healthy controls (HC). Results indicated elevated GMV in comorbid MDD+ANX striatal regions (i.e., putamen) and global GMV relative to HC, perhaps indicating a defining feature of ANX comorbidities. Ethan's research interests include affective neuroscience, eating pathology, substance use/addiction, and posttraumatic stress disorder. Ethan's goal is to obtain a Ph.D. in clinical psychology with a neuroscience concentration to further the scientific community's understanding of the brain concerning behavior and mental illness.



Diversity in Research
And Multidisciplinary
Neuroscience
(DREAM-Neuro) PostBaccalaureate Fellowship.
Dr. Evan White and LIBR's
Diversity Training and

Fellowship Subcommittee created the training and career development plan for the DREAM-Neuro Fellowship supported by LIBR. This fellowship enables a recent college graduate to gain up to 2 years of neuroscientific-based mental health research

experience prior to applying for graduate or professional degree programs. Lizbeth Rojas is LIBR's second DREAM-Neuro fellow from Oklahoma City, Oklahoma. She is a first-generation college graduate and received her B.S. in psychology with a minor in neuroscience from Oklahoma State University in 2022. As an undergraduate student she worked in the Laboratory of Emotion And Psychophysiology (LEAP) under Dr. DeMond Grant focusing on research in anxiety disorders, with an emphasis on EEG. As a DREAM-Neuro Fellow, she continued her training on EEG and event-related potentials as part of the Neuroscience of American Indian Resilience and Risk (Neu-AIRR) Lab under the mentorship of Dr. White. Lizbeth is currently applying for programs to pursue a Ph.D. in clinical psychology, with a long-term goal of a career in mental health research. Currently, her research interests focus on the interrelationship between the body and the brain, and how those connections influence psychopathology and cognitive functions, specifically within depression and anxiety disorders in communities experiencing mental health inequity. In her work with Dr. White, Lizbeth has written a paper ready for submission examining the role of inflammation in disrupted reward processing among American Indians (AI) with major depressive disorder using multi-modal neuroimaging analysis and has a follow-up project examining a similar question with respect to response inhibition.

## New Postdoctoral Associates



**Dr. Navid Hakimi** earned his Ph.D. in mechanical engineering from the University of Toronto, focusing on computational fluid mechanics and microfluidics-based 3D bioprinting for manufacturing tissue substitutes.

Dr. Hakimi joined LIBR in December 2022 to work with Dr. Ryan Smith on Bayesian modeling of decision-making as well as experimental investigation of associative learning in interoceptive tasks via breathing perception.



**Dr. Toru Takahashi** earned his Ph.D. in human sciences from Waseda University in Japan, focusing on mechanisms of mindfulness interventions for depression and anxiety. Dr. Takahashi joined LIBR in

June 2023 to work with Dr. Ryan Smith on computational modelling of acceptance and electrophysiological mechanisms of predictive processing.

## **Research Day**



Danielle Bethel
Crowd Favorite



Jolene Tay

Judges' Favorite

On July 28, 2023, LIBR held its 2nd annual Research Day open to the public, coordinated by Drs. Jennifer Stewart, Ricardo Wilhelm, and Evan White. Research assistants presented posters on research they conducted within their respective labs at LIBR. Internal LIBR judges reviewed all posters and scored them on various criteria, and everyone in attendance was encouraged to vote for their favorite poster. **Danielle Bethel** won the Crowd Favorite poster award focused on "Development and Validation of American Indian Cultural Identity Stimulus Set: Implications For Future Research and Addressing Mental Health Disparities", and Jolene Tay won the Judges' Favorite poster award focused on "Internalizing Symptoms in Children of Healthcare Workers Before and During the COVID-19 Pandemic". LIBR's Research Day gave research assistants an opportunity to showcase their hypothesis testing, data analysis, and poster presentation skills, providing additional experience for graduate and medical school applications.

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#### William K. Warren Frontiers in Neuroscience Lecture Series Speakers

Suicide Circuit Therapeutics: Leveraging the Efficacy of ECT and the Focality of TMS

Joan Camprodon, M.D., Ph.D. February 7, 2023

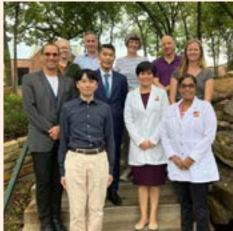
Social Regulation of Human Gene Expression

Steve Cole, Ph.D. May 2, 2023



Why Does My Child Not Eat?
The Complex Relationships
Between Behavior and
Neurobiology in Eating Disorders

Guido Frank, M.D. January 11, 2023



Microglia and Extracellular Vesicles in Neurologic Disorders

Tsuneya Ikezu, M.D., Ph.D. October 3, 2023



Inflammation and Anhedonia in Depression: Biomarkers, Mechanisms, and Therapeutic Implications

Jennifer Felger, Ph.D. November 7, 2023



Addressing Mental Illness with Neuroscience, Advocacy, Diversity, Equity, and Inclusion Tools

Nii Addy, Ph.D. March 24, 2023 Putative Neurobiological Mechanisms of Race-related Trauma: Pathways for Vulnerability and Strategies for Resilience

Negar Fani, Ph.D. January 24, 2023

Trauma, Substance Misuse, and Juvenile Justice

Micah Johnson, Ph.D. March 2, 2023

#### **Visiting Scientists and Distinguished Guests**



Rethinking Neurodevelopmental Models, Metrics, and Intervention for Adolescent Invisible Symptoms

Sarah Feldstein-Ewing, Ph.D. April 21, 2023



Meeting the Needs of Justice-Involved People with Serious Mental Illnesses: Embracing the complexity

Amy Blank Wilson, Ph.D., MSW August 3, 2023

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The Effects of Climatic Stressors on Day-To-Day Emotional States

Nick Obradovich, Ph.D. February 28, 2023

Using Neuromodulation and Unpredictable Threat to Understand the Mechanisms of Anxiety Expression and Regulation

Nicholas Balderston, Ph.D. August 15, 2023

**Self-Injurious Thoughts & Behaviors in Youth: Finding Gaps & Building Bridges** 

Melinda Schreiner, Ph.D. July 18, 2023

Revealing the Dual Nature of Brain Diseases: Micro and Macrostructural Insights Using Diffusion MRI and Tractography

Fang-Cheng (Frank) Yeh, M.D., Ph.D. October 19, 2023



Principal Investigator Highlight

**EVAN WHITE, PH.D.** 



roots in Northeastern Oklahoma.
He attended local public schools:
Lanier Elementary, Edison Middle,
and Edison High School. He and
his wife Natalie have two children,
Benjamin (3) and Lois (1). He is an
enrolled member of the Absentee
Shawnee Tribe of Oklahoma and
actively engaged with the Shawnee
Chapter of the Native American
Church of Oklahoma; he also
belongs to the Whiteoak Shawnee
Ceremonial Grounds. He received
his bachelor's degree in psychology

Dr. White is a Native Tulsan with deep

from Oklahoma State University, where he also advanced to receive his master's and doctoral degrees in Clinical Psychology, working under the mentorship of DeMond M. Grant, Ph.D.

Dr. White's graduate research was focused on the innovative use of psychophysiological techniques to explore cognitive models of mood and anxiety disorders. His clinical training, which covered a broad spectrum of generalist clinical science, emphasized evidence-based psychotherapy for adult outpatient treatment of anxiety, mood, and trauma-related disorders. Following his graduate training he completed a comprehensive predoctoral clinical internship at the Charleston Consortium in South Carolina. While on internship, he deepened his expertise in the field of

psychophysiology and empirical study of emotion and behavior under the mentorship of Lisa McTeague, Ph.D.

In 2019, Dr. White joined the Laureate Institute for Brain Research as a postdoctoral fellow under the mentorship of Dr. Robin Aupperle. Here, he began to increase his empirical toolkit to include translational neuroimaging methodologies, aiming to predict treatment responses in mood and anxiety disorders. During his time as a postdoctoral fellow. Dr. White received a MOSAIC K99/ ROO award for his project "Neuroscientific Exploration of Cultural Protective Factors in American Indians" from the National Institute on Minority Health and Health Disparities (K99R00MD015736) with his mentorship team including Dr. Martin Paulus and Dr. Robin Aupperle. He took a position as an Associate Investigator in July of 2020 and established his lab, "Neuroscience of American Indian Resilience and Risk." More recently, his commitment to integrating clinical and cultural neuroscience burgeoned into a leadership role in 2022, when he was promoted to Principal Investigator and assumed the roles of Director of Native American Research and the Electroencephalography Core at LIBR.

In this capacity, Dr. White spearheads research that is not only at the forefront of neuroscience but also culturally resonant, seeking to improve mental health outcomes among American Indians. Dr. White's program of research was recently awarded the prestigious NIH Director's Pioneer Award for the collaborative project "Kipiyecipakiciipe - Coming Home: Establishing clinical cultural neuroscience as a tool for understanding the role of traditional cultural engagement in mitigating substance misuse and disorder" with the Shawnee Tribe. This work is distinguished by a focus on multi-modal neuroscience in combination with a community-based participatory research approach to ensure the work is conducted in a culturally informed manner. With an eye toward the protective role of cultural engagement against poor mental health outcomes, his research is pioneering a functional framework for identifying neuroscientific signatures of cultural protective factors.

In addition to his research, Dr. White places significant importance on the mentorship and development of emerging scholars in the field. His efforts extend to supervising clinical psychology trainees and mentoring the research of postbaccalaureate scholars, graduate students, and postdoctoral scholars. Inspired by the

support and encouragement he received during his own academic journey, Dr. White places a high importance on providing a similar foundation for his mentees.



Dr. White actively engages students in a range of research activities, allowing them to develop and refine their ideas, pose scientific questions, undertake analytic training, and present their findings to wider audiences. He has established and directed training programs at LIBR that reflect this ethos: The LIBR Accelerated Summer Research (LASR) internship that affords undergraduate students valuable research experience, and a postbaccalaureate research fellowship (Diversity in Research and Multidisciplinary Neuroscience (DREAM-Neuro) fellowship) aimed at promoting research on underserved communities. These initiatives are designed to build confidence and expertise, fostering an environment where trainees can passionately pursue their research interests by combining hands-on learning with career development and mentorship.

Overall Dr. White is committed to rigorous, impactful research. He advocates for the inclusion of community partners at each stage of the research, to ensure that the work is informed by and beneficial to the communities it intends to serve. Through these efforts and a dedication to mentoring the next generation of scientists, Dr. White hopes to affect positive change in mental health among American Indian communities and the field more broadly.

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**ELISABETH AKEMAN**Research Therapist

JACOB ARMSTRONG
Clinical Psychology Intern

NICOLE BAUGHMAN Lab Coordinator

**HANNAH BERG, PH.D.** *Postdoctoral Research Associate* 

JAYA CHAKKA Lab Coordinator

EMILY CHOQUETTE, PH.D.

Associate Investigator

AARDRON ROBINSON
Software Engineer
CASSANDRA STURYCZ, PH.D.
Postdoctoral

#### **Current Research Focus**

Dr. Aupperle is Principal Investigator at Laureate Institute for Brain Research (LIBR) and Associate Professor at The University of Tulsa. She currently serves as Chair of LIBR's Diversity, Equity, and Inclusion Committee and Director of the LIBR training site for the Northeastern Oklahoma Psychology Internship Program (NOPIP). The mission of her lab, Neurocognitive Aspects of Anxiety, Trauma and Treatment (NeuroCATT), is to conduct translational neuroscience research that has the potential to inform the understanding and optimization of psychotherapy interventions for individuals experiencing anxiety, depression, or trauma-related symptoms. Much of her work focuses on understanding approach/avoidance drives and threat/reward processing in relation to symptoms and treatment outcomes for anxiety, depression, and co-occurring conditions.

