



LIBR

Laureate Institute for Brain Research



**SCIENTIFIC
REPORT**

2021

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The Laureate Institute for Brain Research (LIBR) facilities consist of 27,000 square feet of space entirely dedicated to neuropsychiatric and neuroscience research on the campus of the Laureate Psychiatric Clinic and Hospital (LPCH) at Saint Francis Hospital in Tulsa, Oklahoma.

42 Offices, including 3 large shared spaces for students and volunteers

5 Conference rooms

3 Bioassay rooms

3 Psychophysiology testing rooms

2 Behavioral observation rooms

2 Float rooms

2 Medical/blood draw rooms

2 MRI bays and adjoining control rooms

1 Mock scanner room

1 Neuropsychological testing room

1 Transcranial magnetic stimulation (TMS) room



Letter from the President

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

Mental health conditions continue to be among the most challenging problems human beings face. This is true even more so in 2021 and into 2022 given the waves of SARS-CoV2 over the past two years and an ever-changing environment that is presenting new challenges with a changing climate. LIBR aims to contribute cutting-edge neuroscience-based tools or techniques to better identify the brain processes that put individuals at risk for mental health problems, that indicate the severity of a problem or determine whether an individual has recovered from a mental health condition. We are also using neuroscience approaches to develop more targeted interventions, i.e., interventions that modulate specific brain processes so that people can improve faster and stay healthy longer.

However, there are significant headwinds, which makes progress difficult. First, the biological basis for mental health conditions is still largely unknown. There are few mechanistic pathways robustly associated with the risk for, exacerbation of, recurrence of, remission of these conditions. Second, the effect sizes of biological differences across groups of individuals with/without mental health conditions tend to be small, which supports the idea that there is no single overarching process that underlies a particular mental health condition. Third, the relationships between levels of analyses (i.e., molecular, cellular, physiological, circuit, behavioral, or symptomatic) tend to be weak, such that the variation on one level

explains little variance on another level. Fourth, there is some evidence for heterogeneity among causes and effects. For example, some individuals who develop a depression may show altered inflammatory responses in the brain whereas others may experience an inability to adequately process positive events. On a practical level, the acceptance, scalability, and adherence to mental health interventions has been limited such that few individuals who might benefit from an intervention consider it necessary, have access, or adhere to it for sufficiently long to make a difference. Finally, mental health conditions may result from causal processes on different levels of analyses. For example, individuals who develop a major depressive episode might have a genetic predisposition for it, experience ongoing inflammatory processes, and experience a significant adverse life event, which together result in the condition observed.

Yet, despite all these difficulties, investigators at LIBR have been working tirelessly to identify processes that can be targets for intervention or can become biological markers of mental health conditions. Moreover, several groups are working on behavioral, pharmacological, and neuromodulatory approaches that are firmly based on neuroscience. As an institute we need to focus on targeted areas of excellence that are based on the expertise of our investigators. At this stage, I have identified five areas that we are working in to make an impact: (1) Neuromodulatory approaches to modify

mental health conditions, (2) Brain-based mechanisms underlying behavioral interventions for mental health conditions, (3) Interoceptive dysfunctions in mental health conditions, (4) Innate and adaptive immunity, inflammation, and related processes in mental health conditions, (5) Culture, lifestyle, and environmental influences (CLE) on mental health conditions.

There are several noteworthy discoveries that LIBR investigators made over the past year. Dr. Haixia Zheng and collaborators found that positive cytomegalovirus serostatus is associated with altered connectivity of regions that are important for stress and emotion processing, which provides further evidence of a possible etiological role of viruses in depression. Robin Aupperle and Jonathan Savitz found a profound metabolic change occurs within the kynurenine pathway, which raises the possibility that a common therapeutic mechanism underlies diverse forms of anti-depressant treatment. Along similar lines, Aki Tsuchiyagaito who worked with Jerzy Bodurka as a post-doctoral fellow showed that real-time neurofeedback decreases metabolism down the so-called neurotoxic branch of the kynurenine pathway. Ryan Smith and colleagues reported that dysfunctions in decision processes among individuals with mood, anxiety, and substance use disorders are pervasive and persist over time. Justin Feinstein and colleagues reported that floatation interventions have profound effect on brain systems most responsible for creating and mapping our sense of self. Kai-Ping Burrows and colleagues found that individuals who show high levels of inflammation show reduced brain processing of positive events, which supports the idea that peripheral inflammation may impair the ability of depressed individuals to appropriately process positive experiences. These findings provide building blocks to identify and delineate processes that could become targets for intervention or could be used as biological markers for mental health conditions.

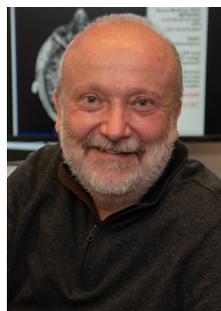
However, identifying targets is not enough. LIBR, as an independent research institute in an environment with a continuously developing research infrastructure, faces the challenge of maintaining a competitive research workforce to ensure future viability of the institute and novel discoveries. We have committed to recruiting talented researchers from diverse backgrounds to ensure that different perspectives, histories, interests, and approaches are considered. We have developed several approaches ranging from internship opportunities for high-school students and post-baccalaureate fellowships,

to structured mentoring of junior investigators to ensure that we are developing a pipeline of talent.

Lastly, LIBR is more than a purely research-based institution. Part of our mission is to create “products” that can be useful for our stakeholders (patients, providers, public health officials, payers). The “product focus” of



LIBR requires that investigators think through how a particular study may affect stakeholders and how the outcome can be used to develop tangible interventions to address stakeholders' concerns. We challenge our investigators to consult with stakeholders to ensure that meaningful aspects are measured which can be used to advance the outcome into a product. Therefore, our research cannot be viewed in isolation from the community we live in but rather, it must be integrated with society. I am very excited that our investigators have lived up to that challenge and have engaged with the community in a variety of different ways as you will see in the pages of this annual report. My hope is that we will further extend our community reach in the coming years.



I cannot end this letter without emphasizing the enormous loss that the institute experienced over the past year. Dr. Jerzy Bodurka was a founding member of the researchers that started the institute, he was an internationally recognized scholar, a force of nature, and a joy of a human being to be around. His contribution to real-time functional magnetic resonance imaging

research will have an impact far beyond his life, which was cut short much too prematurely. In his honor, we have named our MRI facilities “The Dr. Jerzy Bodurka Imaging Center” and we will organize a Festschrift with colleagues from other academic institutions to celebrate his accomplishments.



LIBR Mission, Vision and Values

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.

SPECIFIC AIMS

1 To identify, characterize and develop targetable, disease modifying processes in mental health.

2 To develop neuroscience-based interventions to improve mental health.

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

4 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.



2021 LIBR BY THE NUMBERS

3,417 inquiries for study participation

2 research associates

3 staff scientists



10 distinguished speakers for the William K. Warren, Jr. "Frontiers in Neuroscience" conferences

2 research investigators

6 principal investigators

2 affiliate investigators

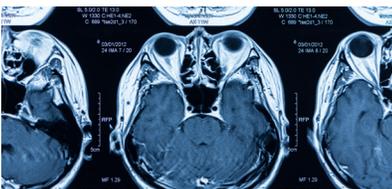
5 associate investigators

4 new externally funded grants

3.9 million in external grant funding

14 active grants and clinical trials

6 post-doctoral fellows



792 magnetic resonance imaging (MRI) scanning sessions

5 graduate students

306 participants enrolled in their first MRI study

2,139 participants enrolled across all studies

60+ collaborative institutions

128 journal article publications by LIBR investigators



2021 FUNDING SOURCES

ACTIVE AND AWARDED GRANTS

National Institute of Drug Abuse (NIDA)

Adolescent Brain Cognitive Development (ABCD) Study
04/15/2020 - 03/31/2027

Principal Investigator: Martin Paulus, M.D.

Plasticity of Aversive Salience in Opioid Use Disorder
03/01/2021 - 12/31/2025

Principal Investigator: Jennifer Stewart, Ph.D.

National Institute of Mental Health (NIMH)

Neural Response to Inflammatory Challenge in Major Depressive Disorder
05/14/2021 - 4/20/2026

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.

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 - 06/30/2022

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

Acute Modulation of Neural Circuitry Regulating Immune Function
in Depression

08/01/2018 - 07/31/2021

Principal Investigator: Jonathan Savitz, Ph.D.

Approach-Avoidance Conflict: A Multi-Level Predictor for
Exposure Therapy Response

04/12/2016 - 03/31/2021

Principal Investigator: Robin Aupperle, Ph.D.

National Institute of General Medical Sciences (NIGMS)

The Center for Neuroscience-based Mental Health Assessment
and Prediction (NeuroMAP)

09/15/2017 - 06/30/2022

Principal Investigator: Martin Paulus, M.D.

National Center for Complementary & Integrative Health (NCCIH)

Investigating Floatation-REST as a Novel Technique for Reducing Anxiety
and Depression

09/25/2018 - 07/31/2022

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

National Institute on Minority Health and Health Disparities (NIMHD)

Neuroscientific Exploration of Cultural Protective Factors in American Indians
12/27/2020 - 11/30/2022

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 - 01/14/2022

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

Oklahoma Center for the Advancement of Science and Technology (OCAST)

Neurocognitive Empowerment for Addiction Treatment (NEAT):
A Randomized Controlled Trial for Opioid Addiction

07/01/2018 - 03/31/2022

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

Presbyterian Health Foundation (PHF)

Structural and Functional Markers of Injury in Cervical Spinal Compression
07/01/2020 - 08/31/2021

Principal Investigator: Jerzy Bodurka, Ph.D.

Oklahoma Shared Clinical and Translational Resources (OSCTR)

Prognostic Utility of MRI Based Bio-markers in Degenerative
Cervical Myelopathy

01/01/2021 - 12/31/2021

Principal Investigator: Ryan Smith, Ph.D.

2021 DONORS

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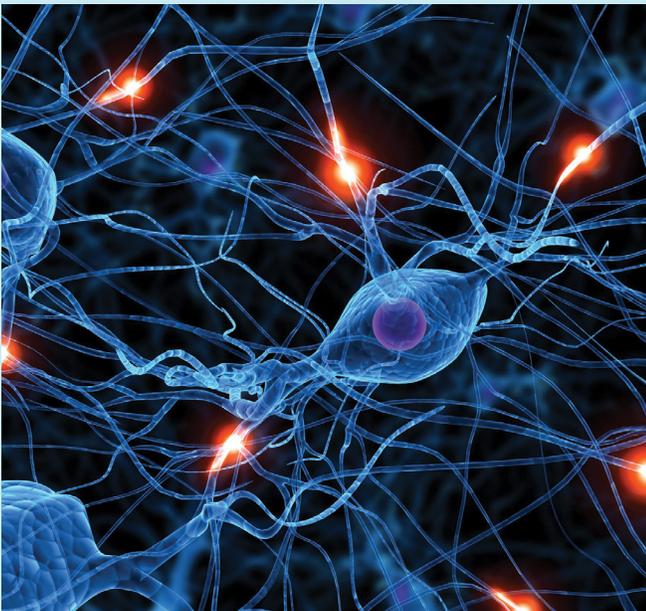
LIBR Leadership



Martin Paulus, M.D.
Scientific Director and President



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



The goal for LIBR is to identify disease-modifying processes 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, or substance use disorder.

CURRENT AREAS OF EXCELLENCE

Neuromodulatory approaches to modify mental health conditions

- To further develop real-time fMRI neurofeedback as a treatment for mood disorders.
- To determine the utility of focused ultrasound and direct current stimulation as interventions in mental health conditions.

Brain-based mechanisms underlying behavioral interventions for mental health conditions

- To determine the neural processes that change as a function of evidence-based behavioral interventions in mood and anxiety disorders.
- To determine the baseline characteristics of neural processes that predict efficacy of a behavioral intervention in mood and anxiety disorders.
- To relate changes across levels of analyses that are a consequence of behavioral interventions in mood and anxiety disorders.
- To determine whether baseline levels of genetic, molecular, cellular, physiological, circuit, behavior or symptom level of analysis predict efficacy of behavioral interventions in mood and anxiety disorders.

Interoceptive dysfunctions in mental health conditions

- To determine the effects of interoceptive perturbations on individuals with mental health conditions.
- To develop a theoretical and quantitative framework that helps to explain interoceptive dysfunctions in mental health conditions.
- To delineate across levels of analyses the alterations in interoceptive dysfunctions in individuals with mental health conditions.
- To determine the utility of measures of interoceptive function as predictive biological markers and potential targets of interventions in mental health conditions.

Innate and adaptive immunity, inflammation (IAII), and related processes in mental health conditions

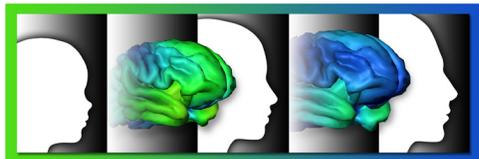
- To determine the alterations of IAII as a function of inflammatory perturbation in individuals with mood disorders.
- To relate alterations in IAII across levels of analysis because of inflammatory perturbation in mood disorders.
- To determine the role of external infectious agents in the pathophysiology of mental health conditions.
- To determine the utility of measures of IAII as predictive biological markers and potential targets of interventions in mental health conditions.

Culture, lifestyle, and environmental influences (CLE) on mental health conditions

- To determine the biological characteristics of CLE on mental health conditions.
- To develop a theoretical and quantitative framework that help to explain CLE on mental health conditions.
- To determine the utility of measures of CLE as predictive biological markers and potential targets of interventions in mental health conditions.



ABCD Study



Adolescent Brain Cognitive Development
Teen Brains. Today's Science. Brighter Future.

We are in our 6th year of the Adolescent Brain Cognitive Development (ABCD) study. LIBR is one of 21 research sites across the country that had to face a difficult situation with COVID-19. The ABCD study is funded by a U01 grant from the National Institute on Drug Abuse (NIDA), with Drs. Paulus and Aupperle serving as Principal Investigator (PI) and Co-PI for the LIBR site. This study originally recruited >11,000 youth ages 9-10 to join the study, which involves tracking of biological and behavioral development through adulthood.

As with so many other studies, the COVID-19 pandemic has affected ABCD and we had to adjust to the changing demands. Since the end of 2020 and throughout 2021, ABCD has moved towards supporting both in-person and remote sessions as needed to meet these changing demands and the needs of our participants. LIBR has completed the 3rd year assessments, continues with the 4th year assessments, and has begun 5th year assessments with participants, who are now age 14-15 years of age.

The study sponsors (various NIH institutes foremost among them the National Institute on Drug Abuse) have continued their dedication to open

science and in October the ABCD4.0 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 and 30-month assessments. The ABCD consortium, along with scientists from all over the world have begun examining the data, available at [ABCD Publications](#). The LIBR group has continued to contribute to this literature including recent publications reporting how [involvement in extracurricular activities, screen media activity, and sleep may relate to children's cognitive functioning](#) (led by Dr. Namik Kirlic) and that examine [relationships between parent-child relationships, gastric symptoms, and eating disorder symptoms among adolescent girls](#) (led by Dr. Kara Kerr).

The ABCD team is continuing to change and grow. Dr. Bodurka was an important part of ABCD, serving as Co-Investigator, contributing to ABCD's initial design and data collection plan for neuroimaging, maintaining high quality neuroimaging data collection at LIBR, contributing to numerous publications, and informing previous and ongoing research utilizing ABCD neuroimaging data. We were saddened by his passing and will forever miss his presence on the ABCD team. We have welcomed Dr. Masaya Misaki, who worked with Dr. Bodurka for several years, to the team to provide his expertise in neuroimaging.

In the past year, Hope Doyle was also promoted to site study coordinator. Hope has been a research assistant with LIBR and the ABCD study for three years and brings her wealth of knowledge and experience of the study to this role. We have also welcomed several new research assistants, including Andrew Helt, Gisella Gaytan, Alexa Gillham, Trinity Lasswell, Maria Acosta, Kailyn Deavens, and Katherine Martinez. Most recently, Dr. Cassandra Sturycz was hired as a postdoctoral fellow to provide additional research and study mentorship and supervision. Dr. Sturycz completed her doctoral degree in clinical psychology at The University of Tulsa and brings an expertise in clinical study management, student and research assistant mentorship, and research related to mental health and suicide. While 2022 may bring its own set of challenges, the ABCD team has learned to be flexible and adapt and looks forward to working hard and accomplishing great things in the coming year.



Tulsa 1000

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 over 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 one-year completion mark. Yearly follow-up assessments continued throughout 2021. The goal for this study is to determine whether neuroscience-based measures can be used to predict outcomes in patients with mental illness. In particular, we are trying to determine what factors best predict who will respond well to a particular treatment. The study is a definitive step towards developing a science-based personalized medicine approach in mental health.

To date, over 30 papers have been published by the T-1000 project authors and their collaborators. Data analysis of the T-1000 variables is ongoing, with over 50 individual scientific papers in progress for publication. Publications thus far have covered the topics of the relationship between gray matter volume and childhood trauma, the development of automatic pipelines for pre-processing 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

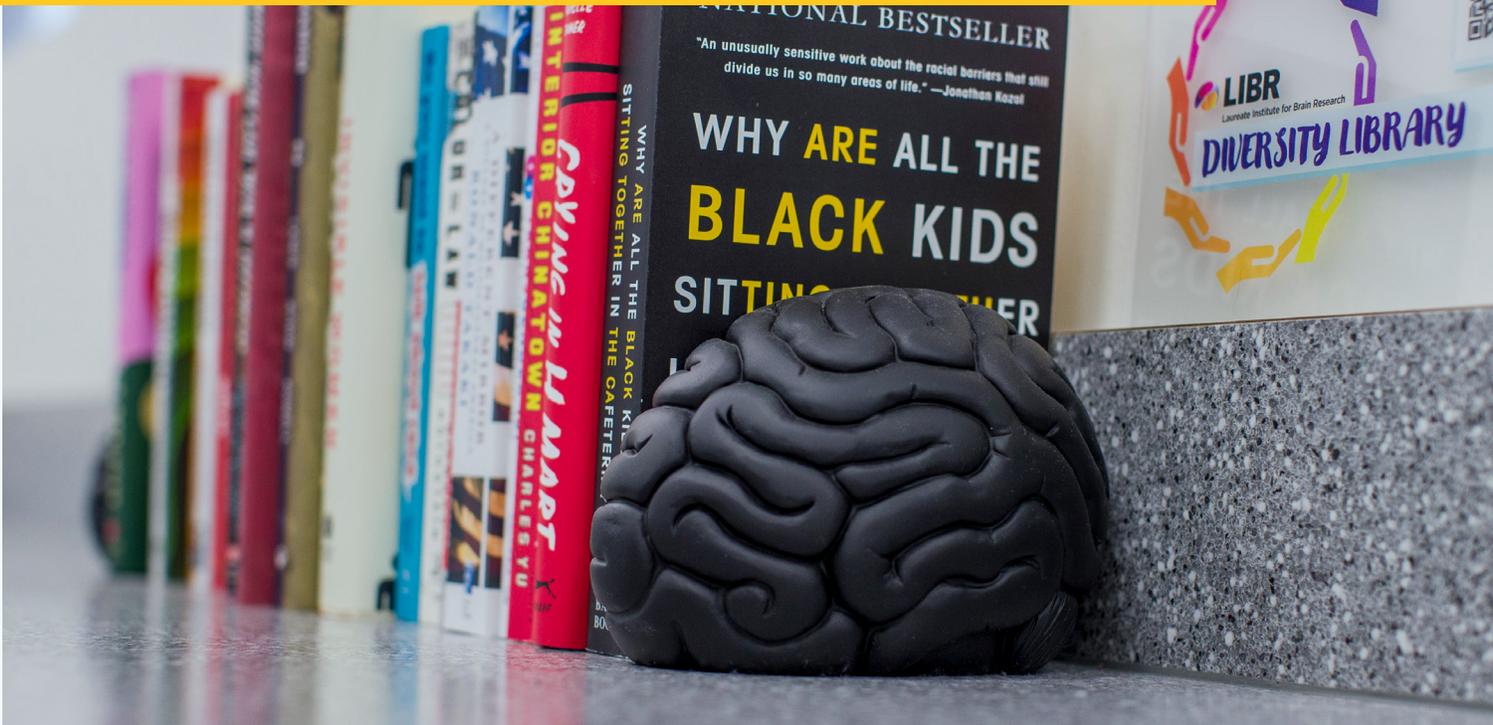
effect of neighborhood factors on brain structure and function, how body characteristics predict motion in the scanner, how early life stress and adult cytomegalovirus infection are related in mood and anxiety disorders, how processing of body signals differs in individuals with opioid and stimulant 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” include 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., Teresa A. Victor, 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 towards developing a personalized treatment approach through the knowledge gained with this comprehensive dataset.

“Racism and Science: A Call for Action”

Martin Paulus, M.D.
Scientific Director and President
Laureate Institute for Brain Research



The position statement “Racism and Science: A Call for Action” was written by Dr. Paulus last year (2020) after the murder of George Floyd. Given the events of the last 12 months, it continues to hold true in 2021. There are three key elements:

- 1 to disaggregate our data to determine how much we can learn about the issues of minority mental health problems;
- 2 to make an effort to diversify our workforce so that we can bring as many perspectives to our research as possible;
- 3 to work with community stakeholders to arrive at better research questions that can solve problems that affect minority communities.

This work is a process and there is not a finish line to aim for. Through this work, we as individuals and we as an institute have and continue to learn how racism has contributed to science and the systems that support science, our role in these racist systems, and how our actions can either contribute to the ongoing racism or help move us towards healing. Dr. Aupperle, chair of the Diversity and Inclusion Workgroup, said “Perhaps one of the most powerful things I have learned over the past year is how improving diversity in science – including having diverse representation of races, ethnicities, genders, and backgrounds in the scientific workforce and as study participants – enhances the quality of the science itself. To make progress towards improving mental health for the diverse world we live in, one must have input from as many different diverse minds as possible, with knowledge and lived experience from a plethora of varied and unique backgrounds.”

In 2021, our quarterly seminar series dedicated to Diversity in Neuroscience brought an exciting group of speakers to Tulsa – virtually or in person: Dr. Sierra Carter from University of Georgia, Dr. Marguerite Matthews, a scientific program manager from Office of Programs to Enhance Neuroscience Workforce Diversity with the National Institute of Neurological Disorders and Stroke (NINDS), Dr. Chad Forbes, Department of Psychological and Brain Sciences, University of Delaware, and Dr. Victoria O’Keefe, the Mathuram Santosham Chair in Native American Health at Johns Hopkins Bloomberg School of Public Health. In addition, a monthly reading and discussion group has been ongoing throughout 2021, where all faculty and staff at LIBR are invited to join a discussion of readings related to topics such as structural racism in science, issues facing women in science, issues facing LGBTQIA+ individuals in science, racial disparities in mental health, the Tulsa Race Massacre, and research relevant to American Indian people.

The Diversity and Inclusion Workgroup also supported the development of the Diversity in Research And Multidisciplinary Neuroscience (DREAM-Neuro) Fellowship and the Summer internship Program, both of which have been successful in not only supporting students in their educational and professional goals but also



in recruiting new talent to LIBR. In the National community, Dr. Evan White (Diversity and Inclusion Workgroup member) consulted with the Anxiety and Depression Association of America (ADAA) to update their [webpage](#) regarding American Indian/Alaska Native mental health information and resources. Through the Workgroup, we have also increased our presence in the local community, attending events such as the [American Foundation for Suicide Prevention Out of Darkness Walk](#) in September, at [Tulsa Pride](#) in June, and multiple Pow Wows in the region. We are also looking forward to volunteering together at the [Iron Gate food pantry and soup kitchen](#) in December.

The Diversity and Inclusion workgroup is proud of the accomplishments since being established in 2020 but also has numerous goals for this coming year and into the future. We look forward to establishing new community partnerships, further increasing the representation of under-represented minorities in science, and further enhancing our research through consideration of modifiable factors that may increase risk or protect against mental health problems for individuals of diverse races, ethnicities, and backgrounds.



LIBR MRI Neuroimaging Facility

Established in July 2009 and in research operation since June 2010, the MRI facility provides advanced state-of-the-art 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 interacting two subjects are measured simultaneously.

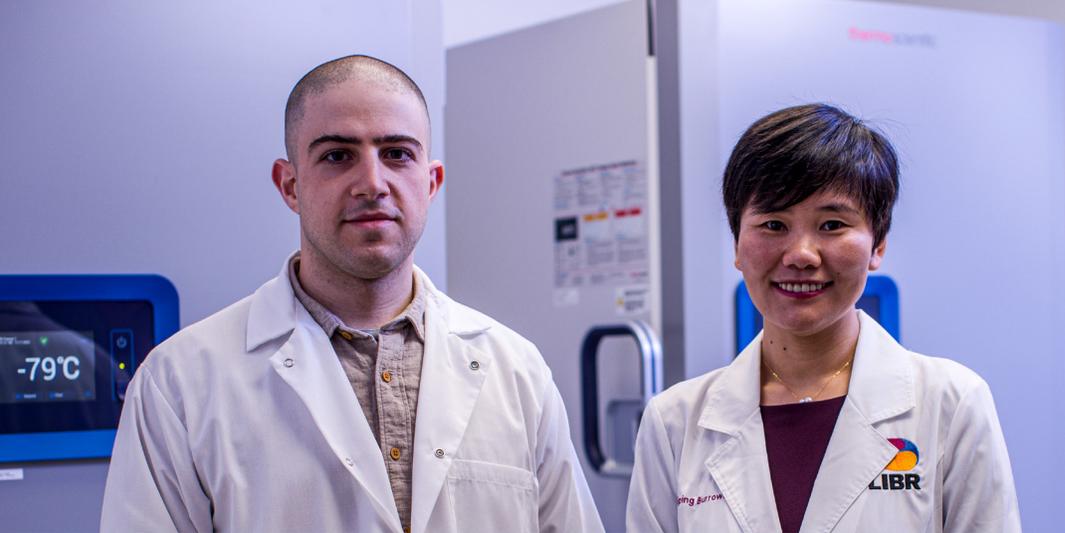
The facility provides all the latest technology, tools, and resources necessary to conduct and support brain neuroimaging studies focused on advancing clinical research to discover causes of and cures and novel interventions for mood, anxiety, eating, and memory disorders.

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 ECG waveforms), and EEG data simultaneously acquired with fMRI. These capabilities enable live monitoring of ongoing brain activation in real-time with extensive multimodal information. The application of real-time neuroimaging in LIBR is expanding from an online data quality check to a neurofeedback treatment for psychiatric disorders, in which a patient is trained to self-modulate a dysfunctional brain activation with feedback of own brain state, and 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 LIBR MRI facility also supports collaborative neuroimaging research with researchers from local academic institutes, including The University of Oklahoma, Oklahoma State University, and The University of Tulsa.



The MRI facility was created from the bottom up and had been overseen by Jerzy Bodurka, Ph.D., an expert in MRI/EEG-fMRI/real-time fMRI. Since September 2021, Masaya Misaki, Ph.D., an expert in multimodal neuroimaging data analysis and information technology, and Julie Owen, chief of MRI technologists, have led the facility management. Other staff includes two MRI technologists, Leslie Walker and Amy Ginn. Beginning in 2022 EEG technologies and data collection and processing will be led by Dr. Evan White, an expert in EEG/event-related potentials (ERPs) and clinical translation psychophysiology and Dr. Xi Ren, EEG Core staff scientist.



LIBR Biomedical Laboratory Facilities

The LIBR Lab houses three laboratory rooms dedicated to human blood processing, specimen long-term biobanking, and bioassays. Human blood and saliva will be routinely collected, and blood processed, for human serum, plasma, and peripheral blood mononuclear cells (PBMCs), aliquoted, and appropriately bio-banked for LIBR investigators.