## **Research Highlights**

The NeuroCATT lab received an R34 award from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in collaboration with Dr. Charles Taylor at the University of California San Diego and Dr. Kate Wolitzky-Taylor at the University of California Los Angeles. The grant will fund work furthering the development of an intervention focused on amplification of the positive valence system and reducing alcohol use (AMP-A) for individuals with alcohol use disorder and symptoms of anxiety or depression. The first phase of the project involved collecting input from substance use providers and prior participants concerning the intervention and piloting the treatment with eight individuals. This will lead into a randomized clinical trial comparing the novel intervention with a more traditional cognitive-behavioral therapy intervention.

The NeuroCATT lab also received a sub-award for a U.S. Department of Defense (DoD)-funded study led by Dr. Amy Jak at the San Diego VA Healthcare System. The grant will fund work examining the benefit of cognitive processing therapy (CPT) modified utilizing cognitive rehabilitation principles, as compared to traditional CPT, for veterans with post-traumatic stress disorder (PTSD) and history of mild traumatic brain injury.

Dr. Hannah Berg led a paper reporting clinical outcomes from Dr. Aupperle's previous NIMH K23 award entitled "Approach-Avoidance Conflict – a multi-level predictor for exposure therapy response". This paper, published in the Journal of Mood and Anxiety Disorders, reported that both behavioral activation (BA) and exposure-based therapy (EXP) were effective in reducing symptoms of anxiety and depression for individuals with generalized anxiety disorder (GAD), with similar outcomes at a 6-month follow-up. However, BA was associated with faster improvement in symptoms and better outcomes at post-treatment. BA has been considered as a gold-standard intervention for depression and these results suggest it may be an effective treatment option for anxiety disorders as well.

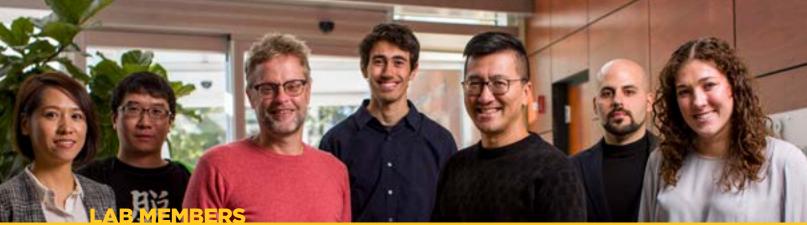
Dr. Aupperle and coauthors Drs. Timothy McDermott (previous graduate student in the NeuroCATT lab), Namik Kirlic, and Evan White published a review "The neuropsychology of anxiety: An approach-avoidance decision-making framework" within the American Psychological Association (APA) handbook. This review provided a summary of the literature concerning the neuroscientific and neurocognitive factors that likely play a role in anxiety disorders.

Dr. Berg initiated a pilot study investigating the neurobiology of effortful threat-neutralization, a behavior with clinical relevance for obsessive-compulsive disorder (OCD). The project draws on previous findings demonstrating overgeneralization of conditioned fear and avoidance in clinical anxiety, and adapts methodology from previous studies eliciting fear-conditioning, generalization, extinction, and effortful behavior. Findings will elucidate the neural underpinnings of this behavior, and the extent to which behavioral and neural indices of effortful threat-neutralization are associated with anxiety-related and obsessive-compulsive traits.

#### **Select Publications**

- 1. Joshi, S.A., Aupperle, R.L. and Khalsa, S.S. Interoception in fear learning and post-traumatic stress disorder. Focus. 2023;21(3):266-277.
- 2. Berg, H., Akeman, E., McDermott, T. J., Cosgrove, K. T., Kirlic, N., Clausen, A., Cannon, M., Yeh, H.-W., White, E., Thompson, W. K., Choquette, E. M., Sturycz-Taylor, C. A., Cochran, G., Ramirez, S., Martell, C. R., Wolitzky-Taylor, K. B., Craske, M. G., Abelson, J. L., Paulus, M. P., & Aupperle, R. L. A randomized clinical trial of behavioral activation and exposure-based therapy for adults with generalized anxiety disorder. Journal of Mood and Anxiety Disorders. 2023;1:100004.
- 3. Kirlic, N., Akeman, E., DeVille, D.C., Yeh, H.W., Cosgrove, K.T., McDermott, T.J., Touthang, J., Clausen, A., Paulus, M.P. and Aupperle, R.L. (2023). A machine learning analysis of risk and protective factors of suicidal thoughts and behaviors in college students. Journal of American College Health. 2023;71(6):1863-1872.
- 4. Aupperle, R.L., McDermott, T.J., White, E., Kirlic, N. The Neuropsychology of Anxiety: An Approach-Avoidance Decision-Making Framework. Invited Chapter In G. Brown, B. Crosson, K. Haaland, & T. King (Eds.), APA Handbook of Neuropsychology. 2023.





JONATHAN AHERN, B.S. Staff Research Assistant

**ASHLEY BARROWS, B.S.**Proiect Manager at LIBR

WENJIE CHENG
Staff Programmer at LICS

AHMAD KAANAN, PH.D. Staff Scientist

ROBERT LOUGHNAN, PH.D.

FIRAS NABER, B.S.
Staff Research Assistant
on Data Analytics at LIBP.

**LUCY SHAO** *Graduate Student at UCSD* 

BOHAN XU, PH.D.
Researcher

HAIXIA ZHENG, PH.D.

Associate Investigator

## **Research Highlights**

- Dr. Fan was invited to moderate a panel on the genomic analysis of the human brain data at the American Society of Human Genetics held in Washington, D.C.
- Co-edited with Drs. John Hewitt and Sylia Wilson, Dr. Fan published a special issue on genetic data from the Adolescent Brain Cognitive Development Study in Behavior Genetics.
- Dr. Fan was invited to give a workshop on geospatial data analysis at the BERTHA summer school in Denmark in July 2023.

#### **Current Research Focus**

Dr. Fan continues his efforts to develop novel and multi-level approaches to investigate the etiology of human brain disorders by analyzing population neuroscience data. With access to large scale datasets, including ABCD, UK Biobank, All of US, and Taiwan Biobank, Dr. Fan's team strives to find the common threads across scales, identifying the key factors that can shape the human mind and brain.

- Xin Wang, Iris Broce, Yuqi Qiu, Kacie D Deters, Chun Chieh Fan, Anders M Dale, Steven D Edland, Sarah J Banks, Alzheimer's Disease Neuroimaging Initiative. A simple genetic stratification method for lower cost, more expedient clinical trials in early Alzheimer's disease: A preliminary study of tau PET and cognitive outcomes. Alzheimer's and Dementia. 2023 Jan 26.
- 2. Linda Ejlskov, Sussie Antonsen, Jesper N Wulff, Esben Agerbo,
  Oleguer Plana-Ripoll, Clive E Sabel, Chun Chieh Fan, Wesley K
  Thompson, Pearl LH Mok, Carsten Bøcker Pedersen, Roger T
  Webb. Multilevel interactions between family and neighbourhood
  socioeconomic indices in childhood and later risks of self-harm and
  violent criminality in Denmark: a national cohort study. The Lancet
  Public Health. 2023;8(2)e99-e108.
- 3. Chun Chieh Fan, Robert Loughnan, Sylia Wilson, John K Hewitt, ABCD Genetic Working Group Agrawal Arpana Dowling Gaya Garavan Hugh LeBlanc Kimberly Neale Michael Friedman Naomi Madden Pamela Little Roger Brown Sandra A. Jernigan Terry Thompson Wesley K. Genotype Data and Derived Genetic Instruments of Adolescent Brain Cognitive Development (ABCD) Study™ for Better Understanding of Human Brain Development. Behavior Genetics. 2023 Apr:1-10.
- 4. Jonathan Ahern, Wesley Thompson, Chun Chieh Fan, Robert
  Loughnan. Comparing Pruning and Thresholding with Continuous
  Shrinkage Polygenic Score Methods in a Large Sample of Ancestrally
  Diverse Adolescents from the ABCD Study™. Behavior Genetics.
  2023;53(3):292-309.
- 5. Sylia Wilson, Chun Chieh Fan, John Hewitt. ABCD Behavior Genetics: Twin, Family, and Genomic Studies Using the Adolescent Brain Cognitive Development (ABCD) Study™ Dataset. Behavior Genetics. 2023;53(3):155-158.





BREANNA MCNAUGHTON
Research Assistant
CIBONEY WARE

Mentee, LIBR ABCD Research Assistant

## **Research Highlights**

Dr. Figueroa-Hall has completed the 2-year K99 phase of her K99/R00 Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC-NIGMS) grant, entitled "In vivo inflammatory challenge to elucidate the role of the toll-like receptor 4 (TLR4) pathway in depression," which was funded by the National Institute of Mental Health (K99MH126950). Dr. Figueroa-Hall will begin the 3-year R00 phase in April 2024.

Dr. Figueroa-Hall's collaboration with Dr. Kaiping Burrows has led to the advancement in brain-enriched extracellular vesicle (EV) research at LIBR, specifically investigating neuronal- and astrocyte-enriched EVs in mental health research. The study of brain-enriched EVs provides a unique, and possibly, revolutionary approach to examine brain biology from a blood sample.

Dr. Figueroa-Hall presented her research at international and national conferences in 2023: poster presentation for the International Society for Extracellular Vesicles (ISEV; Seattle, Washington, May 2023); oral presentation for the Zarrow Mental Health Symposium (October 2023); poster presentation for ISEV's 1st annual Nervous System EV (INEV; Rome, Italy, December 2023); and poster presentation for the American College of Neuropsychopharmacology (Tampa, Florida, December 2023).

Dr. Figueroa-Hall was selected for the NIH Early Career Reviewer Program and ACNP's Under-Represented Minority (URM) Mentorship Program.

#### **Current Research Focus**

Dr. Figueroa-Hall's training and expertise in toll-like receptor 4 (TLR4) inflammatory signaling is the basis for her research interests in examining how the TLR4 system via regulating inflammatory processes affects mental health. Her overarching goal is to understand how the immune system is dysregulated in MDD and identify novel targets/biomarkers for inflammationassociated depression. Her current research aims include investigating peripheral and central immune responses in depressed vs. healthy individuals and delineating astrocyteenriched EV-mediated immune mechanisms in MDD. Dr. Figueroa-Hall is also involved in LIBR's Diversity, Equity, and Inclusion Committee and the Philanthropy/Community Outreach Subcommittee and organizes LIBR's William K. Warren Frontiers in Neuroscience Lectures.