The specimen sample processing room contains recently purchased state-of-the-art equipment including a 1) Biosafety Level 2 (BSL-2) laminar flow cabinet for making sterile aliquots of samples; 2) refrigerated and unrefrigerated centrifuges for blood cell processing; 3) small clinical centrifuges for serum and plasma processing; 4) automated counters for cell counting; and 5) a label-maker for labeling storage vials.

The biobanking room contains recently purchased large, ultralow (-80°C) temperature freezers for specimen biobank and long-term storage. 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 email, send text messages, and make phone calls to Dr. Kaiping Burrows and Valerio Coussa 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.

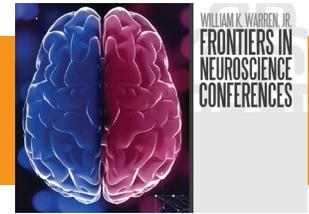
The bioassay room is used to measure blood or saliva-based biomarkers using enzyme-linked immunosorbent assay (ELISA) to assess immune, metabolic and stress related markers (e.g., IL-1ra, IL-6, leptin, adiponectin, HSP70, cortisol, etc.). The equipment/software in this room includes BioTek 50 TS automated microplate washer; BioTek 800 TS Absorbance Microplate Reader with onboard software through color touchscreen interface; and Gen5 software for advanced reader control, powerful data analysis; and flexible exporting/reporting tools. The automated microplate washer instrument is important for ensuring rapid and even washing of plates which reduces intra- and inter-assay variability. The Gen5 software is designed for ELISA

data and generates standard curves and statistics, which are then downloaded in standardized electronic reports for the investigators. Other equipment in the bioassay room



include a large laboratory refrigerator; a freezer (-20°C), and an ultralow temperature freezer (-80°C) for storing ELISA kits or reagents that require 2°C to 10°C , $< -20^{\circ}\text{C}$ or $< -70^{\circ}\text{C}$ controlled temperatures; an ice maker to create ice flakes for defrosting frozen plasma/serum samples and keeping some reagents cold during lab experiments; centrifuges to centrifuge plasma, serum, or saliva samples after defrosting; and single and multi-channel pipettors for bioassay precision and accuracy.

The William K. Warren Foundation “Frontiers in Neuroscience” Speaker Series



Peter Strick, Ph.D.

The Neural Basis of the “Brain-Body” Connection

Stephen Higgins, Ph.D.

Contingency Management in the Treatment of Substance Use Disorders and Other Health Conditions

Ned Kalin, M.D.

The Childhood Risk to Develop Anxiety and Depression: A Translational Neuroscience Approach

John Markowitz, M.D.

Interpersonal Psychotherapy for Posttraumatic Stress Disorder

Tanja Jovanovic, Ph.D.

Neurobiological Effects of Trauma in Adults and Children

Professor Klaas Stephens

Translational Neuromodeling, Computational Psychiatry, and Computational Psychomatics

Erin Hazlett, Ph.D.

Studying Emotion Processing in Individuals at Risk for Suicide: Psychophysiological and Neuroimaging Approaches

Dean Mobbs, Ph.D.

Space, Time and Fear

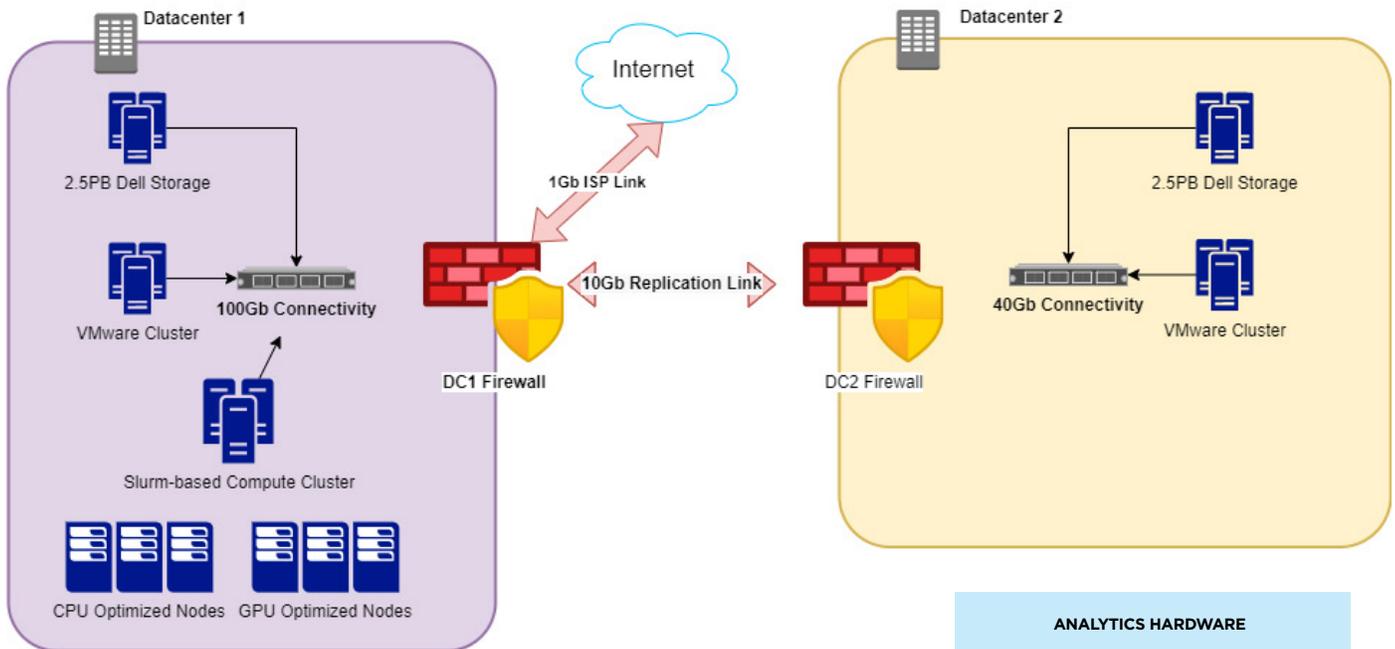
Manpreet Singh, M.D., M.S.

Evolving Neuroscience-Informed Interventions for Pediatric-Onset Mood Disorders

Catherine Tallon-Baudry, Ph.D.

From Visceral Signals to Subjectivity

Data Analytics



Data analytics is integral to research at LIBR, allowing researchers to test hypotheses and answer questions quantitatively. The computational power available allows complex analyses of neuroimaging and behavioral data to be done **on-site with remotely accessible computing resources**.

LIBR maintains an analysis cluster using the **SLURM** batch scheduler, which coordinates hundreds of simultaneous jobs. This centralized architecture is particularly efficient, giving all researchers access to much more computational power than would be feasible using local workstations.

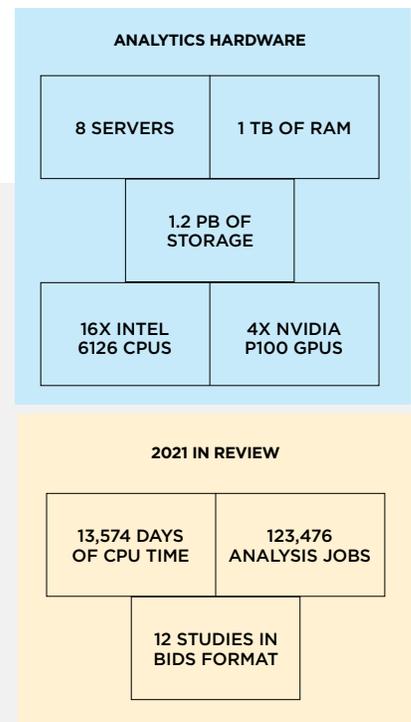
Throughout 2021, researchers used over **13,000 days of CPU processing time**. It would take over 30 years to do the same work on a typical personal computer.

LIBR also maintains all data on-site at using a massive network attached storage system, with replication at an **off-site backup in Oklahoma City**.

This system provides excellent security and performance on-site as well as a disaster recovery plan should something happen to the LIBR campus.

All new studies conducted at LIBR are

organized in accordance with the **Brain Imaging Data Structure (BIDS)**. BIDS is a standard outlining best practices for the organization and description of complex datasets. Using BIDS facilitates collaboration with the neuroimaging community, which is increasingly adopting this standard.



The LIBR Float Clinic & Research Center (FCRC)

The Laureate Institute for Brain Research 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 including anxiety, depression, or eating disorders.



The FCRC is now directed by Dr. Sahib Khalsa following the departure of Dr. Justin Feinstein from LIBR, and it is in its 5th year of operation. Initial studies published in 2018 found that floating appears to quickly 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 led by Dr. Feinstein found patterns of reduced functional

connectivity between regions of the brain involved in mapping body sensation and self-representation in healthy individuals. This study provides the first functional neuroimaging evidence of the effects of floating on brain function.

Building from this base of knowledge, ongoing clinical trials are examining the potential therapeutic impact of Floatation therapy on several psychiatric conditions. The first study is an NIH-funded clinical trial led by Dr. Khalsa investigating the feasibility and tolerability of floatation therapy as a technique for reducing anxiety and depression in individuals with high levels of stress, anxiety, and depression. Despite the Covid pandemic, the study recently completed the primary data collection phase and has entered the analysis phase. The second study is a LIBR-funded clinical trial led by Dr. Khalsa investigating 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 is conducted in partnership with Dr. Scott Moseman, the medical director of the Laureate Eating Disorders Program, and the clinical staff from the program. The primary data collection phase is also complete, and the study has now entered the analysis phase. Results from both studies will be reported in the upcoming year, so please stay tuned for further updates.

The FCRC was featured by CNN in the Staying Well series, which focuses on techniques for improving physical and mental well-being.

2021 AWARDS



Dr. Martin Paulus was named to the 2022 Board of Directors for the Anxiety and Depression Association of America (ADAA). The board members are distinguished researchers, clinicians and psychiatrists serving the public and mental health community.

Dr. Jennifer Stewart was awarded tenure at The University of Tulsa.

Dr. Jennifer Stewart was named one of 12&12, Inc.'s "12 Faces of 2021". The focus of her research partnership with 12&12 is to better understand the process of early recovery from opioid addiction.

Dr. Leandra Figueroa-Hall won 1st place and a \$1000 travel award at the "Pitch Your Research Section" of the End2Cancer conference. Her central hypothesis is that toll-like receptor 4 (TLR4) signaling is altered in inflammation-associated depression.

Dr. Robin Aupperle was accepted as an Associate Member of the American College of Neuropsychopharmacology.

Elisabeth Akeman completed her Master's degree in counseling psychology in May 2021.

Kelly Cosgrove received predoctoral national research service awards (F31) from the National Institute of Mental Health (NIMH) related to her graduate dissertation projects examining the role of social and neural connectedness in predicting neurodevelopmental functioning in the Adolescent Brain and Cognitive Development (ABCD) study.

Tim McDermott also received a predoctoral national research service awards (F31) from the National Institute of Mental Health (NIMH) related to his graduate dissertation project examining dorsolateral prefrontal cortex (dlPFC) fMRI-based neurofeedback during emotional inhibition.

Danielle DeVille defended her dissertation focused on using machine learning methods to identify factors relating to suicidal thoughts and behaviors in the ABCD study and began a clinical psychology internship at the University of California – San Diego (UCSD).



Ebony Walker received the LIBR Diversity in Research and Multidisciplinary Neuroscience (DREAM-Neuro) Fellowship early in 2021. This fellowship allows Ebony to gain rounded research, analysis and writing experience to help her succeed in applying and being admitted into a graduate training program.

Dr. Sahib Khalsa was awarded a five-year R01 grant from the NIMH entitled "A neurocomputational assay of gastrointestinal interoception in anorexia nervosa". This study combined an experimental medicine approach focused on gastrointestinal interoception with computational modeling to probe neural circuits of interoception and appetite-related gastric processing in anorexia nervosa.

Dr. Sahib Khalsa was appointed as an Associate Editor at the journal Biological Psychology.

Dr. Sahib Khalsa was elected as an Associate Member at the American College of Neuropsychopharmacology.

Dr. Bart Ford received a NARSAD Young Investigator award and secured a tenure-track faculty position at OSU.

Dr. Evan White was accepted into the Alies Muskin Career Development and Leadership Program, Anxiety and Depression Association of America.



Dr. Evan White was awarded funding from the Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) program at the National Institute on Minority Health and Health Disparities. The MOSAIC National Institute of General Medical Sciences program supports investigators from diverse backgrounds embarking on careers at research-intensive institutions.

Mara Demuth, M.S. from Dr. Evan White's lab was accepted into multiple medical school programs and is currently in the process of deciding where to attend.

CLINICAL COLLABORATORS



[12&12, Inc.](#) is the largest Comprehensive Community Addiction Recovery Center in Oklahoma. At 12&12, the only focus is to help men and women battle the brain disease of addiction and co-occurring substance abuse/mental health disorders. 12&12's complete continuum of care provides multiple levels of treatment including detoxification, intensive residential treatment, outpatient and intensive outpatient treatment, counseling, transitional living, and sober living.

For over 35 years, 12&12 has helped thousands of Oklahomans in the fight to get their lives back. 12&12's service model is based on a multi-disciplinary approach that integrates medical oversight, psychiatry, nursing, counseling and case management.

Independently operated and located in the heart of Tulsa, 12&12 has Behavioral Health Care accreditation from the Joint Commission, and certification by the Oklahoma Department of Mental Health and Substance Abuse Services (ODMHSAS) as a Comprehensive Community Care Addiction Recovery Center (CCARC). For more information on 12&12, Inc. visit www.12and12.org.

Reba Harvey serves as Chemical Dependency Technician (CDT) Assistant Supervisor at 12&12 and acts as liaison for the organization on the LIBR Plasticity of Aversive Salience in Opioid Use Disorder (PASO) study. Her role includes communicating with the research team when a client is interested in participating in the study, and coordinating transportation to and from the facility. Reba has been at 12&12 since January 2019 and a part of the PASO study since 12&12's initial involvement. She thoroughly enjoys being the point of contact to LIBR for the various needs of the research team and clients. In Reba's words, she is fortunate to play a very small part of a big mission!