#### **Select Publications**

- Burrows K\*, Figueroa-Hall LK\*, Stewart J, Alarbi A, Kuplicki R, Hannafon B, Tan C, Risbrough V, McKinney B, Ramesh R, Victor T, Aupperle R, Savitz J, Teague K, Khalsa S, Paulus M. Exploring the role of neuronal-enriched extracellular vesicle miR-93 and interoception in major depressive disorder. Res Sq [Preprint]. 2023 Jun 16:rs.3.rs-2813878.
- \*Shared co-first authorship

#### Abstracts

- Leandra K. Figueroa-Hall, Kaiping Burrows, Rayus Kuplicki, T. Kent Teague, Michael Irwin, Sahib Khalsa, Salvador Guinjoan, Martin P. Paulus, Jonathan Savitz (December 2023). Astrocyte-Enriched Extracellular Vesicle Vascular Injury Proteins and HSA-LET-7f-5p Expression after in Vivo Immune Challenge in Major Depressive Disorder. Virtual poster presentation at the annual meeting for the American College of Neuropsychopharmacology; Tampa, Florida.
- 2. Leandra K. Figueroa-Hall, Ahlam M. Alarbi, Chibing Tan, Kaiping Burrows, Bethany Hannafon, Rajagopal Ramesh, Victoria B. Risbrough, Kent Teague, Martin P. Paulus (December 2023). Four distinct methods for exosome isolation and enrichment of astrocyte-enriched extracellular vesicles. Poster presentation at the ISEV's 1st symposium on eVs in the Nervous Systems; Rome, Italy.
- Figueroa-Hall LK and Burrows K (2023). A window into the depressed brain.
   Oral presentation at Zarrow Symposium; the Mental Health Association; Tulsa, OK.
- 4. Figueroa-Hall LK, Burrows, K., Alarbi, A. M., Tan, C., Kuplicki, R., Stewart, J. L., Aupperle R., Hannafon, B.N., Ramesh, R., Savitz, J. B., Risbrough, V. B., Teague, T. K., Khalsa, S.K., Guinjoan S., & Paulus, M. P. (2023). Neuronal-enriched extracellular vesicle miR-182 and miR-486 expression display opposing directionality in non-suicidal and suicidal individuals with major depressive disorder. Poster presented at the annual meeting of the International Society for Extracellular Vesicles; Seattle, Washington.



## **Research Highlights**

Dr. Gueguen, in collaboration with the neurosurgical and neurology departments of the University Hospital of Grenoble Alpes and the Grenoble Institute of Neuroscience, provided the first electrophysiological study in human subjects of the role of the thalamus in reinforcement learning. This is of particular relevance to the field of Computational Psychiatry as the thalamus is at the intersection of several neural circuits supporting emotion regulation, memory, learning and decision-making; all of them are known to be altered in neuropsychiatric disorders such as substance use disorders.

As part of another collaboration with the psychiatry department of the University Hospital of Grenoble Alpes and the Grenoble Institute of Neuroscience, Dr. Gueguen participated in a study which leveraged computational modeling to identify sub-populations with bipolar disorder on the basis of the reinforcement learning deficits they present. This is in line with Dr. Gueguen's advocacy for the use of computational modeling as a research-informed clinical tool when working with neuropsychiatric populations.

During her postdoctoral fellowship at Rutgers University, Dr. Gueguen's work identified that, contrary to the popular belief of an altered valuation system in substance use disorders being responsible for biased decision-making towards drug options, the neural encoding of subjective value under uncertainty is preserved. Instead, this study points towards biases due to their current affective state, highlighting the need to better understand how affective states alter value-based decision-making in substance use disorders.

#### **Current Research Focus**

Dr. Gueguen joined LIBR as an Associate Investigator in the summer of 2023 after a postdoctoral fellowship at Rutgers University where she used model-based behavioral and neuroimaging techniques to identify signatures of maladaptive value-based decision-making in populations with opioid use disorder.

Dr. Gueguen's laboratory at LIBR employs behavioral, neuroimaging and computational modeling techniques to investigate the neurocomputational mechanisms underlying maladaptive appetitive and aversive outcome processing in people with methamphetamine use disorder, how they are amplified by negative affective states and how they can make someone vulnerable to drug reuse.

A major overarching goal is to identify actionable behavioral intervention targets to promote long-term abstinence in this population for whom no pharmacological therapeutic solution is currently available.

#### **Select Publications**

- Collomb-Clerc A, Gueguen MCM, Minotti L, Kahane P, Navarro V, Bartolomei F, Carron R, Regis JM, Chabardès S, Palminteri S, Bastin J. Human thalamic low-frequency oscillations correlate with expected value and outcomes during reinforcement learning. Nature Communications. 2023;14:6534.
- Pouchon A, Vinckier F, Dondé C, Gueguen MCM, Bastin J, Polosan M. Reward and punishment learning deficits among bipolar disorder subtypes. Journal of Affective Disorders. 2023;340:694-702.

#### **Abstracts**

- Gueguen MCM, Anlló H, Bonagura D, Kong J, Hafezi S, Palminteri S, Konova AB (2022 - in revision). Recent opioid use impedes range adaptation in reinforcement learning in human addiction. Also presented at College on Problems of Drug Dependence (poster) and Society for NeuroEconomics (select talk).
- 2. Anlló H, ..., Gueguen MCM, Bonagura D, Konova AB, ..., Palminteri S (2023 preprint currently in revision). Outcome context-dependence is not WEIRD: Comparing reinforcement- and description-based economic preferences worldwide. Also presented at Federation of European Neuroscience Societies Forum (poster).
- 3. LoFaro FM\*#, Gueguen MCM\*, Kapoor A#, Alvarez EE#, Bonagura D, Konova AB. (2023). Preserved Neural Encoding of Subjective Valuation Under Uncertainty in Human Opioid Addiction. College on Problems of Drug Dependence (select talk).
- \* indicates equal contributions
- # denotes a graduate student mentee



#### **Current Research Focus**

Dr. Guinjoan's lab strives to discover and characterize circuits that subserve repetitive negative thinking (RNT) in persons with depression. His lab established that persons with intense RNT display specific changes in the disposition and size of white matter tracts connecting psychosurgical targets useful in MDD and obsessive compulsive disorder. This work is now being followed by an attempt to directly modulate such circuits employing low-intensity focused ultrasound (LIFU), an emerging reversible and noninvasive technique of neuromodulation. If successful, this method may pave the way to larger trials addressed at 1) establishing causal relationships between large-scale brain circuits and rumination, an important symptom of MDD, and 2) attempting to alleviate RNT in a safe, noninvasive manner.

## **Research Highlights**

Dr. Guinjoan's lab has completed the recruitment of 20 persons who suffer from major depression and varying degrees of rumination intensity, and expect to complete recruitment of 10 persons who are healthy and will serve as a comparison group for the low-intensity focused ultrasound (LIFU) pilot study targeting white matter tracts in the anterior limb of the internal capsule in the right brain hemisphere. The lab observed consistent target engagement with this method in a preliminary analysis, and a trend towards resulting clinical effects. The results were presented at the American College of Psychopharmacology annual meeting on December 5, 2023. This was the first time that white matter tract functional modulation had been demonstrated with a noninvasive method such as LIFU, which before was only possible with costly, invasive, and risky methods involving electrode implantation or tissue ablation. This observation will allow for the testing of additional participants with the goal to make causal inferences about brain mechanisms of symptom generation in major depression and other psychiatric disorders.

2 Dr. Guinjoan's lab obtained a detailed characterization of rumination as a prominent and incapacitating symptom of depression, often associated to suicidal ideation and behavior, by different methods:

- Employing a machine learning approach to understand how much behavior and genetic predisposition result in higher risk of rumination in persons with depression.
- Observing that highly ruminative persons with depression have greater connectivity between brain regions involved in the processing of language, and those involved in the processing of emotion, which is germane to the phenomenology of rumination as a mental experience.
- Discovering psychosurgical methods that are useful in the treatment of the most severe forms of treatment-resistant depression engage white matter tracts that are overrepresented in persons with depression who are also highly ruminative.

#### **Select Publications**

- Sánchez SM, Tsuchiyagaito A, Kuplicki R, Park H, Postolski I, Rohan M, Paulus MP, Guinjoan SM. Repetitive negative thinking-specific and
  -nonspecific white matter tracts engaged by historical psychosurgical targets for depression. Biological Psychiatry. 2023;94(8):661–671.
   Commentary in: Belforte JE. Moving forward precision medicine in psychiatry. Biological Psychiatry. 2023;94(8):607–608.
- 2. Tsuchiyagaito A, Sánchez SS, Misaki M, Kuplicki R, Park H, Paulus MP, **Guinjoan SM**. Intensity of repetitive negative thinking in depression is associated to greater functional connectivity between semantic processing and emotion regulation areas. Psychological Medicine. 2023;53(12):5488–5499.
- 3. Forthman KL, Kuplicki R, Yeh HW, Khalsa SS, Paulus MP, Guinjoan SM. Transdiagnostic behavioral and genetic contributors to repetitive negative thinking: a machine learning approach. Journal of Psychiatric Research. 2023;1672:207–213.
- 4. Guinjoan SM. Personalized definition of surgical targets in major depression and obsessive-compulsive disorder: a potential role for low-intensity focused ultrasound? Personalized Medicine in Psychiatry. 2023;38:100100.
- 5. Tsuchiyagaito A, Misaki M, Cochran G, Philip NS, Paulus MP, **Guinjoan SM**. Thalamo-cortical circuits associated with trait- and state-repetitive negative thinking in major depressive disorder. Journal of Psychiatric Research. 2023;168:184-192.

8 - 1





KYLE GOLDMAN Research Assistant

**LAKIN GREEN**Student Volunteer

**TATE POPLIN**Research Assistant

## **Research Highlights**

Dr. Ironside was awarded a \$2.1 million 5-year R01 grant from the National Institute of Mental Health to investigate "Processes and circuitry underlying threat sensitivity as a treatment target for comorbid anxiety and depression." The study employs a pharmaco-fMRI approach to study threat sensitivity using a novel predator task in patients with major depressive disorder (MDD), anxiety disorders (AD), and comorbid MDD and AD. The ultimate aim of this work is to establish treatment targets for comorbid MDD and AD for novel interventions and provide evidence for the separation of MDD from comorbid MDD and AD in future clinical trials.

The Mechanisms of Depression and Anxiety Laboratory (MoDAL) completed a 3-year project funded by the National Institute of General Medical Sciences (NIGMS) focusing on the effects of non-invasive brain stimulation on threat sensitivity in comorbid MDD and AD.

Dr. Ironside presented her lab's work at the Society for Biological Psychiatry's Rising Star session and at the British Association for Psychopharmacology.

#### **Current Research Focus**

Dr. Ironside has a background in cognitive neuroscience with a focus on threat sensitivity using neuromodulation and neuroimaging in clinical populations. Her main interests include establishing unique targetable phenotypes of anxious depression and understanding the mechanisms of action of novel treatments such as non-invasive neuromodulation. Dr. Ironside uses acute pharmacological and neuromodulatory probes and behavioral, electrophysiological and neuroimaging measures with a view to establishing potential biomarkers of treatment response. The goal of this research program is to identify novel treatment targets, inform patient selection for future clinical trials and, ultimately, treatment selection in the clinic.

#### **Select Publications**

- Poplin, T., Ironside, M., Kuplicki, R., Aupperle, R. L., Guinjoan, SM., Khalsa, SS., ... & Kirlic, N. The unique face of anxious depression: Increased sustained threat circuitry response during fear acquisition. bioRxiv. 2023.
- 2. Ironside, M., DeVille, DC., Kuplicki, RT., Burrows, KP., Smith, R., Teed, AR., ... & Khalsa, SS. The unique face of comorbid anxiety and depression: increased interoceptive fearfulness and reactivity. Frontiers in Behavioral Neuroscience. 2023.
- Walker, EA, Aupperle, RL, T-1000 Investigators, Paulus, MP, Ironside, M. Distraction is associated with increased avoidance behavior under approachavoidance conflict. Current Psychology. 2023.
- 4. Ironside, M, et al. Reductions in rostral anterior cingulate GABA are associated with stress circuitry in females with major depression: A multimodal imaging investigation. Neuropsychopharmacology. 2021.
- Ironside M\*, Amemori K\*, McGrath CL, Lund Pedersen M, Kang MS, Amemori S, Frank MJ, Graybiel AM, Pizzagalli DA. Approach-avoidance conflict in major depression: Congruent neural findings in human and non-human primates. Biol Psychiatry. 2020.