Dr. Jennifer Stewart was selected and interviewed as one of 12&12, Inc.'s "12 Faces of 2021" honorees.



Sahib S. Khalsa M.D., Ph.D.
Director of Clinical Operations
Laureate Institute for Brain Research

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

Laureate Eating Disorders Program Collaboration

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

Laureate 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 neuroimaging, to variances in brain functionality of those with eating disorders, to body image and treatment evaluation, LIBR remains on the cutting edge of investigation into eating disorder neurobiology and intervention.

When an individual receiving treatment with Laureate qualifies for ongoing research studies, she may be offered the opportunity to participate. The clinical team assists in evaluating how participation will support her recovery and whether the individual might benefit from engaging in the study. Current areas of research include a treatment study examining the impact of Floataction-REST (reduced environmental stimulus therapy) on anxiety and body image concerns in anorexia nervosa, development of a mobile app for a new understanding of body image concerns in eating disorders and a neurobiological investigation of the gut-brain connection in anorexia nervosa. LIBR has made important findings relevant to individuals struggling with eating disorders as well as to those who love, support and provide treatment for these individuals.



Women in Recovery (WIR)

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

- 1 Determine how the brain recovers from trauma, substance use, depression, and/or anxiety through the unique diversion program, Women in Recovery.
- 2 Identify factors that may predict success within the Women in Recovery program.
- 3 Inform modifications to the program in order to potentially enhance success for future clients.

These goals have been supported by three separate projects thus far. **Project 1 is a longitudinal investigation involving clinical, behavioral, and neurobiological assessments at LIBR focused on identifying predictors of treatment outcome, as well as markers of substance use and mental health recovery.** This project was conducted as part of the Tulsa 1000 study and primary investigators on this study include Drs. Paulus and Aupperle. Recruitment has been completed for this project, though longitudinal follow-up assessments are

ongoing. A total of 169 women enrolled in the study. Several publications have come from this collaboration. One publication led by Dr. Stewart reported that WIR women have greater levels of some inflammatory markers in blood than women with other psychiatric diagnoses (IL-8 and IL-10), but lower levels of other markers (C-reactive protein). This is different than what we observe for men with substance use disorders and may provide insights into unique relationships between substance use and inflammation/immune responses in women

(published in *Drug and Alcohol Dependence*). Another paper, led by Dr. Moradi, reported that neither a diagnosis of substance use nor the severity of previous use were associated with the “resource allocation index” (RAI), a measure of connectivity between different networks. This suggests that global connectivity between brain networks may be resilient to substance use. This paper was published in the journal *Drug and Alcohol Dependence*. Drs. Smith and Aupperle examined how substance use and depression/anxiety may relate to how people make decisions to approach or avoid outcomes associated with both reward and threat. They reported that individuals with substance use may be less likely to avoid distressing images but more uncertain in their decisions. These results were published in the *Journal of Psychiatry and Neuroscience*.

Researchers at LIBR have also begun using a machine learning approach to identify psychosocial predictors of graduation from WIR. While the ability to predict outcome at the individual person level was not high, results were useful for identifying potential variables that may be important to consider in relation to one’s ability to graduate. Specifically, these preliminary results suggest that those individuals with lower impulsivity, greater interoceptive awareness, and a history of trauma were more likely to graduate from the program. These results suggest potential treatment targets for future clinical research collaborations between WIR and LIBR.

Project 2 is a randomized clinical trial examining the potential benefit of an intervention focused on cognitive functioning for enhancing outcomes for WIR. This study is funded by the Oklahoma Center for Advancement of Science and Technology (OCAST) and is led by Dr. Ekhtiari and Dr. Aupperle (Co-Investigator). The researchers are utilizing a new group-based therapy called “Brain Gym” focused on the role of neuropsychological functioning (for example, memory, attention, executive functions) in substance use recovery. The intervention uses cartoons, brain awareness games and real-life scenarios to ensure the intervention is interactive, engaging, and likely to be consolidated. Cartoons were specifically designed to incorporate female characters

and were modified in response to feedback from WIR staff and participants. Our attention, memory, cognitive control, and ability to monitor what is important (salient) in our environment as well as our own physical sensations (termed “interoception”) play a role in substance use recovery. Thus far, 45 women have enrolled in this project and completed baseline assessment, of which 22 were provided Brain Gym (while 23 completed WIR as usual). The COVID-19 pandemic caused a delay in enrolling participants in the Brain Gym study; however, the study is now actively enrolling participants.

Project 3 is a new collaborative WIR/LIBR project: A five-year grant funded by the National Institute on Drug Abuse examines 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 12&12.

Participants are recruited into the study within a month of entering WIR and complete neuroimaging scans, behavioral testing, physiology (heart rate, respiration, skin conductance), questionnaires, and interviews at four timepoints: baseline and one-, two-, and three-month follow-up 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. Our preliminary data from the Tulsa 1000 study suggest that people reporting opioids as their drug of choice report lower body awareness, higher depression, anxiety, and pain, greater intensity of heartbeat sensations, and lower brain responses to losses and heartbeat sensations than people without a history of drug use. We want to see if these responses change during the first three months of treatment and if there are sex differences in these responses to guide future treatment targets for addiction.

LIBR Training and Mentoring

Summer Internship Program. Dr. Evan White coordinated LIBR's first summer internship program, which enabled three undergraduates to be full-time paid research interns at LIBR for two 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 Dr. White and other LIBR staff members. The consensus was that the first year of the internship program was a great success!



Grace Cardenas, a senior pre-health student at Washington University in St. Louis majoring in cognitive neuroscience, worked with Dr. Salvador Guinjoan on secondary data analysis from the T-1000 study.

Her project examined associations between repetitive negative thinking (RNT) and various cognitive functions in individuals with eating disorders relative to those with major depression and healthy controls. Results indicated that RNT seems to be associated with cognitive functioning differently in eating disorders compared to both healthy controls and participants with depression.



Jayla Melvin, a current senior undergraduate student at Oklahoma State University majoring in psychology and minoring in social justice worked with **Dr. Namik Kirlic** on preliminary data analysis for

his ongoing A-MindREaL project (P20GM121312-05, 8736). This project examined the socio-economic and environmental factors that convey risk for psychopathology amongst adolescents with and without early life stress exposure. Results indicated that family income, experience of bullying, and substance use contributed to development of psychopathology above and beyond neighborhood of residence in the Tulsa area.



Samantha Ramirez, a recent psychology graduate from Oklahoma State University, worked with **Dr. Evan White** on preliminary data analysis for his K99 project (K99MD015736)

examining mental health protective factors among American Indian people. This project examines potential protective factors against poor mental health among American Indian peoples in the Tulsa area. Results indicated that social support may play a key role in protecting against anxiety and depression among American Indian individuals with high enculturation in their traditional culture.

Diversity in Research And Multidisciplinary

Neuroscience (DREAM-Neuro) 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 two years of neuroscientific-based mental health research experience prior to applying for graduate/professional degree programs. Job duties to be undertaken by the fellow may include assisting in experimental design, recruiting participants, administering study sessions, collecting, and analyzing data, and preparing study results for reports, posters, and manuscripts. Funds are made available to the fellow to present their work at conferences and attend other educational training activities. Additionally, DREAM fellows will participate in specialized career development trainings to support their transition to advanced doctoral programs (Ph.D, Psy.D., M.D., or similar), including workshops on preparing competitive applications and navigating interview days.



Ebony Walker, LIBR's first DREAM-Neuro fellow, is working with **Dr. Maria Ironside** on multiple projects, including running research participants through a study investigating the acute

effects of neuromodulation probed using behavioral and neuroimaging measurements designed to capture threat sensitivity and stress response. Ebony has also learned how to process and analyze eyeblink startle data and presented a poster at Society for Research in Psychopathology's 2021 conference on her project

examining relationships between approach-avoidance behavior and the emotion regulation strategy of distraction. Moreover, Ebony has learned statistical programming using R statistics software and has been teaching other research assistants about the usefulness of this coding. Ebony earned her BA in Psychology from University of Arkansas Fayetteville and her BA in Interdisciplinary Studies at University of Nevada Las Vegas and is currently applying to Clinical Psychology PhD programs.

New Post-Doctoral Associates



Dr. Emily Choquette earned her PhD in Clinical Psychology from the University of South Florida in 2021, focusing on women's health and particularly the functional relationship between disordered eating behaviors and alcohol use. Dr. Choquette completed her clinical internship with the Michael E. DeBakey

VA Medical Center in Houston, TX from 2020-2021. She joined LIBR in September, 2021 to work with Dr. Sahib Khalsa and Dr. Robin Aupperle on research to enhance the clinical utility of the Tulsa Life Chart, a web-based graphical representation of psychosocial history relevant for mental health treatment and to continue her research related to understanding the intersection of body image, eating behaviors, and substance use.



Dr. Xi Ren earned her PhD in Psychology: Cognition and Neuroscience from the University of Missouri, Columbia in 2018, focusing on the role of event related potentials (ERPs) in motor learning and Parkinson's disease during electroencephalography (EEG) recordings. Next, Dr. Ren completed

a post-doctoral research position at the University of Pittsburgh studying ERPs in first-episode psychosis and schizophrenia recorded during EEG and magnetoencephalography (MEG). Here at LIBR, Dr. Ren is working with Dr. Jennifer Stewart and Dr. Evan White on ERP analyses and EEG source localization related to reward anticipation in major depressive disorder.



Dr. Stella Sanchez earned her PhD in Physics from the University of Buenos Aires (Argentina) in 2021. In her PhD she specialized in analyzing MRI data to study early abnormalities in brain function and structure in persons who are asymptomatic but are at risk of late-onset Alzheimer's

disease given their family history of the disorder. Under the supervision and mentorship of Dr. Salvador Guinjoan at LIBR, she is analyzing MRI data to identify patterns in brain connectivity on a sample composed of patients who suffer a similar severity of depression, but differ in the intensity of Repetitive Negative Thinking (RNT).



Dr. Charles Verdonk received his MD degree from the University Paris XI (France) in 2013, and then served as general practitioner for two years. He subsequently received a master's degree in cognitive science from the University Paris V (France) in 2017. He earned his PhD in neuroscience

from the Paris Sciences et Lettres University (France) in 2021, focusing on the physiological assessment of body awareness, including neurophysiological and postural signals, and on how body-brain interactions may affect cognitive functions. Here at LIBR, Dr. Verdonk investigates the neural and physiological basis of the Heartbeat Evoked Potential, a candidate biomarker of cardiovascular interoception, in healthy individuals and individuals with anxiety, depression, or eating disorders.



Dr. Xiaoqian (Sophy) Yu earned her PhD in Psychology with Cognition, Neuroscience, and Social concentration from the University of South Florida, Tampa in 2020. Her research interest was two-fold: a) to focus on both basic research and applied research of the event related

potential (ERP), P300, particularly in the use of P300-based brain-computer interface (BCI) spellers; 2) and to understand how individual differences in baseline attention capacity impacts the training outcome of mindfulness. Dr. Yu then joined the post-doctoral fellowship at Cincinnati Children's Hospital Medical Center (CCHMC) to explore the electrophysiological markers of attention deficit in children with Attention-deficit/hyperactivity disorder (ADHD) and adolescents with sluggish cognitive tempo (SCT) recorded during EEG and magnetoencephalography (MEG). Under mentorship of Dr. Namik Kirlic at LIBR, Dr. Yu is continuing her interest in understanding the neural mechanisms of mindfulness through neuroimaging methods.



In the News 2021



Scientific Retreat 2021

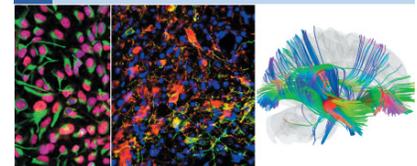
In November, LIBR investigators gathered at PostOak Lodge and Retreat in Tulsa for their annual scientific retreat. This gathering was an opportunity to reflect on the past year and welcome future endeavors to fulfill LIBR's mission of improving mental health through neuroscience.



Dr. Kirlic's work was featured on [Good Day Tulsa](#) during a discussion about one of his teen studies looking at the effects of stress and mindfulness training on the brain.

Tulsa's [KOTV - News On 6](#) spoke with Dr. Namik Kirlic about ways to manage stress and anxiety during the holiday season.

Congratulations to Drs. Savitz and Zheng and fellow research colleagues on their recently published *Neuropsychopharmacology* paper and featured cover artwork from the article [“Replicable association between human cytomegalovirus infection and reduced white matter fractional anisotropy in major depressive disorder”](#).



Calls to advance equity, diversity, and inclusion
Modeling puberty suppression in mice
Childhood maltreatment and cognitive function





LIBR's first annual summer intern poster session was a success! The excellent research work by Grace Cardenas, Jayla Melvin and Samantha Ramirez was presented to LIBR faculty and staff at a morning reception on July 30th. We are proud of what they've accomplished in such a short time under the direction of their mentors, Drs. Evan White, Namik Kirlic and Salvador Guinjoan.



Dr. Martin Paulus, joined [KOTV - News On 6](#) to explain how the recovery process works as part of a 5-year study to better understand opioid addiction recovery. "A 2016 study found Oklahoma ranked in the top 10 for the highest rates of prescribing opioids and it's estimated that 43% of drug overdose deaths in the state involve opioids."

On May 18th, 2021, Dr. Martin Paulus presented a free webinar on "Connectedness and Mental Health" during the pandemic in collaboration with [ResearchMatch](#) and the [Anxiety and Depression Association of America \(ADAA\)](#). The recorded version is now available on [ResearchMatch's YouTube channel](#).

Dr. Martin Paulus was interviewed by FOX23 News and Shae Rozzi about the potential effects of social media on the brain and current social media trends for kids and teens.