\*indicates equal contributions





**EMILY ADAMIC, M.S.** *Graduate Student, The University of Tulsa* 

EMILY CHOQUETTE, PH.D.

Associate Investigator

KELLER MINK, B.S.

Research Assistant

**ABHINITA PREMKUMAR, B.S.**Research Assistant, LIBR Float Clinic and Research Center

CHARLES VERDONK, M.D., PH.D. Postdoctoral Research Associate

## **Research Highlights**

An ingestible vibrating capsule produced reliable changes in gastric-evoked brain activity and stomach sensation in healthy individuals. This minimally invasive mechanosensory approach serves as the basis for an ongoing NIH-funded study focused on identifying abnormal gut-brain interactions in women with anorexia nervosa as well as in individuals with functional gastrointestinal disorders.

An adrenaline-like challenge during functional brain imaging revealed that abnormal brain connectivity in regions associated with the heart is associated with anxiety and body image disturbance in women with anorexia nervosa. This study provides a new explanation for how an abnormal balance of brain-body communication could contribute to the increased anxiety and body image disturbance in certain eating disorders.

A randomized clinical efficacy trial demonstrated that floatation-REST (Reduced Environmental Stimulation Therapy) reliably decreases body image dissatisfaction and anxiety in women with anorexia nervosa, with symptom reductions persisting at 6 months, indicating utility for treating body image disturbance and anxiety concerns in anorexia nervosa. This innovative approach could augment existing treatments, offering a new avenue of hope for those struggling with eating disorders.

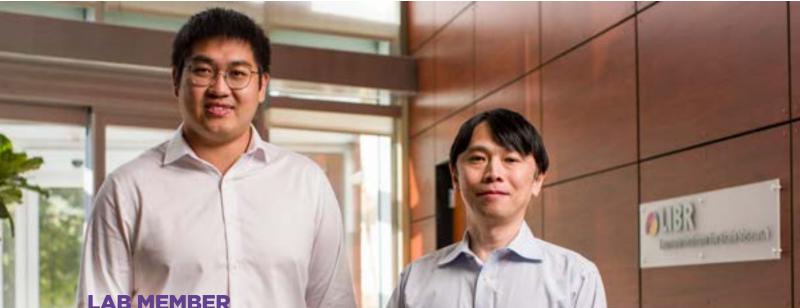
A pre-registered study applied 2 forms of statistical hypothesis testing about the functional connectivity of brain networks in women with generalized anxiety disorder. The study found convergent evidence of abnormal coupling between the insula and ventromedial prefrontal cortices (vmPFC) as well as other previously undescribed regions, providing additional evidence that the vmPFC-insula neurocircuit in generalized anxiety disorder is a key target for future intervention studies.

#### **Current Research Focus**

The beating heart sends one of the most important signals to the brain, and the regulation between these organs is central for health and disease. Dr. Khalsa's research uses an experimental medicine framework and pharmacological modulation of the heartbeat to examine the underlying sensory and regulatory brain circuits using brain imaging, electroencephalography, and computational modeling. They hypothesize that a dysregulated heart-brain relationship contributes to the onset and maintenance of several mental health conditions—e.g., mood, anxiety, and eating disorders. By identifying how the brain and heart are dysregulated, this research will provide the biological basis for new treatments aimed at re-establishing balanced regulation between these organs. Dr. Khalsa has also begun to examine gut-brain relationships from a similar perspective, with a focus on eating disorders. His central goals are to discover modifiable neuroscience-based treatment targets for psychiatric disorders, to develop tests to precisely identify these treatment targets in individual patients, and to design neuroscience-based therapies capable of ameliorating the symptoms and signs of mental illness.

- Mayeli A, Al Zoubi O, White EJ, Chappelle S, Kuplicki R, Morton A, Bruce J, Smith R, Feinstein JS, Bodurka J, Paulus MP, Khalsa SS. Parietooccipital ERP indicators of gut mechanosensation. Nature Communications. 2023;14:3398.
- De la Cruz F, Teed AR, Lapidus RC, Upshaw V, Schumann A, Paulus MP, Bär KJ, Khalsa SS. Central autonomic network alterations in anorexia nervosa following peripheral adrenergic stimulation. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2023;8(7):720-730.
- 3. Garland MM, Wilson R, Adamic E, Thompson WK, Arevian AC, Stein MB, Paulus MP, Feinstein JS, Khalsa SS. Reduced Environmental Stimulation Therapy in anxiety and depression: an experience sampling study. Journal of Mood and Anxiety Disorders. 2023;1:100003.
- Steinhäuser JL, Teed AR, Al-Zoubi O, Hurlemann R, Chen G, Khalsa SS. Reduced vmPFC-insula functional connectivity in generalized anxiety disorder: a Bayesian confirmation study. Scientific Reports. 2023;13:9626.
- 5. Choquette EC, Flux MC, Moseman SE, Chappelle S, Naegele J, Upshaw V, Morton A, Paulus MP, Feinstein JS, Khalsa SS. The impact of floatation therapy on body image and anxiety in anorexia nervosa: a randomized clinical efficacy trial. EClinicalMedicine. 2023;64:102173.





**ZHIYIN CHEN** *Graduate Student* 

## **Research Highlights**

1 Dr. Misaki's lab has shown that repetitive negative thinking (RNT) in major depressive disorder (MDD) is a more active process than previously thought, involving multiple brain regions across functional networks, not just the default-mode activity that is active during rest. Trait RNT scores were more accurately predicted from functional connectivity patterns during a negative thinking state than during the resting state.

2 Dr. Misaki's lab investigated the whole-brain mechanism of real-time fMRI neurofeedback training in treating symptoms of repetitive negative thinking (RNT) in depression. Their machine learning predictive modeling analysis highlighted the significant role of the interaction between brain regulation activities and the response to the feedback signal in achieving effective treatment outcomes.

The real-time fMRI neurofeedback system was further developed to support the Siemens Prisma scanner, one of the most popular scanners for neuroscience research, which has been installed at LIBR.

#### **Current Research Focus**

Dr. Misaki is an Associate Investigator whose research is dedicated to developing novel psychiatric treatments using real-time neuroimaging technologies, including functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). His approach centers on neurofeedback training, in which participants receive real-time feedback on their brain activation signals, enabling them to learn how to self-regulate their brain activation and mental state. His work focuses on understanding the mechanistic aspects of neurofeedback treatment processes and personalizing treatment. In pursuit of this goal, he is working on identifying subtypes of mental disorders using machine learning approaches in large datasets.

- 1. Misaki, M., Tsuchiyagaito, A., Guinjoan, S.M., Rohan, M.L., Paulus, M.P. Whole-brain Mechanism of Neurofeedback Therapy: Predictive Modeling of Neurofeedback Outcomes on Repetitive Negative Thinking in Depression. bioRxiv. 2023;2011.2016:567419.
- 2. Misaki, M., Tsuchiyagaito, A., Guinjoan, S.M., Rohan, M.L., Paulus, M.P. Trait repetitive negative thinking in depression is associated with functional connectivity in negative thinking state rather than resting state. J Affect Disord. 2023;340:843–854.
- 3. Tsuchiyagaito, A., Misaki, M., Cochran, G., Philip, N.S., Paulus, M.P., Guinjoan, S.M. Thalamo-cortical circuits associated with trait- and state-repetitive negative thinking in major depressive disorder. J Psychiatr Res. 2023;168:184–192.
- Tsuchiyagaito, A., Misaki, M., Kirlic, N., Yu, X., Sanchez, S.M., Cochran, G., Stewart, J.L., Smith, R., Fitzgerald, K.D., Rohan, M.L., Paulus, M.P., Guinjoan, S.M. Real-Time fMRI Functional Connectivity Neurofeedback Reducing Repetitive Negative Thinking in Depression: A Double-Blind, Randomized, Sham-Controlled Proof-of-Concept Trial. Psychother Psychosom. 2023;92:87-100.
- 5. Tsuchiyagaito, A., Sanchez, S.M., **Misaki, M.**, Kuplicki, R., Park, H., Paulus, M.P., Guinjoan, S.M. Intensity of repetitive negative thinking in depression is associated with greater functional connectivity between semantic processing and emotion regulation areas. Psychol Med. 2023;53:5488–5499.



## **Research Highlights**

Dr. Obradovich collaborated with Dr. Martin Paulus to delineate potential challenges that the adoption of large language models in psychiatric care might present to both clinicians and patients alike; parts of their work were published as a viewpoint in JAMA Psychiatry.

Dr. Obradovich continued his participation as a core member of the Lancet Countdown team of scientists, working to develop novel indicators of the relationship between climatic exposures and human health and well-being, and to aid in outlining the future of the Countdown's global orientation and direction.

Dr. Obradovich's work to develop methods for evaluating the interplay between human and machine behaviors—and their potential implications for mental health—was supported by OpenAI via the company's Researcher Access Program grant on which Dr. Obradovich is a co-PI.

#### **Current Research Focus**

Dr. Obradovich applies tools from computational behavioral science, methods from statistical inference, and large social trace data to study a complex array of environmental and technological determinants of mental health. The overarching goal of the lab is to identify exposures that modify mental health—both protective and harmful ones—and to isolate the causal mechanisms underlying identified relationships to enable successful intervention. His prior studies have included the use of billions of social media posts to study how the weather alters online emotional sentiment as well as the use of global fitness band data to study how environmental factors alter human sleep patterns as a potential precursor to altered mental health status.

- Obradovich, N., Johnson, T., Paulus, M. Managerial and organizational challenges await psychiatry in the age of Al. JAMA Psychiatry. (in press).
- 2. Romanello, M., Di Napoli, C., Green, C., ..., Obradovich, N., et al. The 2023 report of the Lancet Countdown on health and climate change: the imperative for a health-centered response in a world facing irreversible harms. The Lancet. 2023.
- Fan, Y., Wang, J., Obradovich, N., & Zheng, S. Intraday adaptation to extreme temperatures in outdoor activity. Scientific Reports. 2023;13(1):473.
- 4. Minor, K., Bjerre-Nielsen, A., Jonasdottir, S. S., Lehmann, S., & **Obradovich, N.** Rising temperatures erode human sleep globally. One Earth. 2022;5(5):534-549.
- Wang, J., Fan, Y., Palacios, J., Chai, Y., Guetta-Jeanrenaud, N., Obradovich, N., ... & Zheng, S. Global evidence of expressed sentiment alterations during the COVID-19 pandemic. Nature Human Behaviour. 2022;6(3):349-358.





KAIPING BURROWS, PH.D. Staff Scientist

LEANDRA FIGUEROA-HALL, PH.D.

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Data Scientist

AHMAD KAANAN, PH.D.
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RAYUS KUPLICKI, PH.D. Lead, Data Analyst

**DALE PEASLEY** *Graduate Student* 

AARDRON ROBINSON

HYEJIN SHIM, PH.D.

Postdoctoral Research Fellow

TERESA VICTOR, PH.D. Staff Scientist

BOHAN XU, PH.D.