A reporter referenced a recent LIBR study in a column on the relationship between investment decisions, gut feelings, and interoception in the Wall Street Journal on February 19th, 2021. Dr. Khalsa, the senior author of the study was quoted: "What we're really talking about [with] gut feelings is how people sense their internal milieu, which encompasses a multitude of different signals, coming from all over the place within the body," says Sahib Khalsa, a neuroscientist at the Laureate Institute for Brain Research in Tulsa, Okla. "The brain is constantly sampling and receiving all these signals, even if you're not consciously aware of that."





Assessment Team Feature

Tim Collins continues to manage the assessment team, as he has since 2013. Throughout 2021, Tim and the team have worked, despite the continuation of COVID, to return screening assessments to pre-COVID numbers. To ensure subject comfort and offer flexibility to the subject, the team has become proficient in the process of remote assessments and the return of in-person assessments. This has led to a 101% increase in the number of screening assessments from 2020 to 2021.

The assessment team focuses on three main objectives:

- 1** Recruit participants living in the Northeastern Oklahoma region using a multi-pronged approach, including social media, digital, radio advertising, direct on-site facility recruitment, direct recruitment at the Laureate Psychiatric Clinic and Hospital, and in-person activity-based recruitment.
- 2** Clinically assess participants: Masters-educated interviewers (licensed therapists or licensed social workers) complete diagnostic interviews to determine DSM-5 diagnoses for each participant. Additionally, interviewers discuss current and past suicidal thinking and/or attempts of self-harm with each person. The team completes clinical interviews with adults and teens.
- 3** Medically assess participants: The medical team (registered nurses and medical technicians) complete comprehensive interviews to determine the history of chronic, recent, and current medical conditions. The team also collects biological samples including CRP and A1c in addition to completing standard medical assessments.

The assessment team also completes COVID-19 testing as directed, clinical interviews, clinical ratings, blood collections, and assists participants in completing study-directed tasks for multiple LIBR studies for the following investigators: Drs. Paulus, Guinjoan, Aupperle, Khalsa, Stewart, Savitz, Smith, Ekhtiari, Kirlic, and Tsuchiyagaito.

The assessment team, over the past 5 years, has completed:

Number of
phone screens:

19,686

Number of screening
consents signed:

6,005

Number of blood
collections:

3,704

Assessment Team Highlight: Lisa Kinyon



Over the last 5 years, Lisa has completed screening consents with 1,591 subjects, both adult and teen.



I have worked various jobs in the Saint Francis system since 1996. I started as a psychiatric technician while working on my master's degree. I have worked in various positions within the system including clinical assessment (CAD) completing level of care assessments, as a psychiatric social worker, and as an outpatient therapist at Laureate. I have worked at LIBR with the assessment team since 2009. I have interviewed a variety of populations including teens, children, adults, and veterans. I enjoy having the privilege of getting to talk to so many different types of people and hearing about their unique personal history.

LIBR Principal Investigator Highlight

JONATHAN SAVITZ, PH.D.
Principal Investigator,
Laureate Institute for Brain Research

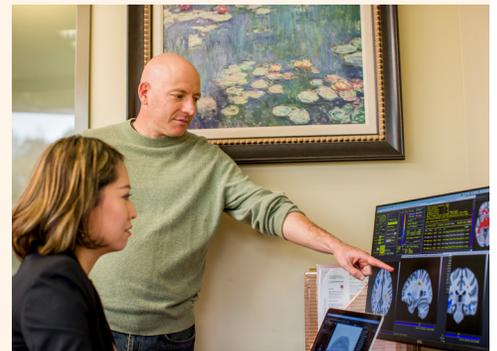


Jonathan Savitz (2nd from left), Leandra Figueroa-Hall (far left), Haixia Zheng (2nd from right) and MacGregor Thomas (far right)



I was born in Johannesburg, South Africa and completed an undergraduate degree there at the University of the Witwatersrand (BSc) majoring in genetics and psychology. I studied further in psychology completing honors and master's degrees in clinical psychology and research psychology, respectively. I wanted to become a neuropsychologist but at that time there was no pathway available for training and practice in the country, and I had no patience for psychodynamic models which dominated in psychology departments. The closest fit to a neuroscience graduate program was a study on the genetics of bipolar disorder run by Prof. Rajkumar Ramesar out of the Human Genetics department at the University of Cape Town. This was before the GWAS era and the emphasis was on performing linkage and candidate gene studies on South African families with bipolar disorder. For my project, I used personality and neuropsychological metrics as endophenotypes of bipolar disorder. I drove all over the Cape Town metro area for 5 years administering these tests to participants in their own homes! While I was doing my PhD, Prof. Mark Solms returned to South Africa to set-up a neuropsychology training program and I was able to obtain some clinical experience seeing patients in the neurology ward at Groote Schuur Hospital (where the first human heart transplant was performed).

While the genetics work was interesting, I was not good at, and did not enjoy the lab work. I was also frustrated by the limitations of neuropsychological testing for understanding what was going on in the brain. Therefore, I decided to learn neuroimaging and interviewed at several labs at the NIH before accepting a post-doc position with Dr. Wayne Drevets. During my post-doc I mostly worked on PET although I maintained contact with the genetics field through collaborations with Drs. David Goldman and Francis McMahon. After about 2 years, Wayne left to take the position of Scientific Director at LIBR and I followed a few months later. I discovered during my post-doc that I did not really have much of an aptitude for neuroimaging - at least as far as the modeling of PET data was concerned. I had always been interested in immunology because of the autoimmune disorders that ran in my family and Wayne mentioned that Tulsa had an excellent immunologist, Kent Teague, who would be willing to work with us. Thus, after my arrival in Tulsa in 2009 I started to learn some immunology and was awarded a K01 to study the relationship between kynurenine pathway metabolites and brain abnormalities in the context of depression. While I am still working on the kynurenine pathway, I also use lipopolysaccharide (LPS) as an experimental model of inflammation and I am very interested in the role of viruses, especially cytomegalovirus (CMV), in psychiatric disorders.



ROBIN AUPPERLE, PH.D.

Principal Investigator,
Laureate Institute for Brain Research
Associate Professor, The University of Tulsa
Volunteer Faculty Member,
Department of Psychiatry,
The University of Oklahoma



LAB MEMBERS

ELISABETH AKEMAN

Research Therapist

HANNAH BERG

Clinical Psychology Intern

EMILY CHOQUETTE, PH.D.

Post-Doctoral Research Associate

MALLORY CANNON

Lab Coordinator

KELLY COSGROVE

Graduate Student

TIM MCDERMOTT

Graduate Student, TU

SAMANTHA RAMIREZ

Research Assistant

JAMES TOUTHANG

Software Engineer

Research Highlights

- 1.** Dr. Aupperle's NIMH K23 award entitled "Approach-Avoidance Conflict - a multi-level predictor for exposure therapy response" was completed. As part of this project, 96 individuals experiencing symptoms of generalized anxiety were offered either behavioral activation or exposure-based therapy. Thus far, this study has resulted in two publications that point towards potential predictors and biomarkers of treatment response: (1) The P300 event-related potential (ERP) during reward anticipation was predictive of individuals likelihood of being able to complete treatment; (2) Completion of behavioral activation therapy results in a robust decrease in quinolinic acid, which is a neurotoxic inflammatory metabolite.
- 2.** The NeuroCATT lab collaborated with Dr. Charles Taylor at the University of California - San Diego and Dr. Kate Wolitzky-Taylor at the University of California - Los Angeles on a feasibility and pilot study of an intervention focused on enhancing positive emotions and social connections and reducing alcohol use for individuals with alcohol use disorder and symptoms of anxiety or depression.
- 3.** The NeuroCATT lab reported on the reliability and stability of behavioral and neural responses during the approach-avoidance conflict (AAC) task developed by Dr. Aupperle. This included reports of fair to excellent reliability across behavioral and neural responses to the task for healthy controls and reports that relationships between substance use and depression and anxiety diagnoses and behavior on the task is stable over a one year period.

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](#). Her research focuses on using neurocognitive methods to enhance our understanding of anxiety, depression, and trauma. She is particularly interested in (1) The intersection between cognitive and emotional processing and decision-making and how this may relate to the development and maintenance of anxiety, depression, and trauma-related symptoms and (2) How knowledge from neuroscientific research may be used to enhance treatment and prevention efforts.

Select Publications

1. White, E.J., et al. (2021). P300 amplitude during a monetary incentive delay task predicts future therapy completion in individuals with major depressive disorder. *Journal of Affective Disorders*, 295, pp.873- 882.
2. Cosgrove, K.T., et al. (2021). Impact of ibuprofen and peroxisome proliferator activated receptor gamma on emotion related neural activation: A randomized, placebo-controlled trial. *Brain, Behavior, and Immunity*, 96, pp.135-142.
3. Smith, R., et al. (2021). Long-term stability of computational parameters during approach-avoidance conflict in a transdiagnostic psychiatric patient sample. *Scientific reports*, 11(1), 1-13.
4. McDermott, T.J., et al. (2021). Test-retest reliability of approach-avoidance conflict decision-making during functional magnetic resonance imaging in healthy adults.
5. Akeman, E.A., et al. (2021). Amplification of Positivity Therapy for Co-occurring Alcohol Use Disorder with Depression and Anxiety Symptoms: Feasibility Study and Case Series. *Behavior Modification*, p.01454455211030506.

SALVADOR M. GUINJOAN, M.D., PH.D.

Principal Investigator
Laureate Institute for Brain Research



LAB MEMBER

STELLA SANCHEZ, PH.D.
Post-Doctoral Research Fellow

Research Highlights

1. In persons with Major Depressive Disorder, repetitive negative thinking (RNT, including symptoms like rumination or worry) results in a worsened prognosis; the group has confirmed RNT is a major predictor of suicidal thinking and behavior in outpatients with a variety of psychiatric disorders.
2. Proposed RNT could be in part understood as a cycle of fear memory retrieval and reconsolidation throughout the day-night cycle, and possibly that some treatments effective in refractory depression act in part by interrupting such an emotional learning cycle.
3. Supporting this view, the lab made the observation that fear learning (but not reward processing) is abnormal in persons with depression and high RNT.

Current Research Focus

Dr. Guinjoan's lab strives to discover and characterize circuits that subserve RNT in persons with depression. To this end, with the help of functional magnetic resonance imaging they have observed that persons who ruminate excessively display higher functional connectivity between areas of the brain regulating "inner speech," and those involved in emotional processing. Dr. Guinjoan's group is now trying to establish if this is in turn related to increased number of neuronal connections (structural MRI) between those areas. They are also setting up a state-of-the-art noninvasive and reversible neuromodulation device that uses focused ultrasound to probe these circuits and attempt to establish causal relationships between brain circuits and RNT. They plan to do that with the help of neuronavigation software that allows for very precise targeting of deep cerebral structures.

Select Publications

1. Wainsztein AE, et al. (2021): *Childhood adversity modulation of central autonomic network components during cognitive regulation of emotion in major depressive disorder and borderline personality disorder. Psychiatry Research: Neuroimaging.* 318:111394.
2. Guinjoan SM, et al. (2021): *Cognitive effects of rapid-acting treatments for resistant depression: Just adverse, or contributing to clinical efficacy? Journal of Psychiatric Research,* 140: 512-521.
3. Villarreal MF, et al. (2021): *Distinct Neural Processing of Acute Stress in Major Depression and Borderline Personality Disorder. Journal of Affective Disorders* 286: 123-133.
4. Chandler JA, et al. (2021): *International Legal Approaches to Neurosurgery for Psychiatric Disorders. Frontiers in Human Neuroscience* 14:588458. doi: 10.3389/fnhum.2020.588458.
5. Crossley NA, et al. (2021): *Structural brain abnormalities in schizophrenia in adverse environments: examining the effect of poverty and violence in six Latin American cities. British Journal of Psychiatry* 218(2):112-118.

MARIA IRONSIDE, DPHIL

Associate Investigator
Laureate Institute for Brain Research



LAB MEMBERS

CHELDYN RAMSEY
Research Assistant

EBONY WALKER
Research Assistant

Research Highlights

1. CoBRE funding was awarded from NIGMS for a three-year project focusing on the effects of non-invasive brain stimulation on threat sensitivity in anxious depression. The project was launched in May 2021 and is steadily collecting multi-level data from participants with anxious depression.
2. The lab utilized multi-level (self-report, behavioral, electromyography, structural and functional neuroimaging) data from the Tulsa 1000 study to characterize unique phenotypes of anxious depression, resulting in one paper currently under revision and two in preparation. These data will inform a federal funding application planned for Summer 2022.
3. Dr. Ironside presented a *Faces of the Future* flash talk at the Society for Psychophysiological Research Meeting.

Current Research Focus

Dr. Ironside has a background in neuromodulation and neuroimaging. Her main interests include understanding the mechanisms of action of non-invasive neuromodulation as a treatment for psychiatric disorders and establishing unique targetable phenotypes of anxious depression. Dr. Ironside uses behavioral and neuroimaging measures to investigate acute effects of transcranial direct current stimulation 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

1. Dong, D., et al. (accepted) Sex-specific Neural Responses to Acute Psychosocial Stress in Depression. *Translational Psychiatry*.
2. Rolle, CE, et al. (2021) The role of the dorsal-lateral prefrontal cortex in reward sensitivity during Approach-Avoidance Conflict. *Cerebral Cortex*.
3. Ironside, M, et al. (2021) Reductions in rostral anterior cingulate GABA are associated with stress circuitry in females with major depression: A multimodal imaging investigation. *Neuropsychopharmacology*.
4. Pedersen, ML, et al. (2021) Computational phenotyping of brain-behavior dynamics underlying approach-avoidance conflict in major depressive disorder. *PLOS Computational Biology*. 2021;17(5): e1008955.
5. Duda, JM, et al. (2021) Repeatability and reliability of GABA measurements with magnetic resonance spectroscopy in healthy young adults. *Magnetic Resonance in Medicine*. 2021;85:2359-2369.

SAHIB KHALSA, M.D., PH.D.

Director of Clinical Operations,
Laureate Institute for Brain Research

Associate Professor,
Oxley College of Health Sciences,
The University of Tulsa

Director, LIBR Float Clinic and
Research Center

Volunteer Faculty Member,
Department of Psychiatry,
The University of Oklahoma



LAB MEMBERS

EMILY ADAMIC, M.S.

Graduate Student, TU

JAMIEE BRUCE, R.N.

Clinical Research Coordinator

EMILY CHOQUETTE, PH.D.

Post-Doctoral Research Associate

MCKENNA GARLAND, B.S.

Graduate Student, TU

ALEXA MORTON, B.S.

Research Specialist

ADAM TEED, PH.D.

Post-Doctoral Research Associate

CHARLES VERDONK, M.D., PH.D.

*Post-Doctoral Research Affiliate,
French Armed Forces Biomedical
Research Institute*

RAMINTA WILSON, M.D., M.P.H.

*Psychiatric Research Coordinator, LIBR
Float Clinic and Research Center*

Research Highlights

- 1.** Partial sympathectomy for refractory ventricular arrhythmias is associated with reduced anxiety but not depression or PTSD symptoms shortly after successful treatment. This finding provides the groundwork for prospective clinical surveillance and interventions focused on mental health in this population.
- 2.** An ingestible vibrating capsule produces changes in stomach sensation and gastric-evoked brain activity. This minimally invasive approach could serve as a useful tool for understanding gut-brain interactions in healthy and clinical populations.
- 3.** Applied computational modeling to the vibrating capsule experiment showed that this computational approach offers promise as a tool for studying individual differences in gastrointestinal interoception.

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.

Select Publications

1. Khalsa SS, et al. Cardiac sympathetic denervation and mental health. *Autonomic Neuroscience* 2021 May; 232:102787.
2. Ralph-Nearman C, et al. Visual mapping of body image disturbance in anorexia nervosa reveals objective markers of illness severity. *Scientific Reports* 2021 Jun 10;11(1):12262.
3. Smith R, et al. Gut inference: A computational modelling approach. *Biological Psychology* 2021 Jul 24;164:108152.
4. Paulus MP, Khalsa SS. When you don't feel right inside: homeostatic dysregulation and the mid-insular cortex in psychiatric disorders. *American Journal of Psychiatry* 2021 Am J Psychiatry. 2021 Aug 1;178(8):683-685.
5. Paulus MP, et al. Methylphenidate augmentation of escitalopram to enhance adherence to antidepressant treatment: a pilot randomized controlled trial. *BMC Psychiatry* 2021 Nov 19;21(1):582.

NAMIK KIRLIC, PH.D.

Associate Investigator
Laureate Institute for Brain Research



LAB MEMBERS

GABRIELLA COCHRAN, B.S.

Lab Manager

XIAOQIAN YU, PH.D.

Post-Doctoral Research Associate

Research Highlights

- 1.** Dr. Kirlic published 12 peer-reviewed papers and one book chapter. Further, Dr. Kirlic presented his research at Anxiety and Depression Association of America and American College of Neuropsychopharmacology annual meetings. He also conducted a number of workshops at local schools and agencies serving at-risk youth, as well as educational seminars at local clinical psychology training programs on topics related to early life stress, adolescent mental health, and mindfulness training.
- 2.** With respect to grantsmanship, Dr. Kirlic entered the third year of his CoBRE career development award. He has also submitted an NCCIH grant, which received favorable reviews and is under resubmission. Finally, Dr. Kirlic joined Dr. Robin Aupperle in developing the clinical psychology internship program at LIBR, and serves as one of its clinical supervisors.
- 3.** Dr. Kirlic's research coordinator, Zsofia Cohen, enrolled in a clinical psychology doctorate program at Oklahoma State University, and her position was filled by Gabriella Cochran, who hails from Atoka, OK and is also interested in pursuing a doctorate in clinical psychology. Finally, our ranks were reinforced by arrival of Xiaoqian Yu, a post-doctoral associate with expertise in measuring attentional capacities in youth, coming on board to continue our work on understanding neural mechanisms of mindfulness training.

Current Research Focus

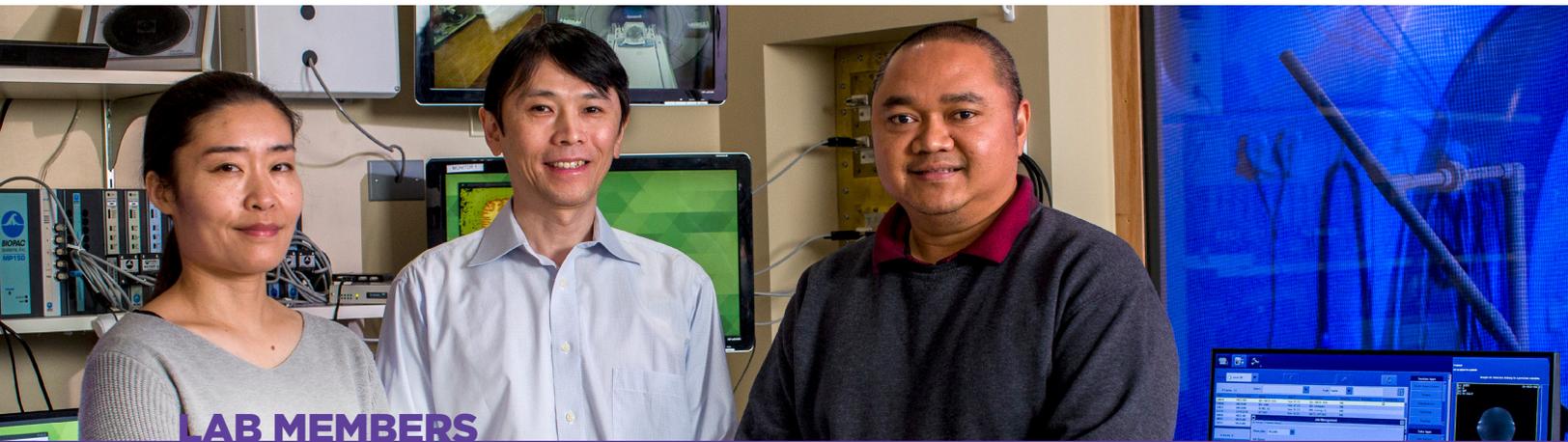
Dr. Kirlic's Laboratory for Neuroscience-Informed Resilience in Early Life focuses on improving our understanding of emerging psychopathology in adolescence and young adulthood, the broad consequences of early life adversity, and augmentation and enhancement of mental health interventions. His laboratory employs several methods, including 1) comprehensive assessment of life experiences, affective functioning, and neurocognitive abilities via self-report and clinician-administered interviews, 2) behavioral and psychophysiological responses during experimental tasks, 3) structural and functional neuroimaging while the brain is at rest or engaged in a particular task, 4) neurofeedback during behavioral interventions, and 5) biospecimen collection to understand immune, endocrine, and epigenetic functioning. They have leveraged advanced statistical approaches, such as machine learning, to aid in this process.

Select Publications

- 1. Kirlic, N., Colaizzi, J., et al. (2021). Extracurricular activities, screen media activity, and sleep may be modifiable factors related to children's cognitive functioning: Evidence from the ABCD Study®. Child Development, 92(2), 2035-2052.*
- 2. Kirlic, N., et al. (2021). Neurocircuitry of Mindfulness-Based Interventions for Substance Use Prevention and Recovery. Current Addiction Reports.*
- 3. Kirlic, N., Akeman, et al. (2021). A machine learning analysis of risk and protective factors of suicidality in college students. Journal of American College Health.*
- 4. Cohen, Z., et al. (2021). The impact of COVID-19 on adolescent mental health: Preliminary findings from a longitudinal sample of healthy and at-risk adolescents. Frontiers Pediatrics, 9, 1-8.*
- 5. Cohen, Z., et al. (2021). The effect of mindfulness-based stress intervention on neurobiological and symptom measures in adolescents with early life stress: A randomized feasibility study. BMC Complementary Medicine and Therapies, 21(123), 1-14.*

MASAYA MISAKI, PH.D.

Associate Investigator,
Laureate Institute for Brain Research



LAB MEMBERS

BENI MULYANA
Graduate Student, OU

AKI TSUCHIYAGAITO, PH.D.
Post-Doctoral Research Associate

Research Highlights

1. Development of an advanced real-time fMRI processing system with extensive denoising for the online measurement of brain activation.
2. The advantage of comprehensive online denoising for computing robust neurofeedback signals was confirmed by simulation analysis.
3. The lab found that positive emotional training with left amygdala neurofeedback restored hippocampal volume reduction in patients with post-traumatic stress disorder.

Current Research Focus

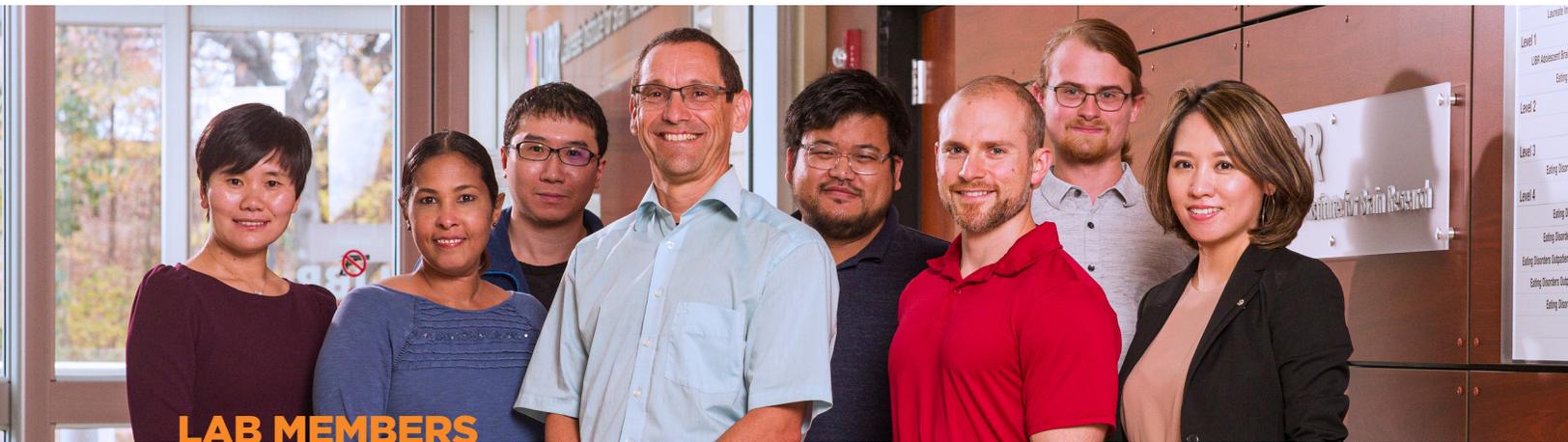
Dr. Misaki is an Associate Investigator. His research aims to develop a novel psychiatric treatment utilizing real-time neuroimaging technology with functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). His research employs neurofeedback training where the brain activation signals are measured and presented for patients in real-time to self-regulate their brain activation and mental state.

Select Publications

1. Misaki, M., et al. (2021). Hippocampal volume recovery with real-time functional MRI amygdala neurofeedback emotional training for posttraumatic stress disorder. *J Affect Disord* 283, 229-235.
2. Misaki, M., et al. (2021). Beyond synchrony: the capacity of fMRI hyperscanning for the study of human social interaction. *Soc Cogn Affect Neurosci* 16, 84-92.
3. Misaki, M., Bodurka, J. (2021). The impact of real-time fMRI denoising on online evaluation of brain activity and functional connectivity. *J Neural Eng* 18.
4. Tsuchiyagaito, A., et al. (2021). Prevent breaking bad: A proof of concept study of rebalancing the brain's rumination circuit with real-time fMRI functional connectivity neurofeedback. *Hum Brain Mapp* 42, 922-940.
5. Ratliff, E.L., et al. (2021). Into the Unknown: Examining Neural Representations of Parent-Adolescent Interactions. *Child Dev*. Nov;92(6):e1361-e1376.

MARTIN PAULUS, M.D.

Scientific Director and President
Laureate Institute for Brain Research



LAB MEMBERS

KAIPING BURROWS, PH.D.
Staff Scientist

KATIE FORTHMAN
Data Scientist

PHILIP SPECHLER, PH.D.
Post-Doctoral Research Associate

RAYUS KUPLIICKI, PH.D.
Lead, Data Analyst

JAMES TOUTHANG
Research Assistant

LEANDRA FIGUEROA-HALL, PH.D.
Post-Doctoral Research Associate

BOHAN XU
Researcher

SAMUEL TAYLOR
Research Specialist

HAIXIA ZHENG, PH.D.
Post-Doctoral Research Associate

Research Highlights

1. Substance using individuals have a unique oral microbiome, the oral microbiome may help to understand the dysfunctional biological processes that promote substance use or may be pragmatically useful as a risk or severity biological marker.
2. Individuals with a higher genetic risk for neuroticism may have a limited ability to process positive and/or negative events influencing their current mood state.
3. In individuals with depression an increased inflammatory process might limit their ability to process positive events.

Current Research Focus

Dr. Paulus' research focuses on three main areas:

- (1) To use a neuroscience-based approach for
 - a. objective markers for psychiatric disorders
 - b. better disease models
 - c. better access to efficacious treatments
 - d. brain-based and more effective interventions
- (2) To use computational approaches in order to move from "one size fits all" towards precision psychiatry.
- (3) To develop prevention strategies for psychiatric disorders.

Dr. Paulus has a Google Scholar h-index of 108 and has published over 400 peer-reviewed manuscripts. 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. 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, or substance use disorder. Dr. Paulus' program of research is to delineate DMPs and provide pathways towards the development of process-specific transdiagnostic interventions that have pragmatic utility, i.e. improve a patient's condition faster with fewer side effects and fewer recurrences, and explanatory value, i.e. refine our understanding of the causal relationships between specific processes and a mental health condition.