HAIXIA ZHENG, PH.D. Associate Investigator

## **Research Highlights**

Many computational measures have poor psychometric properties, which could invalidate previous findings and hinder ongoing research. The Paulus lab recommended steps to address these issues and facilitate the translation of computational assays to clinical practice.

Individuals with MDD have lower expression of miR-93, which is associated with higher levels of certain inflammatory markers. Unlike healthy individuals, those with MDD don't show an adaptive epigenetic regulation of a brain region (insula) involved in processing internal body signals, hinting at the molecular mechanisms that might be altering brain responsivity to these signals in MDD.

The Paulus lab found that higher screen media activity (SMA) in youth at ages 9-10 is associated with more internalizing issues 2 years later, partially mediated by specific changes in brain structures.

#### **Current Research Focus**

The current focus of Dr. Paulus and LIBR is to explore the underlying neural mechanisms of conditions like anxiety, depression, and substance use disorders across diverse populations.

Leveraging neuroimaging and neuroscientific methods, LIBR seeks to uncover the intricate neurobiology involved in validating and enhancing clinical assessments and prediction tools. There is also a concerted effort to develop innovative non-invasive treatments and interventions and identify disease-modifying processes (DMPs) that could affect the risk, severity, or recurrence of mental health conditions. Dr. Paulus' research aims to develop transdiagnostic interventions that improve patient outcomes, providing pragmatic utility and refining the understanding of causal relationships in mental health.

Dr. Paulus has a Google Scholar h-index of 116 and has published more than 450 peer-reviewed publications (some in top-tier journals like Science, Nature Reviews Neuroscience, PNAS, JAMA Psychiatry, Lancet Psychiatry, Biological Psychiatry, Neuropsychopharmacology, and the American Journal of Psychiatry) which have been cited more than 47,000 times. Dr. Paulus is the Deputy Editor of JAMA Psychiatry, a Series Editor for Current Topics in Behavioral Neuroscience, and is on several editorial boards of top-tier psychiatric journals. He has served on numerous NIH and International Study Sections and is currently on the National Institute of Mental Health Board of Scientific Councilors and on the Scientific Advisory Board for the Max Planck Institute of Psychiatry. Dr. Paulus is also on the Board of Directors of Anxiety and Depression Association of America.

- Stewart JL, Burrows K, Davis CB, Wilhelm RA, McNaughton BA, Kuplicki R, Paulus MP, Khalsa SS, White EJ. Impulsivity in amphetamine use disorder: Examination of sex differences. Addiction. 2023 Sep;118(9):1787-1800.
- Karvelis P, Paulus MP, Diaconescu AO. Individual differences in computational psychiatry: A review of current challenges. Neurosci Biobehav Rev. 2023 May;148:105137.
- 3. Colaizzi JM, Flagel SB, Gearhardt AN, Borowitz MA, Kuplicki R, Zotev V, Clark G, Coronado J, Abbott T, Paulus MP. The propensity to sign-track is associated with externalizing behavior and distinct patterns of reward-related brain activation in youth. Scientific Reports. 2023 Mar 16;13(1):4402.
- 4. Burrows K, Figueroa-Hall L, Stewart J, Alarbi A, Kuplicki R, Hannafon B, Tan C, Risbrough V, McKinney B, Ramesh R, Victor T, Aupperle R, Savitz J, Teague K, Khalsa S, Paulus M. Exploring the role of neuronal-enriched extracellular vesicle miR-93 and interoception in major depressive disorder. Res Sq. 2023 Jun 16.





**JULIE ARTERBURY** Chief MRI Technologist

**ZHIYIN CHEN** *Graduate Studen* 

ISAAC EWERS
Research Specialis

AMY GINN
MRI Technologist
MASAYA MISAKI, PH.I

AKI TSUCHIYAGAITO, PH.D Associate Investigator LESLIE WALKER

## **Research Highlights**

Dr. Rohan initiated an investigation of image acquisition and processing methods for functional MRI. Imaging research at LIBR relies on robust data acquisition and this project evaluates new developments in magnetic resonance technology for inclusion in the research protocols at LIBR.

2 Dr. Rohan continues to study the mechanisms of Low Field Magnetic Stimulation, a novel electromagnetic therapy for bipolar depression. His first investigation at LIBR will be an imaging study of the immediate effects of this treatment.

Data from the Tulsa 1000 study, as well as the CoBRE NeuroMap study, contain the results of a unique tissue characterizing scan that may contain clues to neuroinflammation. Dr. Rohan plans to perform an analysis of this data in collaboration with Dr. Jonathan Savitz to search for biomarkers of inflammation.

#### **Current Research Focus**

In 2023, Dr. Rohan supervised the installation of a 3.0 Tesla Prisma-NX MRI system to replace LIBR's original system purchased in 2009. The increase in signal-to-noise, scan coverage and scan rate made possible by the new system will enable more robust imaging results. Dr. Rohan directs the MRI Core and is responsible for the scan procedures, equipment, and data quality.

Dr. Rohan's main research focus is to ensure that the most recent and robust magnetic resonance data acquisition methods are available to the LIBR community. Improved acquisition methods are possible with the arrival of new hardware, coils and electronics that support higher resolution and faster scanning, which are being evaluated against existing methods. Image processing methods have also advanced recently and will be evaluated against existing methods using the strength of cognitive imaging results.

Dr. Rohan has developed a novel electromagnetic treatment for bipolar depression, Low Field Magnetic Stimulation (LFMS). LFMS has undergone clinical pilot studies over the last several years. In 2024, Dr. Rohan will investigate the immediate effects on the brain of this treatment with the goal of identifying a fast method for estimating effect size.

#### **Select Publications**

- Misaki M, Tsuchiyagaito A, Guinjoan SM, Rohan ML, Paulus MP. Trait repetitive negative thinking in depression is associated with functional connectivity in negative thinking state rather than resting state. J Affect Disord. 2023 Nov 1:340:843-854.
- Tsuchiyagaito A, Misaki M, Kirlic N, Yu X, Sánchez SM, Cochran G, Stewart JL, Smith R, Fitzgerald KD, Rohan ML, Paulus MP, Guinjoan SM. Real-Time fMRI Functional Connectivity Neurofeedback Reducing Repetitive Negative Thinking in Depression: A Double-Blind, Randomized, Sham-Controlled Proof-of-Concept Trial. Psychother Psychosom. 2023;92(2):87-100.
- Stella Sanchez; Aki Tsuchiyagaito; Rayus Kuplicki; Heekyeong Park; Ivan Postolski; Michael Rohan; Martin Paulus; Salvador Guinjoan. Repetitive Negative Thinking-Specific and Nonspecific White Matter Tracts Engaged by Historical Psychosurgical Targets for Depression. Biol Psychiatry. 2023 Oct 15;94(8):661-671.
- 4. Ali Fahim Khan; Fauziyya Muhammad; Esmaeil Mohammadi; Christen O'Neal; Grace Haynes; Sanaa Hameed; Michael L. Rohan; Andriy Yabluchanskiy; Zachary Adam Smith. Beyond the Aging Spine A Systematic Review of Functional Changes in the Human Brain in Cervical Spondylotic Myelopathy. Geroscience. 2023 Oct 6.
- 5. Ali Fahim Khan; Esmaeil Mohammadi; Grace Haynes; Sanaa Hameed; Michael Rohan; David B. Anderson; Kenneth A. Weber II; Fauziyya Muhammad; Zachary A. Smith. Evaluating Tissue Injury in Cervical Spondylotic Myelopathy with Spinal Cord MRI – A Systematic Review. Eur Spine J. 2023 Nov 5.





ISAAC EWERS

## **Research Highlights**

- Dr. Savitz continued his work with cytomegalovirus (CMV). Drs. Haixia Zheng and Savitz published a paper in Molecular Psychiatry showing that CMV infection is associated with suicide, increased expression of inflammatory markers and microglial "activation" postmortem.
- The Savitz lab also published a Hot Topics paper on herpesviruses and psychiatric disorders in Neuropsychopharmacology.
- Drs. Tim Meier and Savitz reported in Brain that CMV-positive athletes with concussion showed evidence of white matter abnormalities (greater axial and radial kurtosis) as well as reduced cortical thickness compared to their CMV-negative counterparts.

#### **Current Research Focus**

Depression is one of the most serious and common psychiatric disorders, yet we know very little about the underlying disease process. Our lab is examining whether inflammation of the brain is one cause of depression. In particular, we are using blood-based immune markers, viral antibodies, and experimental medicine designs to examine how inflammatory processes affect the healthy and diseased brain. Ultimately, this research can help to identify new treatments for depression that are based on modifying the inflammatory process.

- 1. Savitz, J., Goeckner, B. D., Ford, B. N., Teague, T. K., Zheng, H., Harezlak, J., Mannix, R., Muftuler, L. T., Brett, B. L., McCrea, M. A., Meier, T. B. The effects of cytomegalovirus on brain structure following sport-related concussion. Brain. 2023;146:4262-4273.
- 2. Zheng, H., Webster, M., Weickert, C., Beasley, C., Paulus, M., Yolken, R., Savitz, J. Cytomegalovirus antibodies are associated with mood disorders, suicide, markers of neuroinflammation, and microglia activation in postmortem brain samples. Molecular Psychiatry. 2023.
- 3. Zheng, H. and Savitz, J. Herpesviruses and neuropsychiatric disorders: overlooked adversaries or innocent bystanders? Neuropsychopharmacology. 2023.
- 4. J. Savitz and R.H. Yolken (Eds). Microorganisms and Mental Health. Springer-Nature. 2023.
- Meier, T.B., Savitz, J. The kynurenine pathway in traumatic brain injury: Implications for psychiatric outcomes. Biological Psychiatry. 2022;91:449-458.





**KO-PING CHOU** *Graduate Student* 

**CARTER GOLDMAN**Research Assistant

NAVID HAKIMI, PH.D.

Postdoctoral Research Associate

**ROWAN HODSON** *Graduate Student* 

**CLAIRE LAVALLEY** *Research Assistant* 

NING LI Study Coordinator MARISHKA MEHTA Graduate Student

TORU TAKAHASHI, PH.D.

Postdoctoral Research Associate

**TAYLOR TORRES** *Research Assistant* 

## **Research Highlights**

Dr. Smith had 13 research articles published in 2023. He also gave 6 invited international talks and 3 national talks presenting his research including presentation of his research at the University of Zurich; Nagoya University; Japan's National Center of Neurology and Psychiatry (NCNP); and Dartmouth College, as well as a keynote talk at a symposium held by the University of Tokyo, among others.

2 Dr. Smith began data collection on a new pilot study examining computational mechanisms of breathing perception in anxiety disorders. His lab also continues to make progress on a 3-year project funded by a grant from the Well-being for Planet Earth Foundation. This project investigates neurocomputational predictors of subjective well-being. Data collection was also completed this year for a study examining the influence of an interoception-based anxiety induction on decision-making mechanisms associated with information-seeking and planning. These data have now begun to be analyzed.

Dr. Smith also recently submitted an R01 grant application to NIDA to extend his work on learning mechanisms in individuals with substance use problems.

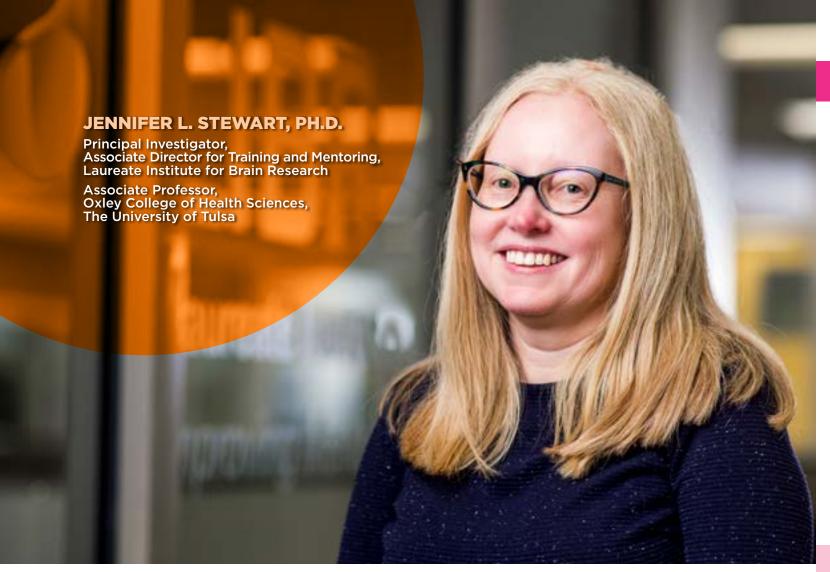
Dr. Smith welcomed several very bright and talented researchers to his lab in 2023, including 3 research assistants (Carter Goldman, Ning Li, and Taylor Torres), one graduate student (Ko-Ping Chou), and 1 postdoctoral research fellow (Toru Takahashi).

#### **Current Research Focus**

Dr. Smith's lab focuses on understanding the neurocomputational mechanisms underlying emotioncognition interactions and how they relate to brain-body interactions, with a special focus on information-seeking behavior, prospective planning, and interoception. Lab projects also focus on how these mechanisms are affected in depression, anxiety, and substance use disorders. The primary research methods used in the lab are neuroimaging (fMRI and EEG), electrophysiology (pupillometry, EKG, Skin Conductance), and computational modeling, including a wide range of modeling approaches (e.g., drift-diffusion models, reinforcement learning models, active inference models). A major overarching focus is to characterize information processing differences between mentally healthy and unhealthy individuals with the goal of improving diagnosis and treatment selection within psychiatry and clinical psychology.

#### **Select Publications**

- Smith R, Lavalley CA, Taylor S, Stewart JL, Khalsa SS, Berg H, et al. Elevated decision uncertainty and reduced avoidance drives in depression, anxiety, and substance use disorders during approach-avoidance conflict: A replication study. Journal of Psychiatry & Neuroscience. 2023;48(3):E217-E31.
- 2. Taylor S, Lavalley CA, Hakimi N, Stewart JL, Ironside M, Zheng H, ... Smith R. Active learning impairments in substance use disorders when resolving the explore-exploit dilemma: A replication and extension of previous computational modeling results. Drug Alcohol Depend. 2023;252:110945.
- 3. Smith R, Persich MR, Cloonan S, Woods-Lubert R, Skalamera J, Berryhill SM, et al. Improvements in Mindfulness, Interoceptive and Emotional Awareness, Emotion Regulation, and Inter-Personal Emotion Management Following Completion of an Online Emotional Skills Training Program. Emotion. 2023.
- 4. Da Costa L, Sajid N, Parr T, Friston K, Smith R. Reward Maximization Through Discrete Active Inference. Neural Computation. 2023;1-46.
- 5. Smith R, Versluis A, Chuning AE, Allen JJB, Weihs KL, Brosschot JF, et al. Early adversity and emotional awareness: A partial confirmation and extension of their relationship. Journal of Family Trauma, Child Custody & Child Development. 2023;1–21.



## **Research Highlights**

Compared to individuals with a history of major depressive disorder (MDD) and healthy controls, individuals with amphetamine use disorder 1) report greater positive and negative urgency (taking rash action when feeling good or bad); and 2) exhibit greater right hemisphere brain signals (in right anterior/middle insula, amygdala, and ventral striatum) during successful behavioral inhibition. These findings point to heightened impulsivity during emotional arousal and recruitment of more brain resources to exert inhibitory control.

Compared to healthy controls, individuals with major depressive disorder (MDD) show higher leptin concentrations that are in turn associated with reduced left hemisphere (insula, dorsal striatum) brain signals during reward anticipation. These findings suggest proinflammation linked to appetite processes could exert effects on the brain's reward pathway in depression.

Within an American Indian sample, individuals with substance use disorders show lower striatal brain signals when anticipating losses than those without these disorders, suggesting reduced resources devoted to the processing of potential negative consequences in addiction.



CHRYSANTHA DAVIS
Research Assistant

NATOSHA MARKHAM
Clinical Research Interviewe

BREANNA MCNAUGHTON

Possarch Assistant

ABIGAIL PLEIMAN
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MEGAN POSEY

Posparch Assistan

RICARDO WILHELM, PH.D.

Postdoctoral Research Associate

#### **Current Research Focus**

Dr. Stewart uses electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) methods to identify biobehavioral markers of major depressive disorder (MDD) and substance use disorders symptom presentation, treatment outcome, and recovery.

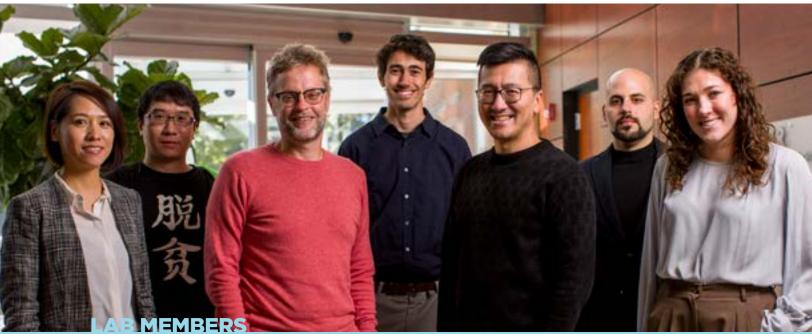
- Burrows, K., McNaughton, B., Figueroa-Hall, L. K., Spechler P., Kuplicki, R., Victor T., Aupperle, R. L., Khalsa, S., Savitz, J., Teague, T. K., Paulus, M. P., & Stewart, J. L. Elevated serum leptin is associated with attenuated reward anticipation in major depressive disorder independent of peripheral C-reactive protein levels. Scientific Reports. 2023;13:11313.
- 2. Stewart, J. L., Burrows, K., Davis, C. B., Wilhelm, R. A., McNaughton, B. A., Kuplicki, R., Paulus, M. P., Khalsa, S. S., & White, E. J. Impulsivity in amphetamine use disorder: Examination of sex differences. Addiction. 2023;118:1787–1800.
- 3. Taylor, S., Lavalley, C. A., Hakimi, N., **Stewart, J. L.**, Ironside, M., Zheng, H., White, E., Guinjoan, S., Paulus, M. P. & Smith, R. Active learning impairments in substance use disorders when resolving the explore-exploit dilemma: A replication and extension of previous computational modeling results. Drug and Alcohol Dependence. (in press).
- 4. White, E. J., Demuth, M. J., Nacke, M., Kirlic, N., Kuplicki, R., Spechler, P., McDermott, T. J., DeVille, D. C., T1000 Investigators, Stewart, J. L., Lowe, J., Paulus, M. P., & Aupperle, R. L. Neural processes of inhibitory control in American Indian peoples are associated with reduced mental health problems. Social Cognitive and Affective Neuroscience. 2023;18.
- Wilhelm, R., Spechler, P. A., Demuth, M. J., Gonzalez, M., Kemp, C., Walls, M., Aupperle, R. L., Paulus, M. P., Stewart, J. L., & White, E. J. Striatal hypoactivation during monetary loss anticipation in individuals with substance use disorders in a heterogenous urban American Indian sample. Drug and Alcohol Dependence. 2023.



## **Research Highlights**

- Dr. Thompson gave a talk at the Joint Statistical Meetings on August 7, 2023, on "Annotation-Informed Polyvertex Scores for Brain-Wide Association Studies."
- 2 Dr. Thompson served as the managing guest editor for a special issue of Developmental Cognitive Neuroscience on novel methods for population neuroscience.
- Dr. Thompson was invited to give a 2-day workshop on geospatial data analysis at the BERTHA summer school in Denmark, July 2023.

Dr. Thompson continues his efforts as Director of Biostatistics for three national consortia on longitudinal neurodevelopment: the National Consortium of Alcohol and Neurodevelopment in Adolescence (NCANDA), the Adolescent Brain Cognitive Development (ABCD) Study<sup>SM</sup>, and the HEALthy Brain Child Development (HBCD) Study.



ONATHAN AHERN, B.S. Staff Research Assistant

**ASHLEY BARROWS, B.S.**Proiect Manager at LIBR

WENJIE CHENG

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LIN LI

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Data Scientist at LIRR

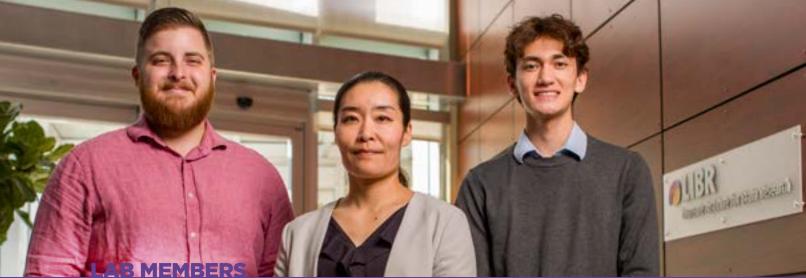
#### **Current Research Focus**

Dr. Thompson continues his effort in development and application of semi-parametric Bayesian hierarchical and mixture models for multivariate data, with applications to diverse areas of biological psychiatry, including human brain imaging and other biological markers of mental illness and estimation of developmental trajectories and prediction of outcomes from incomplete longitudinal data.

#### **Select Publications**

- Cao Z, McCabe M, Callas P, Cupertino RB, Ottino-González J, Murphy A, Pancholi D, Schwab N, Catherine O, Hutchison K, Cousijn J, Dagher A, Foxe JJ, Goudriaan AE, Hester R, Li CR, Thompson WK, Morales AM, London ED, Lorenzetti V, Luijten M, Martin-Santos R, Momenan R, Paulus MP, Schmaal L, Sinha R, Solowij N, Stein DJ, Stein EA, Uhlmann A, van Holst RJ, Veltman DJ, Wiers RW, Yücel M, Zhang S, Conrod P, Mackey S, Garavan H; ENIGMA Addiction Working Group. Recalibrating single-study effect sizes using hierarchical Bayesian models. Front Neuroimaging. 2023 Dec 21;2:1138193.
- 2. Gebru NM, Goncalves PD, Cruz RA, Thompson WK, Allegair N, Potter A, Garavan H, Dumas J, Leeman RF, Johnson M. Effects of parental mental health and family environment on impulsivity in preadolescents: a longitudinal ABCD Study™. Front Behav Neurosci. 2023 Oct 24;17:1213894.
- 3. Vaez M, Montalbano S, Sánchez XC, Georgii Hellberg KL, Rasekhi Dehkordi S, Dybdahl Krebs M, Meijsen J, Shorter J, Byberg-Grauholm J, Mortensen PB, Børglum AD, Hougaard DM, Nordentoft M, Geschwind DH, Buil A, Schork AJ; iPSYCH Investigators; Helenius D, Raznahan A, Thompson WK, Werge T, Ingason A. Population-based Risk of Psychiatric Disorders Associated with Recurrent CNVs. medRxiv [Preprint]. 2023 Sep 5;2023.09.04:23294975.
- 4. Ottino-González J, Cupertino RB, Cao Z, Hahn S, Pancholi D, Albaugh MD, Brumback T, Baker FC, Brown SA, Clark DB, de Zambotti M, Goldston DB, Luna B, Nagel BJ, Nooner KB, Pohl KM, Tapert SF, Thompson WK, Jernigan TL, Conrod P, Mackey S, Garavan H. Brain structural covariance network features are robust markers of early heavy alcohol use. Addiction. 2024 Jan;119(1):113-124.
- 5. Park H, Forthman KL, Kuplicki R, Victor TA, Yeh HW, Thompson WK, Howlett JR, Guinjoan S, Paulus MP. Polygenic risk for neuroticism is associated with less efficient control in more difficult situations. Psychiatry Res Neuroimaging. 2023 Oct;335:111716.