Select Publications

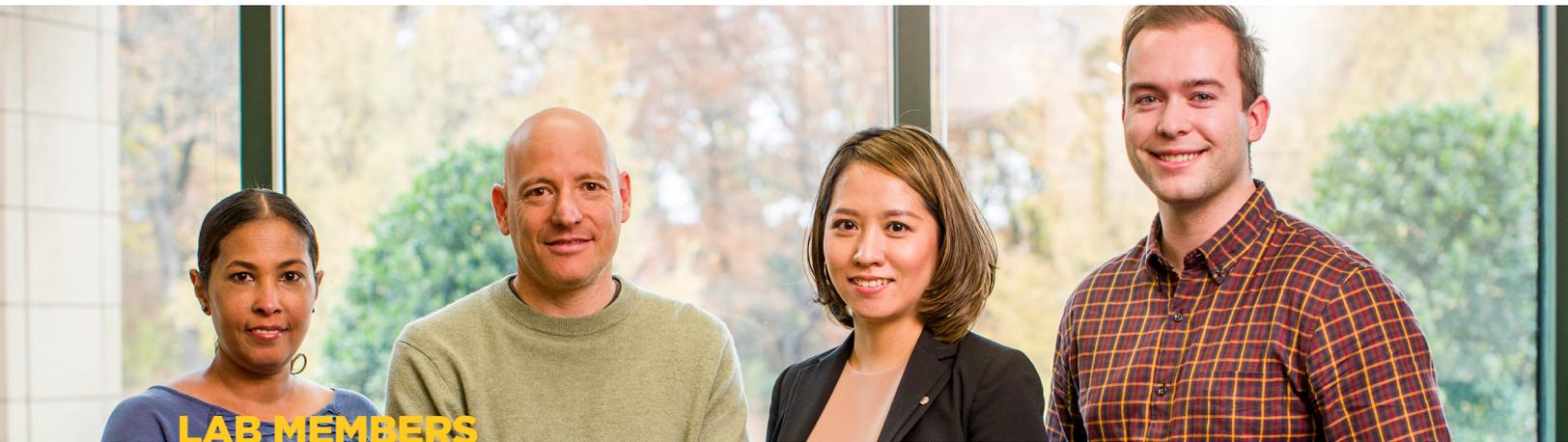
1. Ekhtiari H, et al. It is never as good the second time around: Brain areas involved in salience processing habituate during repeated drug cue exposure in treatment engaged abstinent methamphetamine and opioid users. *Neuroimage*. 2021 Sep;238:118180.
2. Smith R, et al. An Active Inference Approach to Dissecting Reasons for Nonadherence to Antidepressants. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2021 Sep;6(9):919-934.
3. Dick AS, et al. Meaningful associations in the adolescent brain cognitive development study. *Neuroimage*. 2021 Oct 1;239:118262.
4. Paulus MP, Thompson WK. Computational approaches and machine learning for individual-level treatment predictions. *Psychopharmacology (Berl)*. 2021 May;238(5):1231-1239.
5. Paulus MP, et al. The effects of FAAH inhibition on the neural basis of anxiety-related processing in healthy male subjects: a randomized clinical trial. *Neuropsychopharmacology*. 2021 Apr;46(5):1011-1019.

JONATHAN SAVITZ, PH.D.

Principal Investigator,
Laureate Institute for Brain Research

Associate Professor,
Oxley College of Health Sciences,
The University of Tulsa

Volunteer Faculty Member,
Department of Psychiatry,
The University of Oklahoma



LAB MEMBERS

LEANDRA FIGUEROA-HALL, PH.D.

Post-Doctoral Research Associate

HAIXIA ZHENG, PH.D.

Post-Doctoral Research Associate

MACGREGOR THOMAS

Research Specialist

Research Highlights

1. Based on work spearheaded by Dr. Haixia Zheng, the lab published three papers demonstrating reductions in gray matter volume and white matter integrity in depressed individuals who tested positive for cytomegalovirus (CMV) compared to matched individuals who tested negative for CMV. These results raise the possibility that in some cases, CMV may be a treatable cause of the subtle brain abnormalities associated with depression.
2. Together with Dr. Robin Aupperle and colleagues, we showed that behavioral activation therapy for depression may lead to a decrease in the neurotoxic kynurenine pathway metabolite, quinolinic acid. Similarly, together with Drs. Jerzy Bodurka, Aki Tsuchiyagaito, and colleagues, we showed that real-time fMRI neurofeedback training of the amygdala for the treatment of depression is associated with an increase in the neuroprotective kynurenine pathway metabolite, kynurenic acid. The results raise the possibility that normalization the kynurenine pathway is a common mechanism of action underlying different anti-depressant therapies.
3. Dr. Savitz and Dr. Tim Meier published a review paper in *Biological Psychiatry* highlighting the role of the kynurenine pathway in the psychiatric sequelae of traumatic brain injury.

Current Research Focus

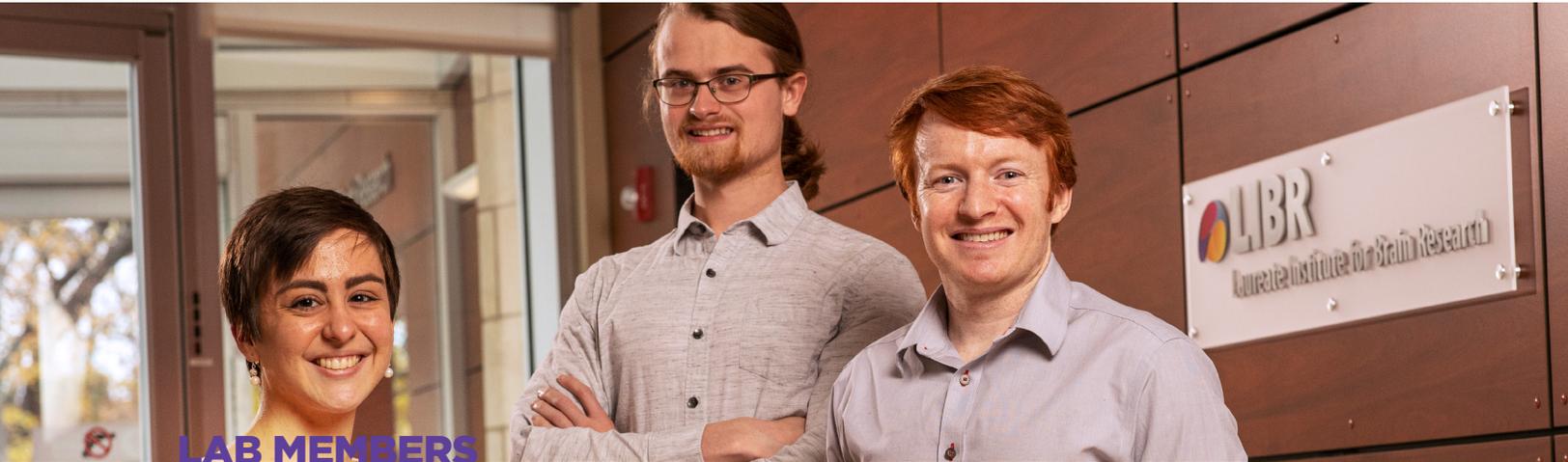
Depression is the most devastating mental health problem on the planet, yet we know very little about the underlying disease process. Our lab is examining whether inflammation of the brain is one cause of depression. In particular, we are using blood-based inflammatory and immune markers and experimental 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.

Select Publications

1. Zheng, H., et al. (2021). A Hidden Menace? Cytomegalovirus Infection is Associated with Reduced Cortical Gray Matter Volume in Major Depressive Disorder. *Molecular Psychiatry*. 26, 4234-4244.
2. Zheng, H., et al. (2021). Replicable Association between Human Cytomegalovirus Infection and Reduced White Matter Fractional Anisotropy in Major Depressive Disorder. *Neuropsychopharmacology*. 46, 928-938.
3. Savitz, J., et al. (2021). Behavioral Activation Therapy for Depression is Associated with a Reduction in the Concentration of Circulating Quinolinic Acid. *Psychological Medicine*. In press.
4. Tsuchiyagaito, A., et al. (2021). Real-time fMRI Neurofeedback Amygdala Training May Influence Kynurenine Pathway Metabolism in Major Depressive Disorder. *NeuroImage Clinical*. 29, 102559.
5. Meier, T.B., Savitz, J. (2021). The kynurenine pathway in traumatic brain injury: Implications for psychiatric outcomes. *Biological Psychiatry*. In Press.

RYAN SMITH, PH.D.

Associate Investigator,
Laureate Institute for Brain Research



LAB MEMBERS

ANNIE CHUNING
Research Assistant

SAMUEL TAYLOR
Research Specialist

Research Highlights

- 1.** Dr. Smith had 14 research articles and 1 book chapter either published or accepted for publication. Dr. Smith presented his research at the Society of Biological Psychiatry annual conference, the Society for Research in Psychopathology Annual Conference, and the American Psychosomatic Society Annual Conference in 2021. He also gave internationally attended tutorial talks on computational methods at the Zurich Computational Psychiatry Course and the MAPs (Methods and Primers for Computational Psychiatry and Neuroeconomics) lecture series.
- 2.** Dr. Smith submitted an NIMH grant in November of 2020 and started collecting data for a new study examining the influence of anxiety on information-seeking and planning processes.
- 3.** Dr. Smith welcomed a very bright and talented research project coordinator named Annie Chuning as a new member of his lab.

Current Research Focus

Dr. Smith's main research interests include understanding how emotion and decision-making processes are realized within the brain, and in how these processes may be altered in mood and anxiety disorders. A major overarching focus is to characterize differences between mentally healthy and unhealthy individuals with the goal of improving diagnosis and treatment selection within psychiatry and clinical psychology. Dr. Smith employs several methods aimed at providing multiple levels of description in characterizing emotion-related psychological and biological processes, including self-reported experience, decision-making tasks, behavioral and physiological responses measures, functional neuroimaging, and computational modeling. Dr. Smith's lab aims to establish (1) the role of emotional and decision-making processes in psychiatric disorders at a cognitive, computational, and neurobiological level of description, (2) how such processes contribute to the vulnerability to, and the onset and maintenance of psychiatric symptoms, and (3) how characterizing such processes in individual participants might inform more individualized and targeted treatment selection.

Select Publications

1. Smith R, et al. Simulating the computational mechanisms of cognitive and behavioral psychotherapeutic interventions: insights from active inference. *Sci Rep.* 2021;11(1):10128.
2. Smith R, et al. Long-term stability of computational parameters during approach-avoidance conflict in a transdiagnostic psychiatric patient sample. *Sci Rep.* 2021;11(1):11783.
3. Smith R, et al. Gut inference: A computational modelling approach. *Biol Psychol.* 2021;164:108152.
4. May AC, et al. Sex differences in circulating inflammatory mediators as a function of substance use disorder. *Drug Alcohol Depend.* 2021 Apr 1;221:108610. Epub 2021 Feb 15. Erratum in: *Drug Alcohol Depend.* 2021 Jul 1;224:108743.
5. Smith R, et al. Perceptual insensitivity to the modulation of interoceptive signals in depression, anxiety, and substance use disorders. *Sci Rep.* 2021 Jan 22;11(1):2108.

JENNIFER L. STEWART, PH.D.

Principal Investigator,
Associate Director for Training and Mentoring
Laureate Institute for Brain Research

Assistant Professor,
The University of Tulsa
Department of Community Medicine



LAB MEMBERS

CHRYSANTHA DAVIS

Research Assistant

MARYKATE DYKES

Research Specialist

MARIAH NACKE

Research Assistant

XI REN, PH.D.

Post-Doctoral Research Associate

Research Highlights

1. Dr. Stewart's five-year longitudinal grant project with Dr. Martin Paulus and Dr. Rayus Kuplicki entitled "Plasticity of Aversive Salience in Opioid Use Disorder" (PASO) was funded by the National Institute on Drug Abuse in March 2021 (R01DA050677), which aims to identify symptom, behavior, physiological, and neuroimaging markers of opioid addiction recovery.
2. Dr. Stewart hired two outstanding research assistants for the PASO project, Chrysantha Davis and Mary Kate Dykes, who coordinate study visits and participant retention efforts.
3. Dr. Stewart's collaboration with Dr. Evan White and Dr. Robin Aupperle, made possible by our valued research assistant Mariah Nacke, demonstrated that electrical brain responses in depressed patients at baseline can predict whether or not they go on to complete 7-10 weeks of therapy (either behavioral activation or exposure).

Current Research Focus

Dr. Stewart use electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) methods to identify brain alterations in cognitive and emotional processing in individuals struggling with symptoms of major depressive disorder and substance use disorders (methamphetamine and opioids). She is working on testing whether these brain alterations can predict future treatment completion/response as well as success in reducing substance use.

Select Publications

1. Burrows, K., et al. (2021). Elevated peripheral inflammation is associated with attenuated striatal reward anticipation in major depressive disorder. *Brain, Behavior, and Immunity*, 93, 214-225.
2. Kirlic, N., et al. (2021). Neurocircuitry of Mindfulness-Based Interventions for Substance Use Prevention and Recovery. *Current Addiction Reports*, 8, 520-529.
3. May, A. C., et al. (2021). Sex differences in circulating inflammatory mediators as a function of substance use disorder. *Drug and Alcohol Dependence*, 221, 108610.
4. Smith, R., et al. (2021). Perceptual insensitivity to the modulation of interoceptive signals in depression, anxiety, and substance use disorders. *Scientific Reports*, 11, 1-14.
5. White, E. J., Stewart, J. L. et al* (in press, *Journal of Affective Disorders*). P300 amplitude during a monetary incentive delay task predicts future therapy completion in individuals with major depressive disorder. * = co-senior authors.

EVAN WHITE, PH.D.

Associate Investigator,
Laureate Institute for Brain Research
Neuroscience of American Indian Resilience
and Risk (Neu-AIRR) Lab



LAB MEMBERS

MARA DEMUTH, M.A.
Lab Coordinator

SAMANTHA RAMIREZ
Research Assistant

Research Highlights

- 1.** Dr. White launched the first neuroimaging research project to examine culturally based resilience factors in American Indian communities. This project is aimed at 1) understanding validity of protective factors identified in broader populations and 2) examine potential unique protective factors against mental health condition in these communities.
- 2.** Preliminary evidence derived from the Tulsa 1000 project indicates that cognitive control may be a particularly relevant protective factor against suicide ideation among AI participants in the project. These findings are currently under peer review.
- 3.** In collaboration with Drs. Stewart and Aupperle, along with other LIBR investigators and trainees, Dr. White documented event-related brain potential markers that predicted diagnosis of depression and individuals with depression who would go on to complete treatment or drop out.

Current Research Focus

Dr. White's laboratory 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. The broad goal of this work is to integrate clinical and cultural neuroscience to identify modifiable factors as candidate treatment targets for mental health intervention and prevention research. Dr. White's research is currently funded by the Laureate Institute for Brain Research and National Institute of Minority Health and Health Disparities through a K99/R00 award, K99MD015736. In addition to his work with American Indians, Dr. White employs translational neuroscience and psychophysiological research (especially event-related potentials) to understand development, maintenance, and treatment of anxiety and mood disorders. He collaborates with investigators at LIBR to examine concurrent EEG-ERP/fMRI indicators of cognitive processing relevant to mental health disorders.

Select Publications

1. White, E.J., et al. (2021). *The influence of state worry on covert selective attention and suppression of threatening distractors: An ERP study.* *Psychology & Neuroscience*, 14(1), 94-109.
2. White, E. J., et al. (2021). *Latent variables for region of interest activation during the monetary incentive delay task.* *Neuroimage*, 230.
3. White, E.J., et al. (2021). *P300 amplitude during a monetary incentive delay task predicts future therapy completion in individuals with major depressive disorder.* *Journal of Affective Disorders*, 291,(1), 873-882.
4. Coser, A., et al. (2021). *For the good of the community: Considering the impact of evidence-based treatment adaptation on tribal communities.* *the Behavior Therapist*, 44(4), 161-170.
5. DeVille, D.C., et al. (2021). *A Multi-level Examination of Interoceptive Processing and Insula Connectivity in Past Suicide Attempters.* *Behavior Therapy*, 52(5), 1080-1092.

SELECT LIBR PUBLICATIONS 2021

Zheng H, Ford BN, Kuplicki R, Burrows K, Hunt PW, Bodurka J, Kent Teague T, Irwin MR, Yolken RH, Paulus MP, Savitz J. Association between cytomegalovirus infection, reduced gray matter volume, and resting-state functional hypoconnectivity in major depressive disorder: a replication and extension. *Transl Psychiatry*. 2021 Sep 7;11(1):464. doi: 10.1038/s41398-021-01558-6. PMID: 34493708; PMCID: PMC8423754.

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IN MEMORIAM

Jerzy Bodurka, Ph.D.



**Chief Technology Officer
Director, MRI-EEG Facility
Laureate Institute for Brain Research**

**Associate Professor (with tenure)
Stephenson School of Biomedical Engineering, The University of Oklahoma**

Dr. Jerzy Bodurka passed away on Friday, August 13, 2021. He was a pioneer and a world-renowned expert in MRI, fMRI and EEG who enjoyed a storied scientific career and many prestigious awards. He worked as a staff scientist at the National Institutes of Health (NIH) and received the NIH Director's Award in 2007 for his advancements in MRI imaging technology. In 2009, he joined the Laureate Institute for Brain Research (LIBR) in Tulsa, OK, where he worked to build an international reputation in magnetic resonance imaging physics and its applications to improving mental health.

He cared deeply about people - those in his group, in his work and in his family. He was a thoughtful and engaging collaborator who advocated for new researchers. He was a loving husband, father, brother, son, mentor and colleague with a knack for technology and tinkering - his wife and daughter joke that they always had a willing IT professional on call. He loved World War II history, space exploration, hiking, tennis, movies, walking with the family dog and most of all, his family.

In lieu of flowers, his family requested that donations be considered to the Laureate Institute for Brain Research to continue Jerzy's life's work in advancing interventions for mental health.

On September 3rd, Dr. Jerzy Bodurka's family and colleagues from LIBR and The University of Oklahoma gathered to celebrate his life and legacy. We shared the immense reach and value of his scientific contributions and impact of the neuroimaging facility and techniques he pioneered at LIBR.

There were also tears of remembrance and joyous laughter as stories were shared of his never-ending enthusiasm for his work and memorable interactions with everyone who had the pleasure of knowing him.

Rest in peace, Jerzy.

You will be missed beyond measure.

ONGOING STUDIES

ABOUT OUR RESEARCH

This study aims to explore how effective Behavioral Activation Depression Therapy is in reducing symptoms of depression.

As a participant you will receive 10 weeks of therapy and complete tasks, questionnaires, blood draws, and EEG.

To see what's happening in your brain we will use magnetic resonance imaging (MRI), a very safe technology that takes live images of your brain as it's working.

Compensation will be provided.

ABOUT THE THERAPY

Depressive symptoms can impact our day-to-day behavior. Feeling down or depressed, and tired all of the time can reduce our desire to seek out and enjoy daily activities. The fewer things we enjoy, the more down or depressed we may feel.

Behavioral activation breaks this vicious cycle by providing opportunities and motivation to engage in more pleasurable and rewarding activities. Behavioral activation also helps us tackle those daunting to-do lists by breaking activities down in a manageable and realistic way.

WE NEED YOU

You may be eligible for this study if you are:

- 18 to 55 years old
- male OR female
- depressed

SYMPTOMS OF DEPRESSION

Loss of pleasure in things you used to enjoy, difficulty sleeping, feeling depressed or blue, changes in weight or appetite, difficulty concentrating, decreased energy or fatigue, moving or talking more slowly.

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Visit us online at www.laureateinstitute.org or email neurocatt@libr.net

Neuroscientific Exploration of Cultural Protective Factors among American Indians

Artwork provided by Comanche artist Timothy Tate Nevaquaya

ABOUT OUR RESEARCH

LIBR is recruiting Native American adults for a new research study to better understand cultural factors and resilience.

HOW TO PARTICIPATE

To be eligible, you must be:

- 21 - 65 years of age
- American Indian
- Fluent in English

We use magnetic resonance imaging (MRI) and electroencephalography (EEG) to take live images of the brain and record brain activity in real time. It's safe, painless, and involves no radiation.

Compensation will be provided

PLEASE CONTACT US: 918-502-5100

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JOIN A RESEARCH STUDY TO IMPROVE MENTAL HEALTH THROUGH NEUROSCIENCE

The Laureate Institute for Brain Research (LIBR) in Tulsa, OK is looking for volunteers to join our treatment studies that aim to personalize mental health care through neuroscience.

Volunteers are needed with and without symptoms of depression and anxiety. You will be paid for your participation. Your information will remain confidential. No insurance is required.

Call for more information: (918) 502-5100
www.laureateinstitute.org | info@libr.net | 6655 South Yale Ave, Tulsa OK 74136

ABOUT OUR RESEARCH

This study aims to explore how anxiety relates to the way we think, feel, and make decisions, as well as how our brain responds to various situations.

As a participant you will complete tasks that trigger parts of your brain involved in decision making and other thought processes.

To see what's happening in your brain, we will use magnetic resonance imaging (MRI), a very safe technology that takes live images of your brain as it's working.

WE NEED YOU

You may be eligible for this study if you:

- Are 18 to 55 years old
- Are male OR female
- Experience high anxiety

OR

- Do not experience any significant mental health symptoms.

You will be paid for your participation.

SYMPTOMS OF ANXIETY

Fear of or distress in social situations, such as public speaking

Fear or distress in performance situations, such as taking tests

Exaggerated or persistent worry about a number of different aspects of life

Panic attacks

Muscle tension

Difficulty sleeping

Irritability

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Laureate Institute for Brain Research



Are You Depressed?

Help us understand how the brain functions in individuals with Major Depressive Disorder (MDD)

ABOUT OUR RESEARCH

The Laureate Institute for Brain Research (LIBR) is studying the biological basis of Major Depressive Disorder (MDD).

We conduct research using magnetic resonance imaging (MRI) to make images of the brain.

These images help researchers understand how the brain processes emotion and motivation.

MRI is safe, painless, and involves no radiation.

WE NEED YOU

You are eligible if you are:

- male or female
- currently depressed
- ages 19-55
- not currently taking psychiatric medication

Joining this research study provides you with an opportunity to contribute to the understanding of MDD, which affects millions of Americans.

Compensation is provided.

SYMPTOMS OF MDD MAY INCLUDE:

Sadness
Hopelessness
Depressed mood
Problems sleeping
Difficulty concentrating
Lack of motivation

For more information, please call LIBR at: 918-502-5100

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Laureate Institute for Brain Research




JOIN A TEEN STUDY

ABOUT OUR RESEARCH

LIBR is a groundbreaking research facility that uses neuroscience to help improve mental health worldwide. We are looking for **teenage research participants from the Tulsa area** to help us improve our understanding of mental health disorders through the use of magnetic resonance imaging (MRI), behavioral testing and biological markers.

Research at LIBR may help us to:

- **Improve** treatment outcomes.
- **Understand** the role of adverse childhood events in the development of mental health disorders.
- **Improve** community partnerships that lead to the **better mental health care.**

STUDY PARTICIPATION

Studies at LIBR typically include questionnaires and testing on a computer, interviews with a researcher, brain imaging scans and the collection of biological samples. Some studies can be completed in a single visit, while others involve multiple visits.

Participation is always **voluntary** and your information is kept **confidential**.

All study assessments and procedures will be provided free of charge to you. No insurance is necessary. You will be paid for your time spent participating in all studies at LIBR.

WE NEED YOU

Qualified teen research volunteers must be:

- Ages 13-17, male or female

AND

- Free of psychiatric symptoms **OR**
- Currently experiencing symptoms of anxiety or depression

• **Accompanied by a parent or legal guardian**

For more information, please call LIBR at: 918-502-5142

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ABOUT OUR RESEARCH

LIBR is recruiting adolescents for a new research study to better understand how mindfulness training may help teens cope with stress and become more resilient.

We use magnetic resonance imaging (MRI) to take live images of the brain. It's safe, painless, and involves no radiation.

HOW TO PARTICIPATE

You may be eligible if you are:

- 13-17 years of age
- Fluent in English
- Have a parent or legal guardian to give permission for your participation

Compensation will be provided.

PARENTS, PLEASE CONTACT US: CALL 918-502-5142



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Mind Full, or Mindful?

A MindREaL Study

Mindfulness for Resilience in Early Life

Are you a teen or the parent of a teen who is interested in learning to become more mindful, concentrate and be more present, and better cope with stress?

LIBR is searching for 13-17 year old volunteers to participate.

Visits involve:

- Completing surveys
- Providing biological samples
- Brain imaging and computer tasks

Compensation will be provided.

ABOUT OUR RESEARCH

The Laureate Institute for Brain Research (LIBR) is conducting research to better understand the relationship between mindfulness training and brain function in teens.

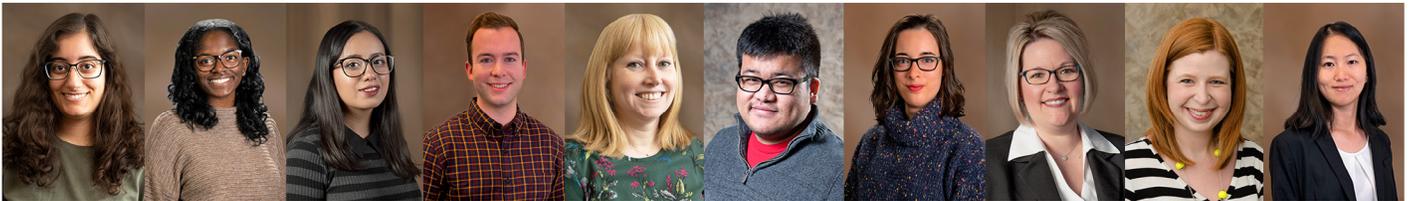
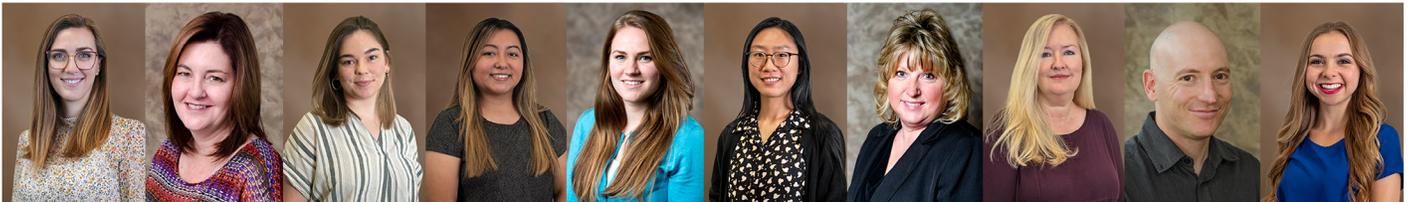
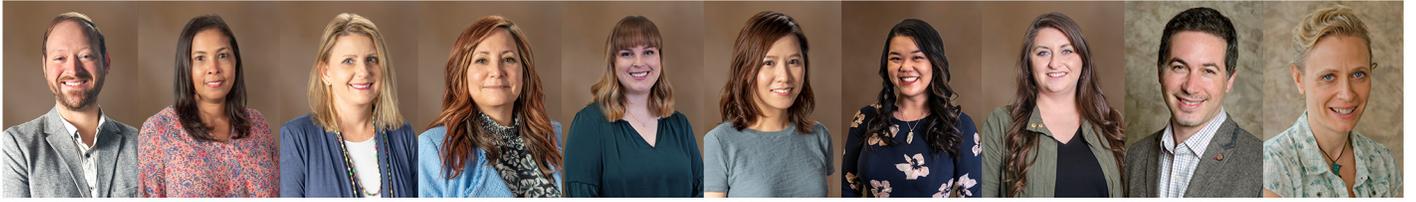


Parents, please contact us: 918-502-5142



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