LANDON EDWARDS, B.S. Research Assistant

**ELI ELLIOTT** 

Volunteer, Undergraduate Student at The University of Tulsa

JOLENE TAY, B.S. Mentee, ABCD Research Assistant

## **Research Highlights**

In collaboration with Dr. Guinjoan's lab, Dr. Tsuchiyagaito employed fMRI scans to investigate brain connectivity patterns associated with repetitive negative thinking (RNT) in adults with MDD. Results revealed distinct patterns between trait- and state-RNT in the right thalamo-cortical circuit, suggesting deep-brain neuromodulation such as a low-intensity focused ultrasound could further elucidate these differences.

Drs. Tsuchiyagaito, Misaki, Guinjoan and Paulus continued a LIBR project with healthy volunteers, where the aim is to decode the brain status associated with rumination, worry, and positive thoughts, exploring methods to counteract RNT through mindfulness and cognitive reappraisal. Gabe Cochran, a former research assistant now pursuing a Ph.D. in Clinical Psychology at Oklahoma State University, played a crucial role in data collection alongside the LIBR assessment team.

Dr. Tsuchiyagaito's lab welcomed Landon Edwards, a dedicated research assistant with doctorate aspirations in Clinical Psychology. As the study coordinator for the CoBRE Phase II Research Project, Landon oversees research into real-time fMRI neurofeedback's influence on the RNT circuit. Eli Elliott, a student at The University of Tulsa majoring Biochemistry with a Neuroscience minor, has also joined the team, assisting in EEG and fMRI analysis with Landon. Additionally, Dr. Tsuchiyagaito mentors Jolene Tay, an ABCD research assistant. Together they are exploring trauma-exposed adolescents' brain functions during reward anticipation and fear conditioning in collaboration with Dr. Namik Kirlic.

#### **Current Research Focus**

About 1 in 10 young adults suffer from major depressive disorder (MDD), which is among the most common mental health conditions in young adulthood and can interfere with the successful transition into middle adulthood, if not effectively treated. Repetitive negative thinking (RNT), a cognitive process that encompasses future-(worry) and past- (rumination) directed thoughts, is associated with both poor prognosis and treatment resistance. Novel treatments designed to modify the neurobiological mechanisms underlying repetitive negative thinking could facilitate recovery in MDD. Dr. Tsuchiyagaito's lab focuses on promoting mental health in young adults and adolescents by understanding the brain mechanisms underlying repetitive negative thinking and developing interventions to enhance the ability to disengage from RNT.

#### **Select Publications**

- 1. Tsuchiyagaito A, Misaki M, Cochran G, Philip NS, Paulus MP, Guinjoan SM. Thalamo-cortical circuits associated with trait- and state-repetitive negative thinking in major depressive disorder.

  J Psychiatry Res. 2023 Oct 27;168:184-192.
- Sanchez SM, Tsuchiyagaito A, Kuplicki R, Park H, Postolski I, Rohan M, Paulus MP, Guinjoan SM. Repetitive Negative Thinking-Specific and Nonspecific White Matter Tracts Engaged by Historical Psychosurgical Targets for Depression. Biol Psychiatry. 2023 Oct 15;94(8):661-671.
- 3. Tsuchiyagaito A, Aoki S, Cochran G, Kawanori Y, Horiuchi S, Hard to let it go: repetitive negative thinking and hoarding in later life in Japan. Aging & Mental Health. 2023 May 13;1–9.
- 4. Tsuchiyagaito A\*, Misaki M\*, Kirlic N, Yu X, Sánchez SM, Cochran G, Stewart JL, Smith R, Fitzgerald KD, Rohan ML, Paulus MP, Guinjoan SM. Real-time fMRI functional connectivity neurofeedback reducing repetitive negative thinking in depression: a double-blind, randomized, sham-controlled proof-of-concept trial. Psychother Psychosom. 2023 Jan 11;92(2):87-100.
- 5. Cochran G, Cohen ZP, Paulus MP, Tsuchiyagaito A\*, Kirlic N\*.

  Sustained increase in depression and anxiety among psychiatrically healthy adolescents during late stage COVID-19 pandemic.

  Front in Psych. 2023 Mar 17;14:1137842.

\*Contributed equally.

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**NICOLE BAUGHMAN** *NeuroCATT Research Assistan* 

**DANIELLE BETHEL**Lab Coordinator

**ERIC MANN** *EEG Core Research Assistal* 

LIZBETH ROJAS

DREAM-Neuro Fellow

RICARDO WILHELM, PH.D.

Postdoctoral Research Associate

## **Research Highlights**

LIBR received a DP1 grant for research to be conducted by Dr. White in collaboration with the Shawnee Tribe of Oklahoma titled "Kipiyecipakiciipe - Coming Home: Establishing clinical cultural neuroscience as a tool for understanding the role of traditional cultural engagement in mitigating substance misuse and disorder." Within American Indian (AI) populations, there is a disproportionate share of negative health and social consequences of substance use disorder (SUD) even after decades of awareness and research. This project aims to integrate community-based participatory research (CBPR) with neuroscience tools to examine the influence of traditional cultural engagement on resilience factors that may protect against poor mental health as well as risk for substance use.

Resilience factors that protect against poor mental health within American Indian (AI) populations have been investigated; however, neural mechanisms of these effects remain under-explored. In a recently published study, Dr. White's group examined reward and loss processing using fMRI data and found that anticipatory processing of high-magnitude losses in some AI individuals may represent a neural mechanism of protective effects against substance use disorders in AI.

Dr. White has built upon previous collaboration with partners at Cherokee Nation regarding Al-participant data from the Adolescent Brain and Cognitive Development (ABCD) Study<sup>sM</sup> through active analysis at LIBR and also external collaboration. Specifically, Dr. White's group has conducted analysis demonstrating that connection to traditional cultural practices may buffer the relationship between maternal depression and internalizing symptoms in children, currently under review. He has also worked with external collaborators examining multilevel indicators of impulsivity in Al youth with some level of reported suicide risk. He is collaborating with internal and external collaborators to publish a framework for studying health disparities using ABCD study data.

#### **Current Research Focus**

Dr. White's research aims to establish and advance neuroscientific understanding of cultural factors that are protective against poor mental health among American Indians utilizing a strength-based framework. A focus of this research is combining multi-modal neuroscience and psychophysiology with communitybased participatory research (CBPR) approaches. This approach to research brings community partners to the table in the scientific endeavor to ensure community priorities are represented and that the results of the work make a positive impact in the community. Dr. White's goal is to integrate clinical and cultural neuroscience to identify modifiable factors as candidate treatment targets for mental health intervention and prevention. Dr. White also is the Director of the Electroencephalography (EEG) Core, overseeing the facility's EEG technology and data-processing infrastructure and ensuring LIBR investigators have support to conduct state-of-the-art research using EEG techniques.

#### **Select Publications**

- Baughman, N. R., Wilhelm, R. A., Spechler, P. A., McNaughton, B. A., Demuth, M. J., Lawrence, G. L., Stumblingbear Riddle, G., Shadlow, J. O., Kominsky, T., Stewart, J. L., Aupperle, R. L., Paulus, M. P., White, E. J. Cognitive control as a potential neural mechanism of protective role of spirituality in anxiety disorders among American Indian people: An ERP study. Psychiatry Research: Neuroimaging. 2023;335:111712.
- Wilhelm, R.A., Spechler, P.A., Demuth, M.J., Gonzalez, M., Kemp, C., Walls, M. Aupperle, R.L., Paulus, M.P., Stewart, J.L., White, E.J. Striatal hypoactivation during monetary loss anticipation in individuals with substance use disorders in a heterogenous urban American Indian sample. Drug and Alcohol Dependence. 2023;246:109852.
- 3. O'Keefe, V. M., Maudrie, T. L., Cole, A. B., Ullrich, J. S., Fish, J., Hill, K. X., White, L. A., Redvers, N., Blue Bird Jernigan, V., Lewis, J. P., West, A. E., Aqpik Apok, C., White, E. J., Ivanich, J. D., Schultz, K., Lewis, M. E., Sarche, M. C., Gonzalez, M. B., Parker, M., Neuner Weinstein, S. E., McCray, C. J., Warne, D., Black, J. C., Richards, J. R., Walls, M. L. Conceptualizing Indigenous strengths-based health and wellness research using group concept mapping. Archives of Public Health. 2023;81:1.
- 4. White, E.J. Racial discrimination, school racial composition and anxiety symptoms in American Indian adolescents:
  Editorial on Barry and Colleagues 2023. Journal of Adolescent Health. (in press).
- 5. John-Henderson, N.A., White, E.J., Crowder, T.L. Resilience and health in American Indians and Alaska Natives: A scoping review of the literature. Development and Psychopathology. 2023;1-12.



**YE ZHANG** *Ph.D. Student, Tohoku University, Japan* 

## **Research Highlights**

Dr. Zheng's group observed individuals infected with cytomegalovirus (CMV) showed a higher likelihood of having neuroinflammation, increased microglia activation, and double the risk of committing suicide in postmortem brain samples, suggesting cytomegalovirus infection may be a targetable source of neuroinflammation that contributes to the development of mental illness.

2 Dr. Zheng's group found the genetic propensity toward a higher level of inflammation (measured by polygenic risk score for inflammation marker C-reactive protein) is associated with the altered neurodevelopmental trajectory and increased risk for psychopathology in adolescents.

Early-life infections are likely to moderate the association between genetic propensity toward a higher level of inflammation and neurodevelopment, thereby amplifying the risk for depression and internalizing and externalizing psychopathologies in adolescents.

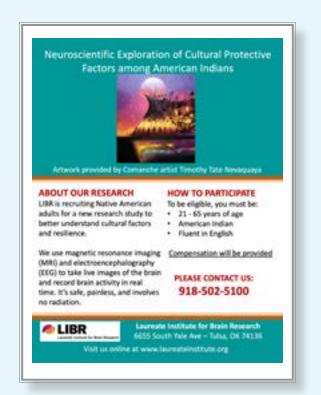
#### **Current Research Focus**

Dr. Zheng's research delves into the role of immune-brain interactions in mood disorders, with an initial focus on how common herpes viral infection (cytomegalovirus, CMV) influences brain structure and function, particularly in relation to depression. Dr. Zheng employs an innovative, multidisciplinary approach, utilizing cutting-edge neuroimaging techniques to examine brain microstructure, alongside blood-based serological assessments to detect viral serostatus and antibody levels. Further, her lab leverages statistical genetic tools to explore how an individual's genetic susceptibility interacts with a viral infection, potentially heightening the risk for neuroinflammation and its clinical presentations, including depression. Dr. Zheng's work is crucial in pinpointing individuals at heightened risk and elucidating the neuroviral underpinnings of depression throughout various stages of life. Her research is setting a solid groundwork for an independent career in population immunopsychiatry, a field that intersects neuroscience, immunology, and psychiatric research. This pioneering work not only advances our understanding of the complex interplay between infectious agents and mental health but also paves the way for new avenues for targeted interventions and preventive strategies in mental health care.

- Zheng H, Webster MJ, Weickert CS, Beasley CL, Paulus MP, Yolken RH, et al. Cytomegalovirus antibodies are associated with mood disorders, suicide, markers of neuroinflammation, and microglia activation in postmortem brain samples. Mol Psychiatry. 2023.
- Zheng H, Savitz J. Herpesviruses and neuropsychiatric disorders: overlooked adversaries or innocent bystanders? Neuropsychopharmacology. 2023.
- Savitz J, Goeckner BD, Ford BN, Kent Teague T, Zheng H, Harezlak J, et al. The effects of cytomegalovirus on brain structure following sportrelated concussion. Brain. 2023;146(10):4262-4273.
- Taylor S, Lavalley CA, Hakimi N, Stewart JL, Ironside M, Zheng H, et al. Active learning impairments in substance use disorders when resolving the exploreexploit dilemma: A replication and extension of previous computational modeling results. Drug Alcohol Depend. 2023;252:110945.
- Zhang Y, Tatewaki Y, Nakase T, Liu Y, Tomita N, Hyreau B, Zheng H et al. Impact of hs-CRP concentration on brain structure alterations and cognitive trajectory in Alzheimer's disease. Front Aging Neurosci. 2023;15:1227325.

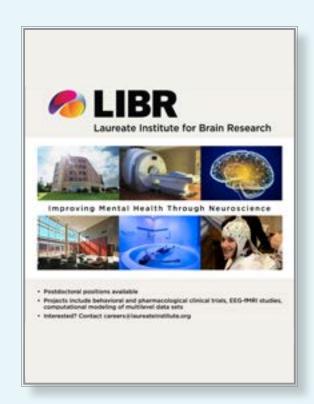
#### **ONGOING STUDIES**



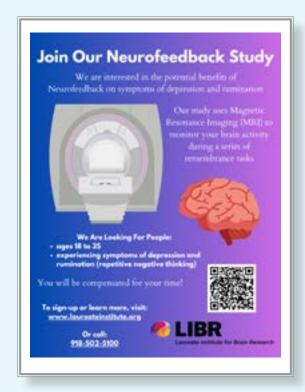














#### **SELECT 2023 PUBLICATIONS**

Verdonk C, Teed AR, White EJ, Ren X, Stewart JL, Paulus MP, Khalsa SS. Heartbeat-evoked neural response abnormalities in generalized anxiety disorder during peripheral adrenergic stimulation. medRxiv [Preprint]. 2023 Dec 22;2023.06.09.23291166.

Adamic EM, Teed AR, Avery JA, de la Cruz F, Khalsa SS. Hemispheric divergence of interoceptive processing across psychiatric disorders. bioRxiv [Preprint]. 2023 Dec 9;2023.12.08.570759.

Zhao Y, Potenza MN, Tapert SF, Paulus MP. Neural correlates of negative life events and their relationships with alcohol and cannabis use initiation. Dialogues Clin Neurosci. 2023 Dec;25(1):112–121.

Tsuchiyagaito A, Misaki M, Cochran G, Philip NS, Paulus MP, Guinjoan SM. Thalamo-cortical circuits associated with trait- and state-repetitive negative thinking in major depressive disorder. J Psychiatr Res. 2023 Dec;168:184–192.

Howlett JR, Larkin F, Touthang J, Kuplicki RT, Lim KO, Paulus MP. Rapid, reliable mobile assessment of affect-related motor processing. Behav Res Methods. 2023 Dec;55(8):4260–4268.

Hodson R, Mehta M, Smith R. The empirical status of predictive coding and active inference. Neurosci Biobehav Rev. 2023 Nov 28;157:105473.

Khalsa SS. Rhythms of the Heart, Echoes in the Brain: Exploring Interoception. JACC Clin Electrophysiol. 2023 Nov;9(11):2236–2239.

Taylor S, Lavalley CA, Hakimi N, Stewart JL, Ironside M, Zheng H, White E, Guinjoan S, Paulus MP, Smith R. Active learning impairments in substance use disorders when resolving the explore-exploit dilemma: A replication and extension of previous computational modeling results. Drug Alcohol Depend. 2023 Nov 1;252:110945.

Misaki M, Tsuchiyagaito A, Guinjoan SM, Rohan ML, Paulus MP. Trait repetitive negative thinking in depression is associated with functional connectivity in negative thinking state rather than resting state. J Affect Disord. 2023 Nov 1;340:843–854.

Poplin T, Ironside M, Kuplicki R, Aupperle RL, Guinjoan SM, Khalsa SS, Stewart JL, Victor TA, Paulus MP, Kirlic N. The unique face of anxious depression: Increased sustained threat circuitry response during fear acquisition. bioRxiv [Preprint]. 2023 Oct 17;2023.10.17.562565.

Sanchez SM, Tsuchiyagaito A, Kuplicki R, Park H, Postolski I, Rohan M, Paulus MP, Guinjoan SM. Repetitive Negative Thinking-Specific and -Nonspecific White Matter Tracts Engaged by Historical Psychosurgical Targets for Depression. Biol Psychiatry. 2023 Oct 15;94(8):661–671.

Lavalley CA, Hakimi N, Taylor S, Kuplicki R, Forthman KL, Stewart JL, Paulus MP, Khalsa SS, Smith R. Transdiagnostic failure to adapt interoceptive precision estimates across affective, substance use, and eating disorders: A replication study. medRxiv [Preprint]. 2023 Oct 12:2023.10.11.23296870.

Savitz J, Goeckner BD, Ford BN, Kent Teague T, Zheng H, Harezlak J, Mannix R, Tugan Muftuler L, Brett BL, McCrea MA, Meier TB. The effects of cytomegalovirus on brain structure following sport-related concussion. Brain. 2023 Oct 3:146(10):4262–4273.

Choquette EM, Flux MC, Moseman SE, Chappelle S, Naegele J, Upshaw V, Morton A, Paulus MP, Feinstein JS, Khalsa SS. The impact of floatation therapy on body image and anxiety in anorexia nervosa: a randomised clinical efficacy trial. EClinicalMedicine. 2023 Aug 29:64:102173.

Paulus MP, Zhao Y, Potenza MN, Aupperle RL, Bagot KS, Tapert SF. Screen media activity in youth: A critical review of mental health and neuroscience findings. J Mood Anxiety Disord. 2023 Oct 3:100018

Park H, Forthman KL, Kuplicki R, Victor TA, Yeh HW, Thompson WK, Howlett JR, Guinjoan S, Paulus MP. Polygenic risk for neuroticism is associated with less efficient control in more difficult situations. Psychiatry Res Neuroimaging. 2023 Oct;335:111716.

Baughman NR, Wilhelm RA, Spechler PA, McNaughton BA, Demuth MJ, Lawrence GL, Riddle GS, Shadlow JO, Kominsky T, Stewart JL, Aupperle RL, Paulus MP, White EJ. Cognitive control as a potential neural mechanism of protective role of spirituality in anxiety disorders among American Indian people: An ERP study. Psychiatry Res Neuroimaging. 2023 Oct;335:111712.

Stewart JL, Burrows K, Davis CB, Wilhelm RA, McNaughton BA, Kuplicki R, Paulus MP, Khalsa SS, White EJ. Impulsivity in amphetamine use disorder: Examination of sex differences. Addiction. 2023 Sep:118(9):1787–1800.

Tsuchiyagaito A, Sánchez SM, Misaki M, Kuplicki R, Park H, Paulus MP, Guinjoan SM. Intensity of repetitive negative thinking in depression is associated with greater functional connectivity between semantic processing and emotion regulation areas. Psychol Med. 2023 Sep:53(12):5488–5499.

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Smith R, Persich MR, Chuning AE, Cloonan S, Woods-Lubert R, Skalamera J, Berryhill SM, Weihs KL, Lane RD, Allen JJB, Dailey NS, Alkozei A, Vanuk JR, Killgore WDS. Improvements in mindfulness, interoceptive and emotional awareness, emotion regulation, and interpersonal emotion management following completion of an online emotional skills training program. Emotion. 2024 Mar:24(2):431–450.

Huys QJM, Paulus M. Special Issue on Reliable Mechanisms for Translational Applications. Biol Psychiatry Cogn Neurosci Neuroimaging. 2023 Aug;8(8):778–779.

Kirlic N, Akeman E, DeVille DC, Yeh HW, Cosgrove KT, McDermott TJ, Touthang J, Clausen A, Paulus MP, Aupperle RL. A machine learning analysis of risk and protective factors of suicidal thoughts and behaviors in college students. J Am Coll Health. 2023 Aug—Sep;71(6):1863—1872.

Burrows K, McNaughton BA, Figueroa-Hall LK, Spechler PA, Kuplicki R, Victor TA, Aupperle R, Khalsa SS, Savitz JB, Teague TK, Paulus MP, Stewart JL. Elevated serum leptin is associated with attenuated reward anticipation in major depressive disorder independent of peripheral C-reactive protein levels. Sci Rep. 2023 Jul 13;13(1):11313.

Joshi SA, Aupperle RL, Khalsa SS. Interoception in Fear Learning and Posttraumatic Stress Disorder. Focus (Am Psychiatr Publ). 2023 Jul;21(3):266–277.

De la Cruz F, Teed AR, Lapidus RC, Upshaw V, Schumann A, Paulus MP, Bär KJ, Khalsa SS. Central Autonomic Network Alterations in Anorexia Nervosa Following Peripheral Adrenergic Stimulation. Biol Psychiatry Cogn Neurosci Neuroimaging. 2023 Jul;8(7):720–730.

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A causal random forest analysis of Adolescent Brain Cognitive Development data. Child Dev. 2023 Jul–Aug;94(4):826–835.

Zheng H, Webster MJ, Weickert CS, Beasley CL, Paulus MP, Yolken RH, Savitz J. Cytomegalovirus antibodies are associated with mood disorders, suicide, markers of neuroinflammation, and microglia activation in postmortem brain samples. Mol Psychiatry. 2023 Jun;30:10.1038/s41380\_023\_02162\_4

Smith R, Lavalley CA, Taylor S, Stewart JL, Khalsa SS, Berg H, Ironside M, Paulus MP, Aupperle R. Elevated decision uncertainty and reduced avoidance drives in depression, anxiety and substance use disorders during approach-avoidance conflict: a replication study. J Psychiatry Neurosci. 2023 Jun 20:48(3):E217–E231.

Burrows K, Figueroa-Hall L, Stewart J, Alarbi A, Kuplicki R, Hannafon B, Tan C, Risbrough V, McKinney B, Ramesh R, Victor T, Aupperle R, Savitz J, Teague K, Khalsa S, Paulus M. Exploring the role of neuronal-enriched extracellular vesicle miR-93 and interoception in major depressive disorder. Res Sq [Preprint]. 2023 Jun;16:rs.3.rs-2813878.

Steinhäuser JL, Teed AR, Al-Zoubi O, Hurlemann R, Chen G, Khalsa SS. Reduced vmPFC-insula functional connectivity in generalized anxiety disorder: a Bayesian confirmation study. Sci Rep. 2023 Jun 14;13(1):9626.

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